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Epidemiology and prevention of measles in rural south India

T. Jacob John, Abraham Joseph, T.I. George, Janaki Radhakrishnan, Rajdayal P.D. Singh and Kuryan George

Departments of Community Health and Virology, Christian Medical College and Hospital, Vellore

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The epidemiology of measles was investigated in a village without any health care supervision, 3 villages with health care supervision but without measles immunization and in 2 villages covered with measles vaccine as part of health care, near Vellore in south India. There was an epidemic of measles in and around Vellore during the last quarter of 1977 and the first of quarter of 1978. In the first village, the attack rate among preschool children was 26 per cent and the overall case-fatality rate 14 per cent. In the second group of villages, the attack rate was 20 per cent and case-fatality 3·7 per cent. In the vaccinated villages, the attack rate was 4 per cent with no death; measles was confined to the unvaccinated children in these villages. No measles occurred among 121 vaccinated children. Complications of measles were predominantly gastrointestinal (35 to 52 per cent) and respiratory (37 to 58 per cent). In the light of the results these and other studies, the inclusion of measles vaccine is strongly recommended in the routine immunization of preschool children in India.

In the planning of health care in India, measles immunization has yet to find a place. Measles vaccine is not included in the current recommendations for routine immunization of infants and children in India, either by the Health Service Agencies or by the Indian Academy of Paediatrics. This situation appears to be due to a general lack of understanding of measles and its adverse effects on the child-population, inadequate knowledge about the efficacy of the vaccine and the relatively high cost of the vaccine.

There have been only four community based studies of measles and its epidemiology, severity, complications and mortality in India[1-4]. Three of them were in rural or low-income urban communities[2-4]. Two of these reports described measles as an important public health problem[2,3]. One of the authors described it as a mild disease without serious complications and with low rate of mortality confined to children with kwashiorkor[4].

Experience with measles vaccine is also limited in India. The World Health Organization (WHO) conducted a vaccination-trial in 408 children in India with 93 per cent seroconversion[5]. The feasibility of mass vaccination was demonstrated[6] in Vellore and surrounding area in 1967. The efficacy of the vaccine in protecting

children against measles has also been repeatedly demonstrated[1,2]. Over 90 per cent antibody response was reported[7] in vaccinated children in New Delhi. Thus the need, feasibility, effectiveness and importance of measles vaccination have been repeatedly pointed out in India[1,2,6-8]. In support of these, we also report our recent observations and experience of measles and its prevention in rural populations.

Material and Methods

The studies were conducted in a village about 5 km west of Vellore town and in 5 villages about 10 km south of Vellore. The first village had no health care supervision by any agency. The remaining five villages were among those under the health care supervision of the Community Health Department. In late 1976 and early 1977, measles vaccine (Attenuvax, Merck Sharp and Dohme) was made available to all preschool children of village No. 2 and the Harijan area of village No. 3.

During the last quarter of 1977 and the first quarter of 1978, an epidemic of measles was prevalent in and around Vellore. Information on measles morbidity, complications and mortality was collected during repeated visits to every house in the 6 villages until the epidemic was over. The diagnosis of measles was made on the basis of history and/or clinical features, *viz.* coryza, cough, sore eyes and a generalised maculopapular rash appearing after 3 or more days of high fever. Desquamation of the skin was characteristic during convalescence.

Death within a month of the onset of measles was attributed to measles or its complications and counted as mortality due to measles.

As many exanthematous diseases are together called[9] '*ammai*' by the community, it was assumed that accurate information on a past history of measles would be difficult to obtain. Therefore, no attempt was made in the first village to classify children according to the past history of measles. In the remaining villages, history of previous attack of measles was elicited by detailed questions addressed to the parents.

Measles antibody was measured in sera as described previously[10].

Results

Morbidity, complications and mortality in the first village : The age-structure of the population, the age-specific attack rates of measles and the case-fatality rates are presented in Table I. The attack rate among the 214 children up to 5 years was 26 per cent (57 cases).

Diarrhoea or dysentery starting with or immediately after measles, occurred in 34 children (52 per cent). Severe and prolonged respiratory disease was reported in 38 children (58 per cent). Otitis media with discharge of pus occurred in 4 children. Among the 65 children with measles 9 died, 6 with diarrhoea or dysentery and 3 with respiratory disease. Thus the case-fatality rate, was 14 per cent (Table I).

Measles in the five villages :

Reliability of a past history of measles : In order to check the reliability of a past history of measles in children, blood was collected from 8 children with and 39 without such history, between 1 and 5 yr of

Table I. Age specific measles morbidity and mortality in village No. 1

Age (yr)	Population	Measles case	Attack rate/100	Deaths	Case-fatality rate
<1	23	9	39	2	22
1	31	14	45	3	21
2	37	8	22	1	13
3	43	10	23	1	10
4	32	9	28	2	22
5	48	6	13	0	0
0-5	214	56	26	9	16
6-9	166	9	5	0	0
⩾10	901	0	0	0	0
Total	1,281	65	5	9	14

age. Among the 8 children with previous history of measles, 6 had measles antibody indicating about 75 per cent accuracy of the history. Two children had presumably some other exanthematous illness. However, among the 39 children without history of measles, 12 (31 per cent) were also seropositive, indicating previous sub-clinical infection with measles virus as has been postulated previously[11].

Measles morbidity in immunized children : In village No. 2 and in the Harijan area of village No. 3, there were 180 preschool children, of whom 30 had previous attack of measles, 121 were vaccinated and 29 had refused to get vaccinated. However, there was not a single case of measles among the 121 vaccinated children during the epidemic, but 6 (21 per cent) among the 29 unvaccinated children contracted the disease (Table II).

Measles morbidity and mortality in unimmunized children : In the remaining villages, there were altogether 775 preschool children, of whom 85 had a previous history of measles. Among the remaining 690 'susceptible' children, 136 developed measles during the epidemic, for an attack rate of 20 per cent (Table II).

Prolonged diarrhoea or dysentery occurred among 56 children (35 per cent), bronchopneumonia in 43 (37 per cent) and suppurative otitis media in 16 (10 per cent). Among the 136 children with measles 5 died, for a case-fatality rate of 3·7 per cent.

Discussion

Morbidity, complications and mortality due to measles : In the first village with no previous health care supervision, the rate of complications following measles and the case-fatality rate were quite high. In the four villages which were provided with health education and care over several years, the rate of complications and mortality were considerably less. In an earlier study on 83 children with measles in a well-nourished group on a university campus, serious complications were virtually absent and there was no death[1]. In a village under nutrition supplementation programme, the case-fatality rate was 3·6 per cent, almost identical to

Table II. Measles morbidity and mortality in pre-school children according to the availability of health care facilities and measles vaccination

Village no.	Health care facilities	Vaccination	No. of children	No. with measles	Attack rate,%	No. died	Case-fatality rate
1	Not available	Nil	214	56	26	9	16
2, 3	Available	Offered and taken	121	0	0	—	—
		Offered not taken	29	6	21	0	—
3-6	Available	Nil	690	136	20	5	3·7

Measles vaccination was offered in village No. 2 and Harijan area of village No. 3

the 3·7 per cent rate in the four villages referred to above[2]. In the first village with no health care supervision, the case-fatality rate was 14 per cent. Thus mortality due to measles is largely preventable by improving the nutrition and health care of a community. In rural communities, such improved living conditions may take a long time to be achieved. Without waiting long for it to happen, measles mortality can be prevented at once by immunization.

Protective efficacy of measles immunization : The protective efficacy of measles immunization was confirmed in this study, since no immunized child developed the disease. The vaccine had been administered only to children above one yr of age and without a past history of measles. While a majority of the children in the second village and the Harijan area of the third village had accepted immunization, the parents of 29 children had refused it. The attack rate (20 per cent) among them was similar to that in the villages where the vaccine was not offered (21 per cent). Thus protection was clearly related to immunization.

In an earlier report of an epidemic in a village, 82 (67·2 per cent) among 122 immunized children and only 2 (2·8 per cent) among 72 immunized children had developed measles[2]. Thus, the degree of protection due to immunization was of the order of 96 per cent. In another report[1] of measles on a university campus, only 1 among 20 previously immunized children developed measles, whereas 22 among 39 unimmunized children of comparable age developed the disease, with an attack rate of 56 per cent. In both these groups, Schwarz strain of measles vaccine, nearing expiry date, not checked locally for potency, had been given to infants and children aged 9 months and above[6]. Thus the few instances of vaccine-failure might have been to interference with immune response on account of residual maternal antibody, or vaccine of low potency. In the present study, Attenuvax strain of vaccine was given to children above one yr and its potency had been

checked and found to be adequate, thus avoiding the two problems identified earlier.

Reliability of past history of measles : It is important to ascertain the reliability of the past history, since immunization is not necessary in children who have had measles. In addition to the serological data presented earlier, the total absence of measles in 115 children who gave a past history of measles, in the five villages, confirms the high degree of reliability of a positive history. In eliciting such history, we have used the precise term used for measles in the local community[9] and also checked if sore eyes, running nose, cough, fever and rash were present.

On the other hand, serological evidence of previous infection was obtained in over 30 per cent of children in whom a history of measles was denied. In earlier (unpublished) studies, we had tested sera from 31 children in New Delhi and 45 children in Ferozpore, between 1 and 5 yr of age, without a previous history of measles. In the former group 19 per cent and in the latter 44 per cent had measurable measles antibody, indicating earlier infection. Such consistent results cannot be ignored as unreliable history; rather, they indicate subclinical infection or very mild, unrecognisable illness. However, in a report on the sero-epidemiology of measles in Bombay, Mehta and co-workers[12] could find no evidence of subclinical infection. On close scrutiny of this report, it was found, that among 47 children between 1 and 5 yr with demonstrable measles virus neutralising antibody, only 29 (62 per cent) had a previous history of measles. In other words, 38 per cent of children had evidence of previous sub-clinical infection[12].

Thus, evidence for previous subclinical or unrecognised infection with measles virus in approximately 20 to 40 per cent of preschool children seems to be a real phenomenon in different parts of India—both urban and rural. As postulated earlier, this may be related to exposure to infection while the infant still has residual antibody transferred from the mother which is sufficient for protection from disease but not enough to prevent infection[13].

The priority for measles immunization : Should measles be included in the expanded programme of immunization in India? Sinha[4] had suggested that measles immunization is of low priority in India because of the mild nature of the disease, lack of serious complications and low mortality. In his experience in a village in West Bengal, measles occurred mainly from May to August, and the prevalence rates were fairly uniform in 1971, 1972 and 1973. These features are very different from what we have observed in southern Indian villages, where it is a disease of the first and last quarters of the year and occurs in a cyclic pattern with epidemics once in 3 to 5 yr. In Punjab, measles is a frequent cause of death among infants and preschool children[14]. The reported picture of measles in rural West Bengal is quite different from that in any other part of India from where reports are available.

As documented in this and other reports[2,3,14] measles and its complications are a major cause of morbidity and mortality among rural Indian children.

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Sero-Epidemiology of Measles—A Three Years Prospective Study in a Rural Population of Rajasthan

D. C. JAIN*, H. S. MEENA*, B. S. YADAV*, K. C. MEENA*
SHASHI KHARE** AND K. K. DATTA**

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ABSTRACT

A community based prospective study on measles was undertaken during 1986 to 1988 in Ramgarh village of Alwar district (Rajasthan) to elucidate epidemiological features of measles. The initial population of the village was 5258 with 2018 children (0-14 years) which rose to total population of 5923 with 2200 children in 1988. During the entire period of study, all the children (0-14 years) were covered regularly through monthly domicilliary visits by trained paramedical personnel under direct supervision of Medical Officers. A total of 208 measles cases were detected which gave an overall incidence rate of 31.5 per 1000 children (0-14 years) per year. Incidence rate was highest in children of 2-5 years of age group and lowest (4.6 per 1000) in 10-14 years of age group. The maximum number (86.5 per cent) of cases occured during the first six months of year. The Kolmogrov-Smirnov statistical method validated the seasonal character of the disease ($Vn = 5.36$, $p < 0.01$). A significant ($P < 0.005$) rise in seropositivity with increase in age was observed in children (6-36 months) who had no previous history of measles and measles immunization during their life time. A higher rate of sero-conversion was observed in children vaccinated after 10-months of age than those before. No significant relationship of seroconversion following vaccination could be seen with age of vaccination ($p > 0.50$), sex and nutritional status ($p > 0.10$).

INTRODUCTION

Measles is a highly communicable disease among children in developing countries, contributing to the high degree of morbidity and mortality[1]. From reports available, the annual incidence of measles in India has been estimated to be 19 per 1000 population[2]. During 1987 a total of 2,28,166 measles cases with 639 deaths were reported from different parts of the country[3]. Although measles is a mild disease but scientific studies indicate that it is a major public health problem as almost all children get measles by the time they attain school going age and its complications rate is significantly high. It has been found that it is the third leading cause of death among pre-school children after respiratory infections and diarrhoea[4].

Hospitals only see the proverbial tip of the iceberg and that also when complications have set in. It is the community which provides the best information on the natural history of the disease. Many seroepidemiological studies[5-8] have been conducted in different parts of the country to draw the attention to the magnitude of measles infection in children but hardly any data are available from rural areas of

*Field Practice Unit, NICD, Alwar-301001 (Rajasthan).
**National Institute of Communicable Diseases, Delhi-54.

Rajasthan. Therefore, a prospective study was undertaken in Ramgarh village of Alwar district (Rajasthan) from January, 1986 to December, 1988 to elucidate epidemiological features of measles. The present paper deals with the findings of this study.

MATERIAL AND METHODS

1. The study village had a population of 5258 comprising of 723 families with 2018 children (0-14 years) in the year 1986 which rose to total population of 5923 with 2200 children (0-14 years). The increase was mostly due to growth of population through births minus deaths.

2. The village was a typical Indian village and the community belonged to the lower socio-economic group.

3. From Jan., 1987 to Dec., 1988 all the children (0-14 years) were covered regularly through monthly domicillary visits by trained paramedical personnel under direct supervision of the Medical Officer.

4. The paramedical personnel enquired about the occurrence of cases of fever with rash and at least one of the symptoms like fever, coryza, and redness of eyes. All the cases of fever were verified by the Medical Officers for the confirmation of the diagnosis.

5. The cases detected were recorded in the prescribed pretested proforma designed for the purpose and followed up till recovery or death and to observe complication, if any, during the study period of three years.

6. Blood samples were collected from children who did not give any history of measles during their life time to know the measles antibody status. The blood samples were collected in filter paper strips. After collection of blood samples the children were immunized with one dose of measles vaccine. A second sample of blood from the same child was collected after 1 month of immunization to know the sero-conversion following use of measles vaccine. The filter paper strips were tested for measles antibody by HI test in the laboratory of the National Institute of Communicable Diseases, Delhi.

7. An HI titre of 1 : 8 or more was considered as sero positive.

RESULTS

A total of 2200 children (0-14 years) were observed in Ramgarh village during the period of three years from January, 1986 to December, 1988. A total of 208 cases of measles were detected (Table 1) which gave an overall incidence rate of 31.5 per 1000 children per year. Incidence rate was found to be high in 2-3 years and in 4-5 years age groups. The lowest (4.6 per 1000) incidence was recorded in 10-14 years of age group. Infants had an incidence rate of 26.5 per 1000. The relationship of measles with age was found to be highly significant ($p < 0.001$). Incidence rate was found almost to be similar in both the sexes ($p > 0.10$).

Table 2 shows the seasonal variation in respect of occurence of measles during the year 1986 to 1988. It reveals that the disease occurred in all the months (except

Table 1—Age & sexwise distribution of cases of measles in Ramgarh village

Age group (Years)	Male			Female			Total		
	Number examined	No. of cases	Attack rate per 1000 per year	Number examined	No. of cases	Attack rate per 1000 per year	Number examined	No. of cases	Attack rate per 1000 per year
0-1	254	23	30.2	173	11	21.2	427	34	26.5
2-3	325	48	49.2	275	44	53.3	600	92	51.1
4-5	147	26	59.0	125	22	58.7	272	48	58.8
6-7	138	11	26.6	113	10	29.5	251	21	27.9
8-9	112	3	8.9	108	4	12.4	220	7	10.6
⩾ 10	270	3	3.7	160	3	6.3	430	6	4.6
Total:	1246	114	30.5	954	94	32.8	2200	208	31.5

Table 2—Seasonal variation with respect to measles incidence in Ramgarh village during 1986-1988

Month	Frequency	Cumulative frequency	Fn	F	Fn—F
1. January	28	28	0.1346	0.0849	0.0497
2. February	33	61	0.2933	0.1616	0.1317
3. March	28	89	0.4279	0.2466	0.1813
4. April	27	116	0.5577	0.3288	0.2289
5. May	48	164	0.7885	0.4137	0.3748
6. June	16	180	0.8654	0.4959	0.3695
7. July	6	186	0.8942	0.5808	0.3134
8. August	5	191	0.9423	0.6657	0.2766
9. September	5	196	0.9423	0.7479	0.1944
10. October	3	199	0.9567	0.8329	0.1238
11. November	3	202	0.9711	0.9151	0.0560
12. December	6	208	1.0000	1.0000	0.0000

Vn = 5.40, $p < 0.01$, Highly significant.

August and November 1988) during the entire period of three years. 86.5 per cent of measles cases occured in the first half of the year and the month of May recorded the highest number of cases (23.1 per cent). Very few cases were observed in the months from July to December (Fig. 1).

Among 333 children of the age group of 6-36 months with no history of measles and measles vaccination, 154 (46.2 per cent) were seropositive while 179 (53.8 per cent) were seronegative (Table 3). A gradual rise in seropositivity was observed with advance in age. The association of seropositivity with age was found to be statistically significant ($p < 0.005$).

Table 4 reflects the seroconversion rates according to age at vaccination. A higher rate of seroconversion could be observed in children vaccinated after 10 months of age than those vaccinated before 10 months of age (Table 4). The relationship of seroconversion with age at vaccination was not found statistically significant ($p > 0.50$).

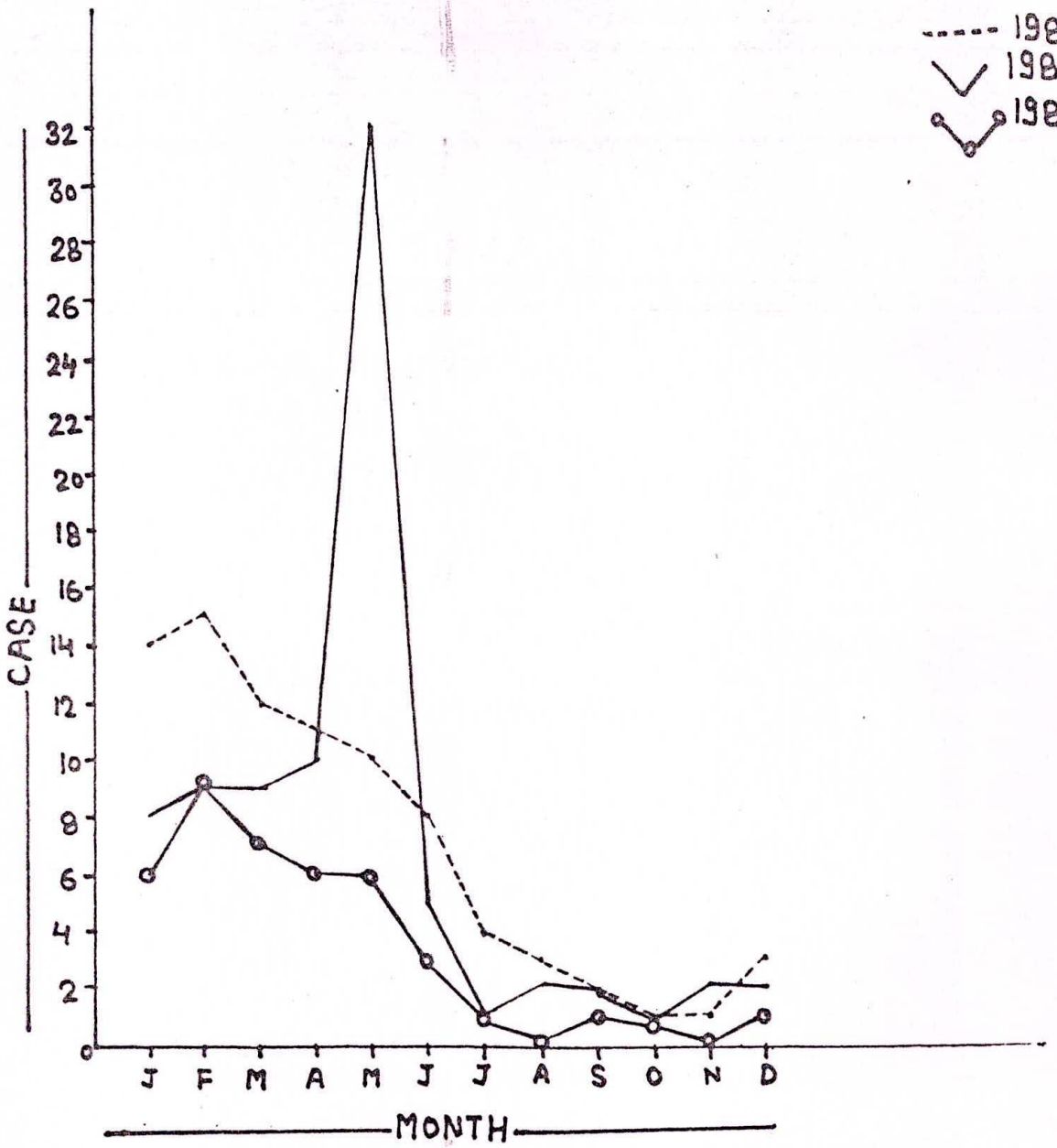

Fig. 1. Seasonal pattern of measles

Table 5 reveals that no significant ($p > 0.10$) association could be obvserved between sex and seroconversion following measles vaccination.

Although the well nourished children had higher seroconversions rate (67.1 per cent) as compared to that of undernourished children (56.6 per cent) following measles vaccination (Table 6), but this difference was found to be statistically not significant ($p > 0.10$).

Table 3—Measles serology status indicating sero positive (HI titre of 1 : 8 or >) and seronegative (HI titre of < 1 : 8) children 6-36 months without any history of measles and measles vaccination during their life time.

Age in months	Sera tested	Positive (⩾ 1 : 8)	Negative (< 1 : 8)
6-10	61	22 (36.1)	39 (63.9)
11-15	46	21 (45.6)	25 (54.4)
16-20	71	24 (33.8)	47 (66.2)
21-25	30	11 (36.7)	19 (63.3)
26-30	52	31 (59.6)	21 (40.4)
⩾ 31	73	45 (61.6)	28 (38.4)
Total:	333	154 (46.2)	179 (53.8)

(Figures in parenthesis indicate percentages)

Table 4—Sero conversion rates according to age at Measles vaccination

Age in months	Number vaccinated	Seroconversion (⩾ 1 : 8)	No sero conversion (< 1 : 8)
6-10	39	21 (53.8)	18 (46.2)
11-15	25	16 (64.0)	9 (36.0)
16-20	47	31 (66.0)	16 (34.0)
21-25	19	11 (57.9)	8 (41.1)
26-30	21	13 (61.9)	8 (38.1)
⩾ 31	28	17 (60.7)	11 (39.3)
total:	179	109 (60.9)	70 (39.1)

(Figures in parenthesis indicate percentages)

Table 5—Sero conversion and sex of Measles vaccinated children

Sex	Number vaccinated	Sero conversion	No sero conversion
Male	101	65 (64.4)	36 (35.6)
Female	78	44 (56.4)	34 (43.6)
Total:	179	109 (60.9)	70 (39.1)

(Figures in parenthesis indicate percentages)

Table 6—Sero conversion and nutritional status at the time of Measles vaccination

Nutritional Status	Number vaccinated	Sero conversion (⩾ 1 : 8)	No. sero conversion (< 1 : 8)
Well nourished	73	49 (67.1)	24 (32.9)
Under nourshed	106	60 (56.6)	46 (43.4)
Total:	179	109 (60.9)	70 (39.1)

(Figures in parenthesis indicate percentages).

DISCUSSION

The present study which was carried out in a rural population (0-14 years) of Alwar district (Rajasthan) showed an overall incidence rate of measles as 31.5 per 1000 children (0-14 years) per year. Approximately similar rates were noted by other workers[8-10] in their studies. Phool Chand *et al*[11] observed higher rate (44.7 per 1000 children) in a similar study in a village Nirmanpur, Varanasi conducted for a period of 13 years (1974-1986). Swami *et al*[12] in a study by monthly home visit in West Rajasthan found annual incidence rate of measles to be13.8 per thousand children (0-14 years), being much lower than that of present study. The difference in incidence rates in various studies is probably due to cyclic trend or nature and design of different studies or both.

In this study the incidence rate was recorded highest (58.8 per 1000 children) in 4-5 years of age group and lowest (4.6 per 1000 children) in 10-14 years of age group (Table 1). Infants had an attack rate of 31.6 per thousand. The relationship of the disease with age was found to be highly significant ($p < 0.001$). No significant ($p > 0.10$) difference could be observed in attack rates of two sexes. Other authors[9-12] also had similar observations.

There has been a definite seasonal variation in the occurence of measles (Fig. 1). Although disease was present through out the year but 86.5 per cent of the cases occured in the first six months of the year (Table 2). The maximum was in month of May (23.1 per cent). It may be due to a small outbreak which occured in May, 1987. The seasonal variation was put to statistical test with the help of Kolmogorov-Smirnow Method[13] which validated the seasonal character of the diseases ($Vn = 5.36$, $p < 0.01$). Labo *et al*[10] in Ballabhgarh and Morley[14] in West Africa has described the same type of seasonal variations. Other authors[11-12, 15] also reported the maximum incidence between January and April. The reason for the seasonal variation could be due to the fact that during winter months the communities remain inside and stay closer enhancing the chances of transmission of the disease. This has a great bearing in planning of immunization programme. It is also pointed out that the transmission and spread of disease can occur in any season depending upon the mobility and susceptibility status of the community.

Seropositivity (HI titre $\geqslant 1 : 8$) rate in children (6-36 months) who gave no history of measles and measles vaccination in our study was higher (46.2 per cent) in comparision to 36.1 per cent and 32.3 per cent recorded by Sehgal *et al*[8] and Bhardwaj *et al*[16] respectively in their studies. In contrast to our findings, higher rates were reported in other studies[7,17-18]. A significant ($p < 0.005$) rise in seropositivity with advance in age was observed in the study. The variation in the seropositivity rates as reported in different studies may be due to geographical difference and peculiar climatic and social conditions prevailing in the study areas. In addition to these, the prevalence of measles infection might have also contributed.

The present study had shown an overall seroconversion in 60.9 per cent children (6-36 months) one month after measles vaccination which is in accordance to the findings of other workers[19-21]. A high rate (83.3 per cent) of seroconversion was reported by Bhardwaj *et al*[16] in their study as compared to the rate of our study.

Interestingly, Swami *et al*[12] reported a positive correlation between seroconversion and increasing age but no such correlation could be observed by us.

Seroconversion following measles immunization showed no significant ($p > 0.10$) difference between two sexes as was reported by Swami *et al*[12]. No significant ($p > 0.10$) difference observed in the seroconversion rate of undernourished and well nourished children. Our findings support the results observed by workers[21-22] in their studies.

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MEASLES OUTBREAK IN A TRIBAL POPULATION OF THANE DISTRICT, MAHARASHTRA

A.R. Risbud
S.R. Prasad
S.M. Mehendale
N. Mawar
N. Shaikh
U.B. Umrani
S.S. Bedekar
K. Banerjee

ABSTRACT

In March 1992, an outbreak of measles, in the tribal population of Vavar village, Mokhada Taluk, Thane district, Maharashtra, was investigated. Two hamlets of Vavar village namely Sagpanipada (epidemic in October, November 1991) and Behedpada (epidemic in January, February 1992) were affected. In both hamlets, measles cases were confined to children below 10 yrs and 96% of the cases occurred in children below 6 yrs. Attack rates were 52.7% and 51.4% and case fatality rates were 31.2% and 15.6% at Sagpanipada and Behedpada, respectively.

All the convalescent patients' sera possessed IgM antibodies against measles. A clear drop in IgM and a rise in IgG antibodies against measles was observed in 35 paired samples from convalescent patients. Fifty four per cent of sera from controls, possessed IgM antibodies.

Migrating population appeared to have imported measles which flared up in an epidemic among the susceptibles. Priority immunization of the children of remote isolated populations may prevent such epidemics.

Key words: *Measles outbreak, Tribals.*

Measles is endemic in urban parts of India. Epidemics of measles have occurred in rural areas and in isolated remote populations(1-4). In March 1992, an outbreak of measles occurred in the tribal population of Vavar village, Mokhada Taluk, Thane district, Maharashtra. We investigated this outbreak on being requested by the Department of Health, Government of Maharashtra. This report presents our observations on the epidemic, which has occurred during the present era, when world wide efforts are being made to overpower measles to the point of eradication(5).

Material and Methods

Vavar village, situated at the south western end of the north Sahyadri mountain ranges is in the Mokhada taluka of Thane district, Maharashtra (*Fig. 1*). The village is comprised of 9 hamlets, locally called 'padas', separated from each other by a distance of 3-5 km. The hamlets are isolated, lack electricity and medical facilities. One had to walk 8 km to avail the nearest bus facility, travel 9 km to visit the nearest market at Ozar and transport a patient 20 km to the nearest Primary Health Centre (PHC) at Sakharshet to seek medical help.

The present outbreak of measles occurred in two hamlets of the Vavar village: Sagpanipada, situated on the top of the hill and Behedpada, situated 3 km away at the foot of the hill. Both these hamlets were

From the National Institute of Virolgy, 20-A, Dr Ambedkar Road, Pune 411 001.

Reprint requests: Dr A.R. Risbud, National Institute of Virolgy, 20-A, Dr Ambedkar Road, Pune 400 001.

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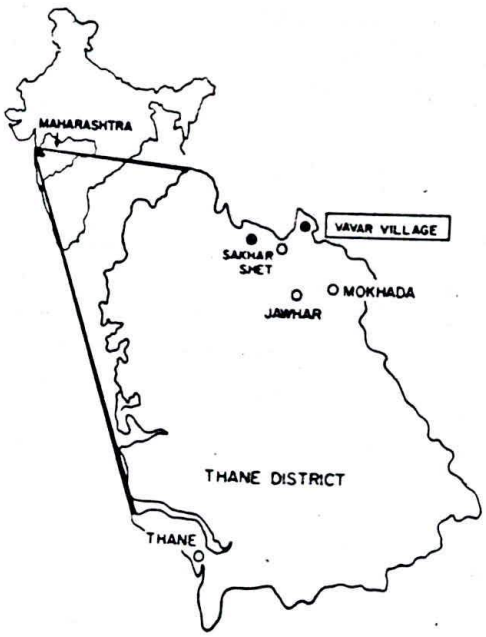

Fig. 1. Location of Vavar village, where measles outbreak occurred.

inhabited by intermingling tribal population.

Enquiries made at PHC Sakharshet revealed that one vaccinator from the PHC used to visit these hamlets for immunizing children with polio, triple and measles vaccines. The vaccinator had to carry the vaccine on foot to these hamlets as no transport facility was available. At the PHC no records of immunization at these hamlets were available.

Locally no qualified medical practitioner was available. However, there was one person locally, who used to treat some ailments with herbs and roots. The villagers preferred him to a Doctor as he did not take any remuneration in cash, instead accepted food/drink or even fowl which was easier for the villagers to pay. He did not treat patients too long and often referred them to PHC.

The team visited all the households in both the hamlets, enumerated the population, examined the patients and noted the details about their illness. In addition, the available children at Behedpada were weighed and their height and mid arm circumferences were noted to assess their nutritional status.

To serologically confirm the epidemic, 8 single convalescent sera from patients of Sagpanipada, 35 paired convalescent and 8 single convalescent samples from patients of Behedpada were collected. There was an interval of 2 months between the paired convalescent samples.

To serve as controls, 7 single serum samples from normal subjects at Sagpanipada and 6 paired sera and 20 single serum samples from normal subjects at Behedpada were collected. These normal subjects belonged to similar age groups and had not suffered an attack of measles during the epidemic.

All serum samples were tested for the presence of IgM and IgG antibodies to measles virus by indirect ELISA(6,7). Briefly the serum samples were diluted 1:100 (in phosphate buffered saline pH 7.2 supplemented with 1% bovine serum albumin). Then the samples were added to Nunc polystyrene plates, coated with purified measles antigen. After appropriate washing steps, goat antihuman IgM (Sigma Chemical Co., 1:1000 dil.) was added for detection of IgM antibodies and goat antihuman IgG (Sigma Chemical Co., 1:1000 dil.) was added for detection of IgG antibodies. This was followed by washing steps and addition of substrate (H_2O_2) and the Chromogen (orthophenylene diamine in phosphate citrate buffer pH 5). After the development of the color, the reaction was stopped with 4N

H_2SO_4 and the wells were read in a Dynatech ELISA reader at 492 nm. Appropriate strong positive, weak positive and negative controls for measles IgM and IgG antibodies were run in each test. Measles IgM and IgG ELISA carried out by us, were standardized by using a commercial kit (Pharmacia) and second international standard antimeasles serum obtained from Staten Serum Institute, Copenhagan, respectively.

A serum giving an optical density (OD) of 0.7 or more in the antimeasles IgM ELISA corresponding to a titre of 1:50 was considered positive for IgM antibodies to measles(8) and a serum giving an OD of 0.6 or more in the IgG ELISA corresponding to a titre of 1:100 was considered positive for IgG antibodies to measles(9).

Chi-square test was used for making comparisons between the males and females, and between the two hamlets Sagpanipada and Behedpada. Student 't' test was used for comparisons of anthropological measurements.

Results

Epidemiological Features

By mid March 1992, when we actually carried out investigations, the outbreak of measles in the two hamlets of Vavar village had waned. The records at PHC, Sakharshet, showed that the outbreak at Behedpada had commenced in the last week of January 1992, reached a peak in the third week of February and ended abruptly in the last week of February. No such information was available for the outbreak at Sagpanipada.

Sagpanipada had 44 households with a population of 270; 176 (65%) were adults and 94 (35%) were children. A total of 48 measles cases occurred and 15 died. In 103 household of Behedpada, 593 people resided, comprising 325 (55%) adults and 268 (45%) children. Among them 128 cases of measles occurred and 20 died.

The age specific measles morbidity at Sagpanipada and Behedpada is presented in *Table I*. In both the hamlets the measles cases were confined to children below 10 years and 96% of the cases occurred in children below 6 years. The overall attack rate of measles for children was 52.7% at Sagpanipada and 51.4% at Behedpada. Infants 9 months and younger had lower attack rate at both the hamlets.

The age specific measles mortality at both the hamlets is presented in *Table II*. The overall case fatality rate was 31.2% at Sagpanipada which differed significantly from 15.6% at Behedpada, ($p<0.05$, $\chi^2=4.414$, $df=1$). Three infants from each of the two hamlets, below nine months, contracted measles and one child expired at each place. At Sagpanipada the high case fatality rate (25-50%) was noticed in all age groups below 5 yrs (60 months), whereas at Behedpada the high case fatality rate of 30% and above was confined to children 2 yrs (24 months) and younger. However, in both the hamlets, majority of deaths occurred in children below 4 years.

The attack rates and case fatality rates for male children did not differ significantly from those for female children in both the hamlets ($p>0.05$).

The precise cause of death in fatal cases could not be ascertained; however, based on the history given by the parents of the survivors, 63% among them had suffered from diarrhea, and or dysentery and 60% from respiratory complications.

Anthropometric measurements of chil-

TABLE I–*Age Specific Measles Morbidity at Sagpanipada and Behedpada*

Age (mo)	Sagpanipada			Behedpada		
	Population	Cases (AR)*	Cumulative percentage	Population	Cases (AR)	Cumulative percentage
0-9	10	3 (30.0)	6.2	16	3 (18.7)	2.3
10-12	10	5[a] (50.0)	16.7	24	18[b] (75.0)	16.4
13-24	21	11 (52.3)	39.6	37	30 (81.1)	39.8
25-36	21	13 (61.9)	66.7	35	27 (77.1)	60.9
37-48	11	8 (72.7)	83.3	31	23 (74.2)	78.9
49-60	11	4 (36.4)	91.7	33	12 (36.4)	88.3
61-72	3	2 (66.7)	95.8	19	10 (52.6)	96.1
73-120	4	2 (50.0)	100.0	54	5 (09.3)	100.0
	91	48 (52.7)		249	128 (51.4)	

AR* = Attack rate.
a = 2 cases 10 months old and 3 cases 12 months old.
b = 2 cases 10 months old, 1 case 11 months old and 15 cases 12 months old.

TABLE II–*Age Specific Measles Mortality at Sagpanipada and Behedpada*

Age (mo)	Sagpanipada			Behedpada		
	Cases	Deaths (CFR)*	Cumulative percentage	Cases	Deaths (CFR)	Cumulative percentage
0-9	3	1 (33.3)	6.7	3	1 (33.3)	5.0
10-12	5	2[a] (40.0)	20.0	18	6[b] (33.3)	35.0
13-24	11	4 (36.4)	46.7	30	9 (30.0)	80.0
25-36	13	4 (30.8)	73.3	27	1 (03.7)	85.0
37-48	8	2 (25.0)	86.7	23	2 (08.7)	95.0
49-60	4	2 (50.0)	100.0	12	0	95.0
61-72	2	0		10	1 (10.0)	100.0
73-120	2	0		5	0	
	48	15 (31.2)		128	20 (15.6)	

CFR* = Case totality rate.
a = Both deaths in 12 months old.
b = 1 death in 11 months old and 5 deaths in 12 months old.

ren (1-5 yrs of age) of Behedpada were compared with the standards from the population of Bombay (ICMR Technical Report Series 26, Studies on pre-school children: 1986). The weights of the children in different age groups did not differ significantly than those for the children in the respective age groups of the standard population. However, arm circumference measurements of the 3-5 yrs old children in the study group were significantly lower than those for the children of the standard population.

Serological Findings

Serological results of the IgM tests and IgG on the single and paired sera from convalescing patients and from the control children are presented in *Table III*. All the single convalescent samples from both the hamlets were positive for IgM antibodies against measles. Among the 35 paired convalescent serum samples of the patients from Behedpada, first samples of all the pairs, obtained in the month of March 1992 possessed IgM antibodies at significant OD values. In the second samples collected after an interval of 2 months, IgM antibody levels showed a clear cut drop and in 16 patients OD values had become insignificant (*Fig. 2*) whereas in the first samples of all the 35 paired sera the IgG antibody titres were low and in 16 patients it was below the cut off values. All the second samples of 35 pairs showed an impressive rise in IgG antibody (*Fig. 3*).

As is seen from *Table III*, many of the samples from the control children also were positive for IgM antibody and most of them were positive for IgG antibody. Five out of six paired samples showed significant IgM levels in the first samples and a fall in the second samples. Both the samples of these pairs from the controls were positive for IgG antibody against measles.

Discussion

In the outbreak of measles described here, all the cases were confined to children below 10 years of age and 96% of the cases occurred in children below 6 years. The overall attack rate was 52.7% at Sagpanipada and 51.4% at Behedpada. These features are common to the measles outbreaks described from the other parts of the country(1,2). However, in an outbreak in a remote isolated population, residing at the Himalayan foot hill, more than 50% of the cases were encountered in children between 5 and 14 years of age(3). The occurrence of this outbreak in the dry season also correlated with some of the rural epidemics described earlier from India and Bangladesh(1,5,10) although outbreaks have been described even in the rainy season by others(2,3,11).

The overall case fatality rate (CFR) seen in the present outbreak was 31.2% at Sagpanipada, situated at the top of the hill and 15.6% at Behedpada, situated at the foot of the hill. The CFR at Behedpada was comparable with that described in a village of Tamilnadu where health care facility was not available(1).

The CFR seen at Sagpanipada appeared to be the highest for the epidemics reported so far from India. Thus, though the determinants of infection, as reflected by the attack rates appear to be similar, the determinants of mortality seem to differ in the two hamlets. The population pattern, socio-economic status, literacy, health seeking behavior were similar in both the hamlets. Both the hamlets suffered equally from lack of medical facility close by. In the light of this, it is difficult to comment as to why

TABLE III–*Results of ELISA to Detect IgM and IgG Antibodies to Measles*

	Sagpanipada		Behedpada	
	IgM	IgG	IgM	IgG
Patients				
Single convalescent samples	8.8*	4/8	8/8	5/8
Paired convalescent samples				
I sample	-	-	35/35	19/35
II sample (2 months later)	-	-	19/35	35/35
Controls				
Single samples	2/7	7/7	10/20	19/20
Paired samples				
I sample	-	-	5/6	6/6
II sample (2 months later)	-	-	4/6	6/6

* Num = Number positive.
Den = Total number of sera tested.

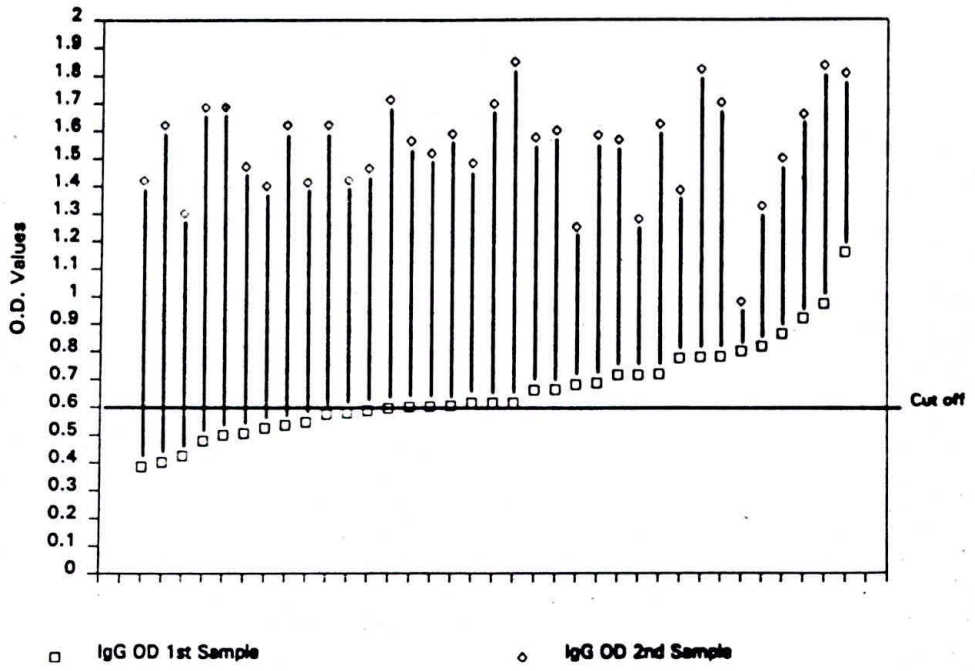

Fig. 2. ELISA OD values for IgM antibodies to measles virus in paired convalescent samples from patients at Behedpada.

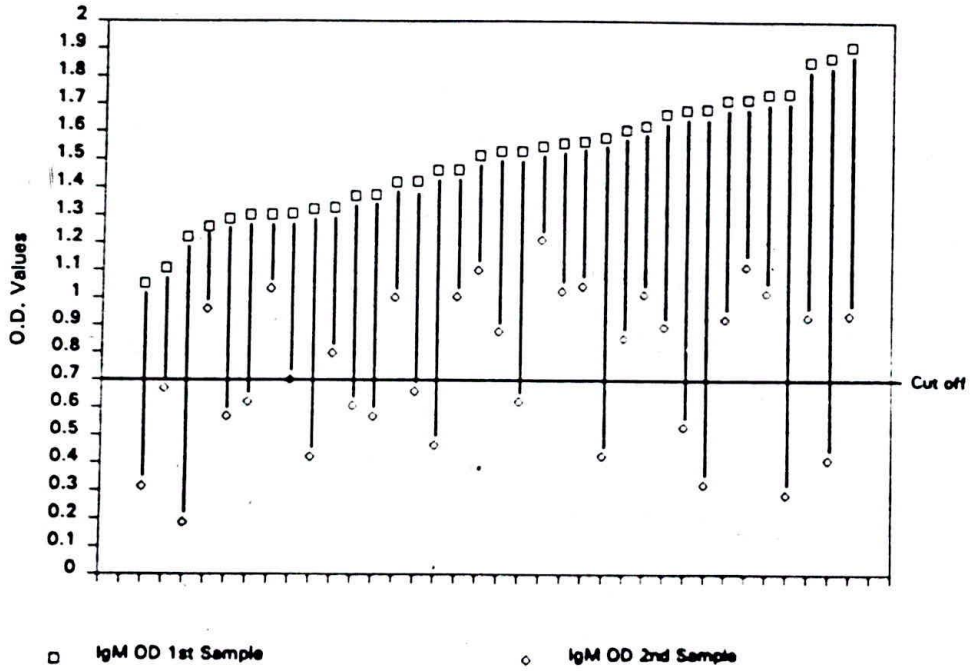

Fig. 3. ELISA OD values for IgG antibodies to measles virus in paired convalescent samples from patients at Behedpada.

there was higher mortality at Sagpanipada. The outbreak at Sagpanipada occurred earlier (October/November 1991) whereas at Behedpada it occurred in February 1992 after a gap of three months. It is possible that during this period a lot of publicity was generated which resulted in active efforts of Health Services personnel to control the outbre which might have resulted in better treatment of very sick children at Behedpada preventing the mortality to some extent.

It has been postulated that malnutrition, lack of easy access to medical facility, bad hygiene, poor management of measles patients at home and local beliefs contribute to high mortality due to measles(1,2). All these factors might have been responsible for the high mortality rates observed in the present epidemic.

Due to non cooperation, we could not assess the nutritional status of children at Sagpanipada. The post epidemic anthropological studies carried out by us on the survivors at Behedpada did not suggest severe malnutrition in children as most of the values did not differ significantly from those described for normal Indian children of similar age groups. However, no comment can be made on the nutritional status of the deceased children. It is quite possible that poor nutrition, dehydration and intercurrent respiratory and gastrointestinal infections might have played a role.

All the convalescent sera tested both from Sagpanipada and Behedpada showed the presence of IgM class of antibodies. The paired convalescent sera tested showed a drop in IgM titres. Both these features were suggestive of a recent measles infection.

The indirect ELISA test performed to

detect IgG class of antibodies to measles virus in 35 paired sera clearly showed a rise in antibody titres in all the patients. This observation confirms the earlier report by Lievens *et al.* on the suitability of indirect ELISA test for the diagnosis of measles infection using paired sera(12).

Fifty four per cent of the control children studied by us showed IgM class of antibodies in addition to good titres of IgG antibodies. These findings suggest a possibility of subclinical measles infections among the controls. Earlier studies using HI test have estimated the subclinical infections to the tune of 30%(1).

Discussions with the local population revealed that many families of Vavar village migrate to adjoining urban areas for work during winter and return home around the month of October for Diwali celebrations. This is the time when the outbreak occurred at Sagpanipada. It is possible that this migrating population imported measles from the urban area, which flared up into an epidemic among the susceptible young children in the village. Spread of measles from urban to rural areas has been described earlier from India and Africa(4,13).

Measles epidemics do not occur in vaccinated villages(1,2). It is unfortunate that the epidemic such as the one described here should have occurred even after seven years of inclusion of measles vaccination in the EPI programme. It seems to reflect the lacunae in the strategy and implementation of our measles control programme.

We feel that for the success of measles control, the population living in isolated villages, far away from the medical facility should receive priority and all the children under five years of age of such population should receive vaccination.

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NOTES AND NEWS

V CONGRESS OF ASIAN PEDIATRC NEPHROLOGY ASSOCIATION

The V Congress of the Asian Pediatric Nephrology Association will be held at New Delhi, India on December 1 to 3, 1994. This will be followed by an Update on Pediatric Nephrology on December 4, 1994. The scientific programme of the Congress and the Update should be very useful to pediatricians.

For further information please write to:

Prof. R.N. Srivastava,
Congress President,
V Asian Pediatric Nephrology Congress,
Department of Pediatrics,
AIIMS, New Delhi 110 029.
India.
Phones : 661123; 6864851 Ext. 3472
Fax : 6862663

Global Campaign Against Epilepsy Agenda for IEA / IES**

K.S. Mani

Consultant Neurologist,
Neurological Clinic,
No.1, Old Veterinary Hospital Road,
Basavanagudi, Banglore-560 004, India.

Introduction

"What disease affects 40 million people worldwide, yet three quarters are untreated ? Paradoxically, the same disease, with early diagnosis and treatment, can be controlled in about three-quarters of those affected. The disease is epilepsy, the commonest serious brain disorder in every country in the world" (Editorial, 1997). Approximately 75% of the 40 million patients with epilepsy worldwide are from developing countries. The population of India is 980 million. If the prevalence of active epilepsy in the country is accepted as around 5.5 / 1000, the number of patients with active epilepsy in India would amount to 5.4 million - which is one-eighth of the worldwide estimate. 70% of the Indian population is rural and thus around 3.8 million epileptics will be in rural areas. Community based studies on epilepsy in Yelandur in Mysore district, Karnataka state have shown that there is a large treatment gap of 78% in rural areas - i.e., they have not had treatment with anti-epileptic drugs (AEDs) except perhaps in a perfunctory manner (Mani and Rangan 1997). This is not only due to poor socio-economic status but due to lack of awareness of therapeutic potential of AEDs and the need for long term medication. The core of the problem is failure to educate the primary care physician and also the general public.

Global campaign against epilepsy in our country can be discussed under three main headings -

1. Training of primary care physicians
2. Public education / health education
3. Dialogue with the Government

70% of the Indian population is rural, but 70% of the medical manpower is urban. 100% of neurologists/ neurosurgeons practice in urban areas, especially in large metropolitan cities because of infrastructural facilities. We have 400 neurologists for 5.4 million epileptics - i.e., one neurologist for 13,500 epileptics which is indeed a skewed distribution ! Epilepsy is an eminently controllable problem in a vast majority of cases, especially of the tonic-clonic seizure variety which poses a potential danger to life or limb. Hence in a developing country with poor infrastructure primary health care should be targeted to achieve epilepsy control, through primary care physician.

Presidential address during EPICON-5 of Indian Epilepsy Association held in Jaipur on December 10, 1997.

Training of Primary Care Physicians

The medical curriculum for undergraduate students with reference to neurological disorders including epilepsy requires revision. The quantum and quality of teaching in epilepsy leaves much to be desired. The emphasis should be on practical epileptology - an opinion shared in UK (Mason et al 1990) and in USA (Devinsky et al 1993). This should include basics of applied neuroanatomy, neurophysiology clinical neuro-pharmacology; recognition of - common seizure types and epileptic syndromes and how to make a quick neurological assessment. Emphasis also should be on the choice of appropriate AED, primarily as monotherapy - very often inexpensive phenobarbitone (PB) or phenytoin (PHT) in minimum effective dose, importance of a seizure calendar, basics of treatment, drug compliance, life style compliance and health education of the patient /relatives regarding their life style. There should be guidelines on when and how to change the dose of drugs; duration of drug treatment, when to reduce / stop the AEDs and the chances of relapse.

A primary care physician should know when to refer a case to secondary/tertiary centre. This is of practical relevance in the present day situation in the country than theoretical expertise on EEG, imaging studies or serum levels of AEDs which are anyway either not available or frightfully expensive for the rural population. However they are very important at a post graduate level. This curriculum on practical epileptology for medical undergraduates is a prime task

for the members of Indian Epilepsy Society (IES), almost all of them members of the Neurological Society of India (NSI) and/or Indian Academy of Neurology (IAN). These medical societies are made up of professionals dealing with epilepsy and include neurologists and neurosurgeons, many of them holding high academic positions in various universities. This view is submitted before them for their consideration and discussion. Recommendation should be made to University Board of Studies and to the Medical Council of India.

Rural Epilepsy Control

In India, if epilepsy has to be controlled early, the treatment facilities should reach the villages and not the other way around, as is the case at present. (Mani and Rangan 1997). Out of 365,000 registered allopaths, only 89% are MBBS degree holders. Non-allopathic doctors account for an additional 510,000. Besides, there are over 4,000 non-governmental organizations (NGOs) committed to rural health care. These could be part of a supervised team for organized primary health care, including epilepsy. There is a vast pool of unemployed local graduates who can be enrolled as paramedical workers (PMWs) to be trained in simplified and practical epileptology. Fool proof arrangements for a 100% unbroken drug chain from manufacturer to patient is a must and the PMWs can be trained to make home delivery of AEDs once a month to ensure better drug compliance. This can be combined with leprosy, tuberculosis and mental health (especially depression) control programs to make it cost effective.

There are over 160 medical colleges in the country. Their departments of medicine should actively train and utilize the services of medical undergraduates in the peripheral decentralized management of epilepsy, tuberculosis, leprosy and depression. The target population could be those in 1 or 2 taluks with in-service training of the local primary care physicians. After a period of 3 - 5 years the college team can shift to another taluk - something like a shifting cultivation leaving it for the local medical manpower to continue the work. The trained PMWs should interact with the local community, identify the suspects - be of epilepsy, leprosy, tuberculosis or depression - and persuade them to attend the primary care clinic where the doctors will examine them, explain about the illness and prescribe drug treatment. They must maintain basic health records and the entire operation must be supervised by a general physician or a neurologist. The emphasis should be on free or subsidized inexpensive AEDs - PB or PHT - supplied in an unbroken drug chain from governmental sources, voluntary NGOs, donations from service organizations like Rotary, Lions etc. Once seizure control has been achieved, the PMWs can be trained to distribute the monthly quota of drugs at nodal points in each village to the patients/carers. These visits can be utilized to enquire about drug/life style compliance, response to drug therapy, side effects and advice to visit the monthly medical clinic for reassessment/ clarification, if required. The all important health education must be emphasized at these monthly visits with adequate regard for socio-cultural ethos.

Is this only an utopian dream, or a practical reality? The experience obtained during the IEA Bangalore chapter / Karuna Trust, Yelandur Rural Epilepsy Control Project From April 1, 1990 to January 1997 is worth a perusal (Mani 1997). The team was made up of specialists - 3 neurologists teamed up with an established local NGO having 2 medical members, 6 PMWs and a transport to go round the villages. The specialists gave their time *gratis* and met their own travel expenses to Yelandur 150 Km (4 hours drive) away from Bangalore. The PMWs trained in epidemiology and practical epileptology by the writer made a door-to-door survey of a population of 64, 963 in 13,562 families, identified the suspects and brought them to the Yelandur clinic once a fortnight for assessment, diagnosis, drug treatment and follow-up. The specialists visited the Yelandur clinic as 2 teams - once a fortnight during the first year, once a month during second year, once in 3 months for the next two years and once in 6 months thereafter. The 3 neurologists also camped twice in the villages for 2 nights and 3 days each during this 6 year period - visited the homes of all the epilepsy patients in all the 40 villages to personally check the follow-up data at the end of 3 and 5 years. Additional 2 other visits were made to gather information on inactive cases who understandably would not visit the medical centre and for a random resample survey to assess the false negatives - i.e., cases missed by the PMWs - the last to arrive at figures for a maximum prevalence rate. This was a 100% clinical study only and the drugs used were PB or PHT essentially as monotherapy. Thanks to the monthly visits of the PMWs, follow-up was available practically in 100% of patients and included data on those who accepted treatment, refused treatment, natural history of untreated epilepsy, follow-up data on febrile seizures, mortality in epilepsy and the all important Knowledge Attitude Practice (KAP) study.

Analysis of data of treated cases at the 3 year follow-up period in 203 patients, showed that complete remission of over 3 years was noted in 40% and 2 - 3 years in an additional 9%. Improved category (no seizures for 1 - 2 years or reduction by more than 50%) accounted for 32%; 15% were unchanged and 4% worse. Thus worthwhile improvement was achieved in (49 + 32) 81% of patients with epilepsy using only inexpensive PB / PHT, with the help of PMWs and without recourse

to investigatory procedures. Side effects interfering with quality of life were minimal - gingival hyperplasis in 7%, somnolence in 1% and no hyperkinesia. This type of beneficial experience with PB in primary rural epilepsy control in developing countries is nothing new and has been noted before by Watts (1989) in Malawi, Feksi et al (1991) in Kenya and Placencia et al (1993) in Ecuador. It is to be noted that Pal et al (1998) found that PB used for rural epilepsy control in children in West Bengal, did not produce behavioural side effects as assessed by a standard questionnaire or parental reports. It is also gratifying that there was not even a single death from status epileptics in those on regular treatment and without any overt brain damage. The total amount spent by IEA for the project over 6 years was of Rs.130,000 (US $3,250) mainly for computerization of demographic data and cost of PB / PHT. To these must be added the cost of the salary of PMWs from Karuna Trust - the local NGO - while travel cost for the specialists was from their own pockets. This proved that with commitment and proper planning, rural epilepsy control is well within the realms of a practical proposition. Collaboration with a willing/ committed partner is very important.

Prevention of Epilepsy

Improved maternal and child welfare programs starting from antenatal care through delivery to childhood immunization and improved nutrition are likely to reduce the prevalence of epilepsy. To this must be added measures for improved public hygiene resulting in protected water supply and established methods of sanitation and sewage disposal - eminently attainable goals if we invest wisely and adequately. Is it not a shame that we should still talk of expensive CT vs. MRI, role of immunology, and whether to start or withhold albendazole for a small single contrast enhancing lesion (SSCEL) when cysticercosis ought to have been eradicated as in the developed countries ? Then we have the preventable scourge of modern times - cranio-cerebral trauma. How to convince the powers that be and the public about the protective value of crash helmets and seat belts ?

Public Education

Till recent times the IEA had to involve itself not only in education of the general public but also in that of the primary care physician. Now that the professional body - IES - has been formed, chapters of IEA ought to give greater attention to public education. These depend on the population to be addressed, their local language and socio-cultural mores. By and large they ought to be in the form of attractive flip charts, posters, pamphlets, booklets, newsletters, TV/radio programs, articles in the lay press, dramas and skits. These should highlight the medical aspects of epilepsy in simple laymens language, therapeutic potential in epilepsy, drugs and life style compliance, positive aspects of life in epilepsy, psychosocial problems and the role of individualization or group discussions as in self-help groups, the ultimate aim being improvement in quality of life. In the Yelandur study, there was a van equipped with TV, video, screen and diesel generator. This would cover all the 40 villages by turns in the evenings for screening educational slides and video programs. This was found to be very popular amongst the village folk and included health educational programs not only on epilepsy but also other common problems like leprosy, tuberculosis, family planning, environmental and individual sanitation and universal immunization. But it must be stressed that in a rural area one well controlled patient is the best advertisement for management of epilepsy rather than a propaganda barrage, which ought to be resorted to judiciously.

Dialogue with the Government

This has to be carried out as a joint endeavour by both the IES and IEA with support from ILAE, IBE and WHO - the latter 3 being the originators of the global campaign against epilepsy. The Government of India must be persuaded to include epilepsy in its National Health Program (NHP) along with malaria, tuberculosis, leprosy etc. We ought to emphasize that 85% of the patients with epilepsy are absolutely normal in between their seizures like anyone else and all quite capable of contributing their mite to society. Control of disease under NHP is a priority item with greater allocation of funds from both the Union and State Governments. This would also enable AEDs to be included under the category of life saving drugs with resultant waiver of import (customs) duty and excise duty. The IEA Bangalore chapter had successfully persuaded the State Government of Karnataka to exempt AEDs from sales tax. This was nearly a decade ago. Other chapters of the IEA/NSI and other State Governments should follow suit? Epilepsy should be included in Health Insurance Schemes and we should do away with barbaric laws linking epilepsy with insanity and divorce. The present over-liberalized driving license regulations with regard to epilepsy for heavy duty vehicle drivers need to be tightened keeping in mind individual liberty and aspirations on one hand and public safety on the other.

Conclusion

Ramamurthi (1997) has cautioned neurologists and neurosurgeons to shed their "super speciality status", come down to terra firma and involve themselves in primary health care. Can't we make a start with epilepsy, an eminently controllable and most common

neurological problem ? In the global campaign against epilepsy, it is suggested that the role of IES and IEA along with NSI and /or IAN are well defined and needs active encouragement and support from the ILAE, IBE and WHO. This is a challenge which must be faced and can be overcome if there is a sense of commitment, unity of purpose, and a dogged pursuit towards the objective of total welfare of patients with epilepsy. Try we should, try we ought to and try we must.

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Antiepileptic Pharmacotherapy : Prevalence of Polytherapy and its Implications

K. Radhakrishnan, S. Dinesh Nayak

Comprehensive Epilepsy Program,
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Trivandrum, Kerala, India

Introduction

Since epilepsy is a common condition affecting 0.5 to 1.5% of the population (Hauser and Hesdorfer, 1990), antiepileptic drugs (AEDs) are frequently used in clinical practice (Masland, 1978; Beghi and Perucca 1995). More than 90% of the burden of epilepsy is carried by the developing countries (Pedley and Kale, 1996).

The approach to pharmacological treatment of epilepsy has changed substantially in the past two decades. This change has resulted from improved knowledge of the efficacy and tolerability of available standard AEDs such as phenobarbitone (PB), diphenyl hydantoin (DPH), carbamazepine (CBZ) and valproate (VPA) (Mattson et al, 1985; Heller et al, 1995), acquisition of new information through observational studies and clinical trials (Beghi and Perruca, 1995), introduction of new AEDs (Marson et al, 1996) and availability of surgical treatment for refractory partial epilepsy. (Engel, 1996; Radhakrishnan, 1997). Recent trends in the management of patients with epilepsy focus on monotherapy in preference to polytherapy all over the world (Reynolds and Shorvon, 1981; Pellock, 1994; Chadwick, 1994).

Very little information regarding the current epilepsy pharmacotherapy practices and its economics are available from developing countries, including India. Considering the greater economic constraints, there is a need for the widespread use of monotherapy with less expensive AEDs in developing countries.

AED usage profile and cost

We recently compared the AED usage profile at entry and at last follow-up of 972 patients seen during 1993 through 1995 in the Comprehensive Epilepsy Care Program of SCTIMST, Trivandrum, Kerala (Radhakrishnan et al, 1997). SCTIMST is a tertiary referral center which receives patients from all over Kerala and from neighbouring states. The patients referred to our comprehensive epilepsy program came from general practitioners, and primary and secondary care facilities. A majority of them had had multiple consultations prior to seeing us. Hence, we concluded that the AED usage profile at entry to SCTIMST is likely to represent the pharmacotherapeutic pattern in the general epilepsy care in this geographical region.

Our patient sample comprised 570 male and 402 female subjects. The mean age was 22.8 ± 14.5 years, range, (0.7 - 86 years). 33.7% of patients were younger than 15 years of age. Idiopathic generalized epilepsy was diagnosed in 39.6% patients, while 49.2% had cryptogenic or symptomatic partial epilepsies. Among the patients with idiopathic generalized epilepsy, 14.8% had juvenile myoclonic epilepsy and 2.9% had childhood absence epilepsy. Among patients with partial epilepsies, 67.6% had temporal lobe epilepsy. Thus, the distribution of the age and epilepsy syndrome in our sample of patients is remarkably similar to other recently reported studies from the West. (Loiseau et al 1991; Osservatorio Regionale per L' Epilessia, 1996).

The distribution of our patients according to AED usage at entry and at last follow-up in SCTIMST is depicted in Table I. At entry 58% of patients were receiving multiple AEDs. We attempted to change them over to monotherapy. At the last follow-up, 76% of patients were on monotherapy. CBZ was the most frequently used AED, followed by DPH, VPA and PB. The absolute percentage increase in the prevalence of monotherapy through our comprehensive epilepsy program was 34%.

We calculated the absolute daily cost of therapy with AEDs from their local price and daily dosage. The relative annual cost of AED therapy was calculated as a percentage of the gross national produce (GNP) per inhabitant. Thus, a patient who is being treated

Reprint request to : Dr. K. Radhakrishnan, Professor and Head, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum - 695 011.

Table I
Distribution of 972 patients according to antiepileptic drug (AED) usage at entry and at last follow-up at SCTMST

	At entry		At last follow-up	
	n	%	n	%
Monotherapy	**409**	**42.1**	**743**	**76.4**
Phenobarbitone*	43	4.4	57	5.9
Phenytoin (DPH)	131	13.5	189	19.4
Carbamazepine**	169	17.4	329	33.8
Valproate (VPA)	63	6.5	159	16.4
Other AEDs	3	0.3	9	0.9
Polytherapy	**562**	**58.0**	**223**	**22.9**
2 AEDs	327	33.6	194	20.0
3 AEDs	164	16.9	27	2.7
> 4 AEDs	71	7.3	2	0.2
Specific combinations				
PB+DPH	58	6.0	29	3.0
PB+CBZ	65	6.7	19	2.0
DPH+CBZ	66	6.8	40	4.1
DPH+CBZ	26	2.7	5	0.5
VPA+CBZ	59	6.1	62	6.4
Other duotherapy	53	5.5	39	4.0
No AED	**1**	**0.1**	**6**	**0.6**

*PB, **CBZ

with PB will spent 4% of GNP for AED therapy, while those on DPH, CBZ and VPA monotherapy will spent 5%, 27% and 30%, respectively, for AED therapy. These figures may be compared with corresponding figures from France for PB, DPH, CBZ and VPA monotherapy of 0.2, 0.3, 1.2 and 1.5%, respectively. Among our patients with polytherapy, the cost increased enormously: PB + DPH 9% GNP to VPA + CBZ 57% GNP. Through our change over to monotherapy from 42% at entry to 76% at last follow-up, the money saved per patient per year was Rs.816 (7.5% of GNP).

Our study shows that better availability of AEDs in recent years in this geographical region has not been supplemented adequately by education of the primary and secondary care physicians about the current trends in the pharmacotherapy of epilepsy. Although the results obtained through our study from a relatively affluent society of Kerala with a literate and health conscious population cannot be extrapolated to rest of India, we presume that the data from elsewhere will not be vastly different. More studies on the epidemiology and econonics of epilepsy treatment from our country are warranted.

Monotherapy versus Polytherapy

There was a long tradition of using several AEDs simultaneously for the treatment of epilepsy. It is now generally accepted that monotherapy is the best therapeutic option when a diagnosis of epilepsy has been established (Reynolds and Shorvon, 1981; Pellock, 1994; Chadwick, 1994). Reynolds and Shovon (1981) showed that 70-80% of patients can be controlled of their epilepsy with monotherapy. Among patients entering the Medical Research Council AED Withdrawal Study (1991) in the United Kindom, 83% of the patients were treated with monotherapy. The percentage of patients on monotherapy was almost 80% in a community dwelling Dutch epilepsy population. (Lammers et al 1996).

Even with most effective AEDs, the proportion of patients who become seizure-free after adding a second or third AED is very small (Mattson 1994; Beghi and Perucca 1995). In a prospective study of the reduction in the number of AEDs among 44 institutionalized patients with multiple handicaps, who were receiving 4 or 5 AEDs, Mirza et al (1993) achieved monotherapy in 64% and duotherapy in the remaining 36% with significantly improved seizure control. Although newer AEDs, such as gabapentin, vigabatrin, lamotrigine, tiagabine and topiramate are becoming available, most patients do not become seizure free with add-on therapy with these new AEDs (Marson et al, 1996; Walker and Sander 1996). In many patients, a 50% seizure reduction may have little effect on the quality of life, especially when such an improvement is achieved at the expense of added AED toxicity and several fold increase in the cost of pharmacotherapy.

Choice of AEDS

Althogh several factors influence the choice of AEDs, the best AED is the one that control seizures (ie efficacy) without causing unacceptable side effects (ie tolerability). VPA or ethosuximide is the drug of choice for absence seizures. In contrast, no evidence convincingly indicates that substantial differences exist among the primary AEDs in their ability to control partial seizures (the most common type of seizure) and secondarily generalized seizures, although PB is significantly less well tolerated than DPH, CBZ and VPA (Mattson et al, 1985; Heller et al, 1995).

There are wide regional differences in the prescribing patterns of AEDs. Multiple factors such as efficacy, tolerability, recommendation from peers, past experience with epilepsy treatment and the system of health care prevailing in an area influence the selection and acceptance of AEDs by physicians and patients. The availability of AEDs and its cost are additional important factors relevant especially for developing countries like India.

We observed that in Kerala, CBZ is the commonest AED used either alone or in combination, followed by DPH, VPA and PB which is similar to the practice in most European nations (Reynolds, 1994; Lammers et al, 1996). In the United States, DPH continues to be most commonly used AED (Pellock, 1994). VPA appears to be the most prescribed AED in France (Genton et al 1992), while PB is more

frequently used in Italy (Collaborative Group for Epidemiology of Epilepsy, 1988).

Conclusions

A majority of patients with epilepsy in developing countries are treated by clinicians without specific training and expertise in this disorder. There is only one qualified neurologist per one million population of Kerala; this ratio will be far worse elsewhere in our country. Based on the result of our study in Kerala, we conclude the following: polytherapy is still quite prevalent in this part of India, less expensive AEDs such as PB and DPH remain underutilized in this geographical region, and polytherapy and the use of expensive drugs such as CBZ and VPA have escalated the cost of AED therapy. Our observations need to be confirmed by more studies on the epidemiology and economics of epilepsy in other regions of India.

There is ample evidence to illustrate that more than 70% of patients with epilepsy can be controlled by treatment with one of the primary AEDs. Even in the small group of patients in whom polytherapy improves seizure control, it often does so at the expense of undesirable side effects, unaffordable cost and disturbed quality of life. Alternate modes of therapy such as epilepsy surgery should be considered early in patients with medically difficult to control partial epilepsies. The mean duration of epilepsy among 55 patients who underwent anterior temporal lobectomy in SCTIMST for intractable complex partial epilepsy was 16.6 years (Radhakrishnan et al, 1997), which reflects the late referral for epilepsy surgery prevailing in this region. Surgical treatment of epilepsy should not be considered as a last resort after all combinations of AEDs (including the newer AEDs) have been tried. As neurologists, we should educate the primary and secondary care providers about these recent trends in the management of epilepsy.

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Randomised controlled trial to assess acceptability of phenobarbital for childhood epilepsy in rural India

DIS 15.3

Deb K Pal, Tulika Das, Gautam Chaudhury, Anthony L Johnson, Brian G R Neville

Summary

Background The use of phenobarbital for childhood epilepsy is controversial because of reported behavioural side-effects; however, whether this research can validly be extrapolated to developing countries is not clear. We undertook a randomised comparison of phenobarbital and phenytoin to assess the acceptability and efficacy of phenobarbital as monotherapy for childhood epilepsy in rural India.

Methods Between August, 1995, and February, 1996, 109 unselected children aged 2–18 years with partial and generalised tonic-clonic epilepsy were identified by population screening. 15 families declined to take part. 94 children were randomly allocated treatment with phenobarbital (1·5 mg/kg daily for 2 weeks; maintenance dose 3·0 mg/kg daily; n=47) or phenytoin (2·5 mg/kg daily then 5·0 mg/kg daily; n=47). Children were followed up for 12 months. The primary outcome measure was the frequency of behavioural side-effects; behaviour was assessed by the Conners parent rating scale for children aged 6 years and older, and by the preschool behaviour screening questionnaire (BSQ) for those aged 2–5 years, at 12 months or at withdrawal from treatment. Analysis was by intention to treat.

Findings The mean log-transformed scores on the behaviour rating scales did not differ significantly between the phenobarbital and phenytoin groups (Conners 2·64 [SD 0·71] *vs* 2·65 [0·89], p=0·97; n=32 in each group: BSQ 2·12 [1·31] *vs* 2·18 [1·02], p=0·94; n=4 *vs* 3). The odds ratio for behavioural problems (phenobarbital *vs* phenytoin) was 0·51 (95% CI 0·16–1·59). There was no excess in parental reports of side-effects for phenobarbital. We found no difference in efficacy between the study drugs (adjusted hazard ratio for time to first seizure from randomisation 0·97 [0·28–3·30]).

Interpretation This evidence supports the acceptability of phenobarbital as a first-line drug for childhood epilepsy in rural settings in developing countries.

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Neurosciences Unit, Institute of Child Health, University College London, London, UK (D K Pal MRCP, Prof B G R Neville FRCP); **SANCHAR-AROD, Pallan, West Bengal, India** (D K Pal, T Das MA, G Chaudhury); **MRC Biostatistics Unit, Institute of Public Health, University Forvie Site, Cambridge, UK** (A L Johnson PhD); **and Child-in-Need Institute, Daulutpur, West Bengal, India** (D K Pal)

Correspondence to: Dr Deb K Pal, Neurosciences Unit, Institute of Child Health, University College London, Wolfson Centre, London WC1N 2AP, UK
(e-mail: d.pal@ucl.ac.uk)

Introduction

Phenobarbital is recommended by the WHO as the first-line drug for the treatment of partial and generalised tonic-clonic epilepsies in developing countries.[1] Widespread use of phenobarbital, one of the oldest antiepileptic drugs, has been encouraged because its efficacy for a wide range of seizure types and its low cost make it suitable for use in primary health care in developing countries.[2] However, studies from the USA and Europe raised concerns about the suitability of phenobarbital as an antiepileptic drug for children, and use of the drug in developing countries has become controversial,[3–5] especially as newer, more expensive alternatives, such as carbamazepine and sodium valproate, became available. In India, phenobarbital is the cheapest antiepileptic drug, with a cost of about US$20–30 for a year's treatment.[6] Phenytoin costs slightly more, whereas carbamazepine and sodium valproate cost 15–30 times more, and imported drugs such as lamotrigine and vigabatrin are not available outside specialist centres.

Several clinical trials have recorded higher frequencies of behavioural problems associated with phenobarbital than with other drugs or no treatment;[7–9] another study found a significantly reduced Stanford-Binet test score after 2 years of phenobarbital treatment, which persisted for 6 months after withdrawal of the drug, although there were no differences in behavioural problems after 2 years.[10] In three other trials, no excess of adverse effects was found when phenobarbital was compared with other active drugs.[11–13]

The strength and generalisability of evidence of serious behavioural and cognitive effects of phenobarbital in recurrent childhood afebrile seizures is controversial, largely because of methodological problems of published trials. Establishment of the acceptability of phenobarbital in appropriate context is of enormous importance in developing countries.[14] Several other considerations also have to be taken into account before available research can be validly applied to such populations. These include the ecological factors influencing the labelling and social significance of mental disorders,[15] cultural perceptions of epilepsy, physiological differences (such as age at diagnosis, number of seizures before treatment, and aetiology),[16] and the feasibility, sustainability, and cost-effectiveness of alternative interventions within an existing framework of local and national needs and health priorities.

Our aim was to assess through a randomised trial the acceptability and efficacy of phenobarbital as monotherapy for childhood epilepsy in a rural Indian setting. The primary hypotheses were that children treated with phenobarbital would have a 25% greater frequency of behavioural problems than those treated with phenytoin, and that there would be equivalence of seizure control to within 15%. We also aimed to assess the feasibility of conducting a randomised controlled trial where such a design had not been used before.

Methods

The study took place in 24 Parganas(S), a rural district of West Bengal, India, south of Calcutta, of area 213 km². Income is seasonal, from farming and local trades. The median monthly income of US$30 and the infant mortality of 65 per 1000 livebirths

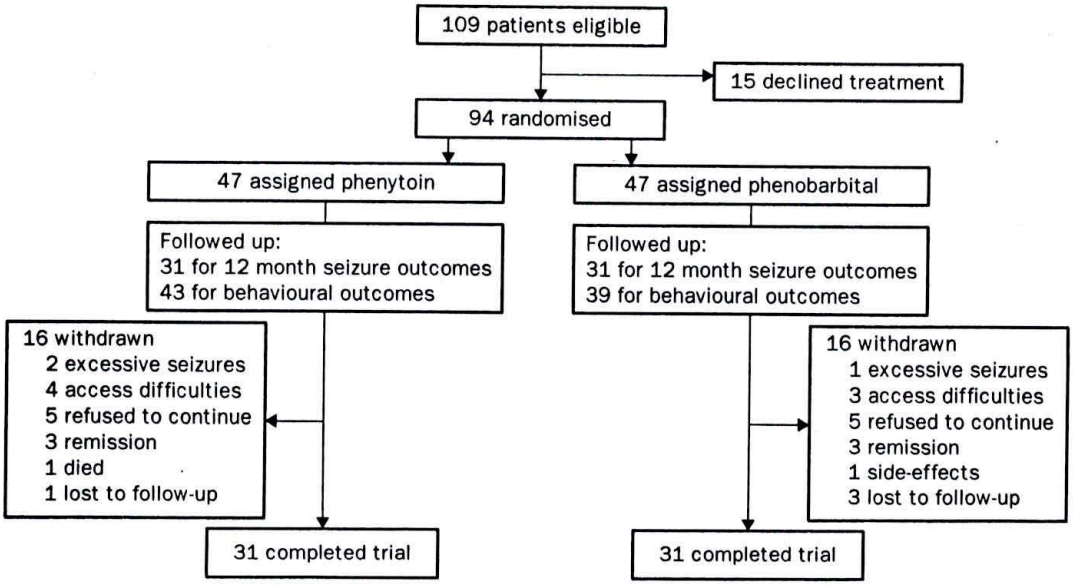

Figure 1: **Trial profile**

are fairly typical of the rest of India. Families are mostly nuclear in terms of living arrangements, but retain strong intergenerational ties. SANCHAR-AROD is a non-governmental organisation that has been working in community-based rehabilitation for children and their families in this area since 1988. An epilepsy service was offered for the first time, jointly by SANCHAR-AROD and another long-standing NGO providing mother and child health services in the area (Child-in-Need Institute).

The study took place between August, 1995, and February, 1997. Children identified by population ascertainment (to be published elsewhere) through house-to-house survey or key informants were invited to attend the clinic. Operational definitions for epileptic seizures were used.[17] After clinical assessment and counselling, parents were asked for verbal consent for their child to take part in the trial, provided that they satisfied the entry criteria. Eligible children were aged 2–18 years, were resident in the field area of either organisation, had had two or more unprovoked seizures within the previous 12 months, and had not been treated during the previous 3 months. Children with myoclonic, absence, or multiple seizure types were treated but not enrolled in the study. Children with febrile convulsions alone were excluded. Any child with clinical evidence of a progressive neurological disorder was referred to the metropolitan neurology centre. Ethical approval for the study was obtained from the local research ethics committee and from the Institute of Child Health, London.

Participants were randomly assigned treatment with phenobarbital or phenytoin in clinic immediately after the diagnosis had been confirmed and parental consent obtained. The first ten children were assigned treatment by means of a pre-prepared, balanced random number list. Thereafter, randomisation was by the technique of minimisation with stratification by age-group and presence of cerebral impairment (severe mental retardation or cerebral palsy). Five separate index cards were used to maintain lists of participants in five categories: aged 2–12 years, aged 13–18 years, with cerebral impairment, without impairment, and overall treatment allocation. All randomisation was carried out by a research assistant who kept the cards in a locked cabinet and took no part in management of patients.

For practical and ethical reasons, the treating physician, child, and parents were aware of the treatment assigned. Outcome was assessed by an investigator unaware of the treatment assignment.

Treatment started with a small, weight-related dose, and was increased after 2 weeks to a maintenance dose consistent with WHO recommendations.[1] Phenobarbital was started at 1·5 mg/kg daily; the maintenance dose was 3·0 mg/kg daily, and one increment was allowed to 5·0 mg/kg daily if seizures were not controlled. Phenytoin was started at 2·5 mg/kg daily; the maintenance dose was 5·0 mg/kg daily, and one increment was allowed to 7·0 mg/kg daily. Any child who had intolerable adverse effects was withdrawn from the trial if necessary. If the seizures were not controlled despite full-dose monotherapy, treatment was changed to the other study drug.

Participants were medically reviewed every month. Occasionally, the interval between reviews was longer if the child was stable and if access to the clinic was difficult. Blood concentrations of drugs were not monitored because of expense. Fieldworkers visited families at home to check on the child's health, to count tablets, to educate the family about first aid, and to encourage the rehabilitation of the child. Children who withdrew from the treatment programme were visited by a senior disability worker and DKP. Thus, possible data loss was kept to a minimum.

Participants were followed up for 21 months after randomisation. Antiepileptic efficacy was measured as time to first seizure after randomisation and the actuarial proportion of each treatment group free of seizures in each treatment quarter. Behavioural side-effects were measured by means of a Bengali adaptation of the Conners parent rating scale (CPRS-48) for children aged 6 years or over,[18] and by the preschool behaviour screening questionnaire for 2–5-year-olds.[19] Assessments were made at 12 months or at the time of withdrawal from treatment. Total and cut-off scores were compared between treatment groups. A checklist of side-effects was used for systematic collection of parental reports of side-effects at clinic visits.

We expected that there would be an important excess of side-effects with phenobarbital and consequently the frequency of side-effects was chosen as the primary outcome. To demonstrate a difference of 25% in side-effects, with an assumed incidence of side-effects with phenytoin of 15%, 80% power, and a one-sided significance level of p=0·05, 39 children were required in each treatment group. We were aware that the trial would have limited power to establish equivalence of the two drugs for late seizure control (between 9 and 12 months after randomisation). On the assumption that 40% of patients in each treatment group are seizure-free during this period, to demonstrate equivalence of

	Phenytoin (n=47)	Phenobarbital (n=47)
Median (IQR) family size	6 (5–7)	6 (5–8)
Occupation of head of household		
Waged labourer	23 (49%)	18 (38%)
Business	6 (13%)	6 (13%)
Skilled trade	7 (15%)	9 (19%)
Salaried	7 (15%)	7 (15%)
Not recorded	4 (9%)	7 (15%)
Maternal literacy		
Illiterate	19 (40%)	23 (49%)
Intermediate	10 (21%)	9 (19%)
Proficient	14 (30%)	9 (19%)
Not recorded	4 (9%)	6 (13%)
Household type		
Nuclear	36 (77%)	34 (72%)
Joint	7 (15%)	7 (15%)
Not recorded	4 (9%)	6 (13%)
Religion		
Hindu	28 (60%)	27 (57%)
Muslim	19 (40%)	19 (40%)
Christian	0	1 (2%)
Median (IQR) monthly income (Rs)	1000 (675–1500)	1000 (700–1500)
Age-group (years)		
2–5	8 (17%)	6 (13%)
6–12	18 (38%)	21 (45%)
13–18	21 (45%)	20 (43%)
Sex		
Male	25 (53%)	24 (51%)
Female	22 (47%)	23 (49%)
Cerebral impairment		
Absent	35 (75%)	35 (75%)
Present	12 (25%)	12 (25%)
Median (IQR) age at onset (years)	6·75 (3·75–10)	8 (5–12)
Mean (SD) body-mass index (kg/m²)	13·3 (5·5)	14·8 (3·3)
Aetiology		
Idiopathic	34 (72%)	38 (81%)
Symptomatic	13 (28%)	9 (19%)
Seizure type		
Partial only	16 (34%)	7 (15%)
Secondary generalised	19 (40%)	18 (38%)
Primary generalised	12 (26%)	22 (47%)
Median (IQR) number of seizures		
Lifetime	61 (6–1002)	51 (5–200)
3 months before study	12 (4·5–93)	9 (4–27)
Febrile convulsions		
Negative history	24 (51%)	26 (55%)
Positive history	5 (11%)	5 (11%)
Not recorded	18 (38%)	16 (34%)
Family history of seizures		
Absent	26 (55%)	29 (62%)
Present	3 (6%)	2 (4%)
Not recorded	18 (38%)	16 (34%)
Previous exposure to antiepileptic drugs		
Negative	22 (47%)	29 (62%)
Positive	25 (53%)	18 (38%)

Data are number of participants (% of group) unless otherwise stated. *Rs30 approximately $1; Rs50 approximately £1.

Table 1: **Baseline characteristics of treatment groups**

effect to within 15% at a two-sided significance level p=0·1 with 50% power, 58 children were required in each group (88 for 65% power). We aimed to recruit 70 children to each group. The design did not allow for early stopping or interim analysis.

Analysis was by intention to treat. Treatment effects, adjusted for design (age and cerebral impairments) and prognostic variables (total number of seizures, interval between first seizure and randomisation, seizures in 3 months before randomisation, previous antiepileptic treatment, sex, seizure type, symptomatic epilepsy) were estimated by means of the Cox proportional hazards model. Log-transformed total behaviour rating scores were compared by Student's *t* test at a significance level of p=0·05. A dichotomous variable was created from cut-off scores for behaviour. The effects of age-group, sex, cerebral impairment,

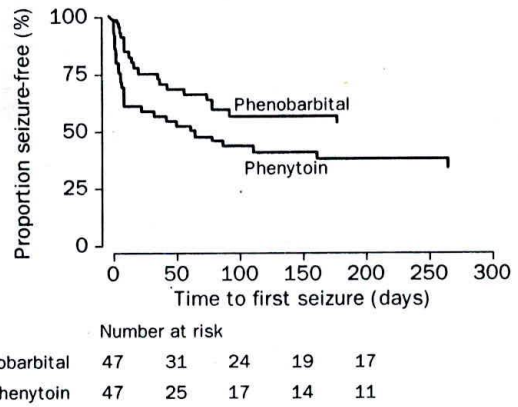

Figure 2: **Kaplan-Meier curves of seizure-free interval by treatment group**

antiepileptic drug, and first-order interactions between these variables, were tested in a multiple logistic regression model, summarised as odds ratios with 95% CI, by means of STATA (version 5·0) for Macintosh software.

Results

Between August, 1995, and February, 1996, 109 eligible children were identified by population screening; 15 families declined any treatment (figure 1). 94 children were randomly assigned one of the trial drugs. 62 (66%) remained on treatment and were followed up for 12 months. In the phenytoin group, 31 children completed 12 months of follow-up; 16 withdrew (four during the first quarter, six during the second, four during the third, and two during the fourth). One child in the phenytoin group drowned in a pond; this death may have been seizure related, but it was unwitnessed. In the phenobarbital group, 31 children completed 12 months of follow-up; 16 withdrew (six during the first quarter, seven during the second, and three during the fourth). 82 (87%) had behavioural outcomes recorded at 12 months or at the time of withdrawal from treatment. In all, 61 (65%) children had complete follow-up data, with similar proportions of missing data between treatment groups.

Most of the participating families were nuclear, with a median size of six (table 1). 59% of families were Hindu, the rest predominantly Muslim. 50% of households were headed by a daily-waged labourer. 45% of mothers were unable to read, write, or tell the time. Reported monthly income varied from Rs300 to Rs6000 (median Rs1000). The typical house was made of mud with a thatch or tile roof, two rooms, no latrine, no other land, and no electricity. Families had to travel for up to 3 h to reach the clinic, often with substantial hardship, by bus, foot, and

Side-effects reported	Phenytoin group		Phenobarbital group	
	Number of participants	Number who did not complete trial*	Number of participants	Number who did not complete trial*
No side-effects	33	13	34	12
Single side-effect				
Behavioural	6	1†	6	3
Sleep disturbance	2	2	2	..
Anorexia/nausea	1	..	..	..
Dizziness	1	..	..	..
Several side-effects	4	..	5	1
Total	47	16	47	16

*For any reason. †Died.

Table 2: **Side-effects reported at clinic and numbers of children who did not complete the trial for any reason**

	Phenytoin group	Phenobarbital group	p
Mean (SD) log total score*			
Conners	2·65 (0·89)	2·64 (0·71)	0·97
BSQ	2·18 (1·02)	2·12 (1·31)	0·94
BSQ (adapted)	3·03 (0·38)	3·51 (0·33)	0·07
Number with behavioural problems/total in group			
Male	6/22 (27%)	3/20 (15%)	
Female	7/21 (33%)	4/18 (22%)	
Aged 2–5 years	3/7 (43%)	3/6 (50%)	
Aged 6–12 years	5/17 (29%)	3/16 (19%)	
Aged 13–18 years	5/19 (26%)	1/16 (6%)	
Cerebral impairment	4/11 (36%)	4/11 (36%)	
No cerebral impairment	9/32 (28%)	3/27 (11%)	
Total	13/43 (31%)	7/38 (18%)	

*Conners parent rating scale for 32 children in each group aged ≥6 years; preschool behaviour screening questionnaire (BSQ) for children aged 2–5 years (4 phenytoin, 3 phenobarbital); adapted BSQ for children with cerebral impairment (7 phenytoin, 4 phenobarbital). Information was not available for 4 children in phenytoin group and 9 in phenobarbital group.

Table 3: **Distribution of behavioural problems at outcome**

cart, at the expense of housework and agriculture, and with significant costs (eg, to buy meals and pay bus fares for themselves and accompanying relatives).

There was balanced distribution by age-group, cerebral impairment, and treatment (table 1). The median age was 12 years, with a median age at seizure onset of 8 years and a median of 50 seizures before randomisation. 64% of children had partial seizures, the remainder primary generalised seizures. A history of febrile convulsions was recorded in 11%. 43 (46%) children had been treated with antiepileptic drugs previously; nine had received phenobarbital and eight carbamazepine, for a median of 18 months (IQR 0·5–60). Homoeopathic treatments had been tried by ten families, and expensive "brain tonics" and vitamins were commonly prescribed concurrently with allopathic drugs (n=12).

Compared with the phenobarbital group, children in the phenytoin group were slightly younger, smaller, and younger at onset of epilepsy and they had a higher cumulative number of seizures, both lifetime and within the 3 months before the trial; higher proportions had a remote symptomatic cause, partial seizure semiology, a first-degree family history of seizure disorder, and previous exposure to antiepileptic drugs. Overall, therefore, children in the phenytoin group had a worse outlook.

Compliance was estimated by tablet counting in the home by fieldworkers. In each treatment group, there was an 8% excess of tablets at the end of the trial, which suggests reasonable compliance for both drugs. In the phenytoin group, two children required increases in dose to 7 mg/kg daily and three required dual therapy (after cross-over) for seizure control. In the phenobarbital group, six children required increases in dose to 5 mg/kg daily, but none needed to switch to the other study drug.

Variable	Odds ratio (95% CI) for behavioural problems	
	Unadjusted (95% CI)	Adjusted (95% CI)*
Single variables		
Phenobarbital *vs* phenytoin	0·52 (0·18–1·48)	0·51 (0·16–1·59)
Male *vs* female	1·44 (0·52–3·97)	0·44 (0·11–1·75)
Cerebral impairment, present *vs* absent	2·24 (0·76–6·56)	0·35 (0·04–3·29)
Age 13–18 *vs* 2–12 years	0·47 (0·16–1·39)	0·42 (0·13–1·39)
Sex×cerebral impairment interaction		
Male, no impairment	1·0	1·0
Male, impairment	0·33 (0·04–3·06)	0·35 (0·04–3·29)
Female, no impairment	0·52 (0·14–1·97)	0·44 (0·11–1·75)
Female, impairment	24·2 (1·60–363·6)	25·1 (1·57–402·0)

*For antiepileptic drug, sex, cerebral impairment, age-group, and sex×cerebral impairment interaction.

Table 4: **Multiple logistic regression model for behavioural problems at outcome**

At the beginning of each successive quarter the proportion of participants entering that quarter who were seizure free was 42%, 49%, 48%, and 56% in the phenytoin group and 56%, 64%, 67%, and 73% in the phenobarbital group. Seizure recurrence occurred earlier in the phenytoin group than in the phenobarbital group (figure 2: log-rank test, p=0·046). After adjustment for design factors (age and cerebral impairment) by the Cox proportional hazards model, the difference between treatments remained (hazard ratio 0·57 [95% CI 0·32–1·00]). However, once all prognostic variables (log lifetime seizures, log pretrial seizures, time between first seizure and randomisation, seizure type, and previous exposure to antiepileptic drugs) had been entered into the model, there was no evidence of a significant difference in efficacy between the drugs, although the hazard ratio of 0·97 had wide 95% CI (0·28–3·30).

27 parents or children reported symptoms that they ascribed to treatment (table 2). The frequency of side-effects was similar in the phenytoin and phenobarbital groups (14 [30%] *vs* 13 [30%], p=0·77). Two families in the phenytoin group who reported sleep disturbance withdrew the child from treatment. Three families in the phenobarbital group who reported behavioural problems (hyperactivity) left the study; two migrated and were lost to follow-up and one withdrew.

There were no significant differences between the treatment groups in behaviour rating scores (table 3). 20 children were rated as having behavioural problems on the basis of cut-off scores—13 in the phenytoin group and seven in the phenobarbital group. Behavioural problems were more common among children with cerebral impairments, those under 5 years old, and girls. All these patterns were stronger in children treated with phenytoin than in those who received phenobarbital.

There was no evidence of association between behavioural problems and age, sex, cerebral impairment, or antiepileptic drug by multiple logistic regression (table 4). We looked for first-order interaction between combinations of these variables but found evidence of interaction only for sex and cerebral impairment—girls with cerebral impairment were significantly more likely to have behavioural problems than boys without cerebral impairment (p=0·02). There was, therefore, no evidence of an excess of behavioural problems in the phenobarbital group. The adjusted odds ratio even suggested fewer behaviour problems with phenobarbital (0·51 [95% CI 0·16–1·59]).

Discussion

We aimed to recruit 70 children to each group but could not achieve this target in the time available. In this trial in India, we achieved 67% of the target sample size, which is similar to rates achieved in clinical trials in Europe and the USA. Despite substantial logistical difficulties in mounting the study, we achieved a follow-up rate similar to that in clinical trials in western countries.[8] Poverty, difficulties with travel, the seasonal pattern of work, the monsoon, and the wide choice of other health practitioners were all obstacles to regular clinical follow-up. This service could not have been offered, and this study could not have been undertaken, without regular home visits by disability workers within the setting of community-based rehabilitation.

Among this representative sample of children with epilepsy in rural India, the overall age distribution was wider than in some previously reported trials.[8,11] The age at onset of epilepsy was similar to that in the UK monotherapy study.[9] Compared with that study, our participants had poorer prognostic features: 25% had cerebral impairments, and they had had many seizures before randomisation, a pattern typical of unselected patients in developing countries.[21] A high proportion (46%) had received drugs in the past, compared with 6–26% in other developing countries.[16,21] Many of these families had consulted a doctor in Calcutta at the onset of their child's epilepsy and could not afford to continue treatment with carbamazepine or expensive, concurrent "brain tonics".

This trial did not show a difference in efficacy between phenobarbital and phenytoin when design and prognostic factors were taken into account, although we lacked the sample size to demonstrate equivalence of efficacy to our desired level of precision. This equivalence of effect is consistent with other studies of monotherapy in childhood,[8–10] and does not allow any conclusion about absolute efficacy to be drawn. Overall, 65% of children were seizure free in the final quarter, a success rate similar to that obtained in community-based studies in Kenya and Ecuador.[13,20] These results therefore confirm the usefulness of first-line antiepileptic drugs for the primary-care treatment of partial and generalised tonic-clonic childhood epilepsy in developing countries.

We found no difference in the incidence of serious behavioural side-effects between phenytoin and phenobarbital, using both objective, masked assessments and parental reports. We were seeking a difference of 25% and had the intended statistical power, and our instruments were validated in a standard manner. Behavioural problems, on our adapted rating scales, were as common as reported in western population studies.[19,22] The finding of no excess of serious behavioural problems with phenobarbital accords with results of other clinical trials that used objective, masked outcome assessment[8,9,23] and suggests that previous reports of intolerable adverse effects may have been influenced by observer bias.[7,10] Another explanation is that the context of the study influenced the outcomes we measured, and that the threshold at which childhood hyperactivity becomes intolerable is higher in this setting, which would explain the low rate of withdrawal due to adverse effects. However, this factor would not explain the lack of a difference in side-effects between the two drugs. In view of the equivalence of effect, frequency of other side-effects, and careful tablet counting, we do not believe that differential non-compliance could explain these findings. Although our results do not support an excess of behavioural effects with phenobarbital in the preschool age-group or in children with cerebral impairments, we cannot rule out this possibility. A separate study would be necessary to answer this question and examine long-term effects on cognitive functioning.

This study was carried out within a primary-health-care service structure, at low cost, and using a model integrated within community-based rehabilitation. Access was an important issue in follow-up, and emphasised the lack of choice in terms of drug cost and availability. International trade agreements will further restrict the transfer of new pharmaceutical technology to developing countries[24] and make replacement of phenobarbital as a first-line drug in developing countries impossible in the near future. Therefore, the main conclusion of this study, that phenobarbital is an effective and acceptable antiepileptic drug for rural Indian children, has great relevance for WHO strategy and epilepsy-control programmes in developing countries.

Contributors

All five investigators contributed to the design of the study. Deb Pal took the baseline measurements and with Gautam Chaudhury and Tulika Das adapted the outcome measures, which were undertaken by Tulika Das. Data handling and statistical analysis were done by Deb Pal with assistance from Anthony Johnson, who also gave advice about practical issues during the trial. Deb Pal wrote the first draft of the paper, and all the investigators contributed to the final version.

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Effect of diagnosis on survival benefit of lung transplantation for end-stage lung disease

Jeffrey D Hosenpud, Leah E Bennett, Berkley M Keck, Erick B Edwards, Richard J Novick

Summary

Background Although certain forms of end-stage lung disease are debilitating, whether the associated mortality rate exceeds that of transplantation is unclear. We undertook analysis to clarify the survival benefit of lung transplantation for various types of end-stage lung disease.

Methods We analysed data for all patients listed for transplantation in the USA for emphysema, cystic fibrosis, or interstitial pulmonary fibrosis in the years 1992–94. The numbers of patients entered on the waiting list, post-transplantation, died waiting, and currently waiting were: emphysema group 1274, 843, 143, and 165; cystic fibrosis group 664, 318, 193, and 59; interstitial pulmonary fibrosis group 481, 230, 160, and 48. A time-dependent non-proportional hazard analysis was used to assess the risk of mortality after transplantation relative to that for patients on the waiting list.

Findings The clearest survival benefit from lung transplantation occurred in the cystic fibrosis group. The relative risks of transplantation compared with waiting were 0·87, 0·61, and 0·61 at 1 month, 6 months, and 1 year (p=0·008), respectively. For interstitial pulmonary fibrosis, the corresponding relative risks were 2·09, 0·71, and 0·67 (p=0·09). No survival benefit was apparent in the emphysema group. The risks of transplantation relative to waiting were 2·76, 1·12, and 1·10 at 1 month, 6 months, and 1 year, respectively, and the relative risk did not decrease to below 1·0 during 2 years of follow-up.

Interpretation These findings suggest that lung transplantation does not confer a survival benefit in patients with end-stage emphysema by 2 years of follow-up. Other benefits not accounted for in this analysis such as improved quality of life, however, may justify lung transplantation for these patients.

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Joint United Network for Organ Sharing/International Society for Heart and Lung Transplantation Thoracic Registry, Richmond, VA, USA (J D Hosenpud MD, L E Bennett PhD, B M Keck MPH, E B Edwards PhD, R J Novick MD)

Correspondence to: Dr Jeffrey D Hosenpud, Division of Cardiovascular Medicine, Medical College of Wisconsin, 9200 West Wisconsin Avenue, Milwaukee, WI 53226, USA

Introduction

Although lung transplantation has become an invaluable approach for the treatment of end-stage respiratory disease, rates of successful outcomes are not yet as good as those for other transplanted organs. Based on data from the Joint United Network for Organ Sharing (UNOS)/International Society for Heart and Lung Transplantation (ISHLT) Thoracic Registry, 1-year mortality is more than 25% and 5-year mortality is greater than 50%.[1] In addition, obliterative bronchiolitis affects more than 50% of patients late after transplantation[2] and accounts for 57% of the deaths after 1 year.[1]

The most common indication for lung transplantation is emphysema.[1] Although emphysema is debilitating, mortality from this disorder may not be as high as that from other forms of end-stage lung disease, especially in patients younger than 60 years.[3-6] Moreover, for some patients with emphysema, volume-reduction surgery[7-9] may be an alternative. To clarify the actual survival benefit of lung transplantation for the more common causes of end-stage lung disease, including emphysema, we undertook an analysis of data from the Joint UNOS/ISHLT Thoracic Registry.

Methods

The cohort for this study included all patients listed for transplantation with UNOS (listed for transplantation in the USA) between Jan 1, 1992, and Dec 31, 1994. The cohort included patients with the three most common indications—emphysema, cystic fibrosis, and interstitial pulmonary fibrosis.

	Cystic fibrosis	Interstitial pulmonary fibrosis	Emphysema
Total cohort	664	481	1274
Outcome at time of analysis			
Died on waiting list	193	160	143
Underwent transplantation	318	230	843
Removed from waiting list and censored for other reasons	94	43	123
Still on waiting list	59	48	165
Died after transplantation	68	55	142
Mean (SD) days on waiting list			
Non-transplant patients	398 (18)	361 (23)	560 (16)
Transplant patients	304 (17)	250 (14)	260 (17)
Mean (SD) post-transplant follow-up days	354 (19)	327 (21)	391 (12)
Mean (SD) total follow-up (days)			
All patients	512 (15)	454 (17)	616 (10)
Transplant patients only	658 (21)	577 (24)	651 (12)
Mean (range) age in years*	25·8 (1·0–49·3)	49·6 (16·1–71·4)	53·5 (17·8–68·4)
Sex			
M	357 (54%)	293 (61%)	567 (45%)
F	307 (46%)	188 (39%)	757 (55%)
White patients	616 (93%)	382 (79%)	1187 (93%)

*At time of analysis.

Table 1: **Characteristics of patients, outcomes, and time spent in each clinical stage**

JE VIRUS ENCEPHALITIS: 1988 EPIDEMIC AT GORAKHPUR

A.K. Rathi
K.P. Kushwaha
Y.D. Singh
J. Singh
R. Sirohi
R.K. Singh
U.K. Singh

ABSTRACT

Gorakhpur region experienced the most serious outbreak of Japanese encephalitis (JE) in 1988 in which 875 children were admitted in the Department of Pediatrics, BRD Medical College, Gorakhpur. Children between 7-10 years age group constituted half (49.3%) of these cases, convulsions (83.8%), altered sensorium (78.2%), headache (68.8%) and hypertonia (77.0%) were the main presenting features. IgM against JE virus was demonstrated in 18/25 CSF and 27/53 sera collected from these children. Significant titres of III antibodies against JE were present in 498/670 patients.

Patients were managed symptomatically. Dexamethasone and dopamine were given to only 137 (15.7%) children admitted with shock and peripheral circulatory failure.

Almost a third (31.8%) of the patients expired, 51.4% recovered completely and 10.7% recovered partially. Corticosteroids did not improve the outcome.

Twenty four patients had recurrence of symptoms after excellent recovery from acute attack of whom two died and 5 developed neurological deficits.

Key words: *Japanese virus encephalitis, Epidemic, Neurological dificits, Recurrence.*

Japanese encephalitis (JE) has become an important health problem in India, more so in children, who bear the major brunt of the disease. The disease was first reported in India in 1954 by Khan(1) from Jamshedpur. This was followed by several reports of occurrence of JE epidemics from other parts of the country(2). Gorakhpur and surrounding districts of eastern Uttar Pradesh first experienced an epidemic of JE in 1978 and then in 1980, 1985 and 1986(3). A severe epidemic of JE seen in Gorakhpur area in the late rainy season of 1988 is reported in the present communication.

Material and Methods

Patients clinically diagnosed as encephalitis and admitted to the pediatric wards of Nehru Hospital, BRD Medical College, Gorakhpur from September to November, 1988 constituted the case material for the present study. Laboratory investigations done included hemoglobin, total and differential leucocyte counts and complete cytochemical examination of cerebrospinal fluid (CSF). On admission blood samples were taken for demonstrating anti-JE virus antibodies (IgM and IgG) with repeat sampling after 15 days to see the rise in IgG antibody titre. Sera separated were stored in sterile containers at –20°C till tested. CSF samples obtained at the time of admission were examined for IgM antibodies to JE virus. Needle biopsy of brain was also done in 4 children immediately after death for isolation of virus.

From the Department of Pediatrics, Biochemistry and Microbiology, B.R.D. Medical College, Gorakhpur.
Reprint requests: Dr. A.K. Rathi, Lecturer in Pediatrics, B.R.D. Medical College, Gorakhpur.
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Patients were largely managed symptomatically and supportively. Airway was kept clean, fever brought down with antipyretics and cold sponging. Phenobarbitone, phenytoin and diazepam were used for seizures. Brain edema was reduced by mannitol, glycerine and in selected cases by dexamethasone. Most patients were on intravenous fluids for 4-5 days keeping in mind the syndrome of inappropriate release of anti-diuretic hormone. Dopamine was used to maintain blood pressure in patients with peripheral circulatory failure (PCF). Dexamethasone was used only in children with PCF and those with central cardiorespiratory involvement and other features of brain edema, not responding adequately to mannitol and glycerine. Oral prednisolone (1 mg/kg/day) was administered to selected patients not showing recovery in 3 weeks, to see its possible effect on the outcome.

After the initial discharge from the hospital, patients were followed up every fortnight. Cases with neurological deficits, sensory/motor and behavioral problems were managed symptomatically with judicious use of physiotherapy.

The isolation of the virus was done employing infant mice model and was carried out at the Department of Microbiology, KG Medical College, Lucknow. The estimation of IgM against JE by MAC ELISA method(4) using 1:5 dilution of serum or CSF was carried out at the National Institute of Virology, Pune. Hemagglutination inhibition (HI) test for IgG antibodies(5,6) was carried out in Department of Microbiology, BRD Medical College, Gorakhpur. HI antibody titre >80 in single sample and minimum of four fold rise in titre in second sample taken after 10-15 days was considered positive. A titre <80 without subsequent rise was taken as negative.

Results

A total of 875 children (3 months to 15 years) with clinical features of encephalitis were admitted to the Pediatric wards of Nehru Hospital during a period of 3 months (375, 456 and 44 children in September, October and November 1988, respectively). Of them, 431 (42.3%) were between 7-10 years of age and boys outnumbered girls (*Table I*). Fever, headache, convulsions and altered sensorium were the main presenting features (*Table II*).

TABLE I–*Age and Sex Distribution of JE Cases*

Age group	Male	Female	Total
3 mo-3 yrs	18 (72.0)	7 (28.0)	25 (2.9)
3–6 yrs	174 (68.8)	79 (31.2)	253 (28.9)
7–10 yrs	305 (70.8)	126 (29.2)	431 (49.3)
11–15 yrs	119 (71.7)	47 (28.3)	166 (19.0)
Total	616 (70.4)	259 (29.6)	875 (100)

Figures in parentheses indicate percentages.

The total duration of signs and symptoms and the outcome of these cases is shown in *Table II & III*. About one third children (31.8%) died. Most of the patients who expired did so within first 3 days of admission. The causes of death included cardiac failure, respiratory failure, PCF associated with toxemia and gastro-intestinal bleeding. Neurological deficits

TABLE II–*Presenting Features and Outcome in JE*

Features	(n=875)	Outcome of illness			
		Recovery	Partial recovery	Death	LAMA*
Fever	865(98.9)	467(54.0)	94(10.0)	269(31.1)	35(4.1)
Convulsions	733(83.8)	356(48.6)	87(11.9)	259(35.5)	31(4.2)
Altered sensorium	684(78.2)	322(47.1)	99(14.5)	231(33.8)	32(4.7)
Headache	558(63.8)	330(59.1)	65(11.7)	138(24.7)	25(4.5)
Vomiting	476(54.4)	201(42.3)	54(11.3)	178(37.4)	43(9.0)
Constipation	346(39.5)	169(48.8)	25(7.2)	145(41.9)	7(2.0)
Neck rigidity	223(25.5)	107(48.0)	33(10.3)	91(40.8)	2(0.9)
Gastric bleeding	115(13.1)	21(18.3)	14(12.2)	80(69.5)	–
Central respiration irregularities	113(12.9)	15(13.3)	27(23.9)	70(61.9)	1(0.9)
Positive Kernig's	69(7.7)	30(43.5)	11(15.9)	26(37.7)	2(2.9)
Diarrhea	32(3.4)	21(65.6)	1(3.1)	10(31.3)	–
Other					
–PCF	59(6.7)	8(13.5)	5(11.8)	45(77.6)	1(1.6)
–Pneumonia	26(3.0)	13(50.0)	9(34.7)	2(7.6)	2(7.6)

Figures in parentheses denote percentages.

* Left agaisnt medical advice; outcome not known.

and behavioral problems were seen in 94 (10.9%) children comprising mainly of mental retardation, aphasia, paresis, dystonia and seizures (*Table IV*).

Dopamine and corticosteroids were administered to 137 (15.7%) cases admitted in the acute stage with PCF and shock. Of the 35 children who were administered prednisolone at 3 weeks of illness, 20 (57.1%) recovered completely, 10 (28.6%) partially and 3 expired (*Table V*). When compared with non-steroid group (56 children) findings were not statistically significant.

TABLE III–*Duration of Signs and Symptoms in Patients who Survived*

Presenting features	(n=597)	Duration in days			
		3	3–7	7–10	10
Fever	531	185 (34.8)	239 (45.0)	76 (14.3)	31 (5.8)
Convulsions	542	178 (32.8)	291 (53.6)	47 (8.6)	26 (4.7)
Altered sensorium	378	172 (45.5)	153 (40.4)	29 (7.6)	24 (6.3)
Headache	317	317 (100)	–	–	–
Vomiting	223	223 (100)	–	–	–
Constipation	162	126 (77.7)	36 (22.2)	–	–
Neck rigidity	177	21 (11.8)	119 (67.2)	37 (20.9)	–
Gastric bleeding	34	23 (67.6)	11 (32.3)	–	–
Central respiratory irregularities	59	34 (57.6)	16 (27.1)	9 (15.2)	–
Positive Kernig's	54	9 (16.6)	33 (61.1)	12 (22.2)	–
Diarrhea	32	14 (43.7)	8 (25.0)	–	–

Figures in parentheses indicate percentages.

Out of the 278 children who were discharged after complete recovery in one week, 24 had recurrence of symptoms and were readmitted. Two of these children expired and rest showed variable recovery (*Fig. 1, Table VI*).

The laboratory investigations showed moderate leucocytosis in 661 (80.3%) cases (*Table VII*) with neutrophil predominance in 60%. Rise in CSF protein level was seen in 70.8% cases of whom 20% showed levels above 100 mg/dl or more whereas CSF

TABLE IV– *Neurological and Behavioral Problems in Patients Showing Partial Recovery*

Sequelae	Number	Percentage
Mental retardation	38	40.3
Hemiparesis	34	36.2
Aphasia	34	36.2
Dystonia	33	35.1
Seizures	26	27.7
Incontinence of bladder anal canal	19	20.2
Involuntary movement	19	20.2
Cranial nerve palsy	6	6.4
Monoparesis	5	5.3
Irrelevant behaviour	11	11.7
Irrelevant talk	10	10.6
Insomnia	10	10.6
Tongue protrusion	10	10.6
Weeping	8	8.5
Excitement	7	7.5
Irritability	6	6.4
Inappropriate laughing	2	2.1
Assaultive behavior	2	2.1

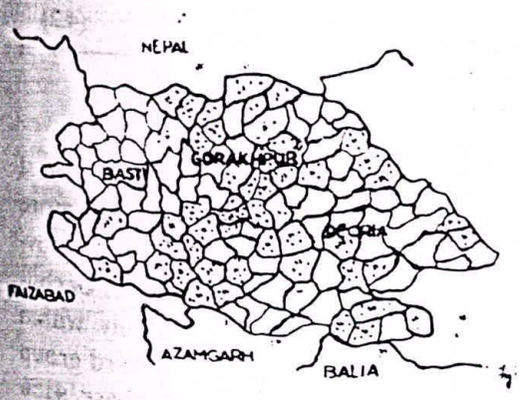

Fig. 1. Geographical distribution of cases of JE (1988-89).

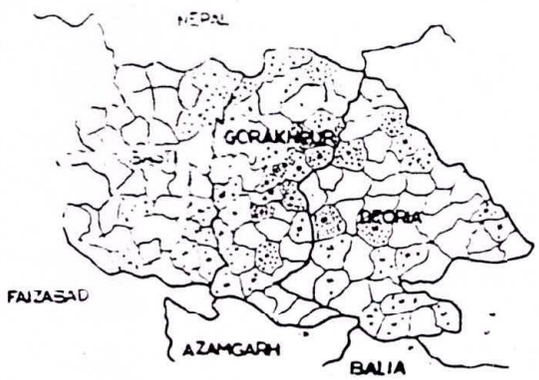

Fig. 2. Geographical distribution of cases of JE (1987-88).

sugar levels were not much altered. Majority of CSF samples had cell count upto 50 × 10^6/L, in 17% samples count was still higher. The virological investigations showed evidence of IgM antibodies in 18/25 CSF and 27/53 sera. HI antibodies (IgG) to JEV in significant titres were seen in 498/670 sera tested (*Table VII*). A four fold or more rise in HI antibodies was seen in sera of 13/14 patients tested out of 24 children readmitted with recurrence of symptoms.

Discussion

The 1988 epidemic of encephalitis in Gorakhpur region was one of the most serious epidemics in India so far with 875 children admitted to Nehru Hospital alone in a period of 3 months. Most of the cases from Gorakhpur and Deoria districts and some were from Basti and Azamgarh districts and bordering towns of Nepal (*Fig. 2*). As in past epidemics (1978, 1980, 1985, 1986)(3,7) the present epidemic too occurred at the end of rainy season. Occurrence of these epidemics at the end of rainy season has also been reported from West Bengal(8).

Encephalitis affected all age groups but the brunt of the disease fell on children

TABLE V–*Effect of Steroids in Chronic Phase*

Groups	Cases	Complete recovery	Partial recovery	Expired	LAMA*
Steroid	35 (4.0)	20 (57.1)	10 (28.6)	3 (8.6)	3 (5.7)
Non-steroid	56 (6.4)	38 (67.9)	14 (25.0)	-	4 (7.1)

χ^2 2df = 1.448; $p > 0.05$.

Figures in parentheses indicate percentages.

* Left against medical advice.

TABLE VI–*Profile of Patients Admitted with Recurrence*

Presenting features	(n = 24)	Complete recovery	Partial recovery	Expired	LAMA
Fever	13 (54.2)	10 (76.9)	2 (15.4)	-	1 (7.7)
Altered sensorium	3 (12.5)	1 (33.3)	1 (33.3)	1 (33.3)	-
Involuntary movements	6 (25.0)	4 (66.7)	2 (33.3)	-	-
Convulsions	14 (58.3)	11 (78.6)	2 (14.3)	1 (7.1)	-
Total	24 (100.0)	16 (66.7)	5 (20.8)	2 (8.3)	1 (4.2)

Figures in parentheses indicate percentages.

between 7-10 years of age. Males were often affected in all age groups and is in line with the earlier reports(9, 10).

Clinical features of JE epidemic were similar to these reported earlier(11,12), as were the findings in CSF(10,11,13) and blood showing marked polymorphonuclear leucocytosis(11,13). The early and high mortality and the causes of death are also similar to previous reports(14,15). Most patients came in the acute stage and more than half of them showed complete recovery in 7-10 days. Significant number of children died in acute phase, mainly within first three days of admission. a third group of children went into a chronic phase, 41% of them developing neurological deficits and behavioral problems. A fourth course

TABLE VII–*Laboratory Findings in JE*

	Feature	Investigation	Result
Blood (n=823)	Hemoglobin (g/dl)	>12	101 (12.3)
		10–12	268 (32.6)
		<10	454 (55.1)
	Leucocyte counts ($\times 10^9$/L)	TLC	
		18	243 (29.5)
		12–18	418 (50.8)
		4–11	162 (19.7)
		Neutrophils (10^9/L)	
		>10	486 (59.1)
		5–10	309 (33.5)
		<5	28 (7.4)
CSF (n=768)	Proteins (mg/dl)	≤40	242 (70.6)
		>40	226 (29.4)
	Pleocytosis ($\times 10^6$/L)	50	131 (17.1)
		5–50	434 (56.5)
Virology (n=745)	Virus isolation from brain		2/4 (50.0)
	IgM – CSF		18/25 (72.0)
	Serum		27/53 (51.0)
	IgG Serum		498/670 (74.3)

Figures in parentheses indicate percentages.

also came to light in the present epidemic. Twenty four children who had shown complete recovery in early phase of epidemic and were sent home in 7 days came back after variable period with recurrence of symptoms (*Table VI*). On readmission, 16/24 recovered completely, 5/24 partially and 2 died. Such a course of JE has not been reported so far. It has been suggested that host defence mechanisms play an important role in viral encephalitis, dominance of which by the virus in early post recovery phase from first attack led to the recrudiscence of illness which again was controlled due to further stimulation of the immunological apparatus chiefly cell mediated immune response. It is as best a speculation as investigations were not carried out to see the behavior of immune mechanisms in these children. Role of auto-antibodies in recurrence too can be possible(16). It has been shown that JE virus persists in body in lymphocytes particularly in thymus and spleen for many months and can be reactivated at a later date (Mathur A, personal communication). In our cases this may be the source of relapse.

Mental retardation, hemiparesis, aphasia and seizures were the chief

neurological deficits noted in the present epidemic. Behavioral problems occurred during phase of recovery in chronic cases. Neurological deficits and behavioral problems following encephalitis are well known(17,19).

In the acute phase, use of corticosteroids was restricted to very sick children, generally with dopamine in PCF and in patients with raised intracranial tension refractory to other measures. When used in children with prolonged illness 5/35 patients showed remarkable recovery. However, the difference in steroid and non-steroid groups was not statistically significant suggesting that steroids do not hold the key to management in chronic cases.

Poor availability of medical care facilities to the masses was also exposed during this epidemic. All State Hospitals and Private Nursing Homes in Gorakhpur were overflowing. This led to shortage of essential drugs and medical and paramedical personnel. Nursing staff being short even at other times, adequate nursing care could not be provided. Advanced medical facilities to maintain respiration, circulation and temperature were also not available. Probably, the outcome of epidemic would have been much better, had these facilities been available to us.

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NOTES AND NEWS

THIRD COMMONWEALTH CONFERENCE ON DIARRHEA AND MALNUTRITION

The Third Commonwealth Conference on Diarrhea and Malnutrition is to be held in Shatin, New Territories, Hong Kong from *November 11th–14th, 1994*. This conference is organized jointly by the Department of Pediatrics, The Chinese University of Hong Kong and the Hong Kong Pediatric Society. Participation by over 300 delegates from throughout the Commonwealth is anticipated and, in this special meeting, we will be joined by colleagues from China.

Further details are available from:

Dr. Peter B. Sullivan,
Organizing Secretary,
Department of Pediatrics,
Prince of Wales Hospital,
Shatin, N.T.,
Hong Kong.
Tel: [852]-636-2854
Fax: [852]-636-0020

STUDIES ON THE MOSQUITO VECTORS OF JAPANESE ENCEPHALITIS VIRUS IN MANDYA DISTRICT, KARNATAKA, INDIA

G Geevarghese, AC Mishra, P George Jacob and HR Bhat

National Institute of Virology, 20-A, Dr Ambedkar Road, Pune-411 001, India

Abstract. Entomological investigations were carried out in areas affected by Japanese encephalitis (JE) in Mandya District, Karnataka, India, from 1983 to 1988, to determine species composition and the density of mosquito vectors, in relation to the incidence of JE cases. JE cases occurred in two spells in a year, one during April-June (summer epidemic) and another during October-December (winter epidemic). There was very high incidence of JE cases in extensively irrigated areas and a low incidence in some of the taluks with less or no irrigation systems. Among culicines, *Culex tritaeniorhynchus* was the most predominant species (20.54%), followed by *Cx. fuscocephala* (16.94), *Cx. vishnui* (16.48%), *Cx. gelidus* (10.70%) and other species. The overall mosquito population showed two peaks in a year, one during the March-April, and another during September, usually preceding the human epidemics. Relative abundance of certain species varied in different years.

INTRODUCTION

Among Japanese encephalitis (JE) endemic areas in India, Mandya District in Karnataka state is unique in having two seasons of epidemics, one during April to June and other during October to December (Mishra *et al*, 1984; Geevarghese *et al*, 1991). Outbreaks of JE of varying intensity have been occurring in Mandya District since 1979 with a major outbreak in 1983. Entomological studies were carried out in Mandya District from April, 1983 to December, 1988 to study the vector density and seasonal prevalence in relation to JE epidemics. The results of preliminary studies carried out during the initial 4 months, *ie*, April-July 1983, has been already reported earlier (Mishra *et al*, 1984). The present paper reports the results of the studies carried out during the entire period from 1983 to 1988.

MATERIALS AND METHODS

Description of the area

Mandya has a total area of about 4,961 km^2 with a population of about 14.14 lakhs with an average density of about 285 persons/km^2. It is divided into two sub-divisions : Mandya subdivision comprising Mandya, Maddur and Malavalli taluks; and Pandavapura sub-division comprising Srirangapatna, Nagamangala, Pandavapura and Krishnarajpet taluks. The Mandya sub-division is mostly irrigated by Vishweshwaraiah canal systems, from Krishnarajasagar reservoir on the Kaveri river. Pandavapura sub-division was comparatively dry during the initial stage of the study but was brought under irrigation recently via the east bank canal from Hemavathi dam in Hassan District, Karnataka State. The average rainfall in the district is 691.2 mm. South-west (June to September) and north-east monsoons (October to December) share 37.9% and 35.6% of the annual rainfall, respectively. The showers during the interventing periods contribute 26.5% of the total rainfall. Rice and sugarcane are the major crops. Usually 2 crops of paddy are cultivated, the first crop from March to June and the second from August to January. One of the largest wetland bird sanctuaries in the country is located at Ranganathittu in Srirangapatna taluk. In addition, breeding places of ardeid and other wetland birds are found in many localities in the district.

Mosquito collections

Four villages under Mandya sub-division, viz Hemmige, Madarahalli, Peehalli and Bevinahalli were selected for periodic mosquito collections. These localities had records of JE cases in earlier outbreaks. Regular fortnightly mosquito collections were carried out around animal sheds and hosts

tethered in the open during dusk hours with mouth aspirators and with the help of torch lights. This type of collection is considered superior quantitatively as well as qualitatively for monitoring the population (Mitchel and Chen, 1973; Mahadev *et al*, 1978; Mishra *et al*, 1984). A total of 4 man hour collections were made from each locality every fortnight.

RESULTS

In all 200,295 specimens representing 45 species were obtained by 1,120 man hour collections, with a man hour density (MPH) of 178.83. 98.29% of the total collection were represented by thirteen species as follows: 1. *Culex tritaeniorhynchus* (20.54%); 2. *Cx. fuscocephala* (16.94%); 3. *Cx. vishnui* (16.48%); 4. *Cx. gelidus* (10.70%); 5. *Anopheles peditaeniatus* (10.51%); 6. *Mansonia uniformis* (9.63%); 7. *An. subpictus* (4.33%); 8. *An. vagus* (3.92%); 9. *Cx. pseudovishnui* (2.53%); 10. *Cx. quinquefasciatus* (0.73%); 11. *An. culicifacies* (0.72%); 12. *An. nigerrimus* (0.64%); 13. *Aedes vexans* (0.62%).

Other species which constituted less than 0.5% of the catch were: 1. *An. barbirostris*, 2. *An. tesselatus*, 3. *An. aconitus*, 4. *An. pallidus*, 5. *An. annularis*, 6. *An. fluviatilis*, 7. *An. minimus*, 8. *An. varuna*, 9. *An. jamsii*, 10. *An. karwari*, 11. *An. stephensi*, 12. *Ae. linneatopennis*, 13. *Ae. pseudomediofasciatus*, 14. *Ae. pipersalatus*, 15. *Ae. jamesi*, 16. *Ae. vittatus*, 17. *Ae. albopictus*, 18. *Ae. unilineatus*, 19. *Cx. infi.* 0. *Cx. whitmorei*, 21. *Cx. bitaeniorhynchus*, 22. *Cx. minutissimus*, 23. *Cx. malayi*, 24. *Cx. fuscanus*, 25. *Cx. univittatus*, 26. *Cx. sitiens*, 27. *Coquillettidae crassipes*, 28. *Mimomyia luzonensis*, 29. *Mi. hybrida*, 30. *Armigeres subalbatus*, 31. *Ma. annulifera*, 32. *Uranotaenia recondita*.

Seasonal prevalence

The mosquito population in general showed two peaks of density in a year, one during March-April and another during September, preceding the epidemic (Fig 1). The same seasonal trend was observed in the mosquito catches of all the years except in 1983 during which the second peak was observed in November instead of September. Culicine species such as *Cx. tritaeniorhynchus*, *Cx. vishnui*, *Cx. psuedovishnui* and *Cx. fuscocephala* showed the above pattern in their seasonal activity

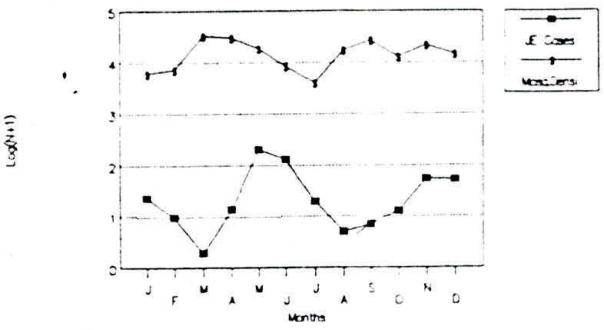

Fig 1—Mosquito populations and JE cases.

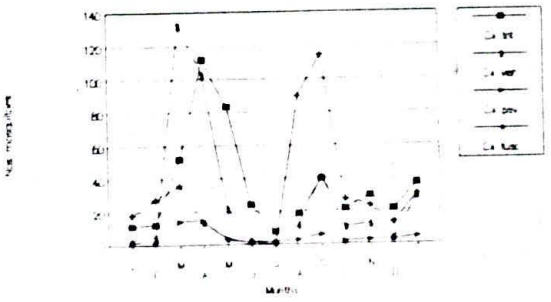

Fig 2—Seasonal prevalance of some culicines.

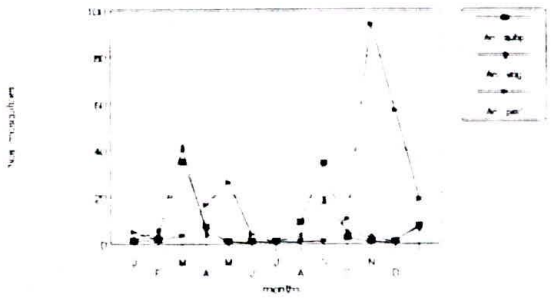

Fig 3—Seasonal prevalance of some anophelines.

(Fig 2). Similar pattern was also observed in certain anophelines such as *An. subpictus*, *An. culicifacies* and *An. vagus* (Fig 3). However, *An. peditaeniatus* and *An. nigerrimus* showed peaks later in May and October. *Ma. uniformis* which breeds mainly in puddles and ponds with aquatic vegetation was found having a stable population throughout the year with a peak in September month. The highest prevalence of *Cx. gelidus* was observed in July.

Mosquito species occurring in peak densities preceding the summer and winter epidemics were different. *Cx. vishnui* (38.63%), *Cx. tritaeniorhynchus* (15.14%), *Cx. fuscocephala* (10.46%) and *An. subpictus* (10.24%) occurred in peak densities during March whereas *Cx. fuscocephala* (38.38%), *Cx. tritaeniorhynchus* (13.46%), *Cx. vishnui* (13.85%) and *An. subpictus* (11.63%) occurred in peak densities in September. Peak density of *Cx.*

vishnui was in March, preceding by a month that of *Cx. tritaeniorhynchus*.

Encephalitis cases in humans

A total of 539 cases were reported during the period, the largest number of cases (233) were recorded in 1983. Maddur (266 cases) was the worst affected taluk followed by Mandya (177 cases) and Malavalli (65 cases) taluks. Nagamangala (15 cases), Srirangapatna (5 cases), Pandavapura (2 cases) and KR Pet (1 case) taluks reported fewer cases (table 2). The incidence of JE cases showed two peaks in a year, one during April-June and another during October-December, the former having more cases. Each peak was generally preceded by a spurt in the vector population (Fig 1).

DISCUSSION

The whole Mandya District was considered to be a dry area before the introduction of Vishveshwaraiah canal system in the early 1930s, which gave an irrigation coverage of approximately 83% of the total irrigated area in the district (Rao, 1981). The network of canals has provided assured irrigation resulting in large scale cultivation of paddy and sugarcane. This has created vast expanse of water bodies for the breeding of mosquitos in the form of paddy-fields, tanks, seepage swamps, numerous ground water pools, etc which appears to have resulted in the increased incidence of mosquito-borne diseases. Rao (1981) had already reported an increase in the incidence of malaria cases in Mandya District when the canal system was

Table 1

Frequency (%) of some predominant mosquito species in different years.

Species	1983	1984	1985	1986	1987	1988
Cx. tritaeniorhynchus	15.65	21.62	22.29	24.14	23.96	15.66
Cx. vishnui	16.09	16.15	14.31	13.81	21.93	19.32
Cx. pseudovishnui	3.66	2.98	2.72	1.59	1.68	1.49
Cx. fuscocephala	10.59	18.84	16.7	21.60	18.54	19.06
An. peditaeniatus	14.94	11.69	12.48	6.43	4.93	8.36
An. subpictus	8.43	2.35	3.20	2.85	4.95	3.99
Cx. gelidus	15.72	5.36	8.75	13.68	10.98	10.95
Total	40,494	41,994	40,742	29,835	24,646	22,581

Table 2

Taluk-wise incidence of JE cases in Mandya District from 1983 to 1988.

Taluk	1983	1984	1985	1986	1987	1988	Total
Mandya	86	5	37	20	18	11	177
Maddur	117	10	67	32	13	27	266
Malavalli	22	5	14	16	7	1	65
Nagamangala	5	3	2	3	2	-	15
Srirangapatna	1	1	2	-	-	1	5
Krishnaraj Pet	-	-	-	1	-	-	1
Pandavapura	-	-	-	2	-	-	2
Other	2	-	3	1	2	-	8
Total	233	24	125	75	42	40	539

initially introduced. During the present study mosquito population showed two density peaks in a year, one during March-April and another during September preceding the JE epidemics and coinciding with the seroconversions against JE virus in the sentinel pigs, reported earlier (Geevarghese *et al*, 1991). An earlier entomological study carried out before the JE activities were recorded in Srirangapatna taluk in 1970-71 had also shown high prevalence of mosquitos twice in a year, corresponding with two paddy crops (Soman, 1984). Eight isolations of JE virus were obtained during the present study from five species, *viz*, *Cx. tritaeniorhynchus*, *Cx. vishnui*, *Cx. gelidus*, *Cx. fuscocephala* and *An. peditaeniatus* (Mourya *et al*, 1989). All these species except *An. peditaeniatus* have been incriminated as the vectors of JE in other count. (Rosen, 1986). *Cx. vishnui* and *Cx. tritaeniorhynchus* were collected in good numbers throughout the epidemic seasons. Preponderance of these two species during the course of the epidemics has been found to be characteristic of the JE affected areas in many countries including India (Rosen, 1986; NIV; 1980). Isolation of JE from *Cx. fuscocephala* and *Cx. gelidus* which appear in large numbers preceding and epidemic incriminates them as the vectors. These species may be playing an important role in the enzootic cycle which usually precedes the epidemic because the peak densities of these mosquitos precede the epidemic. Krishnaraj Peth, Pandavapura, Srirangapatna and Nagamangala taluks showed a low incidence of JE cases. These taluks are comparatively dry with none or partial irrigation systems and limited paddy cultivation. It is obvious that the irrigation system plays an important role in increasing the mosquitogenic conditions and the resultant increase in mosquito-borne diseases in the study areas. The situations prevailing in the study area are comparable to that reported in Sri Lanka, Queensland and Brazil, where increased activities of arboviruses and malaria were observed subsequently to the introduction of irrigation systems. (Ramasamy *et al*, 1992; Smith, 1970; Degallier *et al*, 1989; Kay *et al*, 1990).

Entomological studies carried out in other JE affected areas in India such as North Arcot and Madurai in Tamil Nadu, Bankura in West Bengal and Kolar in Karnataka, have shown only one peak in the mosquito activity preceding the epidemic (NIV, 1980; Mani *et al*, 1991; NIV unpublished data). Mandya is therefore unique in having two spells of JE epidemic coinciding with two peak densities of the vector population.

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A community-based study of subclinical flavivirus infections in children in an area of Tamil Nadu, India, where Japanese encephalitis is endemic*

A. Gajanana,[1] V. Thenmozhi,[2] P. Philip Samuel,[3] & R. Reuben[4]

A characteristic feature of the epidemiology of Japanese encephalitis (JE) is the occurrence of a large number of subclinical infections. The reporting of only overt cases underestimates the total level of virus transmission, a knowledge of which is essential for the evolution of control strategies. We carried out a 3-year prospective serological study between 1989 and 1991 in a primary health centre in Tamil Nadu where JE is endemic. Each year paired specimens, taken before and after the transmission season from a cohort of schoolchildren aged 5–9 years, were tested for haemagglutination inhibition (HI) antibody titres in order to study seroconversion.

The seroconversion rates in the successive years were 37.5, 42.1 and 25 percentage points, and in a third of such seroconversions it was possible to establish a specific diagnosis. Seroconversion was attributable predominantly to JE virus and minimally to West Nile virus. Relatively high dengue virus activity occurred only in 1991. There were statistically significant differences in seroconversion rates between villages and this was related to variations in the ratio cattle:humans:pigs. Very high seroconversion rates occurred among children who were negative for HI antibodies before the transmission season. HI antibodies declined to undetectable levels 6–8 months later in half the children who had seroconverted. The average net annual increase of 16.2 percentage points in seropositivity was nevertheless much higher than values reported from other areas of endemicity. The overall incidence of JE cases was 15 per 10 000 children aged 5–9 years, and the estimated ratio overt:inapparent infection was 1:270.

Introduction

Japanese encephalitis (JE) is an important public health problem in south-east Asia, and its transmission appears to be increasing in several countries (*1*). In India the disease was first reported in 1955 (*2*), and subsequently many epidemics have occurred in different parts of the country. JE virus infects a large number of susceptible individuals but only a few develop overt manifestations of the disease. Differences in the virulence of virus strains, host susceptibility, background immunity, and several other factors may cause variations in the incidence of the disease without affecting the total infection rates. Therefore the current system of reporting only cases of encephalitis does not reflect the total level of transmission, measurement of which is an essential prerequisite for planning control strategies.

Inapparent infection, resulting in the development of measurable antibodies to JE virus, can be used to quantify seroconversion rates among susceptible groups during the transmission season. In India, serological surveys have provided valuable data on the point prevalence of antibodies against JE virus and other flaviviruses,[a] but information on inapparent infection rates and the ratio of inapparent to apparent infections is inadequate. We therefore carried out a 3-year prospective serological study of a cohort of primary-school children in an area in Tamil Nadu where JE is endemic. At the same time we monitored the JE virus infection status of sentinel pigs in the study area.

[1] Centre for Research in Medical Entomology, Post Box No. 4 Sarojini Street, Chinna Chokkikulam, Madurai-625 020, India.
[2] Deputy Director.
[3] Research Assistant.
[4] Research Scientist.
* Requests for reprints should be sent to this author.

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Materials and methods

Study site

In 1981 an extensive epidemic of encephalitis in children was reported in the South Arcot District of Tamil Nadu, in which a serological diagnosis of JE was made for 61% of the patients examined (*3*). Subsequently, many cases of encephalitis have been reported each year, mainly in October and November, coinciding with the period of the north-east monsoon. Nallur Primary Health Centre, which covers about 120 000 people, was chosen for the study because it is located in one of the worst-affected areas. Between 50 and 200 pigs are reared in each village, in addition to other domestic animals. Details of cases and deaths due to encephalitis were obtained from the Tamil Nadu Public Health Service.

Mosquito blood meal identification

A relatively high proportion of recognized vectors of JE virus in the area (*Culex tritaeniorhynchus*, *C. vishnui*, and *C. pseudovishnui*) feed on humans and pigs in addition to cattle. Methods of identifying mosquito blood meals have been described previously (*4*).

Seroconversion in sentinel pigs

Ten locally procured piglets born during the non-transmission season (January–June) and aged 3–6 months were placed in each of four villages. Blood specimens were collected from them in heparinized vials at the time of placement and every fortnight thereafter from June to December. The animals were included in the study only when their maternal antibodies, if present, disappeared.

Human infections

We carried out an exploratory investigation in eight villages in August and November 1988 in order to plan a subsequent seroconversion study. Samples of fingerprick blood (200–300 µl) were collected in heparinized vials from nursery and primary-school children aged 3–14 years, following the informed consent of their parents.

Fifteen villages were selected at random from those in which at least one case of encephalitis had occurred since 1986. In all the schools in these villages, primary-school children, mainly aged 5–7 years but with a small number aged 8–9 years, who were present on the day of the first visit, were recruited for the study, following informed consent. Only these children were followed up prospectively. None had received JE vaccine but they were all covered by the Expanded Programme on Immunization. From each child 200–300 µl of fingerprick blood was collected as described above. Paired surveys were conducted before and after the JE transmission season, as follows: in August and December 1990, August 1990 and January 1991, and August 1991 and February 1992.

Blood specimens were transported on ice to the field laboratory for separation of plasma, which was then shipped on ice to Madurai and stored at –20 °C pending examination.

Serological tests

The haemagglutination inhibition (HI) test (*5*) was performed on microtitration plates on acetone-extracted, goose-erythrocyte-absorbed plasma. Each specimen was tested against JE, West Nile (WN), and dengue (DEN-2) virus antigens. Paired specimens were tested simultaneously and known positive and negative controls were included in each day's run. The diagnostic criteria used were as follows:

- *seronegative*, <1:10 HI titre for all three viruses;
- *seropositive*, ≥1:10 HI titre for at least one virus;
- *seroconversion*, pretransmission season specimen negative and post-transmission season specimen positive, or both specimens positive with a fourfold or greater rise in titre in the post-transmission season specimen;
- *seroreversion*, post-transmission season specimen positive and next pretransmission season specimen negative;
- *specific virus infection*, monospecific response or broadly reacting, with HI titres to one virus that were at least four times greater than those to the others; and
- *unclassified*, less than fourfold difference in titres for more than one virus.

Virus-specific IgM antibodies were detected by IgM-capture enzyme-linked immunosorbent assay (ELISA) (*6*) using kits provided by the National Institute of Virology, Pune. The JE, WN, and DEN-2 virus antigens supplied in the kits were used for each sample.

Statistical analysis

The precision level for the seroconversion rate was determined using the Epi Info software package (Centers for Disease Control, Atlanta, GA, USA, and WHO, Geneva, Switzerland).

Results

Seroconversion in sentinel pigs

Of 124 animals examined, 95 (76.6%) seroconverted during the transmission season. In individual

...e seroconversion rates were as follows: 60–100% ... 1989, 75–100% in 1990, and 58–66% in 1991. ...eroconversions occurred in all the months when ...sts were carried out, i.e., June–December, the peak ...ring in November (Fig. 1). Of the 95 animals that ...eroconverted, 24 (25%) had HI antibodies to JE ...rus alone; and 42 (44%) had HI antibody titres ...ainst JE virus that were at least four times greater ...an the titres against WN/DEN-2. JE virus infection ...s therefore confirmed in 69% of the animals that ...eroconverted; the remaining 29 animals (31%) were ...classified.

...uman cases of encephalitis

...tween 1981 and 1990, a total of 229 patients with ...cephalitis were reported at the primary health ...tre, the numbers corresponding to the successive ...rs bei-- as follows: 24, 5, 18, 11, 15, 49, 39, 9, ... and . Data for 1991 were inadequate and were ...refore not included in the analysis. As shown in ... 2, about 99% of patients were under the age ... 15 years and there was a distinct peak in the inci...ce among 4–5-year-olds. The male:female ratio ... 1:0.8, and 80% of cases occurred in October ... November.

...uman seroepidemiology

... an exploratory study, blood specimens from 793 ...ldren aged 3–14 years were examined for HI anti...ies to flaviviruses, and 271 (34.2%) proved posi... against one or more antigens. Of these seroposi... children, 221 (81.5%) were positive for JE, 131 ...%) for WN, and 112 (41.3%) for DEN-2, alone ... combination. The age-specific prevalence of HI ...odies showed a significant linear regression of ...ntage positivity on age ($y = 1.25 + 4.72x$; $r =$

... ...conversions in sentinel pigs in the area ...ed by Nallur Primary Health Centre, by month, ...-91.

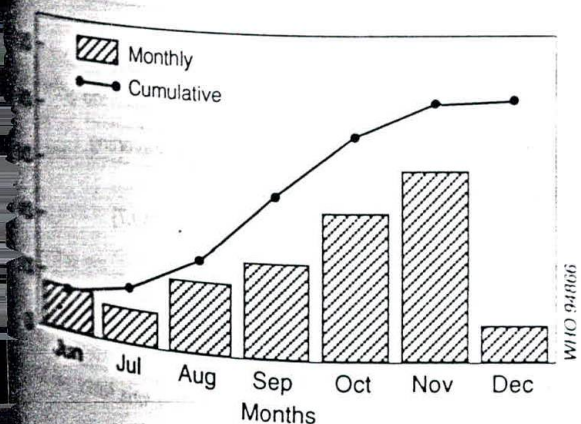
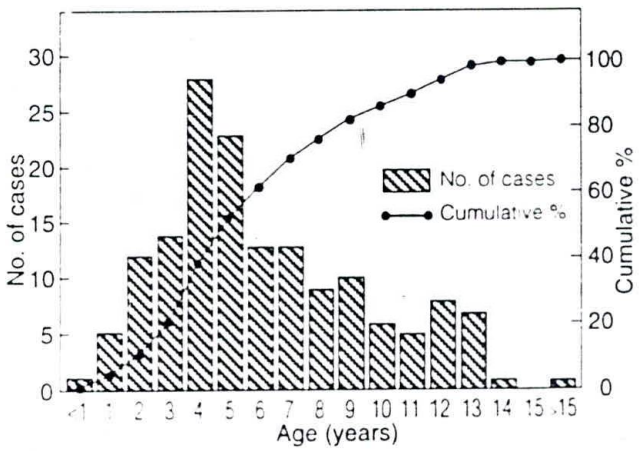


Fig. 2. **Age distribution of human cases of encephalitis recorded at Nallur Primary Health Centre, 1986–90.**



0.9159, $P < 0.005$). The value of the regression coefficient suggested that the annual increment in seropositivity was about 5%, and on this basis it was considered that a sample size of 450 children would be required for a precision of ±2% in estimating this increment. We therefore recruited about 1000 children for the prospective study, in the expectation that about 50% would drop out during the 3-year study period.

Our assumption that the rate of increase in cohort positivity was about 5% per year proved to be incorrect. The precision levels achieved, as calculated from actual sample sizes and rates of increase, varied from 2.9% in the first year to 4% in the third, when blood samples were obtained in only nine of the original 15 villages because of lack of cooperation (Table 1).

Prospective cohort study

Among children from whom paired blood specimens were taken in 1989, 15.8% possessed antibodies to flaviviruses before and 53.3% after the transmission season, an increase of 37.5 percentage points (Table 1). In 1990, 33.7% of children were positive before and 75.8% after the transmission season, an increase of 42.1 percentage points. Before the 1991 transmission season, 48.2% of children were positive; after this season, 73.2% were positive, an increase of 25 percentage points. Table 1 shows that in the non-transmission season, i.e., the period between the post-transmission survey and the following year's pretransmission survey, there was a considerable decline in seropositivity (19.6 and 27.6 percentage points, in 1990 and 1991, respectively). Thus, the net annual increases in cohort positivity to HI antibodies, as determined by comparison of pretransmis-

Table 1: **Haemagglutination inhibition antibody against flaviviruses among the study children, 1989–91**

	No. examined	No. positive	Increase (percentage points)	Precision level (%)[a]	Net annual increase in positivity (percentage points)
1989					
Preseason	1 102	174 (15.8)[b]	37.5	2.9	
Postseason	1 102	587 (53.3)			17.9
1990					
Preseason	650	219 (33.7)	42.1	3.8	
Postseason	650	493 (75.8)			14.5
1991					
Preseason	440	212 (48.2)	25.0	4.0	
Postseason	440	322 (73.2)			

[a] 95% confidence interval.
[b] Figures in parentheses are percentages.

sion samples in successive years, were 17.9 percentage points in 1989–90 and 14.5 percentage points in 1990–91. The geometric mean titres of JE virus antibodies of all the sera titrated in the post-transmission seasons did not reveal differences between age groups or between successive years, varying from 12.3 to 17.1 in December 1989, from 10.8 to 14.5 in January 1991, and from 10.6 to 12.2 in February 1992.

Seroconversion rates were studied on pre- and post-transmission season samples. The rates among children who were negative before the transmission season were 46.2%, 76.6% and 71.9%, respectively, in 1989, 1990, and 1991 (Table 2). The rates among children who were positive before the transmission season were 32.7%, 27.8%, and 7.4%, respectively. Seroreversion rates were studied during the nontransmission period. Among positive children, 49.7% seroreverted in 1989–90, and 50.5% in 1990–91. The probability of seroreversion was inversely related to the initial JE virus antibody titres at the end of the transmission season. Table 3 shows that 56.9% children with an initial titre of ≤1:20 seroreverted while 33.3% did so among those with an initial titre of ≥1:40. The difference was significant (χ^2 test: 28.92, $P < 0.05$).

The postseason percentage point increases in seropositivity were similar for males and females (37 and 38 in 1989, 40 and 42 in 1990, and 23 and 27 in 1991; χ^2 test, not significant). However, statistically significant variations were observed between villages, with the percentage point increases ranging from 23 to 50 in 1989, and from 26 to 58 in 1990 ($P<0.05$). In 1991 only nine villages were followed up; in five of them seropositivity increased (range: 4–69 percentage points); in one village there was a marginal increase (1 percentage point); and in three villages there was a decrease (range: 43–4). For the villages, data on the blood-feeding rates of vectors were available. In Erappavur, where the cattle

Table 2: **Seroconversion and seroreversion rates against flaviviruses in a cohort of school-children covered by the Nallur Primary Health Centre, 1989–91**

	Seroconversion:[a]					
	Preseason HI[b] antibody status:					
	Negative[a]		Positive[a]		Seroreversion[a]	
Year	*n*	No. seroconverting	*n*	No. seroconverting	*n*	No. seroreverting
1989	928	429 (46.2)[c]	158	51 (32.7)	493	245 (49.7)
1990	431	330 (76.6)	97	27 (27.8)	279	141 (50.5)
1991	228	164 (71.9)	135	10 (7.4)		

[a] See text for definitions.
[b] Haemagglutination inhibition.
[c] Figures in parentheses are percentages.

Table 3: Seroreversion rate in relation to Japanese encephalitis virus–haemagglutination inhibition antibody titre among the study children

Post-transmission JE-HI titre[a]	No. examined	No. seroreverting
1:10	281	163 (58.0)[b]
1:20	90	48 (53.3)
1:40	94	36 (38.3)
1:80	75	21 (28.0)
1:160	32	10 (31.3)
Total	572	278 (48.6)
≤1:20	371	211 (56.9)
≥1:40	201	67 (33.3)

[a] JE-HI = Japanese encephalitis virus–haemagglutination inhibition.
[b] Figures in parentheses are percentages.

lation was high relative to that of humans, the percentage of [illegible]E vectors feeding on cattle was greater and the seroconversion rate was lower than in two other villages where the cattle:humans ratio and the percentage of feeding on cattle were relatively low (Table 4). The humans:pigs ratio and the corresponding feeding rates were approximately the same in all three villages.

Among those children who seroconverted, virus specificity was established in about a third, while the rest remained unclassified (Table 5). JE-virus-specific seroconversions occurred in 29.6%, 37.5%, and 15.6% over successive years; the corresponding values for WN virus were 3.8%, 0.3%, and 0. DEN-2-virus-specific seroconversions were seen only in 1991, when they accounted for 15.5% of seroconverters.

Table 4: Seroconversion rates, animal and human population ratios, and blood-feeding rates of Japanese encephalitis vectors in three villages covered by Nallur Primary Health Centre

	Village:		
	Erappavur	Sepakkam	Kodikkalam
Seroconversion in children[a]	26.5	32.5	48.5
Cattle:humans	1:12:25	1:4:20	1:4:29
Culex tritaeniorhynchus			
Feeding on:			
Cattle	92.3	85.8	85.2
Humans	1.6	3.8	5.9
Pigs	1.6	5.9	5.4
C. vishnui			
Feeding on:			
Cattle	93.5	86.3	83.3
Humans	2.4	5.1	11.5
Pigs	0.6	11.5	7.9

[a] Rates for 1989 and 1990.

Table 5: Virus-specific seroconversions among schoolchildren covered by Nallur Primary Health Centre, 1989–91

Seroconversion to:[a]	1989	1990	1991	Total
JE	142 (29.6)[b]	134 (37.5)	41 (23.6)	317 (31.4)
WN	18 (3.8)	1 (0.28)	0	19 (1.9)
DEN	0	0	27 (15.5)	27 (2.7)
Unclassified	320 (66.7)	222 (62.2)	106 (60.9)	648 (64)
Total	480	357	174	1 011

[a] JE = Japanese encephalitis virus; WN = West Nile virus; and DEN = dengue virus.
[b] Figures in parentheses are percentages.

JE-virus-specific IgM antibodies were demonstrated in 10 of 134 postseason samples from children who seroconverted in 1989, but in none of the 60 similar samples tested in 1990. No WN- or DEN-2-virus-specific IgM was detected in either year.

Apparent:inapparent infection ratio

In the first 2 years of the study, seroconversions were mainly due to JE virus, and it was therefore assumed for the purposes of calculation that the post-transmission rise in positivity was due to JE virus infections. On this basis we estimated the number of cases of inapparent infection among the 10 400 children aged 5–9 years who were covered by the primary health centre and compared this with the number of clinically diagnosed cases of encephalitis in this age group, also presumably due mainly to JE virus (Table 6): the ratio was 1:282 in 1989 and 1:257 in 1990, with an average of 14.9 cases per 10 000 population. No calculations were attempted for 1991, since DEN-2 virus was also active and data on encephalitis cases were inadequate.

Discussion

The present study followed the temporal changes in transmission rates over 3 years in an area where JE was endemic, unlike previous investigations that have covered only one transmission season (7–9). Schoolchildren aged 5–9 years were selected so that there would be an adequate number of susceptible individuals and sufficient participation. Of the 10 400 children aged 5–9 years covered by the primary health centre, the study sample size ranged from 10% in 1989 to 4.2% in 1991. The HI test has several advantages making it particularly appropriate

Table 6: **Apparent:inapparent infection ratios for children aged 5–9 years in the area covered by Nallur Primary Health Centre (population 10 400), 1989–90**

	Proportion seroconverted	Estimated number of inapparent infections	Observed number of cases of encephalitis	Apparent:inapparent infection ratio
1989	0.38	3 952	14	1:282
1990	0.42	4 368	17	1:257

for following the same cohort through more than one transmission season. It is a sensitive and accurate indicator of subclinical infection with JE virus in the early postinfection phase (*10*), needing only a small quantity of serum or plasma, easily obtainable from fingerprick blood specimens. HI antibodies develop faster than neutralizing antibodies and previously infected persons may show measurable HI antibody responses (*7*, *11*).

There was intense flavivirus activity in all 3 years, and the annual seasonal increase in HI seropositivity ranged from 42.1 to 25 percentage points. This was considered to be caused predominantly by JE virus activity in 1989 and 1990, when the majority of the seroconversions diagnosed serologically were attributable to this virus. The fact that only JE-virus-specific IgM antibodies were identified in a sample of children provided supporting evidence; furthermore, 69% of the sentinel pigs in the area, all primary responders, exhibited mainly monospecific JE virus seroconversions during the season. WN virus activity was either absent (in 1991) or present at a low level (in 1989 and 1990), whereas in a post-epidemic survey in South Arcot District in 1982 the prevalence of WN neutralizing antibodies was significantly higher than that of JE (*12*). This indicates shifting patterns of virus activity in the area. Thus DEN-2 virus, which was not active in 1989 and 1990, exhibited relatively high activity in 1991, when 16% of seroconversions in children were due to it.

Previous studies in southern India have shown that, among cases of serologically confirmed JE, HI antibody titres began to fall about 3–4 months after onset (*13*). In the present study, for about half the children who suffered inapparent infections during the transmission season HI antibody titres had declined to undetectable levels 6–8 months later, before the start of the next transmission season; also, there was an inverse relationship between seroreversion rates and initial antibody titres. Similarly, in Chiangmai Valley, Thailand, 21% of people who had monospecific JE virus titres of 1:20 as a result of subclinical infection had reverted to <1:20 within 12 months, while none of those with titres of ≥1:40 reverted (*11*). The high seroreversion rate in the present study arose at least partly because only small children were investigated. It is interesting th only other record of high seroreversion (28% among American servicemen in Korea, all of were nonimmune before the transmission s who lost detectable HI antibodies in 7–9 m (*10*).

Notwithstanding the high seroreversion the net annual increases in HI positivity (on a 16.2 percentage points, were much higher than reported for populations in other areas of ende although the data are not strictly comparable bec of differences in the study designs and the groups observed. Among Japanese schoolch aged 6–12 years, annual rates of increase of 5 and 9–10% (*8*) have been reported. In the Chia Valley, annual increments were in the 2.5–11% in individual villages, while among schoolchildren the increment was 4.3% (*11*), and under-40-year-olds in Sarawak the overall es was 6% (*14*). However, 50% of a group of sus tible American servicemen at an airbase in developed antibodies in a single season (*15*).

Very high seroconversion rates were obser children who did not possess HI antibodies b the transmission season (46.2%, 76.6% and 71 successive years). Each seroconversion was pr ably the result of at least one infective mosquit The minimum probability of a child receiv infective bite during the transmission season the range 0.47–0.77. Studies are in progress to virus in wild-caught vectors in order to co whether such intense transmission can take Presumably the children who were already HI tive at the beginning of the season received the number of infective bites, but they did not all a detectable response. In successive years increasing acquisition of immunity, the seroc sion rate in the group of positive children decr

Statistically significant differences observed between seroconversion rates in indi villages. At least, in part, these differences we sibly caused by variations in cattle populations a low seroconversion rate in children was ass with a high cattle:humans ratio. Vector abu was approximately the same in these villages (C for Research in Medical Entomology, M unpublished data).

The overall incidence of JE cases in the Nallur Primary Health Centre was 6.0 per 10 000 population in the age group 1–19 years, higher than in Chiangmai Valley (Thailand) where it was 3.8 per 10 000 for the same group (*16*). However, in Nallur the incidence among 1–9-year-olds was strikingly higher (9.4 per 10 000) than that among 10–19-year-olds (2.3 per 10 000), whereas in Chiangmai Valley the incidence for the younger age group was lower than that for the older (3.1 and 4.6 per 10 000, respectively). This suggests that immunity develops early in Nallur as a result of repeated exposure to intense transmission. The ratio of overt:inapparent JE infections (1:270) for children aged 5–9 years in the present study was similar to the ratios observed in Chiangmai Valley (1:300) (*11*), Sarawak and China (Province of Taiwan) (1:250–500) (*11*), Japan (1:590) (*8*), and West Bengal (1:400) (*17*).

The present study has revealed that young children in an area of endemicity in southern India are actively at risk of developing JE during the transmission season because of the high probability of receiving an infective mosquito bite. However, only about 1 in 270 will develop the disease and others will suffer a latent infection resulting in high HI seroconversion rates, followed by high rates of seroreversion during the nontransmission season. Further studies are required to elucidate the implications of these findings for the development of protective immunity in the population.

Acknowledgements

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Résumé

Etude dans la communauté des infections infracliniques à flavivirus chez l'enfant dans une région du Tamil Nadu (Inde) où l'encéphalite japonaise est endémique

Les infections infracliniques par le virus de l'encéphalite japonaise (JE) dépassent de très loin les encéphalites déclarées. La notification des seuls cas déclarés sous-estime donc le niveau général de transmission du virus, dont la détermination quantitative est indispensable pour l'élaboration de stratégies de lutte. Nous avons réalisé une enquête sérologique prospective sur la période 1989–1991, sur une cohorte de 1102 écoliers âgés de 5 à 9 ans, sélectionnés dans 15 villages couverts par le centre de santé primaire de Nallur, au Tamil Nadu, où l'encéphalite japonaise est endémique. Pour chaque enfant, on a déterminé les titres d'anticorps par inhibition de l'hémaglutination (HI), à l'égard du virus de l'encéphalite japonaise (JE), du virus West Nile (WN), et du virus de la dengue type 2 (DEN-2), avant et après la saison de transmission. On a également étudié, parallèlement, les séroconversions chez des porcs sentinelles.

Chez l'enfant, l'augmentation post-saisonnière du pourcentage de positivité en HI était, pour les trois années successives, de 37,5, 42,1 et 25 points. Chez environ un tiers des enfants ayant opéré une séroconversion, un diagnostic viral spécifique a été établi. La séroconversion était due au virus JE chez 29,6%, 37,5% et 23,6% des enfants pour chacune des trois années, alors que pour le virus WN les valeurs correspondantes étaient de 3,8%, 0,3% et 0. Une activité du virus DEN-2 n'a été observée qu'en 1991, au cours de laquelle 15,5% des enfants étaient atteints. La prédominance du virus JE dans la région a été prouvée par la mise en évidence d'IgM anti-virus JE chez 7,5% des enfants ayant opéré une séroconversion, alors qu'il n'a pas été détecté d'anticorps dirigés contre les virus WN et DEN-2. Le taux de séroconversion chez les porcs était de 76,7%, dont 69,9% du fait du virus JE. Chez près de la moitié des enfants ayant fait une séroconversion, les titres d'anticorps avaient baissé jusqu'à n'être plus décelables lors de nouvelles analyses effectuées 6 à 8 mois après la saison de transmission. Il y avait, par conséquent, une augmentation annuelle nette moyenne du pourcentage de séropositivité de 16,2 points dans la cohorte. Les taux de séroconversion variaient de façon statistiquement significative d'un village à l'autre, et dans trois d'entre eux, ces variations étaient liées à des différences au niveau du rapport bovin:homme:porc.

Chez les enfants négatifs pour les anticorps en HI avant la saison de transmission, des taux de séroconversion très élevés ont été observés (46,5% à 76,6%), montrant l'existence d'une intense transmission du virus dans la région. L'incidence des cas de JE diagnostiqués d'après l'examen clinique était de 14,9 pour 10 000 chez

les enfants de 5 à 9 ans. En supposant que la plus grande partie de la séroconversion observée au cours des deux premières années de l'étude était due au virus JE, nous avons estimé que le rapport entre l'infection déclarée et l'infection inapparente était de 1:270.

Il est nécessaire de déterminer plus avant la signification des forts taux de séroconversion, qui peuvent être attribués à des taux élevés d'inoculation par les moustiques, en ce qui concerne l'acquisition d'une immunité protectrice.

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s new area of work. In addition, representatives of fund-lders and non-fundholders will need to cooperate and ave access to specialist advice.

The Nottingham group may be succeeding because ost of these criteria have been fulfilled, but even when ese conditions are achieved some groups will find them-ves in difficulty. Clear agreement on the exact status of ch group, its scope for action, and the limitations of its wer are essential. In contrast with fundholding practices d the newly emerging "multifunds," non-fundholding ups are only advisory to purchasing agencies. Clarity out the nature of this relation should help sustain isory groups and prevent breakdown in the more ficult debates about resources. Doctors will need to erience early positive results from their work; suspicion consultation is purely cosmetic will produce early llusionment. Anecdote and some reports suggest that h disillusionment is not unusual.[7]

Such groups face other problems. The Nottingham up rightly recognises the difference between purchasing planning, and ways must be found of restoring to every lth authority and health board a coherent planning ction, involving not only non-fundholding groups but fundholding practices and multifunds where they

roups will be motivated by aspirations to guarantee ity of access, but defining and proving inequity has ed difficult. To ensure equity requires rigorous con-ing and, better, more accessible information than n seems available to non-fundholders at present. hermore, although the debate about inequity has sed on the impact of fundholders' purchasing de-ns, unpublished reports suggest that some non-fund-

The climate of continuing change is not conducive to the establishment of satisfactory working practices and good relations, and commissioning groups need a period of stability. The function of a group may be undermined if the agency is simultaneously exploring alternative arrangements to secure advice for general practitioners.

Finally, the leaders of general practitioner advisory groups will need to maintain the validity of their mandate, and therefore of their advice, by frequently rechecking that the arrangements they are negotiating are indeed in line with colleagues' views.

The internal market seems with us for the foreseeable future,[9] and some have argued that general practitioners need to get involved or risk isolation.[10] A period of rigorous evaluation of all systems of purchasing remains essential, but the Nottingham non-fundholders have described a model that may merit wider application.

ROGER CHAPMAN
Chairman, Commissioning of Care Task Group,
Royal College of General Practitioners

The Surgery,
Leighton Buzzard LU7 7AR

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ague in India

sons for public health everywhere

See news on p 897

ecades with no confirmed human plague in India, authorities there are simultaneously responding to eaks of bubonic and pneumonic plague in rural and n populations of the south central and southwestern s of Maharashtra and Gujurat. A major concern is the ad of disease by travellers from these epidemic foci.[1] ldwide, public health authorities have been trying revent the introduction of pneumonic plague within borders, requiring national disease surveillance and ntine offices to operate on emergency schedules g with a situation with which almost none has any first experience.[2]

blic fascination, confusion, and incredulity have been ed by press reports. A mass exodus including hospital nts and even staff themselves has occurred from the ntre of the outbreak of pneumonic plague despite ar pronouncements by the medical community that ie is readily treated with antibiotics. Assurances of ffectiveness of public health measures have seemed gruous given the explosive spread of disease, which rities have been slow to confirm and explain. Doctors public health workers have quickly tried to educate themselves about a disease they had long considered in the past tense. And everyone asks, "How could this happen?"

Plague is caused by infection with *Yersinia pestis*, a bacterium carried by rodents and transmitted by fleas in parts of Asia, Africa, and the Americas.[2] India was one of the countries most affected by the pandemic of plague that began in the latter half of the 19th century, experiencing an estimated 12·5 million deaths during 1889-1950.[4] In recent decades plague in India and elsewhere has retreated to rural, natural foci of infection involving mostly wild rodents and their fleas, with occasional spill over to commensal hosts and humans in villages and towns. Although a number of countries regularly experience endemic plague, its pattern of occurrence is mostly sporadic but with occasional limited outbreaks. In the 1990s outbreaks of both bubonic and pneumonic plague have occurred in Myanmar, Vietnam, Tanzania, Zaire, Peru, and Madagascar.[5] In 1992, 1758 cases with 198 deaths were reported to the World Health Organisation.[5] None of these outbreaks has aroused much attention outside the country of occurrence. What is so different about the current situation in India?

Most human plague is the bubonic form, which results

from the bites of infected fleas; plague can also be transmitted direct to humans if they handle infected animals or inhale infectious respiratory droplets from people with pneumonic plague or aerosols from laboratory accidents. The incubation period for plague ranges from one to seven days, and manifestations of the illness include rapid onset of fever, chills, headache, malaise, myalgias, and prostration, often with nausea and abdominal discomfort. In particular, bubonic plague is characterised by painful swelling of lymph nodes (buboes) in the inguinal, axillary, or cervical regions; pneumonic plague is characterised by cough, dyspnoea, and tenacious blood tinged sputum; and septicaemic plague may result in fulminant Gram negative shock in the absence of localised signs of infection.[6]

New cases of bubonic plague were recognised six weeks ago by Indian health authorities in Beed district, Maharashtra state, about 300 km east of Bombay. In a chronology provided by WHO's regional office for South East Asia these cases followed reports of a flea nuisance and large numbers of dead rats (rat falls) in affected villages; the diagnosis was supported by positive results of serum testing in the cases. By 26 September 80 suspected cases had been reported by 15 villages. Routine control measures were instituted. On 22 September reports of cases of suspected pneumonic plague were received from Surat, a port city with a population of more than a million people, many of them migrant workers, in Gujurat state, about 200 km north of Bombay. Significantly, no rat falls and no cases of bubonic plague were reported.

This suggests a spillover from an epizootic cycle of plague in wild rodents to commensal rodents in Maharashtra state, resulting in primary cases of bubonic plague and secondary cases of pneumonic plague and the subsequent importation by travellers of pneumonic plague from the primary focus into Surat. The course of the epidemic in India over the next weeks is unclear; aggressive application of proved methods of actively detecting and of containing cases, contact tracing, and treatment as well as improved hygiene and environmental sanitation are necessary to bring about its early control.

Quarantine

Plague is one of the three remaining diseases for which people can be put in quarantine internationally.[7] The response of countries has ranged from complete termination of air transport to and from India and the requirement of proof of recent vaccination against plague for admittance of anyone travelling from India to the institution of various systems of heightened surveillance based on international regulations.[7]

In Britain recommendations were issued to all doctors, describing the level of risk to travellers and measures to be taken by those who travel to Gujurat state.[8] Britain, Canada, and the United States instituted heightened disease surveillance by flight crews, notification of quarantine officers by pilots of any suspect case before a plane lands, medical examination of the suspect case before the disembarkation of passengers and crew, surveillance of those passengers potentially exposed to the suspect contagious person, providing information to all passengers arriving on direct flights from India advising that their risk of infection is likely to be low, and notifying them to report to a doctor immediately should they develop an illness with fever during the ensuing week. People suspected of having plague have been identified in aircraft landing in North America and Europe, although no cases of plague have been confirmed in travellers at the time of writing.

Travellers to India and other countries in which plague is endemic are considered to be at low risk of infection with *Y pestis*. To reduce risk, travellers should avoid areas with recently reported cases in humans. People who must travel to these areas should avoid rat infested areas, especially areas where dead rats have been observed; apply insect repellants to ankles and legs and apply repellants and insecticides to clothing and outer bedding as directed by the manufacturer; avoid handling dead or sick animals; and, if the risk of exposure is high, take prophylactic antibiotics. For adults the preferred antibiotic for prophylaxis is tetracycline or doxycycline; for children aged 8 or less it is a sulphonamide. Because desired antibody responses to plague vaccine may require the administration of multiple doses over several months these vaccines are not recommended for immediate protection during outbreaks.

Doctors should be alert for evidence of plague in people who have travelled to areas where plague is endemic and who develop a febrile illness within seven days of leaving the area. All patients suspected of having plague should be placed in hospital in isolation, specimens should be obtained from patients for laboratory diagnosis, chest roentgenography should be performed, and antibiotic treatment should be started promptly. Streptomycin is the preferred drug for treating plague, but gentamicin, tetracyclines, and chloramphenicol are also effective.[9,10] Prompt treatment can reduce overall mortality from plague from 60%-100% to less than 15%. Prophylactic antibiotic treatment should be given to all people who have been close enough to a patient with pneumonic plague to allow the transmission of infective respiratory droplets.

The unexpected and dramatic events that are playing themselves out in India, and the public health responses around the world to these events, highlight the continuing threat of emerging and re-emerging infectious diseases and the ill preparedness of the health community to meet these threats.[11-14] The Centers for Disease Control and Prevention in the United States is currently evaluating what strategies will be most useful to meet these challenges; one possibility is for doctors to participate in a sentinel network for the surveillance of emerging infections.[14]

Outbreaks of plague in India remind us once again of the need to maintain a core of skill in infectious diseases and the public health infrastructure to detect, monitor, and combat a wide range of disease agents, some new, some revisiting. Plague may have retreated over the past decades, but it has not gone away.

D T DENNIS
Chief

Bacterial Zoonoses Branch Division of Vector-Borne Infectious Diseases,
National Center for Infectious Diseases,
Centers for Disease Control and Prevention,
Fort Collins,
Colorado 80522,United States

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EDITORIAL

PLAGUE

From 23rd September 1994 reports began to appear in the news papers that 'pneumonic plague' in epidemic form had hit the city of Surat, Gujarat state, India, claiming several lives. A large number of people, constituting one third of population, also left the city. The rumour and panic spread widely throughout the country. According to a report, up to mid October, throughout India (specially Gujarat, Maharashtra, Rajasthan, West Bengal, Delhi, Madhya Pradesh, Uttar Pradesh, Bihar, Orissa, etc.) 6700 people were admitted in the hospitals for the fear of plague and 337 of them were supposedly positive for the plague bacilli. In Surat alone, about 1000 people were admitted with 56 deaths presumably due to plague.

By that time many foreign countries cancelled flights to India and examination of travellers became compulsory, quarantine was imposed and plague-free certificates were demanded during foreign travels. The rumour and panic shattered the prestige of the country throughout the world. Even mother Teressa, the Nobel prize winner had to wait at aero-plane in Rome for several hours for examination.

West Bengal was also in the grip of the panic. Spurious reports of at least three deaths due to plague were published in the news papers on 28.9.94.

The whole condition of the state of West Bengal was examined by a team of experts at a small delay and on solid scientific ground it was pronounced clearly that no plague bacilli were detected from any patient died or admitted in the hospitals with suspected diagnosis of plague. This was done in the first week of October. Then reports began to come from many states that plague bacilli were also not found by them. The panic and rumour which came suddenly, also vanished within a very short time.

The episode which started in Surat raised many questions. Were they all cases of plague? Some of the cases were examined by the serological test. No rising titre could be examined. No culture of bacilli was possible. The features typical of plague were not observed. The pattern did not show actually the pattern of plague infection, either bunonic or pneumonic. No definite history of rat fall was there in Surat. Who knows these might be the cases of dengue haemorrhagic fever or malaria or pneumonia? Were proper investigations carried out keeping all these differential diagnosis in mind? How definitely the concerned authorities diagnosed those cases as the cases of plague? Which methods were actually followed? Different scientists expressed different opinions. These should be classified before finally saying it plague.

So a highpower committee should immediately be constituted taking

knowledgeable personalities and experts from the states who were involved in investigation of the 'epidemic' and thorough investigation must be carried out to state clearly (1) Whether actually plague occurred or not (2) How the diagnosis of plague was done (3) in how many cases and (4) from how many states the cases occurred. Nature and extent of plague should also be given in details. (5) Who were the responsible persons for raising the panic? In this regard role of media and concerned doctors should be analysed thoroughly. (6) Was there any vested interest behind it? Needless to mention that certain campaines did a lot of business with certain antibiotics (7) was there any deep rooted conspiracy to lower down the prestige of our country?

Plague or no plague, it is sure that these unhappy happenings dealt a severe blow to the reliability and authenticity of the existing health structure of our country.

A. K. Hati

LETTERS TO THE EDITOR

From :
Dr. A. S. Bose [PGT in MD(PSM)]
131/55, N.S. Ch. Bose Road
Calcutta - 700 040

12th Sept., 1994.

To
The Editor
Indian Journal of Public Health
Calcutta

Re : Ghosh S, Sengupta PG et al. Maternal behaviour and feeding practices as determinants of childhood diarrhoea : some observations among rural Begalee mothers. Ind. J of Pub. Health 1994 ; 38 (2) : 77-80.

Sir,

The authors of the above paper have stated in their methods section that out of 76 pair-matched control families, 29 families were re-classified as case families and the data analysed in a case control fashion (Table II).

It is inappropriate to change the status of a control family to a case family and thus change the pair-matched study design. A bias will be introduced as shown in the following hypothetical example.

Let us say, there were 20 case families and 20 control families. Let us also assume that 10 families each among the case and control series were exposed to the putative factor under study and that the 20th pair was a 'like' pair, i.e. both the case and the control were exposed to the putative factor. Therefore, initially there was no difference in exposure rates (10/20 i.e. 50%) among cases and controls. But now the child in the 20th control family contracts the disease (diarrhoea) and is reclassified as a case. So, we now have, from the same series, 11 out of 21 case families exposed to the putative factor and 9 out of 19 control families similarly exposed, and a resultant difference in exposure rates. If this happens with a large number of control families (29 in the above paper), the very procedure of re-classification introduces a spurious association where none exists.

The proper method of analysing pair-matched case-control series is to maintain the pairing in the analysis ('rstu' table) and use the Mc Nemar marginal chi-square test for test of association (1). In case of families which turned out to be unsuitable as controls (child developing diarrhoea) both the case and the control should have been excluded from the analysis. The method of reclassification of controls as cases as followed by the authors, gives rise to a paradoxical situation as follows.

The 'like' pairs ('r' and 'u' cells of 'rstu' table), which are excluded in the matched pair analysis design, are the very pairs which will tend to show a spurious association on reclassification and the 'unlike' pairs ('s' and 't' cells, of 'rstu' table), which are used to measure the relative risk and presence of association in matched pair analysis, will tend to conceal any true association on reclassification.

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Thanking you,
Yours truly,
Sd/- A.S. Bose

JIMA

A MONTHLY PUBLICATION
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CALCUTTA

EDITOR–INDRAJIT RAY, MD

Editorial

Return of Plague

The recent outbreak of human plague after 28 years in India does prove the epidemiological features of the disease known by the public health professionals for years. The conquest of plague so long echoed by some has been only limited to control of human plague. Plague in wild rodents has never been eliminated and the same holds true for future. It is therefore to be said that the disease was never eradicated from the country like smallpox.

The so called plague cycle is maintained in wild nature through rodent-rat flea-rodent. The wild rodent is the reservoir of infection and rat flea is the insect or vector responsible for transmission of the disease. There is always a possibility that infected rat fleas may be forced to dwell on the domestic rats thereby infecting them and subsequently infected fleas may bite human being for alternate source of blood meal causing human plague. Human plague is almost always preceded by domestic rat plague.

The epidemiology of an outbreak indicates that there must be a reservoir of infection, an effective vector and a non-immune population. The present outbreak of plague vividly supports the view and as long as such situation persists there is always a chance of outbreak of the disease. Such chances are expected more where there is 'natural foci' of plague, a plague season and the area has witnessed a recent natural calamity specially like earthquake when domestic rodents are easily infected from displaced wild rodents through rat fleas. India has a 'natural foci' and plague season which starts from September and persists till May because in hot summer wild rodents undergo aestivation and live in closed burrows with stored food.

That the present epidemic has started in Maharashtra where a devastating earthquake took place a year ago and the observation of rat flea in those areas together with bubonic plague there, in the month of September does support the epidemiological clues of the present outbreak. Further, there, man has no natural immunity against plague and vaccine produced immunity lasts only for 6 months. The fact that there have been more bubonic plague cases in Maharashtra some of whom have gone to Surat not being treated, causing pneumonic plague reflects more evidences to support the hypothesis. But surely the epidemic could have been prevented had there been awareness of the disease among public and professionals that the disease can never be eradicated and can come back any day and also had there been regular surveillance and monitoring programme by the State and Municipal health departments so as to alert the public in time and to take appropriate preventive measures.

Human plague has been prevented as observed from 1967 onwards and is preventable if proper surveillance is routinely done. This includes testing plague antibody in sera of rats (100 trapping of rats) and measuring flea index in domestic rats. If there is slight indication of positivity in these measurements, preventive action like destruction of commensal rats, extermination of fleas

through insecticides and sanitation at home and public premises, if adopted, human plague may be prevented. Even with stringent preventive measures, if cases with plague occur, it can be arrested with available very effective antibiotics namely, tetracyclines and the disease can be controlled with prophylactic antibiotics to all the contacts. In the present outbreak those who died was due to not taking the treatment in time whether for pneumonic or bubonic plague and no one should die if treatment is instituted in time. The available statistics indicate that there were only 56 deaths among 336 laboratory positive cases giving rise to mortality rate of 17% (some of the deaths were without treatment or not timely treated) which is in sharp contrast with previous epidemics where 50% deaths were observed in untreated cases of bubonic and 100% in untreated cases of pneumonic plague.

The lesson learnt from the present outbreak is t people and professionals were not aware of the fact t plague has not been eradicated and may come back human population. It may also be understood now t weaknesses of the surveillance and the monitor programme of the health authorities. Health workers a professionals need to be more vigilant and monitor t plague status in rats regularly and make sure to cont rat and fleas so that people can live in the States wi safety and health.

S P MUKHOPADHYA

Ex-Dean and Director-Professor and Head of the Department of Preventive and Social Medicine and In-charge, Disaster Management Centre, All India Institute of Hygiene and Public Health, Calcutta 700073.

[*Continued from page 22*]

oedded in the lung abd cause fibrosis of the tissue. This reduces the vital capacity of the lung. A patient of byssinosis is highly susceptible to bronchitis and tuberculosis.

In the agate cutting and polishing industries, the children are engaged in various operations like chipping, grinding and drilling the agate stones. They are exposed to agate dust which contains elements like iron, calcium, aluminium, copper, nickel, chromium and silica. These cause lung diseases like tuberculosis, pneumoconiosis, bronchitis and bronchial asthma.

Table 1 summarises the health effects of children in other occupations.

Table 1 — *Showing Health Effects in Different Working Places*

Working place	Health effects
Bidi industry	Nicotine poisoning causes nausea, headache, blackouts and muscle fatigue, loss of eye sight
Brass industry	Acid burns and tuberculosis
Zari industry	Eye diseases, postural deformities and spinal problems
Carpet industry	Poisoning from colouring agents, lung diseases from fibre dust
Household or shops for domestic workers or shop boys	Overwork, physical and sexual abuse, drug addiction, dependence often develops

Agricultural child workers are also vulnerable to various types of injuries to their health. In general, higher susceptibility to ill-health arises because children are generally deputed to undertake adult jobs and their immatured vulnerable body and mind become more stressful than those of adult workers. Most agricultural work entails prolonged exposure to sun and rai In tropical countries the climatological thermal load is consi erable along with metabolic heat load due to strenuous agricu tural operations. When the air temperature exceeds the bod temperature, it would increase the heat through connective he gain and thus heat-induced disorders are found amongst th agricultural child labourers. Moreover, the children ar employed to operate modern powered agricultural machine and they become vulnerable to mechanical injuries. Childre are also employed in spreading fertilisers, pesticides and he vicides either by hand or with the help of indigenous equipmen without wearing personal protective devices and the childre become susceptible to the systemic toxic effects of such chemi cals causing skin diseases like dermatitis and neurological com plications through skin absorption such as local irritation an stimulation of the central nervous system resulting in hyper excitability, tremor and convulsion[7]. Parasitic infestations, spe cially intestinal helminthiasis are endemic in the tropics an may be contracted in the course of agricultural operations. Bite of poisonous insects, snakes and injuries sustained while at tending farm animals, are the important causes of morbidity and mortality of the agricultural child workers.

CONCLUSION :

Thus health hazards are obviously of varying kinds and the degree of hazards varies. In some instances, the hazard is obvious and in others it is insidious. Though Article 24 of the Indian Constitution states clearly that children below 14 years will not be allowed in any hazardous employment, we are, in reality, a long way from exercising the law to its fullest extent.

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DIS 1d.4

Plague in India

SIR—The laudable sentiments of your Oct 15 editorial on plague notwithstanding, your statement that "In a measles epidemic year more children probably die in a month in India than have died of plague during the past two centuries" cannot be true. White[1] recorded 10·5 million deaths from plague in India in the 20 years from 1898 to 1918 alone. According to Clifford Gill,[2] the highest plague mortality was among children aged 10–15. Gill also reported that in the plague year of 1924, infant mortality in many parts of India more than doubled over the already enormous baseline.

Nigel Paneth
Program in Epidemiology, Michigan State University, College of Human Medicine, East Lansing, MI 48824, USA

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Editor's reply

Paneth makes a good point. We probably went too far in the comparison between measles and plague deaths, although we stand by the underlying point that, both in the present context and in the past, measles is a far more important cause of mortality. As the recent outbreak in India has shown only too clearly, statistics about plague tend to be highly unreliable. We question, therefore, the figure cited by Paneth for plague deaths over 20 years towards the start of this century, but there is certainly now no way of knowing for sure.

SIR—Despite modern diagnostic techniques for identifying plague, your correspondents (Nov 12, p 1359, and Dec 3, p 1574) cast doubt on the diagnosis in 5559 suspected cases in India during late 1994. Jacob John (Nov 12) compounds the situation by questioning whether there was one coherent clinical epidemic in Surat or whether the higher mortality was caused by more than one disease.

This problem is not new. In 1897 in Bombay it was recognised that in its early stages plague might be mistaken for ague, remittent fever, syphilis, pneumonia, epilepsy, cerebral apoplexy, uraemic coma, ulcer with inflammation of lymph glands, diarrhoea, debility, marasmus, and phthisis.[1] If, then, modern plague is so difficult to diagnose, it can scarcely be expected that the retrospective diagnosis of plague 600 years ago will be any easier, yet no such doubts are entertained by most of those writing about either the fourteenth century Black Death or the numerous occurrences of so-called plague that dominated the English epidemic scene until the mid-seventeenth century. In the absence of any data for case mortality, serology, organism culture, the rodent epizootic, fleas, and most other indices, a retrospective diagnosis is confidently presented and as stoutly defended.

This was a very cold epoch in northern Europe yet despite the habitat restrictions imposed by climate, the two warm-adapted vectors, the black rat and the rat flea, are supposed to have been widely present even though their modern distribution has been severely restricted.[2] The Black Death was active at all times of the year, in settlements of all sizes, and in locations from coast to upland, and spread at rates far exceeding those of known plague. In addition, overall mortality rates were extraordinarily high—far greater than any seen in modern plague.

In this unpromising situation it is more realistic to consider true plague to have formed only a part of the high mortality and to have perhaps been confined to favourable urban habitats during hot summers. The acceptance of this supposition would remove the difficulty of devising unrealistic scenarios to equate plague with bubonic plague and make a historical necessity out of a biological improbability. Even in the city true plague was probably only one contributor to high mortality. In my study of epidemic years in London between 1540 and 1665, at least three major patterns of deaths with time are evident[3]—only one of which resembles plague or another single disease causing a steady incremental increase of deaths. Another has the characteristics of enteric disease, a not unreasonable proposition in view of the water supply, general hygiene, and sewage disposal methods. Closely neighbouring parishes showed considerable autonomy in not only mortality patterns but also the timing of epidemics, and the data suggest not a unity of disease (plague) but a complex pattern of different diseases across the city—a view supported by the extensive nature of plague "diagnosticks" that encompassed buboes and most other causes of death as well.

That plague and bubonic plague might not have been the same thing receives support from an early eighteenth century source. Writing in 1721 Dr George Pye argued that plague "differs from an epidemic disease, but in degree of violence only; and consequently any epidemic sickness that rages with more than ordinary violence and which occasions an extraordinary mortality amongst mankind, may be and is properly termed a pestilence, or the plague".[4]

Graham Twigg
Biology Department, Royal Holloway and Bedford College, Egham, Surrey TW20 0EX, UK

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SIR—We appreciate Bharadwaj and colleagues' timely report of melioidosis in Pune in Maharashtra state during October, 1994. We report melioidosis in a boy of 9 years who was a resident of Trichur town in Kerala state.

He had longlasting fever, cervical lymphadenitis, and hepatosplenomegaly with multiple ultrasound hypoechoic lesions in spleen and liver. The illness had started in August, 1994, and gradually progressed until November when a specific diagnosis was made and correct treatment started. The boy had insulin-dependent diabetes mellitus. He had always lived in the town of Trichur and had no particular contact with rice fields or swampy soil. Bone-marrow and lymph-node biopsy specimens showed epithelioid granulomatous lesions, suggestive of tuberculosis, but without acid-fast bacilli. However, the disease had progressed during anti-tuberculosis therapy. We obtained a non-fermenting gram-negative bacillus (NFGNB) from aspirated material from one liver lesion. On the assumption that this was a contaminant, an open-liver biopsy specimen was taken, from which also a similar NFGNB was isolated. Both organisms proved to be *Pseudomonas pseudomallei*. On intravenous ceftazidime and oral co-trimoxazole therapies, the boy recovered and went home.

The importance of this case history is that melioidosis has been identified in Kerala for the first time. Melioidosis can

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C. S. PANDAV
H. VISWANATHAN
D. P. HAXTON
International Council for Control of Iodine Deficiency Disorders
New Delhi

Plague

The plague outbreak is over. It came, caught the health authorities unaware and went leaving us with the grim reality that, in spite of the great advances in science, we cannot afford to forget epidemic diseases. The recent outbreak of plague has shaken the country and the international community as no other disease has done in the recent past.

There has been no plague in India since 1966, but its re-emergence after 28 years conforms to the cyclic nature of this disease—a pattern which has been seen in many other countries.[1] During the periods of quiescence, interest in and awareness of the disease waned and so did the technical expertise and resource allocation for the maintenance and updating of infrastructure. Many other more pressing priorities were allocated scarce resources.

Public health functionaries had, before the recent epidemic, forgotten what little they knew of plague's epidemiology; clinicians had virtually deleted it from the differential diagnosis of bacterial pneumonia or lymphadenopathy with fever and laboratories had lost expertise. Only the frugal infrastructure for plague surveillance at the National Institute of Communicable Diseases (NICD) was left to provide skeletal support.

However, even in this situation, the mortality in the recent outbreak was restricted to 54 cases though several rather controversial statements have been made regarding the aetiology and effects of the outbreak.

Plague is caused by *Yersinia pestis* (*Y. pestis*), a bacterium carried by rodents and transmitted by fleas in parts of Asia, Africa and the Americas.[2] The first human epidemic on record was an outbreak among the Philistines in 1320 BC.[3] There have been three pandemics of plague and India was affected in all of them. It suffered most in the third which started in Southern China in 1866. Between 1898 to 1948 an estimated 12.5 million deaths occurred in this country. Since then, plague in India has been essentially limited to its rodent hosts.

During the period 1978–1992 as many as 14 856 cases of plague with 145 deaths were notified by 21 countries to the World Health Organization (WHO) and even as late as 1992 nine countries notified a total of 1582 cases of human plague including 138 deaths.[1] Six of these countries, viz. Brazil, Madagascar, Myanmar, Tanzania, Vietnam and the United States of America reported cases of plague nearly every year.[1] These facts seem to have escaped the attention of the international community and the mass media in contrast to the minor outbreak of plague in India during 1994.

Yet India was put in international quarantine.[4] Some countries stopped all flights to and from India and others insisted on evidence of vaccination against plague. A few stopped anyone from India entering their countries.[5]

According to the WHO, a case is labelled as 'suspected plague' if one of the following conditions is met:

1. Clinical symptoms are similar.
2. If a Gram-negative bipolar coccobacillus is identified.

A case is labelled as 'presumptive plague' if one or both of the following conditions are met:

1. If the organism is immunofluorescence stain positive for the presence of the *Y. pestis* F1 antigen, or if it is both immunofluorescence and Wayson/Wright-Giemsa stain positive.
2. If a single serum sample is detected to have antibodies against the F1 fraction of *Y. pestis*.

A case is 'confirmed' to be plague if one or both of the following conditions are fulfilled:

1. In addition to Wayson/Wright-Giemsa and immunofluorescence positivity the organism is grown in culture and is positive by both bacteriophage and biochemical reactions.
2. Two serum samples, taken at appropriate times, demonstrate a fourfold difference in end point titres of plague specific antibodies.

Human plague was first diagnosed in the Beed District of Maharashtra on 6 September 1994 on the basis of clinical, epidemiological and laboratory evidence. Facilities for immunofluorescence staining for plague were not available in India at the time of onset of the outbreak. So the NICD was able to provide presumptive diagnoses on the basis of serological investigations.

While action to contain the disease in Beed was in progress, pneumonic plague emerged in Surat, Gujarat on 10 September 1994, the population panicked and an estimated 0.3–0.5 million left the city and fled to other parts of the country. The entire health machinery of India and the rest of the world started aggressive preventive and control measures.

In a serious disease such as pneumonic plague even with the presumptive diagnosis alone institution of control measures assumes primary importance. It would have been improper to wait for laboratory confirmation. Thus we mobilized material resources and personnel for human case surveillance, active case detection, case containment and treatment and contact tracing as well as prophylaxis. This paid rich dividends and large scale mortality and morbidity was avoided.

The increased flea density, rat fall, positive serology in rodents and the nature of the human cases left little doubt about the occurrence of plague in Beed. This was confirmed by the WHO international team who also carried out serological studies. In Surat as well as in Delhi, a fourfold rise of antibodies in paired serum samples of antibodies specific to the F1 antigen of *Y. pestis* was observed in many samples. The WHO international team visited Delhi, Surat and Beed and endorsed the evidence of recent plague infection in man and animals in Beed and Surat. They and the WHO Director General also complimented the Government of India for mobilizing resources to effectively counter the outbreak.[6]

During an outbreak of pneumonic plague if half a million potential carriers of the disease run away to different parts of the country, priorities have to be set and precious resources as well as manpower have to be reorganized effectively and deployed to prevent further spread. After the primary objective of control was achieved efforts were made to purify and characterize the culture isolates.

Apart from purely scientific issues, two more facets of the plague outbreak have been fiercely debated. One of them is the role of the press in exaggerating the facts and thus resulting in huge economic losses. The nation's vernacular and English newspapers as well as the international press and mass media

exaggerated the extent of the outbreak. Though it may be justified to demand that the press takes a rational and prudent view of such happenings, it must also be kept in mind that whatever appears in the media is a reflection of the thinking of the people. Panic was generated so effectively, because the very word 'plague' seems to be associated with hundreds of deaths and because both the public and medical profession were unaware of the changing epidemiology of the disease. Safe and potent antimicrobial agents are now available which have made plague easily treated.

Although a great deal of noise has been made about the tremendous economic loss suffered because of the outbreak of plague, very few have appreciated the role of health authorities in quickly and effectively containing the disease, without which the loss might have been much greater. What is more important is that the recent outbreak has exposed the major failings of our public health system. We need better sanitation, a more effective disease surveillance system and the institution of early warning mechanisms.

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K. K. DATTA
National Institute of Communicable Diseases
New Delhi

Plague in India: A New Warning from an Old Nemesis

> The main outstanding problem of the Black Death, or indeed of the plague in any era, is ... what it is which provokes an epidemic of the air-borne pneumonic variant of the disease (1).

A recent Institute of Medicine report, "Emerging Infections: Microbial Threats to Health in the United States" (2), called attention to the complacency that has developed regarding infectious diseases, highlighted the risk for importation of diseases that develop in remote parts of the world, and stressed the need to strengthen national and international infectious disease surveillance. The report cites the introduction of plague from other continents into Europe in the 14th century and into North America in the late 19th century. The recent epidemic of plague in India highlights the concerns expressed in this report.

In August 1994, an outbreak of bubonic plague was reported from the Beed district, a known plague-enzootic region (3) in Maharashtra State in western India. In late September, news came of an explosive epidemic of suspected primary pneumonic plague in the city of Surat in neighboring Gujarat State (4). Hundreds of suspected cases and more than 50 deaths were reported from Surat. Press accounts described a mass exodus of hundreds of thousands of persons from this industrialized port city of nearly 2 million inhabitants (5). By early October, more than 6300 suspected cases of plague had been reported from 12 Indian states, including Delhi, but only a few were considered laboratory confirmed, primarily by unvalidated serologic techniques (6).

Preliminary results of subsequent studies, done by the Indian government and an independent World Health Organization team, provided presumptive evidence of bubonic plague cases and enzootic plague activity in Maharashtra State (Gage KL, Chu MC, Centers for Disease Control and Prevention [CDC]. Personal communication). In Surat, reviews of clinical records and results of epidemiologic studies confirmed the reports of an outbreak there of acute respiratory illness characterized by fever, cough, hemoptysis, pulmonary infiltrates on radiographs, and a high fatality rate in the early course of the outbreak (Dennis DT, Orloski-Snider KA, CDC. Personal communication). Although some patients studied had antibodies to the plague bacillus, plague could not be established as the cause of this outbreak in the absence of the confirmed isolation of the causative agent. Although large numbers of suspected cases of plague were reported from New Delhi, Bombay, and Calcutta, no convincing evidence suggested transmission in any city but Surat. As of 25 October 1994, 693 suspected cases of plague with unvalidated serologic evidence of infection had been identified in six Indian states, and no new cases were being reported (7).

The initial reports of the outbreak caused considerable international concern about the risk for exportation of pneumonic plague from India. Official responses in various countries ranged from the enhancement of surveillance for ill travelers arriving at airports to the closure of borders, the embargo of flights to and from India, and the restriction of imports of Indian goods. Commerce between the United States and India, however, remained unrestricted during the epidemic. By enhancing surveillance at airports (8), providing written information about plague to all air travelers arriving from abroad, and promptly disseminating information on plague to clinicians and health department personnel, health officials in this country identified and evaluated for plague 13 travelers who had recently arrived from India with febrile illnesses and other conditions (CDC, Unpublished data) (7, 9, 10). Two persons were found to have malaria, one had both dengue and malaria, and one had *Salmonella* bacteremia. No tourists in India are known to have contracted plague, and no patients with plague are known to have departed India during the crisis. The economic costs of emergency response systems implemented internationally during this crisis undoubtedly were substantial, and the resulting losses to the Indian tourism industry and other industries are expected to be staggering (5).

Plague is caused by infection with *Yersinia pestis*, a gram-negative bacillus carried by rodents and their fleas in parts of Asia, Africa, and the Americas (11, 12). Most human plague is the bubonic form, transmitted by the bites of infected fleas; however, persons can also acquire plague by handling infected animals or by exposure to respiratory droplets from persons or animals with pneumonic plague. The incubation period for plague is 1 to 7 days (usually 2 to 4 days in primary pneumonic disease). Manifestations of the illness include acute onset of fever, chills, malaise, myalgias, and prostration, often with nausea. In particular, bubonic plague is characterized by painfully swollen regional lymph nodes (buboes) draining from the cutaneous inoculation site (11, 12). Pneumonic plague is characterized by a productive cough, often with hemoptysis, and pulmonary infiltrates. Septicemic plague may result in endotoxic shock and disseminated intravascular coagulation without localized signs of infection. Plague meningitis is a less common presentation, and overlapping clinical presentations can occur.

Laboratory diagnosis of plague depends on cultural isolation of *Y. pestis* from tissues or body fluids, direct detection of antigens in tissues or fluids by fluorescent antibody staining, or detection of serum antibodies by passive hemagglutination assays (11, 12). Visualization of characteristic bipolar bacilli in Giemsa- or Wayson-stained smears supports a diagnosis of suspected plague. The organism grows slowly on bacteriologic agar media

and is infective for laboratory mice. Tests for plague are highly reliable when done by laboratory staff experienced with *Y. pestis*, but such expertise is usually limited to selected reference laboratories. All patients with suspected plague should be hospitalized and isolated, with precautions taken against transmission by respiratory droplets until pneumonia is ruled out or until specific antibiotic agents have been administered for at least 48 hours (12). Specimens should be obtained promptly for laboratory diagnosis, chest roentgenograms should be done, and specific antibiotic therapy should be promptly initiated. Appropriate diagnostic specimens include sputum samples or tracheal aspirates for suspected cases of pneumonic plague; bubo aspirates for bubonic cases; and cerebrospinal fluid for meningitis cases. All specimens, including blood, should be smeared and examined with a Wayson or Giemsa stain, and all should be cultured. Acute- and convalescent-phase serum specimens should be obtained for antibody testing. Close communication between clinicians and the diagnostic laboratory is essential when a diagnosis of plague is being considered.

Streptomycin is the drug of choice for treating plague. Tetracycline is also highly effective, and gentamicin can be used when streptomycin is not readily available. Chloramphenicol is the preferred treatment for plague meningitis (11–14). Prompt treatment can reduce overall plague mortality from 60% to 100% to less than 15%. Antibiotic prophylaxis is indicated for persons who have had face-to-face contact or who have occupied a closed space with a patient who has pneumonic plague. Recommended prophylactic drugs include tetracycline in adults and older children and sulfonamides in children 8 years of age and younger; chloramphenicol is also effective (14). Prophylactic therapy should be continued for the duration of the potential exposure plus an additional 5 to 7 days. Routine travel to plague-endemic countries presents a low risk for infection with *Y. pestis*; therefore, antibiotic prophylaxis for plague is rarely indicated for travelers to these countries. Inactivated plague vaccine is apparently ineffective against primary pneumonic plague (15), and direct evidence for its effectiveness against bubonic plague in humans is unavailable (16). It is potentially useful for persons who anticipate a visit to an enzootic plague focus (for example, field biologists studying plague), but it is not recommended for immediate protection during epidemics because a maximal antibody response requires the administration of multiple doses over several months (11, 12).

In 1992 (the most recent year for which complete data are available), human plague was reported in nine countries (Brazil, China, Madagascar, Mongolia, Myanmar, Peru, the United States, Vietnam, and Zaire) (17). In addition, cases of bubonic plague have been recently reported in Malawi, Mozambique, and Zimbabwe. In India, large plague epidemics occurred during the first half of this century and resulted in millions of deaths; however, until the recent epidemic, the last laboratory-confirmed cases of human plague in India were reported in 1966 (17–19). Sporadic cases of human plague occur annually in the western United States, particularly in rural and suburban regions of New Mexico, Arizona, and Colorado (20), after exposure to the infected fleas of wild rodents, contact with infected animal carcasses, or (rarely) droplet transmission from domestic cats with pneumonic plague. The extensive yet focal geographic distribution of *Y. pestis* is a reminder that when patients are evaluated for infectious diseases, the importance of a detailed travel history cannot be overemphasized.

The extreme measures taken by some persons and governments in response to the initial recent reports from India can largely be attributed to the widespread impression that pneumonic plague is not only deadly but also highly contagious in all circumstances. The latter impression, however, is not supported by the evidence. Person-to-person transmission of *Y. pestis* occurs by exposure to respiratory droplets from a patient with pneumonic plague who is coughing at close range (probably within 2 meters) (12). Reported rates of secondary transmission of pneumonic disease have varied widely in different plague epidemics (15). In epidemics with reportedly high secondary transmission rates, poverty and overcrowding in households was the rule. In contrast, in the plague-endemic areas of the western United States, no secondary plague cases resulting from person-to-person spread have been reported since 1925 (12), despite the occurrence of at least 37 pneumonic plague cases in the interim (including at least six primary pneumonic cases) (CDC, Unpublished data) (20). In many of these cases, diagnosis and treatment were delayed, resulting in many potentially exposed persons with close contact and hundreds of persons with casual contact who received delayed or no prophylaxis. Thus, the risk for secondary plague transmission in the United States appears to be low. Clearly, the contagiousness of pneumonic plague deserves further study that includes a consideration of sociobehavioral, climatologic, and host-specific factors.

Important lessons can be learned from recent events in India. When an outbreak of uncertain cause occurs, appropriate specimen collection and diagnostic testing for potential causative agents is of paramount importance. With several effective antibiotics widely available with which to treat and prevent clinical plague, draconian measures in response to reports of plague outbreaks are unnecessary. Instead, a measured response based initially on a rapid but thorough assessment by a multidisciplinary team of experts (including clinicians, epidemiologists, entomologists, mammalogists, and microbiologists) is needed. The capacity for such a response depends directly on the quality of the public health infrastructure, including effective surveillance and laboratory systems, epidemiologic response capability, and vector and vertebrate host control programs (21). Clinicians play an increasingly important role in recognizing illnesses and syndromes that require a public health response and alerting health departments to the need for prompt investigation (22). Rational responses to future international public health crises depend on improving linkages between clinicians and public health professionals in all countries.

Although plague is of obvious historic importance (1) and continues to be a global threat, little research is currently being done on the subject. In many countries, including the United States, few clinicians, scientists, or laboratory or public health personnel are plague experts. In all plague-endemic countries, cost-efficient animal-based serosurveillance programs are needed to define and track the geographic distribution of *Y. pestis*, and extensive ecologic studies are needed to define and control

enzootic and epizootic transmission cycles that put humans at risk (23). The pathogenesis of plague and determinants of the virulence of *Y. pestis* should be studied anew using the most up-to-date laboratory methods. The potential for the emergence of resistant strains of *Y. pestis* related to widespread antibiotic use during pneumonic plague epidemics should be studied. Simpler and faster laboratory tests for plague are needed, and these should be made available for use by local or regional laboratories in developing countries in which plague is enzootic.

Largely because of the efficiency of modern air travel, microbial pathogens have shown an ever-increasing disrespect for international borders (24). With the current decrease in political and trade barriers worldwide, this trend will certainly continue. Thus, it is imperative that the United States maintain multidisciplinary expertise in, and that clinicians remain alert for, "exotic" infectious diseases, including tropical diseases. The recent events in India underscore the need for expanding expertise and opportunities for training in arthropod-borne infectious diseases in this country and internationally (25) and for strengthening clinical, scientific, laboratory, and public health expertise in microbial diseases that are rarely recognized in the United States. The CDC has developed a plan to address these critical emerging infectious disease issues in collaboration with partners in state and local health departments, academia, clinical medicine, clinical laboratories, and international organizations (26). The recent plague experience in India provides a clear example of the high price of ignoring global microbial threats (27).

Grant L. Campbell, MD, PhD
Centers for Disease Control and Prevention
Fort Collins, CO 80522

James M. Hughes, MD
Centers for Disease Control and Prevention
Atlanta, GA 30333

Requests for Reprints: Grant L. Campbell, MD, PhD, Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention, P.O. Box 2087, Fort Collins, CO 80522-2087.

Current Author Addresses: Dr. Campbell: Centers for Disease Control and Prevention, P.O. Box 2087, Fort Collins, CO 80522-2087.
Dr. Hughes: Centers for Disease Control and Prevention, Mailstop C12, Atlanta, GA 30333.

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1 of 16

TI: Field trial of an ecological approach for the control of Phlebotomus argentipes using mud & lime plaster.
AU: Kumar-V; Kesari-SK; Sinha-NK; Palit-A; Ranjan-A; Kishore-K; Saran-R; Kar-SK
AD: Rajendra Memorial Research Institute of Medical Sciences, Patna.
SO: Indian-J-Med-Res. 1995 Apr; 101: 154-6
AB: A pilot study for the control of Ph. argentipes, a known vector of kala-azar in India, was carried out using an ecological approach. Of the 15 houses selected for the study 10, including the cattle sheds and latrines, were plastered with a mixture of mud and lime, up to a height of 1.22 m taking care to seal all cracks and crevices. The remaining five houses were left unplastered and were considered as control areas. The pre-treatment and post-treatment resting densities of the sandfly were monitored both in treated and untreated houses. A sudden drop in the sandfly density was noticed in the treated houses, whereas there was no significant reduction in the check houses, suggesting an effective control.

2 of 16

TI: Endemic kala-azar in eastern Sudan: post-kala-azar dermal leishmaniasis.
AU: Zijlstra-EE; el-Hassan-AM; Ismael-A
AD: Department of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Center, University of Amsterdam, The Netherlands.
SO: Am-J-Trop-Med-Hyg. 1995 Apr; 52(4): 299-305
AB: In a longitudinal study between 1991 and 1993 in an endemic area in eastern Sudan, 85 cases of kala-azar (visceral leishmaniasis) were diagnosed, of whom 48 (56%) developed post-kala-azar dermal leishmaniasis (PKDL). Another four cases of PKDL had no clinical history of kala-azar. In children, PKDL was more frequent in the very young; seven of nine kala-azar cases (78%) in the group 0-1 years of age and 13 of 16 (81%) in the group 2-3 years of age developed PKDL. On the average, PKDL occurred 56 days (mean; range 0-180) after the end of treatment of kala-azar. To assess the severity of PKDL, a classification was developed using three grades of severity based on differences in density and distribution of lesions. In young children, PKDL was more severe. Incomplete treatment of kala-azar may be important in the pathogenesis of PKDL. Thirty-one patients were followed-up for at least six months; of these, 20 were not treated (17 healed, two improved, and in one, the condition was unchanged), three healed after incomplete treatment with sodium stibogluconate, and eight were cured after treatment but two required two courses. Considerable morbidity was caused by PKDL and should be taken into consideration in the management and follow-up of kala-azar patients. The high incidence of PKDL may have important implications in transmission.

3 of 16

TI: [Studies on the effect of deltamethrin bath treatment of hamsters infected with Leishmania donovani for interrupting kala-azar transmission]
AU: Jin-C; Xiong-G; Hong-Y; Su-Z
AD: Institute of Parasitic Diseases, Chinese Academy of Preventive Medicine, Shanghai.
SO: Chung-Kuo-Chi-Sheng-Chung-Hsueh-Yu-Chi-Sheng-Chung-Ping-Tsa-Chih. 1994; 12(4): 300-2
AB: Phlebotomus chinensis were fed respectively on two groups of Cricetulus barabensis infected with Leishmania donovani, of which one group had received deltamethrin bath and the other was not treated with insecticide bath. The

results showed that all the sandflies in the former group died within 24 hours, while those in the latter group had a high survival rate. Among the 165 sandflies examined, 114 (69.1%) became infected. The promastigotes not only developed well in the midgut, but also invaded esophagus, pharynx and proboscis. In the control group, the mortality of sandflies in 24 hours was 5.1% (3/59). According to the data obtained in the present study, the authors consider that insecticide bath treatment of infected domestic dogs in endemic villages could be used for interrupting kala-azar transmission.

4 of 16

TI: Indian kala-azar caused by Leishmania tropica.
AU: Sacks-DL; Kenney-RT; Kreutzer-RD; Jaffe-CL; Gupta-AK; Sharma-MC; Sinha-SP; Neva-FA; Saran-R
AD: Laboratory of Parasitic Diseases, National Institutes of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.
SO: Lancet. 1995 Apr 15; 345(8955): 959-61
AB: Kala-azar, or visceral leishmaniasis, in India is generally assumed to be a result of infection with Leishmania donovani. 15 parasite isolates collected over the past 10 years from patients with classical disease were typed by monoclonal antibodies, isoenzymes, and kDNA analysis. 4 were shown to be L. tropica, a species historically associated with cutaneous disease and more recently a mild "visceralising" disease from the Desert Storm experience. The results confirm that L. tropica is a co-endemic agent of visceral leishmaniasis in India, and may shed light on the rising frequency of therapeutic unresponsiveness to sodium antimony gluconate, which complicates treatment of this lethal disease.

5 of 16

TI: Treatment of atypical leishmaniasis with interferon gamma resulting in progression of Kaposi's sarcoma in an AIDS patient.
AU: Albrecht-H; Stellbrink-HJ; Gross-G; Berg-B; Helmchen-U; Mensing-H
AD: Medizinische Kernklinik und Poliklinik, Universitatskrankenhaus Eppendorf, Hamburg, Germany.
SO: Clin-Investig. 1994 Dec; 72(12): 1041-7
AB: Visceral leishmaniasis (kala-azar) affecting HIV-infected patient is being reported in increasing frequency. A 40-year-old German bisexual patient with full-blown AIDS is described who presented with Kaposi's sarcoma, epigastric pain, diarrhea, and weight loss but without fever. Leishmania amastigotes were initially found in biopsies from stomach, duodenum, and a cutaneous Kaposi's sarcoma lesion but were later also recovered from bone marrow and lymph node. The patient received three courses of a combination of pentavalent antimony and interferon-gamma. In addition to the common side effects such as fever, thrombocytopenia, and elevated amylase and lipase, a vivid progression of the Kaposi's sarcoma was noted. Tumor progression was temporally closely associated with treatment with interferon-gamma. Because this phenomenon has also been observed in other patients, we advise caution when using interferon-gamma in patients with Kaposi's sarcoma.

6 of 16

TI: Immunochemotherapy for a systemic intracellular infection: accelerated response using interferon-gamma in visceral leishmaniasis.
AU: Sundar-S; Rosenkaimer-F; Lesser-ML; Murray-HW
AD: Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
SO: J-Infect-Dis. 1995 Apr; 171(4): 992-6
AB: To determine if cytokine immunotherapy accelerates the response to conventional treatment in visceral leishmaniasis (kala-azar), previously untreated Indian patients were given antimony for 30 days (n = 15) or antimony plus interferon-gamma (IFN-gamma; n = 16). After 10 days, 10 (63%) of 16 patients treated with antimony plus IFN-gamma versus 1 (7%) of 15 randomized to antimony alone were considered cured of parasites (P < .005). On day 20, 14

(93%) of 15 versus 6 (40%) of 15 patients, respectively, were apparent clinical cures (P < .006), and treatment was discontinued early in the 14 IFN-gamma treated responders. Day 30 apparent cure rates (100% vs. 73%) and 6-month ultimate cure responses (87% vs. 60%) were higher in IFN-gamma-treated patients but not statistically different from controls (P > .05). All 13 IFN-gamma-treated subjects who were cured (12 of whom received therapy for 20 days) have remained healthy with follow-up of 14-24 months (mean, 18.9). These results indicate that IFN-gamma successfully accelerates the parasitologic and clinical response to antimony treatment, an effect that should permit shortening the duration of conventional therapy in previously untreated kala-azar.

7 of 16

TI: Correction of serum electrolyte imbalance prevents cardiac arrhythmia during amphotericin B administration.
AU: Thakur-CP
SO: Natl-Med-J-India. 1995 Jan-Feb; 8(1): 13-4
AB: Arrhythmias and cardiac arrest have been reported during amphotericin B administration but no effective technique has been described to prevent them. I saw two patients with kala-azar resistant to sodium stibogluconate who developed cardiac arrest after amphotericin infusion (in spite of tolerating a test dose). Both had low levels of serum sodium, potassium and calcium. After these were corrected the amphotericin B was restarted and the course of treatment completed successfully. I suggest that prior to giving amphotericin B to patients with resistant kala-azar their electrolyte imbalance should be corrected.

8 of 16

TI: Diagnosis and treatment of kala-azar.
AU: Chandra-J; Patwari-AK
AD: Department of Pediatrics, Lady Hardinge Medical College and Associated, Katawati Saran Children's Hospital, New Delhi.
SO: Indian-Pediatr. 1994 Jun; 31(6): 741-8

9 of 16

TI: Phase 2 efficacy trial of an oral 8-aminoquinoline (WR6026) for treatment of visceral leishmaniasis.
AU: Sherwood-JA; Gachihi-GS; Muigai-RK; Skillman-DR; Mugo-M; Rashid-JR; Wasunna-KM; Were-JB; Kasili-SK; Mbugua-JM; et-al
AD: Clinical Research Centre, Kenya Medical Research Institute, Nairobi.
SO: Clin-Infect-Dis. 1994 Dec; 19(6): 1034-9
AB: The efficacy of an oral 8-aminoquinoline (8-[[6-(diethylamino)hexyl]amino]-6-methoxy-4-methylquinoline) (WR6026) in the treatment of 16 patients with kala azar was evaluated. The first 8 patients received therapy for 2 weeks at a dosage of 0.75-1.00 mg/(kg.d); 1 patient was cured, and in regard to the other 7, a 1-logarithm decrease in the number of splenic parasites and clinical improvement were noted. The next 8 patients received therapy for 4 weeks at the same daily dosage (1 mg/[kg.d]); 4 were cured, and for the other 4, 1- to 2-log decreases in the number of parasites and clinical improvement (in regard to weight, liver and spleen size, hemoglobin level, and leukocyte count) were noted. The therapy was associated with minimal toxicity; adverse effects included gastrointestinal distress, headache, and methemoglobinemia. The fact that one-half of the patients were cured indicates that future trials with longer regimens and higher dosages are warranted and should include patients for whom existing treatment methods have failed.

10 of 16

TI: Diagnosis of symptomatic visceral leishmaniasis by use of the polymerase chain reaction on patient blood.
AU: Nuzum-E; White-F-3rd; Thakur-C; Dietze-R; Wages-J; Grogl-M; Berman-J

AD: Division of Experimental Therapeutics, Walter Reed Army Institute of Research, Washington, DC 20307-5100.
SO: J-Infect-Dis. 1995 Mar; 171(3): 751-4
AB: To diagnose symptomatic visceral leishmaniasis (kala-azar) using peripheral blood rather than tissue aspirates, a polymerase chain reaction (PCR) technique was developed for which the detection limit is 1 Leishmania-infected macrophage in 8 mL of blood. For Indian, Kenyan, or Brazilian patients with parasitologically confirmed kala-azar, 57 of 63 cases before treatment had blood that was PCR-positive (90% sensitivity). None of 40 clinically healthy persons had PCR-positive blood (100% specificity). Twelve (92%) of 13 clinically cured Indian patients had negative PCR reactions 1-6 months after treatment. This PCR procedure can provide a parasitologic diagnosis for the vast majority of kala-azar cases before therapy, may identify patients who have been successfully treated by chemotherapy, and should substantially reduce the need for invasive tests.

11 of 16

TI: A combination of sulphadiazine, trimethoprim and metronidazole or tinidazole in kala-azar.
AU: Bano-P; Shahab-SM
AD: Sadar Hospital Biharsharif, Nalanda, Bihar.
SO: J-Assoc-Physicians-India. 1994 Jul; 42(7): 535-6
AB: Nine patients of kala-azar showed good response to treatment with a combination of sulphadiazine, trimethoprim and metronidazole or tinidazole given orally for 12 to 25 weeks. No untoward side effect was noticed. Tinidazole sulphadiazine and trimethoprim combination was found to be safer for treatment of kala-azar in pregnant women.

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TI: Daily versus alternate-day regimen of amphotericin B in the treatment of kala-azar: a randomized comparison.
AU: Thakur-CP; Sinha-GP; Pandey-AK; Barat-D; Singh-RK
AD: Patna Medical College and Hospital, Bihar, India.
SO: Bull-World-Health-Organ. 1994; 72(6): 931-6
AB: Using a randomized study, we compared a daily and an alternate-day regimen of amphotericin B for the treatment of kala-azar, with respect to efficacy, adverse reactions, cost-effectiveness, and tolerance. The study subjects were 80 kala-azar patients, drawn from the first four decades of life and matched by age, sex, and parasite load. The patients were randomly allocated to treatment groups A and B (40 patients per group). Patients in group A received a daily regimen of amphotericin B, starting with an escalating dose of 0.05 mg/kg body weight per day until a daily dose of 1 mg/kg was reached; the latter dose was then given daily till a total dose of 20 mg/kg body weight had been administered. The patients in group B also started with an escalating dose of 0.05 mg/kg but when 1 mg/kg was reached the drug was given on alternate days. All 80 patients using the two treatment regimens were cured, no patient relapsed in either group in 6 months of follow-up, and their bone-marrow aspirates were free of amastigotes. Treatment of kala-azar patients with the daily regimen of amphotericin B at a dose 1 mg/kg body weight was as effective, not more toxic, equally well tolerated, and much more cost-effective than the alternate-day regimen and should be adopted for treatment of this condition.

13 of 16

TI: Is one year follow-up justified in kala-azar post-treatment?
AU: Nyakundi-PM; Wasunna-KM; Rashid-JR; Gachihi-GS; Mbugua-J; Kirigi-G; Muttunga-J
AD: Clinical Research Centre, Kenya Medical Research Institute, Nairobi.
SO: East-Afr-Med-J. 1994 Jul; 71(7): 453-9
AB: Sixty-five patients, 51 males and 14 females, with clinical and parasitological evidence of visceral leishmaniasis were initially treated as follows: 44.6% were on intravenous sodium stibogluconate (pentostam) 20 mg/kg/d

for 30 days, 35.4% was on a combination of pentostam as above and allopurinol 21 mg/kg/d in three divided doses for 30 days while 20% was on pentostam 10 mg/kg thrice/d intravenously for 10 days. All patients were parasitologically negative by the end of their respective treatment regimen. All patients were reviewed at 2 months, 6 months, and 12 months periods in order to evaluate the relapse rates and optimal follow-up period. Thirteen patients (20%) relapsed at 2 months and one patient (1.5%) relapsed at 6 months follow-up periods respectively. There was no relapse between 6 months and 12 months follow-up period. The mean liver and spleen sizes in responders showed a dramatic reduction at 2 months follow-up and thereafter a gradual reduction occurred in the next 10 months. Weight gain continued throughout the year. Apart from platelet count which showed a sustained high level from discharge to 12 months follow-up, the peripheral blood indices stabilized from 2 months follow-up. Relapses were retreated until parasitologically negative twice and then followed up, for a period of 12 months. At follow-up the liver and spleen sizes reduced gradually in the next 12 months.(ABSTRACT TRUNCATED AT 250 WORDS)

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TI: Amphotericin versus sodium stibogluconate in first-line treatment of Indian kala-azar.
AU: Mishra-M; Biswas-UK; Jha-AM; Khan-AB
AD: Darbhanga Medical College and Hospital, Bihar, India.
SO: Lancet. 1994 Dec 10; 344(8937): 1599-600
AB: Patients do not always respond to treatment of visceral leishmaniasis with pentavalent antimony, and the drug has toxic effects. Amphotericin B might be useful as an alternative first-line treatment for the disease. We compared the efficacy of amphotericin and sodium stibogluconate in a prospective randomised trial in 80 uncomplicated and parasitologically confirmed cases of Indian kala-azar. None of the patients had received an antileishmanial agent before. Sodium stibogluconate was given at 20 mg/kg in two divided doses daily for 40 days, and amphotericin in fourteen doses of 0.5 mg/kg infused in 5% dextrose on alternate days. All 40 patients randomised to amphotericin were cured; of the 40 patients assigned to sodium stibogluconate, 28 (70%) showed initial cure and 25 (62.5%) showed definitive cure ($p < 0.001$). With amphotericin, there was quicker abatement of fever and more complete spleen regression with no serious adverse effects. Amphotericin is effective in the first-line treatment of Indian kala-azar and superior to antimony therapy.

15 of 16

TI: A further study of LDT and IFAT tests in evaluating the control of kala-azar in China.
AU: Bao-Y; Wang-ST; Shao-QF
AD: Xuzhou Medical College, Jiangsu, China.
SO: J-Trop-Med-Hyg. 1994 Dec; 97(6): 357-61
AB: Kala-azar (KA) used to be highly prevalent in Shandong Province in China and, according to the survey made in 1950, the average prevalence rate was 350 per million. Through mass treatment and sandfly control, the prevalence rate was brought down to 3 per 100,000 in 1958 and the disease was basically eliminated. Since 1972, only 18 residual patients have been detected and no newly infected cases have appeared. In the meantime, the vector density had been reduced to such a low level that sandflies could not be found in 85% of the villages. For further evaluation of the control measures, an immunological survey on a relatively large scale was conducted in 78 townships located in 24 counties of 13 prefectures and cities in 1990. A total of 10,239 rural residents of different ages had the Leishmanin dermal test (LDT). None of the people under 30 years of age was positive (0/8020), while in those aged above 30, the average positive rate was 4.4% (98/2219). During the survey, blood samples were also taken from 4232 people for indirect fluorescent antibody test (IFAT); results were all negative. This indicates that the transmission of KA had been completely interrupted since the early 1960s and the province is now a non-endemic area of KA. Further analyses of the data showed that LDT is of

great value in epidemiological investigation of KA, for the evaluation of control measurements, the ascertainment of the past and present status of the disease, and detection of subclinical infection.(ABSTRACT TRUNCATED AT 250 WORDS)

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TI: The treatment of kala-azar during pregnancy.
AU: Thakur-CP; Sinha-GP; Sharma-V; Barat-D
AD: Department of Medicine, Patna Medical College, Bihar, India.
SO: Natl-Med-J-India. 1993 Nov-Dec; 6(6): 263-5
AB: BACKGROUND. Kala-azar in pregnant women is difficult to treat because for them the two commonly used drugs, sodium stibogluconate and pentamidine, are not considered safe. We assessed the effect of amphotericin B on pregnancy, on the foetus and kala-azar. METHODS. Five pregnant women were administered amphotericin B at a dose of 1 mg/kg body weight daily starting with 0.5 mg/kg body weight till a total dose of 20 mg/kg body weight was given. The progress of pregnancy was monitored ultrasonographically and the mothers and children were followed for six months. RESULTS. All the 5 women were cured of the disease and there was no harmful effect on the children. CONCLUSION. Amphotericin B cures kala-azar during pregnancy with no harmful effects on the foetus.

TI: Successful treatment of refractory visceral leishmaniasis in India using antimony plus interferon-gamma.
AU: Sundar-S; Rosenkaimer-F; Murray-HW
AD: Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
SO: J-Infect-Dis. 1994 Sep; 170(3): 659-62
AB: Fifteen Indian patients with relapsing or drug-refractory visceral leishmaniasis were retreated for 30 days with antimony plus interferon-gamma (IFN-gamma). All 15 had failure of an initial course of antimony and at least one additional course of antimony or pentamidine; 7 patients had failure of three or four prior courses of therapy. During the study, treatment was discontinued in 2 patients because of anemia and congestive heart failure in 1 and intractable vomiting in the other; both subsequently died. In the remaining 13 patients, IFN-gamma plus antimony treatment was associated with daily fever but no other adverse reactions. After 30 days of therapy, 9 (69%) of the 13 patients were apparently cured. Six months after treatment, all 9 were healthy, had parasite-free bone marrow aspirate smears, and were considered cured. None have relapsed during a mean follow-up of 15.9 +/- 1.7 months. These results support the use of antimony plus IFN-gamma as an immunochemotherapeutic alternative for kala-azar patients who have repeated failures of conventional treatment.

TI: Liver morphology and function in visceral leishmaniasis (Kala-azar).
AU: el-Hag-IA; Hashim-FA; el-Toum-IA; Homeida-M; el-Kalifa-M; el-Hassan-AM
AD: Department of Pathology, Faculty of Medicine, University of Khartoum, Sudan.
SO: J-Clin-Pathol. 1994 Jun; 47(6): 547-51
AB: AIM--To study the morphology and function of the liver in visceral leishmaniasis (Kala-azar). METHODS--Percutaneous liver biopsy specimens from 18 patients with confirmed visceral leishmaniasis were examined under light and electron microscopy before and after treatment with pentovalent antimony. The tissue was also examined for hepatitis B surface and core antigens using immunoperoxidase staining. Liver function was investigated in nine patients before and after treatment. RESULTS--Specimens before treatment showed Kupffer cells and macrophages colonised by leishmania parasites in 40% of cases. A chronic mononuclear cell infiltrate had affected the portal tracts and lobules. Ballooning degeneration of the hepatocytes, fibrosis of the terminal hepatic venules, and pericellular fibrosis were common findings. The fibrosis was related to Ito cells transforming to fibroblast-like cells. None of the patients had hepatitis B infection. All patients had biochemical evidence of liver dysfunction before treatment. Liver function improved after treatment. CONCLUSION--Visceral leishmaniasis causes morphological and functional disturbance in the liver. Focal fibrosis rather than cirrhosis occurs. The exact aetiology of hepatic damage is unclear but may have an immunological basis.

TI: Tinea versicolor and visceral leishmaniasis.
AU: Hashim-FA; Elhassan-AM
AD: Physiology Department, Faculty of Medicine, University of Khartoum, Sudan.
SO: Int-J-Dermatol. 1994 Apr; 33(4): 258-9
AB: BACKGROUND. Visceral leishmaniasis (VL) is endemic in several areas in the

Sudan. The disease is associated with depressed cellular immunity. Tinea versicolor is a normal commensal of the skin which can become pathogenic particularly in patients with depressed cell-mediated immunity. Patients with VL have a high prevalence of tinea versicolor. METHODS. One hundred and thirty patients with parasitologic confirmation of VL were screened for tinea versicolor infection. In the suspected cases the diagnosis was made by demonstrating the fungal hyphae and spores in skin scrapings. All patients were treated with sodium stibogluconate. RESULTS. Of the 130 patients with VL, 10.8% were found to have severe tinea versicolor. The fungal infection developed or became worse with the start of VL. After successful treatment of VL, the tinea lesions disappeared completely or decreased in severity. CONCLUSIONS. Depressed cell-mediated immunity that is a feature of VL is the probable underlying cause for fungal infection. Tinea infection during the course of VL is to be distinguished from lesions of post-kala-azar dermal leishmaniasis.

4 of 5

TI: Immunoblotting identifies an antigen recognized by anti gp63 in the immune complexes of Indian kala-azar patient sera.
AU: Sanyal-T; Ghosh-DK; Sarkar-D
AD: Leishmania Group, Indian Institute of Chemical Biology, Calcutta.
SO: Mol-Cell-Biochem. 1994 Jan 12; 130(1): 11-7
AB: In SDS-PAGE the immune complexes (IC) of kala-azar patient sera showed intense bands at 55 kDa and 20 kDa corresponding to heavy and light chains of immunoglobulins. In immunoblot experiment, kala-azar and normal IC after treatment with patient sera showed multiple bands of which the band at 55 kDa was most prominent in kala-azar IC. It is known that in kala-azar sera antihuman IgG is present, so the heavy band at 55 kDa region may be due to higher amount of IgG and/or other antigen(s) present at that region. Immunoblot experiments of kala-azar IC with anti gp63 also developed a major band at 55 kDa. It suggests that the antigen (55 kDa) and gp63 have common antigenic epitope (s). Normal IC did not react with anti gp63 indicating absence of this antigen in normal IC. Antigenic similarity between the IC antigen (55 kDa) and gp63 indicated that the former antigen may have been processed from gp63. In summary, identification of a parasite antigen (55 kDa) in IC of kala-azar patients sera may be useful in developing a serodiagnostic assay for visceral leishmaniasis.

5 of 5

TI: Treatment of post-kala-azar dermal leishmaniasis.
AU: Ramesh-V
AD: Department of Dermatology and Regional STD, Centre Safdarjang Hospital, New Delhi, India.
SO: Int-J-Dermatol. 1994 Mar; 33(3): 153-6

1 of 13

TI: Treatment of Brazilian kala-azar with a short course of amphocil (amphotericin B cholesterol dispersion).
AU: Dietze-R; Milan-EP; Berman-JD; Grogl-M; Falqueto-A; Feitosa-TF; Luz-KG; Suassuna-FA; Marinho-LA; Ksionski-G
AD: Tropical Medicine Unit, Federal University of Espirito Santo, Vitoria, Brazil.
SO: Clin-Infect-Dis. 1993 Dec; 17(6): 981-6
AB: Amphotericin B is an effective but toxic antileishmanial agent. Lipid-encapsulated amphotericin B should have a high therapeutic index for visceral leishmaniasis because reticuloendothelial cells, the sole site in which Leishmania is found, will phagocytize and concentrate the complex. Amphotericin B cholesterol dispersion (Amphocil; 2 mg/[kg.d] intravenously) was administered to 10 Brazilians with kala-azar for 10 days (cohort 1) and to 10 Brazilians with kala-azar for 7 days (cohort 2). All patients were successfully treated: 19 of the 20 patients were without visible parasites in the bone marrow; the mean time to afebrility was 4.2 days; spleen size regressed by a mean of 79% 2 months after therapy; and no patient had clinical or laboratory abnormalities by the end of 6-12 months of follow-up. Side effects were fever and chills accompanied by respiratory distress, but not nephrotoxicity, in children < 3 years of age.

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TI: Leishmaniasis: report of 33 cases and a review of the literature [editorial]
AU: Bouree-P; Belec-L
SO: Comp-Immunol-Microbiol-Infect-Dis. 1993 Oct; 16(4): 251-65
AB: Leishmaniasis are parasitic diseases in extension. They appear in new foci, because of important displacements of populations, and they affect immunocompromised patients (under chemotherapy, transplanted, or HIV infected). Study of 33 cases of leishmaniasis, 22 visceral and 11 cutaneous, at the Hopital du Kremlin-Bicetre, France, showed predominant contamination in Maghreb and in the south of France. In the case of Kala-Azar, fever (18 cases) and hepatosplenomegaly (19 cases) are frequent, and the serodiagnosis and the search of parasites by myelogram are always positive. In HIV-infected individuals, clinical signs are similar, but the serodiagnosis is less reliable. Evolution is bad in transplanted patients who must remain under immunosuppressive drugs. In the case of cutaneous leishmaniasis, diagnosis is based on local sample, while the serodiagnosis remains negative. Treatment is sometimes long, necessitating repeated treatments.

3 of 13

TI: [Childhood kala-azar: the cases of a decade]
AU: Lopez-Pena-LF; Clemente-Yago-F; de-la-Cruz-Amoros-F; Gorostiza-Felipe-P; Monferrer-Fabregat-R; Escriva-Tomas-P
AD: Servicio de Pediatria, Hospital General de Alicante.
SO: An-Esp-Pediatr. 1993 Sep; 39(3): 199-201
AB: The aim of our work was to review the epidemiological, clinical and laboratory features of the cases of Kala-azar in our hospital during a decade in order to outline data that might be useful in helping to make an earlier diagnosis and subsequently, earlier treatment. We report eighteen cases of visceral Leishmaniasis treated in our hospital between January 1981 and December 1990. The ages of the patients varied between five months and seven

years. In our experience, medullar aspirate was the most effective diagnostic method. However, it this test is negative, specific serological tests should be included in the assessment of any pediatric inpatient with fever and splenomegaly. In our opinion, it is very important to keep this disease in mind, especially in non-endemic areas.

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TI: Leishmanin and tuberculin sensitivity in leishmaniasis in the Sudan, with special reference to kala-azar.
AU: Zijlstra-EE; el-Hassan-AM
AD: Leishmania Research Group, Medical Research Council, Khartoum, Sudan.
SO: Trans-R-Soc-Trop-Med-Hyg. 1993 Jul-Aug; 87(4): 425-7
AB: The application of leishmanin and tuberculin skin tests was studied in patients with leishmaniasis in the Sudan. 35 cases of active kala-azar and 3 relapse cases were leishmanin negative. 81% of patients treated for kala-azar showed a positive reaction after 6 months. 17 of 29 patients with post kala-azar dermal leishmaniasis (PKDL) were leishmanin positive. 2 of 16 patients with kala-azar tested with tuberculin were positive; one was diagnosed as tuberculosis. In 7 initially tuberculin negative patients, the tuberculin test became positive after treatment. A new Leishmania major skin test antigen (Pasteur Institute, Iran) was more reactive than other antigens in patients with cutaneous leishmaniasis, mucocutaneous leishmaniasis and PKDL, but not in treated kala-azar cases. In a field study in an area of endemic kala-azar, the new L. major antigen proved more reactive both in individuals previously exposed to L. major (causing cutaneous leishmaniasis) and in those with past exposure to L. donovani. The literature concerning skin testing with leishmanin and tuberculin in kala-azar is reviewed.

5 of 13

TI: Kala-azar in western Upper Nile province in the southern Sudan and its spread to a nomadic tribe from the north.
AU: el-Hassan-AM; Hashim-FA; Ali-MS; Ghalib-HW; Zijlstra-EE
AD: Department of Pathology and Physiology, Faculty of Medicine, University of Khartoum, Sudan.
SO: Trans-R-Soc-Trop-Med-Hyg. 1993 Jul-Aug; 87(4): 395-8
AB: Since the start in 1988 of the present epidemic of kala-azar (visceral leishmaniasis) in western Upper Nile state in southern Sudan, the epidemiology of the disease in all parts of the Sudan where kala-azar has been reported was reassessed by the Leishmaniasis Research Group in Khartoum. In this paper, the spread of the epidemic is described among a nomadic tribe originating from southern Kordofan state, who migrate every year with their cattle to the Bentiu rea in western Upper Nile state where the epidemic is still raging. 200 cases from this tribe were seen in Khartoum; another 56 cases were found during a field trip to the area. In addition, the Bentiu area was visited, where 301 cases were under treatment and another 52 of 1120 individuals screened were confirmed parasitologically. 20 cases of post-kala-azar dermal leishmaniasis were found. Parasites isolated from the nomadic tribe were of the same zymodeme as parasites isolated previously from the Nuer in western Upper Nile. The epidemiological findings in each state are discussed in relation to the tribes that were affected and the ecology of the area.

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TI: Efficacy of amphotericin B in multi-drug resistant kala-azar in children in first decade of life.
AU: Thakur-CP; Sinha-GP; Sharma-V; Pandey-AK; Sinha-PK; Barat-D
AD: Department of Medicine, Patna Medical College.
SO: Indian-J-Pediatr. 1993 Jan-Feb; 60(1): 29-36
AB: Fifty children in the first decade of life, and suffering from multiple drug resistant kala-azar, confirmed by demonstration of amastigotes in aspirates of bone marrow or spleen were treated with amphotericin B in gradually increasing dosage to a total dose of 20 mg/kg. All patients had

classical features of severe kala-azar, and had taken more than one course of antimony and pentamidine, and three patients had taken one additional course of ketoconazole besides many courses of antimony and pentamidine. The clinical response started just after first infusion in 8 patients, and the patients became afebrile. By 5th infusion, all looked better and 18 patients became afebrile. By 15th infusion all patients were afebrile and cheerful. Their spleens became smaller and body weights and total white cell counts increased. Forty eight patients had parasitological cure at the end of treatment, and only 2 patients required an additional 5 infusions for parasitological cure. All patients were ultimately cured. No one relapsed within six months of follow up. All patients had shivering, rigor and rise of temperature on the day of infusion, which could be minimized with prior administration of low dose of hydrocortisone, but could not be eliminated. Eighteen patients had loose motions during treatment, while 14 patients had decrease in appetite which improved quickly when the treatment was over. Fourteen patients had transient rise of blood urea, in six patients serum creatinine also increased and 16 patients had a minor fall in serum potassium.(ABSTRACT TRUNCATED AT 250 WORDS)

7 of 13

TI: The treatment of kala-azar in the Sudan with sodium stibogluconate: a andomized trial of three dosage regimens.
AU: Zijlstra-EE; Siddig-Ali-M; el-Hassan-AM; Hofland-HW; el-Toum-I; Satti-M; Ghalib-HW
AD: Leishmania Research Group, Medical Research Council, Sudan.
SO: Trans-R-Soc-Trop-Med-Hyg. 1993 May-Jun; 87(3): 307-9
AB: In a randomized study in the Sudan, 3 different regimens of sodium stibogluconate were compared in patients with parasitologically confirmed kala-azar (visceral leishmaniasis): 10 mg/kg for 30 d (38 patients), 20 mg/kg for 30 d (29 patients), and 20 mg/kg for 15 d (37 patients). Treatment failures were defined as death, partial response, relapse, or the development of post-kala-azar dermal leishmaniasis. The hazard ratio for failure of 20 mg/kg for 30 d vs. 10 mg/kg for 30 d 2.1 (95% confidence interval [CI] = 0.6, 7.6) and for 20 mg/kg for 15 d vs. 10 mg/kg for 30 d it was 1.7 (95% CI = 0.5, 6.1). No significant difference was detected between the 3 regimens in the rate of return to normal of haematological criteria, regression of spleen size, or weight gain. After 15 d treatment parasite clearance with 20 mg/kg for 30 d and 20 mg/kg for 15 d was more profound than with 10 mg/kg for 30 d ($P < 0.05$), but the difference was no longer present at the end of treatment. Further investigation of the effectiveness of short, intensive treatment regimens in the treatment of kala-azar is warranted.

8 of 13

TI: Visceral leishmaniasis (kala-azar) after a visit to the Mediterranean region.
AU: Rudi-J; Racz-P; Horner-M; Kommerell-B
AD: Medizinische Universitatsklinik, Abteilung fur Gastroenterologie, Heidelberg.
SO: Clin-Investig. 1993 Aug; 71(8): 616-9
AB: The case of a 17-year-old patient is presented who became ill 10 months after a holiday visit to Malta. Symptoms included fever peaking daily at 40 degrees C, pancytopenia, and splenomegaly. There was no evidence of bacterial or virological involvement, and probatory treatment with antibiotics followed by corticosteroids was without success. Examination of bone marrow led to the diagnosis of visceral leishmaniasis (kala-azar). A therapy with pentavalent antimony brought rapid improvement in clinical symptoms and led to complete recovery. A short review is presented of the epidemiology, diagnosis, and therapy of visceral leishmaniasis. The aim of this presentation is to remind the attendant physician of the clinical symptoms involved with the possible case of visceral leishmaniasis.

9 of 13

TI: Amphotericin B therapy in kala-azar.
AU: Giri-OP
AD: Department of Medicine, Darbhanga Medical College and Hospital, Laherisarai.
SO: J-Indian-Med-Assoc. 1993 Apr; 91(4): 91-3
AB: Twenty-seven adult patients of kala-azar unresponsive to sodium stibogluconate (SSG) were given amphotericin B in the dose schedule of 0.50 mg/kg body weight on alternate days for a total of 21 to 31 infusions, depending upon clinical and parasitological response. A 100% cure rate was achieved at the end of the therapy and no relapse was encountered during 12 months follow-up. Only mild adverse reactions were noted on the day of infusion during therapy. Amphotericin B was found to be an acceptable alternative drug for treatment of such cases.

10 of 13

TI: Evaluation of amphotericin B as a first line drug in comparison to sodium stibogluconate in the treatment of fresh cases of kala-azar.
AU: Thakur-CP; Sinha-GP; Sharma-V; Pandey-AK; Kumar-M; Verma-BB
AD: Department of Medicine, Medical College, Patna.
SO: Indian-J-Med-Res. 1993 Jul; 97: 170-5
AB: A total of 150 patients of kala-azar matched for age and sex and parasitologically proved were randomly allocated to two equal treatment groups. Patients in one group received amphotericin B(AMB) in a dose of 1 mg/kg body weight (BW) on alternate days starting with 0.05 mg/kg/bw on first day with daily increments, till a total dose of 20 mg/kg/bw was given; the patients in the second group received sodium stibogluconate (SAG) in the dose of 20 mg/kg/bw, im daily for 30 days. The efficacy, safety and cost-effectiveness of the two drugs were compared. Apparent cure (afebrile at the end of therapy) in 75 (100%) and 69 (92%) patients and ultimate cure (no relapse in six months of follow up) in 75 (100%) and 60 (80%) patients occurred in the AMB and SAG groups respectively. The difference between the ultimate cure in the two groups was significant ($P < 0.001$). Six (8%) and 9(12%) patients of SAG group showed primary (with no response to SAG during treatment) and secondary unresponsiveness (with no response to SAG after relapse) respectively and they were cured with amphotericin B.(ABSTRACT TRUNCATED AT 250 WORDS)

11 of 13

TI: Post-kala-azar dermal leishmaniasis: a clinical and therapeutic study.
AU: Ramesh-V; Misra-RS; Saxena-U; Mukherjee-A
AD: Department of Dermatology and Leprology, Safdarjang Hospital, New Delhi, India.
SO: Int-J-Dermatol. 1993 Apr; 32(4): 272-5
AB: BACKGROUND. Post-kala-azar dermal leishmaniasis is a condition peculiarly confined to the Indian subcontinent. METHODS. The clinical features and investigations in 18 patients of post-kala-azar dermal leishmaniasis were studied. RESULTS. There was a polymorphic picture from hypopigmented macules to nodules and plaques. Mucous membranes were affected in five, the lips and glans penis being the most frequent sites. Histopathologically, a rich dermal infiltrate was seen in indurated lesions and in macules; it was confined to perivascular foci in the upper dermis. Leishman-Donovan bodies were seen in 16. CONCLUSIONS. The lesions cleared in 4 to 5 months after treatment with sodium antimony gluconate intramuscularly 20 mg/kg/day up to a maximum of 1 g/day. The drug was well tolerated.

12 of 13

TI: Heterogeneity of cutaneous leishmaniasis with emphasis on the Old World.
AU: Peters-W
AD: Department of Medical Parasitology, London School of Hygiene and Tropical Medicine, England.
SO: Schweiz-Med-Wochenschr. 1993 Jun 19; 123(24): 1237-49
AB: Leishmaniasis of the integument which may result from infection with a

number of different species of Leishmania can be primary, or can arise as a late manifestation of systemic infection of the reticuloendothelial organs (kala-azar). Infection of the skin and/or mucosae assumes many different clinical forms which are reviewed here. The immune response is essentially a cell-mediated one. Even left untreated, the majority of tegumentary lesions will eventually self-heal but the process may be very prolonged and severe scarring can result. The main features of diagnosis, prevention and treatment are discussed. No vaccines are generally available at present. Organic pentavalent antimonials remain the drugs of choice.

13 of 13

TI: Amphotericin B in resistant kala-azar in Bihar.
AU: Thakur-CP; Sinha-GP; Pandey-AK; Barat-D; Sinha-PK
AD: Patna Medical College and Hospital, Bihar, India.
SO: Natl-Med-J-India. 1993 Mar-Apr; 6(2): 57-60
AB: BACKGROUND. During the recent epidemic of kala-azar in Bihar, we identified a group of patients who were unresponsive to the two commonly used drugs--sodium stibogluconate and pentamidine. We evaluated the use of amphotericin B in these patients because it has been shown to be active in experimental animals against amastigotes and promastigotes, it has been found to be useful in South American patients and is now recommended by the World Health Organization as a second line drug. METHODS. We selected 300 patients who were unresponsive to sodium stibogluconate and pentamidine (out of 500 patients with kala-azar confirmed by demonstration of Leishmania donovani bodies in their splenic aspirates). Amphotericin B was given in a dose of 1 mg/kg body weight on alternate days starting with 0.05 mg/kg body weight with daily increments till a 1 mg dose was reached. A total dose of 20 mg/kg was given initially and repeated if the parasites persisted. The investigations done before and after treatment were splenic or bone marrow aspiration, measurement of the spleen and liver size, body weight, total and differential white cell counts, haemoglobin level, total serum protein, blood urea, serum creatinine, serum potassium, blood sugar, serum alanine and aspartate transaminase, electrocardiography and a chest X-ray. The efficacy of treatment was assessed at the end of treatment and after 6 months of follow up. RESULTS. After treatment with amphotericin B, 298 (99%) of the patients had been cured of their disease as evidenced by the disappearance of fever, reduction of hepatosplenomegaly, clearance of the parasites from the spleen and bone marrow and an absence of relapse on 6 months of follow up. Two hundred and sixty-eight (89%) patients required 1 g of the drug, 24 (8%) required 1.5 g and 6 (2%) required 2 g. All patients had shivering and fever during the infusion. Two had a cardiac arrest from which they could not be revived. Other complications included anorexia, stomatitis, jaundice, hypokalaemia and a rise in blood urea. However, these were only mild and improved after treatment was stopped. CONCLUSION. Amphotericin B is an effective drug for patients with kala-azar unresponsive to treatment with sodium stibogluconate and pentamidine, but it should be administered under close medical supervision.

1 of 16

TI: Treatment of kala-azar in India [editorial]
AU: Thakur-CP
SO: Natl-Med-J-India. 1992 Sep-Oct; 5(5): 203-5

2 of 16

TI: Treatment of visceral leishmaniasis (kala-azar) with aminosidine (= paromomycin)-antimonial combinations, a pilot study in Bihar, India.
AU: Thakur-CP; Olliaro-P; Gothoskar-S; Bhowmick-S; Choudhury-BK; Prasad-S; Kumar-M; Verma-BB
AD: Patna Medical College, Tripolia Social Service Hospital, India.
SO: Trans-R-Soc-Trop-Med-Hyg. 1992 Nov-Dec; 86(6): 615-6
AB: A 20 d drug regimen of aminosidine (= paromomycin) at 12 mg/kg/d in combination with sodium stibogluconate at 20 mg/kg/d proved efficacious and well-tolerated in patients with visceral leishmaniasis in the State of Bihar, India. Eighteen of 22 evaluable patients achieved an ultimate cure. The remaining 4 patients, although not cleared of parasites, had their parasite grade reduced and also improved clinically. This confirms prior findings in Kenyan patients with kala-azar, and indicates that this regimen is a valid alternative to antimonial compounds alone in the State of Bihar, where cases of kala-azar not responding to antimonial drugs and intolerant of pentamidine are increasingly recorded.

3 of 16

TI: Detection of circulating antigen by McAb-AST for evaluating the efficacy of anti-Leishmania chemotherapy.
AU: Hu-X; Lin-F; Kan-B; Yan-W
AD: Laboratory of Parasitology, West China University of Medical Sciences, Chengdu, Sichuan.
SO: Chin-Med-Sci-J. 1992 Sep; 7(3): 157-60
AB: We have adapted the simple and sensitive McAb-antigen spot test (AST) for evaluating the efficacy of anti-Leishmania chemotherapy. Serum samples from 37 kala-azar patients were tested by McAb-AST, and all showed definite positive reactions before treatment. After a course of antimony treatment, 20 turned negative, coupled with the disappearance of clinical symptoms; another 12 cases responded with weak positivity accompanied by an improvement of clinical manifestations; and the remaining 5 antimony-resistant patients showed strong positive reactions, with their conditions gradually worsening. Furthermore, all 6 cases in which the diagnosis was missed by the bone marrow smear method turned McAb-AST negative after chemotherapy. These results suggest that McAb-AST can be used to evaluate the efficacy of chemotherapy as well as to avoid missed diagnosis by the bone marrow smear method.

4 of 16

TI: Rapid and sensitive detection of Leishmania kinetoplast DNA from spleen and blood samples of kala-azar patients.
AU: Smyth-AJ; Ghosh-A; Hassan-MQ; Basu-D; De-Bruijn-MH; Adhya-S; Mallik-KK; Barker-DC
AD: Department of Pathology, University of Cambridge, UK.
SO: Parasitology. 1992 Oct; 105 (Pt 2): 183-92
AB: Following sequence analysis of a Leishmania donovani kinetoplast DNA (kDNA) minicircle, we have developed synthetic oligonucleotides for use in the polymerase chain reaction (PCR). With these primers, we have amplified L.

donovani kDNA from splenic aspirates and blood samples taken from kala-azar patients. Treatment of the samples for PCR requires only limited DNA purification by lysis in SDS, digestion with proteinase K, phenol extraction and ethanol precipitation of the resulting nucleic acid. We have obtained amplified product routinely with DNA prepared from the equivalent of 2.5-25 microliters of splenic aspirate or of 50-500 microliters of blood from infected patients. In dilution experiments a visible product has been obtained on amplification of DNA from the equivalent of 2.5 x 10(-7) microliters of splenic material. We therefore propose the amplification of L. donovani kDNA by PCR as a rapid and highly sensitive method for the diagnosis of kala-azar.

5 of 16

TI: Visceral and cutaneous leishmaniasis in an European paediatric population.
AU: Mattot-M; Ninane-J; Bigaignon-G; Vermylen-C; Cornu-G
AD: Department of Paediatrics, Cliniques Universitaires Saint-Luc, Brussels.
SO: Acta-Clin-Belg. 1992; 47(4): 231-7
AB: Six children with leishmaniasis, aged 10 months to 10 years, were treated in the Paediatric Department. Four patients had visceral leishmaniasis (kala-azar): diagnosis was based on bone marrow examination and therapy consisted of a combination of Glucantime and Lomidine. The remaining two children had cutaneous leishmaniasis: diagnosis was made by skin biopsy and the patients were treated with Glucantime alone. In all children, serology was clearly positive at the time of the diagnosis and all patients improved. The only side effects were cough associated with fever in one child, and supraventricular premature beats in another one. They were ascribed to Glucantime, and proved reversible after discontinuation of the treatment.

6 of 16

TI: Post kala-azar dermal leishmaniasis in the Sudan: clinical features, pathology and treatment.
AU: el-Hassan-AM; Ghalib-HW; Zijlstra-EE; Eltoum-IA; Satti-M; Ali-MS; Ali-HM
AD: Leishmaniasis Research Group, Medical Research Council, Khartoum, Sudan.
SO: Trans-R-Soc-Trop-Med-Hyg. 1992 May-Jun; 86(3): 245-8
AB: The clinical features, pathology, immune responses, diagnosis and treatment of post kala-azar dermal leishmaniasis (PKDL) in the Sudan are described and discussed. The disease is characterized by maculopapular or nodular lesions on the face, limbs or trunk. Lesions appear during or within months after the treatment of visceral leishmaniasis, but in 2 of 19 patients there was no previous history of kala-azar. PKDL may be confused with leprosy both clinically and pathologically. Similarities and differences between the 2 diseases are discussed. Unlike visceral leishmaniasis, the peripheral lymphoid cells of patients with PKDL respond to Leishmania antigen and some are leishmanin positive. The response to intravenous sodium stibogluconate (20 mg/kg for 30 d) was reasonably good but some patients required repeated or more prolonged treatment. Ketoconazole in a dose of 10 mg/kg daily for 4 weeks had no effect on PKDL.

7 of 16

TI: Oral leishmaniasis associated with kala-azar. A case report.
AU: Abbas-K; el-Toum-IA; el-Hassan-AM
AD: Dental School, Faculty of Medicine, University of Khartoum, Sudan.
SO: Oral-Surg-Oral-Med-Oral-Pathol. 1992 May; 73(5): 583-4
AB: Mucosal leishmaniasis as an oral disease in the form of chronic periodontitis with involvement of the oral mucosa is described. Leishmania parasites were isolated from the oral lesions, lymph nodes, and bone marrow. The patient had a low-grade fever and hepatosplenomegaly that regressed along with the oral lesions after treatment with stibogluconate sodium.

8 of 16

TI: Observations on the effect of verapamil with sodium stibogluconate in kala azar.

AU: Thakur-CP; Kumar-M
AD: Department of Medicine, Patna Medical College Hospital, India.
SO: Trop-Geogr-Med. 1992 Jan; 44(1-2): 15-8
AB: 40 parasitologically confirmed cases of kala azar, were randomly allocated into four treatment groups to assess the effect of verapamil on fresh and antimony resistant cases of kala azar. Untreated patients received sodium stibogluconate only or in combination with oral verapamil. Antimony-resistant patients were treated with sodium stibogluconate combined with oral verapamil or pentamidine. The patients were followed up for six months. Verapamil neither shortened the duration of treatment nor increased parasitological cure rate nor improved the ultimate cure. In antimony unresponsive patients it did not reverse unresponsiveness.

9 of 16

TI: Clinical aspects of kala-azar in children from the Sudan: a comparison with the disease in adults.
AU: Zijlstra-EE; Ali-MS; el-Hassan-AM; el-Toum-IA; Satti-M; Ghalib-HW
AD: Leishmaniasis Research Group, Medical Research Council, Sudan.
SO: J-Trop-Pediatr. 1992 Feb; 38(1): 17-21
AB: The clinical presentation of kala-azar in 43 children and 45 adults was mpared. In both groups fever, left upper quadrant abdominal pain and welling, and weight loss were equally the most common presenting symptoms. Lymphadenopathy was observed in 86 per cent of children and 76 per cent of adults. Splenomegaly was absent in 2 per cent of children and 7 per cent of adults. No significant difference was found in frequency distribution of symptoms and signs between children and adults. Haematological indices were compared in both children and adults with kala-azar and their control groups. In both children and adults with kala-azar, haemoglobin concentration, total white cell count, and platelet count were significantly lower before than after treatment. Only haemoglobin concentration was lower in children with kala-azar as compared with adults with the disease. Children in the control group had lower haemoglobin and higher total white cell count than adult controls. Response to therapy was evaluated in 693 patients. Two-hundred-and-fifty children and 373 adults were treated with sodium stibogluconate 10 mg/kg for 30 days; in both groups 12 per cent deaths and 4 per cent relapses occurred. Thirty children and 40 adults were treated with sodium stibogluconate 2 x 10 mg/kg for 15 days. In children, 3 per cent deaths and 7 per cent relapses were noted; in adults there were 8 per cent deaths and 5 per cent relapses. No significant difference in death rate or relapse rate was found between children and adults in both regimens. Both regimens performed equally well in children and adults with regard to death rate and relapse rate.

10 of 16

TI: [Visceral leishmaniasis in HIV infection. A totally opportunistic infection]
AU: Cabie-A; Matheron-S; Lepretre-A; Bouchaud-O; Deluol-AM; Coulaud-JP
AD: Service des Maladies infectieuses et tropicales, Hopital Bichat-Claude Bernard, Paris.
SO: Presse-Med. 1992 Oct 24; 21(35): 1658-62
AB: Visceral leishmaniasis occurring in immunocompromised patients, and in particular during HIV infection, has been described in recent years and differs from the usual Mediterranean kala-azar as encountered in France. In order to define the clinical, diagnostic and therapeutic features of the HIV-Leishmania spp. co-infection, we report 8 new cases and compare them with data from the literature. The co-infection occurs at any stage of HIV infection, usually in drug addicts using intravenous injections. Clinical manifestations, such as fever, weight loss, liver and spleen enlargement and polyadenopathy, and laboratory findings (cytoponia, inflammatory syndrome) are generally present but not specific during the HIV infection course. Moreover, some gastrointestinal and pleuropulmonary forms of the co-infection are misleading. Leishmaniasis serology is negative in 50 percent of the patients. In most cases

the diagnosis is provided by detection of the parasite in bone marrow samples. Culture must be systematic, and samplings must be repeated if they are negative. The first-line treatment consists of pentavalent antimony. Almost 80 percent of the patients respond to this treatment, but relapses occur in 50 percent of the cases. This high risk of relapse and the opportunistic behaviour of leishmaniasis justify a prophylaxis of relapses.

11 of 16

TI: Kala-azar: a comparative study of parasitological methods and the direct agglutination test in diagnosis [see comments]
AU: Zijlstra-EE; Ali-MS; el-Hassan-AM; el-Toum-IA; Satti-M; Ghalib-HW; Kager-PA
AD: Leishmaniasis Research Group, Medical Research Council, Sudan.
SO: Trans-R-Soc-Trop-Med-Hyg. 1992 Sep-Oct; 86(5): 505-7
AB: In a comparative study 88 patients were diagnosed as suffering from kala-azar (visceral leishmaniasis) using 3 parasitological methods simultaneously. Splenomegaly was absent in 4 cases. In 84 patients with splenomegaly, splenic aspiration appeared to be the most sensitive method (96.4%), followed by bone marrow aspiration (70.2%) and lymph node aspiration (58.3%). There was no relation between titres in the direct agglutination test and parasite load as determined by the number of parasitological methods which were positive or parasite density in splenic aspirates. Splenic aspiration and bone marrow aspiration were compared as an assessment of cure in kala-azar. In 6 (13%) of 46 patients tested, parasites were found, all by splenic aspiration. Bone marrow showed parasites in one of these. The literature with regard to parasitological investigations before and after treatment is reviewed.

12 of 16

TI: The treatment of kala-azar: old and new options.
AU: Zijlstra-EE
AD: Department of Infectious Diseases and Tropical Medicine, Academic Medical Centre, Amsterdam, The Netherlands.
SO: Trop-Geogr-Med. 1992 Jul; 44(3): 288

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TI: Post-kala-azar dermal leishmaniasis in the Sudan: peripheral neural involvement.
AU: Elhassan-AM; Ali-MS; Zijlstra-E; Eltoum-IA; Ghalib-HW; Ahmed-HM
AD: Leishmania Research Group, Faculty of Medicine, Khartoum, Sudan.
SO: Int-J-Dermatol. 1992 Jun; 31(6): 400-3
AB: Four patients developed post-kala-azar dermal leishmaniasis and neuritis (PKDL) 1 to 6 months following apparently successful treatment of kala-azar. The duration of the lesion varied between 1 month and nearly 5 years. The lesions were macules, papules, or nodules affecting the face, extremities, and trunk. The diagnosis was made by demonstration of the parasite in slit smear and biopsies and by a positive direct agglutination test (DAT). Histologically, the patients were found to have neuritis affecting the cutaneous nerves in the lesion only. The nerves showed a lymphohistiocytic infiltration and occasionally parasites. There was no impairment of sensation. Response to sodium stibogluconate was good. PKDL may simulate leprosy both clinically and pathologically.

14 of 16

TI: Ketoconazole in the treatment of antimony- and pentamidine-resistant kala-azar [letter]
AU: Wali-JP; Aggarwal-P; Gupta-U; Saluja-S; Singh-S
SO: J-Infect-Dis. 1992 Jul; 166(1): 215-6

15 of 16

TI: [Kala-azar]
AU: Lagardere-B; Chevallier-B; Cheriet-R
AD: Service de Pediatrie, Hopital Ambroise Pare, Boulogne.

SO: Ann-Pediatr-Paris. 1992 Mar; 39(3): 159-64
AB: The incidence of infantile visceral leishmaniasis is currently increasing, at least in the Mediterranean region. Most cases seen in France occur on the Mediterranean coast or are imported from Africa. However, contamination in other regions of France is not an exceptional occurrence and may raise diagnostic problems. The parasite reservoir is the dog population in which the prevalence of Leishmania infection is particularly high in the Provence and Cevennes regions. Both teenagers and young children may be affected by this disease, whose clinical manifestations may be misleading. The typical symptomatic triad, i.e., anemia-fever-enlarged spleen, may be incomplete, especially as a result of the intermittent character of the fever. Patients may remain afebrile for long periods. Diagnosis rests on demonstration of the parasite in bone marrow specimens (several biopsies are often required) or in the spleen. Bacteriologic studies using a special medium are helpful. Serologic tests are sensitive and specific but often become positive only late in the disease. Management still rests on pentavalent antimonial compounds. Advances have been made in the understanding of the toxic effects and rules for optimal use of these drugs. Improved insight into the parasite's biology may result in use of new forms of treatment; allopurinol is at present the only recent addition to the armamentarium which has been proved effective in humans when given in combination with an antimonial compound.

16 of 16

TI: [Kala-azar. Is it possible to treat it with aminoglucosides?]
AU: Tapia-Collados-C; Comino-Almenara-L; Escriva-Tomas-P; Ribera-Delgado-M; Gonzalez-Peraba-J; Tapia-Lopez-M; Lopez-Pena-L
AD: Servicio de Pediatria, Hospital General, Alicante.
SO: An-Esp-Pediatr. 1992 Jan; 36(1): 57-8
AB: We report the case of a 13 month old male infant with visceral leishmanisis. The clinical picture was suggestive of kala-azar, but a bone marrow aspirate was negative, so treatment was not started. During the course of the process an urinary infection was documented and therapy with aminoglycosides was begun. At this time we observed that hepato--and spleno--megaly diminished and then disappeared and clinical manifestations improved. We later received a positive serology for Leishmania donovani. We review the medical literature in respect to this therapeutic possibility.

1 of 9

TI: Amphotericin B for second-line treatment of Indian kala-azar [letter]
AU: Mishra-M; Singh-MP; Choudhury-D; Singh-VP; Khan-AB
SO: Lancet. 1991 Apr 13; 337(8746): 926

2 of 9

TI: Post kala-azar dermal leishmaniasis: the Kenyan experience.
AU: Muigai-R; Gachihi-GS; Oster-CN; Were-JB; Nyakundi-PM; Chunge-CN; Kirigi-G; Rashid-JR
AD: Clinical Research Centre, Kenya Medical Research Institute, Nairobi.
SO: East-Afr-Med-J. 1991 Oct; 68(10): 801-6
AB: Post kala-azar dermal leishmaniasis (PKDL) occurs occasionally after successful cure of visceral leishmaniasis. Twelve patients with diagnosis consistent with PKDL were seen at Clinical Research Centre from 1981 to 1985. Clinical presentation ranged from macular hypopigmented lesion to generalized nodular lesions. All lesions cleared either by self-cure or by treatment with sodium stibogluconate.

3 of 9

TI: Comparison of regimes of treatment of antimony-resistant kala-azar patients: a randomized study.
AU: Thakur-CP; Kumar-M; Pandey-AK
AD: Patna Medical College and Hospital, Patna, Bihar, India.
SO: Am-J-Trop-Med-Hyg. 1991 Oct; 45(4): 435-41
AB: Three hundred twelve patients with antimony-resistant kala-azar were randomized into three groups. The first group (A) received pentamidine isethionate intravenously three times each week until parasitological cure was achieved. Group B received pentamidine concomitantly with a 20-day regimen of sodium stibogluconate. Group C received pentamidine injections that were followed by 20 days of sodium stibogluconate therapy. All patients became afebrile after 10 injections of pentamidine. Parasitologic cure was achieved in approximately 98% of the patients who had 33 or more injections of this drug. The addition of the antimony compound did not appear to enhance the rate of parasitologic cure. Three patients continued to have parasites after 40 injections of pentamidine. After six months, the rate of parasitologic cure was significantly higher in Group C (pentamidine followed by sodium stibogluconate) than in either Group A or B. Forty patients relapsed after apparent parasitologic cure and were successfully treated with five additional injections of pentamidine, followed by a course of antimony therapy. Minor side effects with pentamidine included an uneasy feeling during intravenous injection (12%), intestinal disturbances (6%), cellulitis (5%), abscess formation (1%), and allergic manifestations (2%). Major reactions to this drug included hyperglycemia (10%; reversible in 6% and irreversible in 4%), and delayed hypoglycemia (8%). Four deaths were associated with the administration of this compound. It is concluded that pentamidine is an effective but toxic drug for the treatment of antimony-resistant kala-azar.(ABSTRACT TRUNCATED AT 250 WORDS)

4 of 9

TI: Kala-azar in displaced people from southern Sudan: epidemiological, clinical and therapeutic findings.
AU: Zijlstra-EE; Ali-MS; el-Hassan-AM; el-Toum-IA; Satti-M; Ghalib-HW; Sondorp-E; Winkler-A

AD: Leishmaniasis Research Group, Medical Research Council, Sudan.
SO: Trans-R-Soc-Trop-Med-Hyg. 1991 May-Jun; 85(3): 365-9
AB: Six hundred and ninety-three patients with kala-azar were seen in Khartoum, Sudan, from January 1989 to February 1990. They were almost exclusively from the Nuer tribe, originating from the western Upper Nile province in southern Sudan, an area not known previously to be endemic for kala-azar. Because of the civil war in southern Sudan no treatment was available locally and massive migration to northern Sudan occurred; many died on the way. All age groups were affected; there was a slight male preponderance (56%). In the clinical presentation, marked generalized lymphadenopathy was prominent (84%). Splenomegaly was absent in 4% of cases. Patients usually showed anaemia, leucopenia and/or thrombocytopenia. 623 patients were treated with sodium stibogluconate, 10 mg/kg for 30 d; relapse occurred in 4% and death in 12%. Latterly, 70 patients were treated with sodium stibogluconate at 2 x 10 mg/kg for 15 d, with relapse in 6% and death in 6%. The difference between the 2 regimens in the number of relapses and deaths was not significant. The outbreak may have been caused by a combination of factors: the introduction of the parasite from an endemic area to a non-immune population, the presence of malnutrition caused by loss of cattle and unavailability of other food sources, and possibly an ecological change in favour of the sandfly vector.

5 of 9

TI: Evaluation of efficacy of longer durations of therapy of fresh cases of kala-azar with sodium stibogluconate.
AU: Thakur-CP; Kumar-M; Pandey-AK
AD: Patna Medical College Hospital.
SO: Indian-J-Med-Res. 1991 Mar; 93: 103-10
AB: The efficacy and safety of three regimens of treatment for kala-azar (visceral leishmaniasis) with sodium stibogluconate were evaluated in a randomised clinical trial to ascertain the optimal duration of treatment for Indian patients. The study included a total of 312 (226 male, 86 female) patients with fresh kala-azar, confirmed by demonstration of parasites in aspirates from bone marrow or spleen, who were randomly allocated into three treatment groups of 104 patients in each to receive sodium stibogluconate intramuscularly. The dose of the drug was 20 mg/kg/body weight/daily with a maximum of 8.5 ml for 20, 30 and 40 days (groups A, B, C respectively). The response of treatment was assessed under blind conditions and patients were followed up each month for a period of six months. The number of patients who were apparently cured (i.e., those whose temperature had returned to normal at the end of their respective regimen and aspirates were free of parasites) was 91 (87%) in group A, 98 (94%) in group B, and 102 (98%) in group C. The difference between groups A and C was significant (P less than 0.01). The number of patients who were ultimately cured at six months was 74 (71%) in group A, 86 (83%) in group B and 98 (94%) in group C. These patients had not relapsed and were cured as confirmed by a bone marrow aspirate which was free of parasites. The difference between groups A and C (P less than 0.001) and groups B and C (P less than 0.05) were significant. However, the difference between groups A and B was not statistically significant.(ABSTRACT TRUNCATED AT 250 WORDS)

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TI: Serodiagnosis of Indian kala-azar: evaluation of IFA, ELISA and CIEP tests.
AU: Mittal-V; Bhatia-R; Sehgal-S
AD: National Reference Centre for Kala-azar, Zoonosis Division, National Institute of Communicable Diseases, Delhi, India.
SO: J-Commun-Dis. 1991 Jun; 23(2): 131-4
AB: The sensitivity and specificity of three serological tests viz. indirect immunofluorescent antibody test (IFAT), enzyme linked immunosorbent assay (ELISA) and counterimmunoelectrophoresis (CIEP) for the diagnosis of Indian kala-azar were evaluated. Of the 209 patients in whom Leishmania donovani parasite could be demonstrated in bone marrow, 207 (99.04 per cent) could be

diagnosed with IFAT, 203 (96.6 per cent) with CIEP and 208 (99.5 per cent) with ELISA. None of these serological tests was positive in 40 healthy individuals and 10 patients each with tuberculosis, toxoplasmosis and malaria. In only one out of 10 patients with malaria ELISA alone gave false positive result. Of the 119 patients who had clinical features simulating kala-azar but were negative for Leishmania donovani in bone marrow and responded to treatment other than that for Indian Kala-azar, IFAT, CIEP and ELISA were false positive in three (2.5 per cent), nil and three (2.5 per cent) cases, respectively. The use of serodiagnostic tests like ELISA for mass screening and CIEP in less well equipped peripheral laboratories is suggested.

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TI: Identification of immune complex antigens in sera of Indian kala-azar patients.
AU: Sanyal-T; Ghosh-DK; Sarkar-D
AD: Department of Cell Biology, Indian Institute of Chemical Biology, Calcutta.
SO: Indian-J-Exp-Biol. 1991 May; 29(5): 411-5
AB: Level of circulating immune complex (IC) in visceral leishmaniasis is much higher than that in control sera. In immunoblot experiment, treatment of kala-azar IC with patient sera showed at least 6 bands of which the band around 55 kDa region was most prominent. The band at 55 kDa is primarily due to the resence of an antigen recognized by its corresponding antibody present in the patient sera. This was confirmed by using radiolabelled antibody from kala-azar patient serum and antipromastigote serum. The heavy chain of IgG originating from IC is also present in the same region which was detected by its recognition with antihuman IgG. The IC gave a band at 55 kDa region with sea-urchin antitubulin. Kala-azar sera also reacted with purified rat brain tubulin. The present results suggest that a tubulin like protein is present at 55 kDa region along with the heavy chain of IgG.

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TI: [Transitory acute kidney insufficiency and insulin-dependent after treatment of kala-azar with pentamidine and N-methylglucamine antimony]
AU: Morin-D; Dumas-ML; Valette-H; Dumas-R
AD: Service de Pediatrie I, Hopital St-Charles, Montpellier.
SO: Arch-Fr-Pediatr. 1991 May; 48(5): 349-51
AB: Azotemia and diabetes mellitus are now well-known adverse reactions associated with Pentamidine treatment, especially since its prescription in case of Pneumocystis carinii pneumonia. We report the case of a 2 year-old boy, treated for kala-azar with pentamidine and N-methyl glucamine antimoniate who developed adverse effects, characterized by a nephrotic syndrome associated with the classic acute tubular necrosis, and transient diabetes mellitus.

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TI: [3 cases of visceral leishmaniasis, one in a HIV-positive man]
AU: Balslev-U; Jonsbo-F; Junge-J; Bentsen-KD
AD: Hvidovre Hospital, Kobenhavn.
SO: Ugeskr-Laeger. 1991 May 27; 153(22): 1591-2
AB: Three cases of visceral leishmaniasis (kala-azar) are presented. One of these was in a 43-year-old patient with AIDS who was infected in Southern Spain. Another was in a man aged 25 years infected in West Africa. These cases are the first two adults to be reported in Denmark. The third case was an 18 month old previously healthy boy, infected in Southern Spain. The symptomtology, diagnosis and treatment of the disease are discussed and it is stressed that serological diagnostic tests have limited value in HIV positive patients.

A kala-azar control programme for remote tribal communities

C.P. Thakur, Sister Frances, Sister Therese, Sister Victoria, & Sister Puspa

Indigenous people have been trained to provide a culturally appropriate kala-azar control programme for the tribal population of Sahibganj, Bihar, India. Cultural resistance to modern medicine has been overcome and the influence of village witch-doctors has been countered.

In the district of Sahibganj, Bihar, India there were 23 670 new cases of kala-azar between 1985 and 1990. Under the auspices of the Social Development Centre, Dumka, an emergency plan was drawn up to tackle this situation. Thirty village health workers attended a three-day training course during which they were taught how to administer sodium stibogluconate intramuscularly, spray DDT, conduct door-to-door surveys, and encourage affected persons to go to health centres. Six sisters attached to Christian missions were given a reorientation course in the control of the disease.

In remote and hilly tribal areas it is desirable to have carefully prepared educative, preventive and curative programmes in place, backed up by mobile hospitals carrying simple diagnostic and spraying equipment.

Awareness programmes

With the help of headmen, kala-azar awareness programmes were organized in villages. Information on the importance, treatment and control of the disease was imparted in the local language. Publicity materials were supplied by the government. It was explained to the villagers that the disease could not be controlled by witch-doctors, and that spraying the insides of houses was vitally important. Only after an awareness programme had been undertaken were control measures applied in any particular village. It was found that such programmes had to be repeated from time to time in order to renew the confidence of the people in the measures adopted.

Spraying with DDT

Following an investigation by entomologists into sandfly prevalence and the susceptibility of the vectors to DDT, the insecticide was

Thakur is Emeritus Professor of Medicine, Patna Medical College; his address is Fraser Road, Patna-800001, India. Sisters Frances, Therese, Victoria and Puspa are with the Holy Cross Health Centre, Sita Panar, Sahibganj, India.

sprayed during January/February and May/June on the inner walls of houses and covered cowsheds up to a height of about two metres at 1 g/m^2, using approximately 1.4 kg DDT per 14 litres of water. The numbers of kala-azar and malaria cases were estimated before and after intensive spraying was conducted in several remote villages.

Treatment

A survey was conducted in order to discover persons who had been suffering from fever for more than three weeks and they were persuaded to attend the health centres for further investigation. In each such case, total and differential counts of white blood cells were made, the haemoglobin concentration was measured, the aldehyde test was performed, and thick and thin blood smears were prepared for the detection of malaria parasites.

If the aldehyde test proved positive, treatment for kala-azar was initiated. Sodium stibogluconate was given intramuscularly at 20 mg per kg body weight daily for 20 days in new cases and for 40 days in relapsed patients, with a maximum of of 850 mg. Following diagnosis and the start of treatment at the centres, treatment in the villages was carried out by village health workers, who were requested to ensure

It was explained to the villagers that the disease could not be controlled by witch-doctors, and that spraying the insides of houses was vitally important.

that people newly diagnosed as having kala-azar took 20 injections of the drug and that relapsed cases took 40 injections.

Patients who failed to respond to the 20-day course of treatment were categorized as cases of primary unresponsiveness. Clinical cure was considered to have been achieved if patients became afebrile and their spleens returned to normal size. If no relapse occurred in the following six months the patients were regarded as having been definitively cured.

At the Sohorghati, Kundly, Sahibganj and Sita Pahar centres there were respectively one, one, one and three sisters and two, four, 20 and eight village health workers, and the patients with kala-azar who were treated numbered 191, 84, 403 and 962 respectively. Of the 1640 treated patients, 1592 were cured, and of the 48 patients who relapsed and were treated again with a 40-day course of sodium stibogluconate, eight relapsed a second time. Forty-four patients became unresponsive to sodium stibogluconate and were sent to hospitals for treatment.

Spraying presented difficult problems in remote areas, particularly where the equipment had to be carried by hand for long distances. Without great dedication on the part of local workers it would have been impossible to achieve the desired coverage.

The spraying operations, performed by the village health workers and supervised by the sisters, reduced the incidence of kala-azar and malaria in three villages where monitoring was carried out; increased numbers of cases were recorded in one village, perhaps because heightened awareness resulted in more people going to their health centre for treatment. Strict supervision was the key to the success of the spraying programme.

The ratio of male to female patients was 1.2 to 1, whereas in a hospital-based study a ratio of 2 to 1 had been reported, possibly indicating

tendency to refer males rather than females to hospital when the condition of patients becomes serious. People with kala-azar responded better to drug treatment in newly affected areas than in areas where the disease first appeared in the early 1970s, perhaps because inadequate doses of the drug had been used in the latter areas, giving rise to resistance.

Clearly, when plans are being drawn up for the control of kala-azar it is important to take local circumstances into account. In remote and hilly tribal areas it is desirable to have carefully prepared educative, preventive and curative programmes in place, backed up by mobile hospitals carrying simple diagnostic and spraying equipment. ■

Importance of the blood supply

Without blood transfusion, the treatment of severe haemorrhage is difficult or impossible and many surgical procedures cannot be safely attempted. Haematological conditions such as thalassaemia, haemophilia, leukaemia, and aplastic anaemia cannot be treated effectively without support from the blood transfusion service. No general hospital can be effective unless it can perform blood transfusion, and if blood is not available from an outside source, the hospital itself is obliged to undertake the task of blood collection.

The recruitment and selection of blood donors are critical to the success of a blood programme, and every effort must be made to ensure both the safety of the donor and the safety of the transfusion for the recipient. The process of donor selection is reliable only when information provided by donors can be trusted, and experience has shown that this is most likely when there is no material gain from donation. Problems in donor selection are considerably reduced when a blood transfusion service is founded upon the principle of voluntary, unpaid blood donation.

■ W. N. Gibbs & A. F. H. Britten, ed. *Guidelines for the organization of a blood transfusion service*. Geneva, World Health Organization, 1992: 1.

DIS-1

KALA-AZAR CONQURED !

By

E Varghese SVD[1], PP Hembrom, PV Raj, S Melookunnel & R Tiwary

I.1 INTRODUCTION

Leishmaniasis or *Kala-azar* (as popularly called in India - KA) is considered as one of the six dreaded tropical diseases of human beings by WHO. In its briefing on *Leishmaniasis* published in 1991 WHO listed 83 countries as affected by *Leishmaniasis*. A Briton, Dr. Lainson reported in 1983 (Indo-UK Workshop on Leishmaniasis) that KA is major public health problem faced by the tropical world. He said there are about 4 lakhs (400,000) new cases of *Leishmaniasis* registered each year in the world.

I.2. KA INCIDENCE IN INDIA

In India KA has been occurring in endemic (restricted to certain pockets only), epidemic (seasonal like cholera or gastro-enteritis) and sporadic (sudden outbreak) forms since long. It was reported for the first time in 1824-25 in Jessore (West Bengal) by Dr. Elliot. Later between 1854-75 the fever in Burdwan district of West Bengal and the epidemic fever in Garo Hills in 1870 was described as KA by Dr. Clark in his sanitary report. First epidemic of KA in Bihar occurred in 1882 and after that a gap of about 10 years the epidemic struck in 1891, 1917, 1933. Because of the rising menace of the KA in Bihar, the Government of India constituted an expert committee under the Chairmanship of Dr. Harcharan Singh in 1985, which recommended urgent setting up of a National KA Control Programme. But nothing came of it. If one goes by the reports and the data from the field study KA is ever on the increase, particularly in Bihar. Not even one third of the cases get reported; because, very few patients come to the centres for treatment owing to the distance, high cost of treatment, travel and other expenses; lack of proper information and utter poverty.

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[1] Institute of Indian Culture, Mahakali Road, Andheri East, Mumbai 400093 India

The eastern belt of the country, specially Bihar is the worst hit by KA followed by West Bengal and Uttar Pradesh. Dr. C P Thakur (Patna) reported that there were over 250,000 cases in Bihar in 1991-92. Muzaffarpur, Darbanga, Vaishali, Samastipur, West Champaran, Sahibganj, Pakur, Godda and Dumka, are some of the worst hit of the 33 affected districts in Bihar. In West Bengal in 1949 there were 35,147 reported cases, which in 1964 came down to 804. But in 1982 it was 979 from Malda, Murshidabad and 24-Parganas alone, showing an upward trend reported Dr. Chowdhury of Rajendra Memorial Research Institute (RMRI, Patna). An enquiry at the dispensaries that treat KA in Hiranpur, Sitapahr, and Soharghatty, has shown that when Soharghatty had 720 KA patients, Sitapahar had 1112 and Hiranpur NSM outpost had 175 cases treated in 1996. Sonadani and Magbita villages in Littipara block (Pakur district) have 110 KA positive cases out of 700 population, i.e. over 15 per cent people of this area are KA affected reported Dr. Chandrashekhar, Director of Navjeevan Seva Mandal (NSM).

I.2. THE PARASITE

Leishmaniasis is caused by *Leishmania donovani* (named after William Leishman and Charles Donovan (1903) and oriental sore by *L. tropica*. Species and sub-species of the genus *Leishmania* are parasitic protozoa, related to the *Trypanosomes*. They are digenetic parasites, completing life cycle in two different hosts - mammals and phlebotomie sand flies. There is no conclusive evidence of a sexual cycle in the life history of *Leishmania*, which appears to divide only by simple binary fission in both the vertebrate and invertebrate hosts. In the vertebrate host it occurs in the amastigote form. Spread of the infection in the host may occur when infected macrophages divide and share their parasite among the daughter cells, or on the heavily infected cells and the ingestion of the liberated amasitgotes from the macrophages by the vectors. The incubation period in the vertebrates varies from few weeks to months. Since KA is an immunosupprassant disease the patient is exposed to secondary infections like tuberculosis. And since the parasite is intracellular unresponsiveness to drug therapy is frequent.

I.3. VECTOR

Phlebotomine sand flies of *Phlebotomus* and *Sergentomyia* genus is the vector. *Phlebotomus argentipes* is found in cowsheds and mud walls of thatched houses. July-November is the time they are found in abundance. During this time about 81 percent of flies caught were KA positive reported Dr. Hati, of RMRI, Patna. They usually breed in damp and dark places where the dead organic matter is available. RMRI, Patna, recommends the use of mud and lime plaster for an effective ecological approach to vector control, in the case of sand flies, particularly as *Phlebotomus argentipes* and *P. papatasi* are growing DDT resistant.

I. 4. SYMPTOMS & STRAINS

Anaemia, anorexia, cough, dry and rough skin, fever, hyperipigmentation of skin, jaundice (in some cases) loose motion, loss of weight, swelling feet, hepato and spleenomegaly, sparse and brittle hair, etc. are some of the common symptoms of KA. It can be classified into visceral form and cutaneous form. *Visceral Leishmaniasis* includes Indian KA, African and Mediterranean KA. The *oriental sore, espundia* and *post Kala-azar dermal leishmaniasis* (PKDL) group under the cutaneous form. According to Locksley there are four major clinical syndromes in this, viz. *Visceral Leishmaniasis, cutaneous Leishmaniasis* of the old and new worlds, *mucutaneous leishmaniasis* (espundia) and *diffuse cutaneous leishmaniasis.* This project was primarily concerned with the treatment of *visceral leishmaniasis* only.

I.5. TREATMENT

Researchers say that while Malaria has only 4 major human strains, KA has at least 19 different strains associated with human infection. Added to this, impaired immune system of the host in *visceral leishmaniasis,* doctors opine, is one of the main causes of unsatisfactory chemotherapy. There have been attempts at developing a vaccine since a few years. But no definite result has been reported yet. Following are the frequently used KA remedies:

1. Sodium Stibo-Gluconate (SSG) or **Sodium Antimony Gluconate (SAG)**: First line drug and the drug of choice in KA treatment. Dosage: daily injection of 20 mg/kg/bw for a period 20-40 days. Dr. C.P. Thakur and others advise longer duration SSG / SAG therapy for fresh cases.).
2. **SSG** is the drug of choice in PKDL as well.
3. Pentamidine : Could be used in resistant or relapse cases of KA. Dosage: 4 mg/kg/bw intravenously for 35 days. Drug causes diabetes mellitus.
4. Amphotericine B : It is a potent drug associated with severe toxicity. Duration of treatment with this drug is 45 days. It is usually given on a gradually increasing dosage starting with 0.05 mg/kg/bw to 1 mg from 1-5th day. From the sixth day the injection is on alternate days a 1 mg/kg / bw. Rigor, shivering and fever are manifested during the treatment. This drug is to be administered in hospitals with revival facilities only.

Allopurinol, metronidazole, keto-conazole, 8-aminoquinalone, miltoforine, etc. are some of the oral drugs for KA. KA patients, once cured, are immune to the viscerotropic form of *L. donovani*. But there is apparently reported cadriotoxicity in cases of KA undergoing antimony therapy.

I.6. RATIONALE BEHIND THE CHAI INITIATIVE

All the above mentioned remedies have severe reactions and toxicity. Besides, since the most affected people are illiterate, poor and are largely subsistence labourers and cultivators they cannot afford to go to the nearby dispensaries and hospitals (which are 2-20 km away) daily to get the injection. Nor can they afford to pay. Of course the government has been trying to provide SSG / SAG free of cost through selected outlets monitored by the Civil Surgeon. But mostly the supply is irregular and such dispensing centres are far too few for the vast number of people affected. So, for these various reasons most of them would not complete the prescribed course. This necessitated the search for a viable, cheap and locally available alternative. So the CHAI constituted a project team comprising of Fr. Meloo SJ (Co-ordinator), Dr. E. Varghese SVD (Principal Investigator) Dr. PP Hembrom (Indigenous Practitioner), Dr. PV Raj (Professor and Head of the Department of Kayachikitsa, Ayurveda College, Hyderabad, Honorary Co-PI, and

Consultant), Dr. Rajender Tiwary (Supervising Medical Officer - ayurveda) and other local co-ordinators and supervisors for running a pilot project on treatment for KA with herbal medicine. The team improved on the basic formulation of Dr. PP Hembrom and other local practitioners who claim to have had success in treating the KA cases, and made a herbo-mineral formulation.

I. 7. IMPLEMENTATION

Having already ascertained the need for such an initiative through the member institutions of CHAI serving in the affected areas it entrusted the work of the project to constituted expert team. The team did extensive literature survey and background study, consulting prominent researchers like Dr. C.P. Thakur, Patna, and A. Nandy, Calcutta, before launching the project. Culture tests were also conducted with the medicine on the parasite culture.

It then set up a local Ethical Committee, comprising the Village Headman of Satia village (Pakur), a practising lawyer, five prominent persons from the locality, under the auspices of CHAI, a registered Trust. The committee studied the project proposal well and gave the assent to proceed, considering the benefit and the least risk involved in this. Nodal agencies were intimated regarding this pilot project, which of course is not required for using a known drug under the direct supervision of a registered ayurvedic medical practitioner.

A sample of 49 patients were selected at five centres, namely Chandnahat and Damuruhat (Godda district), Kodma and Sitapahar (Sahibganj district) and Soharghati (Pakur district). The probable patients were screned and selected at these centres as and when patients came in on their own, by the attending physicians, after obtaining the informed consent and fulfilled other WHO recommendations in pilot projects. KA suspected patients were sent to the nearby hospitals for laboratory investigations. Those who exhibited the usual clinical symptoms and tested KA positive in Aldehyde test and DAT, with high ESR were sent for bone marrow smear test. Those tested KA positive in all these tests were administered the medicine prepared under the direct supervision of the project team. Each patient was

monitored and case history and charts on them were maintained at each dispensing centre. After completing the stipulated course aldehyde test and blood tests were done, besides noting the improvement in the general condition and the clinical symptoms noted earlier. Those with no fever, no hepato/spleenomegaly, normal blood count, and negative aldehyde, and in some cases bone marrow smear test , and were considered cured.

II.a. HERBO-MINERAL FORMULATION

Number	Botanical Name	Skt / Hindi Name	Part Used
1	*Boerhaavia diffusa*	*Punarnava* *Beshakapore*	Root
2	*Plumbago zeylanica*	*Chitraka* *Chitrak*	Root
3	*Vitex peduncularis*	*Nagbail* *Charaigorwa*	Bark

PREPARATION:

Treat the finely cut pieces of *Plumbago* roots in lime water for about two hours to purify it before putting it into the mixture. Make decoction of the above medicines taken in 1: 1/2 : 1 proportion and finely cut in 16 parts of water and boil down to half on slow fire. After sieving the decoction add 10 g of *Woodfordia fruticosa* flower powder, 1 g of pepper powder and 50 g of jaggery for 1 litre decotion as preservative. Warm it up again for some time, cool it and bottle it.

DOSAGE:

25 ml x twice daily x 45 days. For children give 15 ml instead of 25 ml.

To activate the medicine each patient is given 125 mg of *Triphala-Mandoor* powder once daily.

Triphala-Mandoor Preparation :

Phyllanthus emblica fruit powder 1 part

Terminalia bellirica seed powder 1/2 part

Terminalia chebula seed powder ½ part

Add 10 g of *Mandoor rasa* to 100 g of the above mixture to make the *triphala mandoor* mixture.

III. RESULT

In all 49 patients took the treatment (Cahndnahat : 15; Damruhat : 3; Kodma : 8; Sitapahr: 14; and Soharghatti : 9). Of these 32 completed the course and 26 had positive resluts, meaning healed or nearly healed. Those who were not healed or those during the course of treatment wanted to switch over to allopathic treatment for whatever reasons, were given free stibnite treatment. Given below is the patient list from the 5 centres who underwent the treatment:

PRE-TREATMENT RECORD (Chandnahat Centre)

Name of patient	Sex	Age	Weight	Village	Remark
1. Agnes Tudu	F	18	42 kg.	Chandana	New Case
2. Babudahan Soren	M	32	35	Langodi	New Case
3. Barka Hansdak	M	16	34	Dumerthari	New Case
4. Berna Hembrom	F	40	44	Chandana	New Case
5. Budhrai Tudu	M	40	44	Sagor	Relapse Case
6. Choto Hansda	M	10	21	Sagor	New Case
7. Chunde Soren	M	40	41	Mohanpur	Relapse Case
8. Marcella Hembrom	F	35	42	Chandna	New Case
9. Rama Paharia	M	10	24	Jolo	New Case
10. Sahal Kisku	M	18	26	Sindri	New Case
11. Saiba Tudu	F	45	43	Borwa	New Case
12. Salomi Murmu	F	35	40	Borwa	New Case
13. Sarojini Murmu	F	27	40	Langodi	New Case
14. Sonoti Hansda	F	12	20	Borwa	New Case
15. Suleman Murmu	M	35	40	Sagor	New Case

No	Fev.	Spl.	Liv	TC	Hb	ESR	Alde	DAT	BM	Wt	Date

1	102	4"	NP	3800	9.2	116	+	-	+	42	070597
2	103	5"	NP	-	-	-	4+	-	-	35	100197
3	104	5"	NP	-	-	-	4+	-	-	30	030397
4	101	4"	NP	-	-	-	4+	-	-	35	230397
5	104	5"	NP	-	-	-	4+	-	4+	44	250497
6	104	5"	NP	2500	7	150	4+	-	4+	21	020497
7	102	5"	NP	-	-	-	4+	-	-	41	161296
8	104	3"	NP	-	-	-	4+	-	-	42	030297
9	103	3"	NP	-	-	-	4+	-	-	24	100397
10	104	5"	NP	-	-	-	+	-	+	26	040497
11	104	4"	NP	-	-	-	4+	-	-	43	030197
12	102	5"	NP	-	-	-	4+	-	-	40	281296
13	102	5"	NP	-	-	-	4+	-	+	40	171096
14	103	4"	NP	4000	5.2	120	4+	-	4+	27	030597
15	104	4"	NP	-	-	-	4+	-	-	40	251096

POST-TREATMENT REPORT (Chandanahat)

No	Fev	Spl	Liv.	TC	Hb	ESR	Alde	DAT	BM	Wt	Date	Rem
1	99	1"	NP	4200	9.2	65	Neg.	-	Neg.	45	240697	good
2	98.8	NP	NP	-	-	-	Neg.	-	-	39	280297	good
3	98.6	NP	NP	-	-	-	Neg.	-	-	32	200497	OK
4	98.2	NP	NP	-	-	-	Neg.	-	-	36	100597	good
5	99	1"	NP	-	-	-	Neg.	-	Neg.	47	090697	good
6	98.6	3"	NP	3500	7	100	Neg.	-	+	23	140797	OK
7	98.2	NP	NP	-	-	-	Neg.	-	Neg.	43	080297	OK
8	99.6	1"	NP		-	-	+	-	-	42	200397	impr
9	99	NP	NP	-	-	-	Neg.	-	-	26	050597	OK
10	99.2	2"	NP	-	-	-	Neg.	-	-	28	200597	OK
11	98.8	2"	NP	-	-	-	Neg.	-	-	45	200297	OK
12	98.2	NP	NP	-	-	-	Neg.	-	-	42	090297	OK

13	98.4	NP	NP	-	-	-	Neg.	-	-	42	160197	good
14	98.6	2"	NP	4300	6	120	Neg.	-	+	28.5	150797	impr
15	98.8	1"	NP	-	-	-	Neg.	-	-	43	080297	OK

PRE-TREATMENT RECORD (Damruhat Centre)

16. Baju Marandi	M	20	38 kg.	Pottamdi	New Case
17. Bernabas Hembrom	M	24	39	Kondapur	New Case
18. Ramchoran Soren	M	30	45	Titria	New Case

No	Fev.	Spl.	Liv.	TC	Hb	ESR	Alde	DAT	BM	Wt	Date
16	99	3"	NP	5300	8	150	4+	-	+	38	081096
17	irreg	2"	NP	9300	11	85	4+	-	+	40	211096
18	102	2"	NP	1020	8	160	4+	-	+	45	091096

POST-TREATMENT RECORD (Damruhat)

No	Fev	Spl	Liv	TC	Hb	ESR	Alde	DAT	BM	Wt	Date	Rem
16	98.4	NP	NP	5300	8.6	20	Neg.	-	-	42	251196	good
17	98.2	1"	NP	9300	11	40	Neg.	-	Neg.	40	121296	OK
18	98.6	NP	NP	6800	8	66	Neg.	-	Neg.	46	261196	good

PRE-TREATMENT RECORD (Kodma Centre)

19. Chundka Hembrom	M	25	41 kg.	Mysol	Relapse Case
20. Chundkae Basky	M	7	14	Bethany	New Case
21. Gabriel Tudu	M	50	45	Kodma	Relapse Case
22. Matti Horon	M	8	24	Kodma	New Case
23. Mongol Hembrom	M	18	35	Kodma	New Case
24. Sumi Tudu	F	12	26	Titalia	Relapse Case
25. Tala Besra	M	8	24	Pakaria	Relapse Case
26. Teresa Besra	F	30	41	Banghi	New Case

No	Fev	Spl	Liv	TC	Hb	ESR	Alde	DAT	BM	Wt	Date

19	irreg	NP	NP	-	8.6	60	4+	+	2+	41	101196
20	,,	4"	1"	-	7	68	4+	+	4+	14	101196
21	102	2"	NP	3900	5.5	45	4+	+	4+	45	290497
22	103	3"	NP	5400	6	68	4+	+	2+	24	060597
23	102	5"	2"	3050	5.2	34	4+	+	2+	35	080597
24	98.4	4"	NP	-	-	-	4+	+	+	26	131196
25	98.8	6"	NP	2750	7.2	80	4+	+	+	24	071196
26	103	4"	NP	2200	5.6	33	+	+	+	41	071196

POST-TREATMENT RECORD (Kodma)

No	Fev	Spl	Liv	TC	Hb	ESR	Alde	DAT	BM	Wt	Date	Rem
19	98.6	NP	NP	-	8.6	6	Neg	Neg.	Neg.	43	281296	good
20	98.2	NP	NP	-	7	16	Neg.	Neg.	Neg.	15	281296	OK
21	98	NP	NP	RA	RA	RA	Neg.	RA	RA	RA	150697	-
22	98.6	NP	NP	RA	RA	RA	Neg.	RA	RA	RA	230697	-
23	98	NP	NP	RA	RA	RA	Neg.	RA	RA	RA	250697	-
24	98	1"	NP	-	-	-	Neg.	-	-	28	150197	OK
25	98.4	2"	NP	-	-	-	Neg.	-	-	27	221296	OK
26	98.2	NP	NP	-	-	-	Neg.	-	-	42	221296	OK

PRE-TREATMENT RECORD (Sitapahar Centre)

27. Abdul Hamid	M	8	16 kg	Borio	Relapse Case
28. Ajnara Khatoon	F	6	12	Udhwa	New Case
29. Bale Hembrom	F	25	33	Barhait	New Case
30. Baso Soren	M	7	19	Dabdiha	New Case
31. Chundby Marandi	F	22	35	Barhait	New Case
32. Clement Kisku	M	10	24	Talbaria	New Case
33. Jetha Hansdak	M	50	48	Satia	Relapse Case
34. Lundhya Besra	M	8	15	Shardharia	New Case

35. Munijan Maria	F	20	44	Denja	New Case		
36. Paruei Khatoon	F	8	16	Jamnagar	New Case		
37. Simon Malto	M	40	46	Ambarpara	New Case		
38. Sukha Khatoon	F	12	32	Bhaia	New Case		
39. Surdhani Hembrom	F	26	25	Sabdrka	New Case		
40. Susani Murmu	M	8	19	Sarmapur	Relapse Case		

No	Fev	Spl	Liv	TC	Hb	ESR	Alde	DAT	BM	Wt	Date
27	100	2"	1"	-	-	-	4+	-	-	16	111096
28	99.6	5"	1"	-	-	-	4+	-	+	12	161096
29	98.6	4"	NP	-	-	60	4+	-	4+	33	181096
30	101	5"	NP	-	10	135	4+	-	3+	19	181096
31	99.2	3"	NP	-	-	-	4+		-	35	271196
32	101	2"	NP	-	12.3	95	4+	-	+	24	111096
33	102	4"	NP	3800	6.2	145	4+	-	4+	48	091096
34	irreg	2"	NP	-	-	-	4+	-	+	15	091096
35	99	3"	NP	-	-	-	4+	-	-	20	041096
36	102	2"	NP	-	-	-	4+	-	-	16	181096
37	99	7"	NP	-	-	-	4+	-	+	46	271196
38	irreg	5"	NP	-	-	-	4+	-	-	31	181096
39	102	4"	NP	-	-	-	4+	-	-	28	111096
40	101	6"	3"	-	8	155	4+	-	4+	19	271196

POST-TREATMENT RECORD (Sitapahar)

No	Fev	Spl	Liv	TC	ESR	Alde	DAT	BM	Wt	Date	Rem.
27	99	2"	NP	-	-	2+	-	-	16	301096	Dis
28	98.8	3"	1"	-	-	+	-	-	14	161196	Dis
29	98.4	4"	NP	-	-	+	-	-	33	181196	Dis
30	98	3"	NP	-	135	Neg.	-	+	18	231296	Dis
31	98.4	1"	NP	-	-	+	-	-	36	271296	Neg.
32	98	NP	NP	-	50	Neg.	-	-	26	161296	good

33	-	-	-	-	-	-	-	-	-	231096	Dis
34	-	2"	NP	-	-	-	-	-	-	241096	Dis
35	98.4	2"	NP	-		Neg.	-	-	46	151196	OK
36	-	2"	NP	-	-	+	-	-	16	181196	Dis
37	98.6	4"	NP	-	85	Neg.	-	Neg.	48	240197	OK
38	98.6	4"	NP	-	-	+	-	-	34	161296	Neg
39	98.8	3"	NP	-	-	+	-	-	28	091196	Dis
40	98	-	-	-	-	-	-	-	-	141296	Dis

PRE-TREATMENT RCORD (Sohaghati)

41. Charles Soren	M	30	49 kg	Amrapara	Relapse case
42. Lukiram Hembrom	M	42	44	Rodgu	Relapse case
43. Manu Giri	M	35	40	Sindrigola	New Case
44. Pargana Murmu	F	30	43	Perak	Relapse Case
45. Ponera Murmu	F	20	33	Amrapara	Relapse Case
46. Rahim Mia	M	35	-	Dengdia	Relapse Case
47. Raju Hansdak	M	40	41	Surejbera	New Case
48. Rani Marandi	F	22	38	Soharghatty	Relapse Case
49. Solet Soren	M	36	-	Margaboni	Relapse Case

NO	FEV	SPL	LIV	TC	Hb	ESR	Alde	DAT	BM	Wt	Date
41	102	4"	NP	1100	7.2	138	4+	-	+	49	311296
42	101	8"	NP	2450	6	120	4+	-	2+	42	281096
43	irreg	2"	NP	-	-	-	4+	-	-	35	211196
44	98.5	6"	2"	2600	7	75	4+	-	4+	43	211096
45	100	8"	NP	-	-	-	4+	-	-	33	021296
46	101	6"	NP	-	6	130	4+	-	4+	40	281096
47	99.8	8"	NP	-	-	-	4+	-	-	41	271196
48	100	10"	NP	1150	5.4	155	4+	-	4+	38	041096
49	102	7"	NP	4600	6	120	4+	-	4+	41	091196

POST TREATMENT RECORD (Sohaghati)

POST-TREATMENT RECORD (Soharghati)

NO	FEV	SPL	LIV	TC	Hb	ESR	Alde	DAT	BM	Wt	Date	Rem
41	99	4"	NP	-	-	-	-	-	-	49	200197	Dis
42	98.8	4"	NP	-	-	-	Neg.	-	-	45	301296	Neg
43	98.6	2"	NP	-	-	-	-	-	-	-	-	Dis
44	98.4	4"	NP	-	-	-	-	-	-	-	251196	Dis
45	99	5"	NP	-	-	-	-	-	-	35	270197	Neg
46	98.6	3"	NP	-	-	-	-	-	-	-	111296	Neg
47	98.6	6"	NP	-	-	-	-	-	-	42	030197	Neg
48	98.4	7"	NP	-	-	-	-	-	-	38	111296	Dis
49	99	5"	NP	-	-	-	-	-	-	41	111296	Dis

IV DISCUSSION

As this was basically a patient-oriented project to popularise natural medicines under normal living conditions the patients were allowed to be on their own. This had some negative influence on the proper running of the project. Many discontinued the medicine after the initial relief, and some others were unhappy about the slow improvement, etc. Of the 49 patients who started taking the decoction only 32 completed the course. Reasons for this large number of drop outs, in addition to the above mentioned reasons, is that despite the best efforts to follow up each patient, because of difficult terrain, long distance and other logistic hurdles kept the patients away from the supervisors and the health workers sent to follow them up.

In spite of the best efforts possible in the given circumstances the result has not been upto the expectations, particularly in getting the follow-up tests done for the patients who completed the course, and in getting all the prescribed laboratory tests done on each of the selected patients. There are several reasons for this lapse - 1. DAT test was available only in Taljhari, which is close to Kodma (while all other centres are far away from Taljhari, the farthest being 150 km away. So getting the technicians to collect the sample, sending someone to get the results, etc. was not practical, as in many centres there were no organised camps to screen patients and even the screened patients had to be taken to the

nearest hospitals for other tests. So except in Kodma the DAT test was not taken, despite the standing instructions to take DAT. 2. Bone Marrow extraction is a very painful procedure which many patients refused to undergo. So only 30 patients underwent BM test before the commencement of the treatment and 13 after the course was completed. 3. Another major problem involved in this pilot project was that the centres selected were very far from each other so even for the local co-ordinator to visit all the centres usually took 3-4 days. Secondly the commitment, understanding and availability of each local team member and the supervising staff in different centres varied, consequent to which some centres had near 100 percent positive turn out and some centres near 100 percent negative results. 4. From the patients part, lack of education, various socio-economic considerations, distance, and poor health consciousness deterred them from completing the prescribed course, reporting periodically, and doing the required pre and post treatment tests. Most patients who dropped out after 20-30 days of treatment went away for lack of speedy recovery, others fell off because the recovery was satisfactory and they regained the 'normal health' which enabled them to work and earn their livelihood. Though the supervising team sent health workers periodically to follow these patients up, most of them were not available at their homes - some on visits, others in the markets, yet others in the fields or forests! Because of these in many cases a second or third visit yielded no result, and a reminder to report to the respective dispensing centres only met with negative compliance Though these were facts known right from the beginning the team kept on, for the simple reason that we are trying to popularise a medicine which has to be taken in the most natural and ordinary life-situations of the patients. 5. Since many of the local supervisors and health workers, though technically competent and very committed and promised full co-operation, were grass-roots level workers, whose only concern is to promote healing, health and well-being, for some of them the conforming the project methods and procedures to the exact technical prescription was not a priority. From this backdrop, the result of this pilot project has been very encouraging and praiseworthy.

26 of those who completed the prescribed course got rather completely cured (those with remark 'good') or there is remarkable progress in their over all well being and the clinical symptoms having disappeared or nearly disappeared (those with the 'OK' remark). They

are still being followed up and even after five months of stopping the medicine no symptoms recurred. All of them have improved health and are leading normal life. Of the six negative results, 2 are suspected tuberculosis cases (one show KA negative, except for spleenomegaly and slight fever. The others too may have other health problems which need to be treated.

Among the 49 patients 16 were relapse cases and others were fresh cases. Even in allopathic treatment there are several instances where even after 45 injection the spleen remain palpable. With 26 people getting cured and the culture test showing that the medicine kills the KA parasites, it is ample enough to contend that this formulation is effective to treat *visceral Leishmaniasis / KA*. But a more systematic research from the Allopathic stream fulfilling the ICMR prescriptions would be highly advisable to get wider acceptability and proper recognition for this new formulation.

ABBREVIATIONS USED:

Alde: Aldehyde Test, + : Positive, BM: Bone Marrow, Cox: Tuberculosis, DAT: Direct Agglutination Test, Dis: Discontinued, ESR: Erythrocyte Sedimentation Rate, Fev: Fever, Hb: Haemoglobin, Impr: Improving (Report Awaited), Irreg: Irregular, Liv: Liver, Neg: Negative, NP: Not Palpable, OK: Satisfactory, RA: Report Awaited, Rem: Remark, Spl: Spleen, TC: Total Cell Count, Wt: Weight

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Kala-azar Research
Report Update:

Dr. E. Varghese SVD

This is a pilot project run by the Catholic Health Association of India, an NGO working since last 54 years in the health sector, and monitored by Dr. E. Varghese SVD (Principal Investigator) and his team for the benefit of the most neglected and suffering people affected by Kala-azar (visceral leishmaniasis), a dreaded disease. This disease has had only antimony compounds as the main remedy, which is not available to patients as and when they need it. Since there are several effective herbs that heal many diseases CHAI constituted a team of experts (Ayurveda doctors, traditional healers and ethnobotanists) to study the literature and local health traditions and come up with a viable formulation for KA. Having done extensive literature survey and survey of the local health traditions the team headed by Dr. E. Varghese under the expert advice of Dr. PV Raj (Professor of Ayurveda) and Dr. P. . Hembrom (Traditional practitioner, whose original formulation was improved upon) and Dr. Rajender Tiwari (Local Supervisor) came up with the above mentioned formulation.

The team briefed the Ethical Committee appointed by CHAI (constituted of legal and medical experts, local Sarpanch, and leaders from various fields in the locality, in all seven of them) of the benefits and the zero risk factor in administering the medicine and appraised the Committee of the probable benefit which is much beneficial to the local people. After considering the various aspects of the expertise and the credentials of project team, their ability to conduct such a project, the logistics, and benefits of such a break through the Ethical Committee at its meeting held on 25 08 1996 at Paharia Samaj Seva Office, Sat Village, Pakur Dt, Bihar, approved the project and gave its approval to go ahead with it.

Accordingly five dispensing centres were selected and through each of these centres patients were screened and sample selected. Allopathic doctors did the screening of patients and the suspected cases were sent for pathological investigations. Those turned positive in the investigations, especially in Aldehyde test, and bone marrow smear test, and those exhibiting the clinical symptoms were posted for treatment. The local team under the supervision of Dr. Rajender Twari a practising Ayurvedic doctor, and qualified nurses at each centre regularly monitored the patients with the progress, charting the observations periodically. The patients thus selected were given medicine for one week and were allowed to go home and be in natural conditions.

49 patients who turned out to be KA positive were administered the medicine. Of them 32 completed the course prescribed (for 45 days). Of them 26 got cured with no relapse till to-date. Those who were willing to go for a second round of confirmatory tests for cure were sent. Others were certified by the doctors as healed for absence of relevant clinical symptoms and pronounced improvement in health and physique.

In its second sitting to evaluate the progress of the project the, on Feb. 08. 1997, the Ethical Committee was briefed with the progress by the Principal Investigator and the team. Having learned that 16 people got cured well and desirous to learn the actual effect of the medicine standardise the course the Ethical Committee suggested for a controlled group of 10 patients to be taken at two centres, Chandanahat Dispensary and Kodma Dispensary. And continue the treatment. Second phase accordingly commenced by March 1997 and was concluded in July 1997. But due to slow inflow of patients and accident of the local co-ordinator (Sebastian Tudu SJ, Director, Paharia Samaj Seva Samiti, Sat) the second phase did not progress as well as expected Hence the results of the second phase is also incorporated with the original reports. Only six patients were treated. And each of them was to be sent for pathological tests 1-2 months after the completion of the prescribed course; the reports of which are awaited.

In the meanwhile the medicine was culture tested by scientists at the School of Tropical Medicine, Calcutta; which showed that the medicine kills the KA parasite. Scientists at the said School are willing to do a thorough research on KA with this formulation following the prescription of the ICMR and apply for a research project from the ICMR in this regard. Presently the medicine is being widely used by patients in the affected areas.

A short paper with the result-up-to-date was presented at the 5th International Conference on Natural Medicines, held at Sri Venkateshwara University, Tirupati, on March 16 1997, by the Principal Investigator, Dr. E. Varghese SVD. Research Paper on this is accepted for publication by Ethnobotany, popular articles on this finding have been published in Health Action, and other vernacular periodicals.

Dr. E. Varghese (PI) and Dr. PP Hembrom (Horopathy Consultant) presented the progress and the details of the research a meeting of the co-ordinating committee (represented by Fr. S. Melookunnel and Sr. Usha) with the Director- Fr. James Culas, Asst. Director - Sr. Ancy of CHAI, President of the Bihar Unitof CHAI - Sr. Prabha, Medical Advisor to CHAI - Dr. C.M.Francis on Oct.30 97. During which it was decided to apply for patent, and licence the medicine; to seek competent personnel to take up a follow up research from the allopathic stream and to seek funds for that from various agencies. CDRI (Lucknow) and CSTM (Calcutta) were suggested to be competent agencies to take up the research. Dr. C.M Francis and Dr. E. Varghese were requested to approach these institutions to explore the possibility of either of them taking it up.

Sincerely Yours,

Dr. E. Varghese SVD

Principal Investigator

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20

Exercise and Coronary Artery Disease

Terence Kavanagh

Ischemic heart disease is the major cause of death in adult males throughout most of the advanced world. Its three clinical manifestations (angina, myocardial infarction, and sudden cardiac death) now seem almost inevitable accompaniments of our modern life-style. The basic pathology involved, atherosclerosis, is a highly complex process which still defies precise scientific explanation.

Broadly speaking, there are two main theories of pathogenesis. The first focuses attention on the lipidlike nature of the atheromatous plaque (1). Low-density and very low-density lipoproteins are said to infiltrate the arterial wall and accumulate in excessive amounts, leading to the formation of fatty streaks and, later, fibrous plaques upon which thrombi can form. Initiation of this process is variously attributed to an inflammatory reaction in the vessel wall, endothelial wear and tear due to prolonged hypertension, or tumorlike proliferation of sick subendothelial muscle cells. Closely associated with this hypothesis is the now largely held view that abnormalities in the plasma lipid levels are a major contributor to the process (2), and that lowering total blood cholesterol levels will reduce the incidence of coronary heart disease (CHD) (3).

The second theory (4,5) proposes that the initial stimulus for atheroma formation comes not from the lipid accumulation, but from the formation of thrombi on the endothelium. The consequent aggregation of red cells, platelets, and enmeshed lipid material become incorporated into the wall of the artery and ultimately evolve into the typical atheroma. Proponents of this school may place more emphasis on the development of antithrombotic agents than on measures to lower plasma lipids.

Our lack of conclusive scientific and statistical proof as to the exact cause of atherosclerosis does not mean that measures should not or cannot be taken toward primary or secondary prevention. There is now a vast body of evidence linking certain risk factors with coronary artery disease (6,7). These are: (a) male sex; (b) heredity; (c) elevated plasma cholesterol (in particular the low-density lipoprotein (LDL) fraction), usually associated with a high dietary

intake of saturated fats; (d) hypertension; (e) cigarette smoking; (f) diabetes mellitus; (g) obesity; (h) psychosocial stress; and (i) physical inactivity.

Many of these factors are interdependent, or may even give rise to one another. Furthermore, the presence of more than one risk factor increases considerably the likelihood of developing the disease. It, therefore, seems entirely reasonable to deduce that a strategem designed to eliminate these risk factors will reduce the disease's incidence.

THE ROLE OF PHYSICAL ACTIVITY AS A PROTECTIVE FACTOR IN CORONARY ARTERY DISEASE

Epidemiological Evidence

Whereas physical inactivity is listed as a risk factor, physical activity can be viewed as a "protective factor." It is almost 40 years since Morris et al. (8) published a report in *The Lancet* which showed that highly active conductors on the London double-decker buses had significantly less heart attacks than their sedentary coworkers, the bus drivers. Since then, a large number of studies have consistently demonstrated the same finding (Table 20.1 (9–18)). Regular physical activity, either at work, or as part of a recreational program, apparently confers a degree of protection from myocardial infarction, both fatal and nonfatal. The reduction in risk for active persons compared with the inactive is about 3-fold. Furthermore, the incidence of sudden cardiac death, a major and common manifestation of ischemic heart disease, is similarly reduced with regular physical activity (19).

The major criticism leveled against these reports, particularly the early ones, is their bias of preselection: constitutionally stronger individuals choose vigorous physical work and/or recreation, while those who are not will choose a more sedentary life-style. The later published reports, in particular those of the Paffenbarger group (15,16,20) dealing with San Francisco longshoremen and Harvard alumni, have refuted the possibility of preselection with elegant methods of statistical analysis.

Table 20.1. Epidemiologic Studies: Comparative Risk for Heart Attacks for Low Physical Activity Members of Groups Compared with High-Level Members of Same Group

Author	Population	Physical Activity	
		High	Low
Morris (UK, 1953) (8)	London transport	1.0	2.2
	Post office	1.0	2.0
Brunner (Israel, 1960) (9)	Kibbutzim dwellers	1.0	3.0
Taylor (USA, 1962) (10)	Railroad	1.0	2.0
Kahn (USA, 1963) (11)	Post office	1.0	1.9
Brunner (Israel, 1966) (12)	Kibbutzim dwellers	1.0	3.0
Kannel (USA, 1967) (13)	Framingham	1.0	2.5
Shapiro (USA, 1969) (14)	Insurance clients (NYHIP)	1.0	4.8
Paffenbarger (USA, 1977) (15)	Longshoremen	1.0	3.0
Paffenbarger (USA, 1978) (16)	University alumni	1.0	2.2
Morris (UK, 1980) (17)	Civil servants	1.0	2.8
Garcia-Palmieri (USA, 1982) (18)	Puerto Rico heart program	1.0	2.0

More recently, Powell and his colleagues (21), from the Centers for Disease Control, Atlanta, subjected a total of 43 such published studies to careful epidemiological and statistical analysis in order to establish their validity. They concluded that "the observations reported in the literature support the inference that physical activity is inversely and causally related to the incidence of CHD." They went on to observe that "the relative risk of inactivity appears to be similar in magnitude to that of hypertension, hypercholesterolemia, and smoking. These observations suggest that in CHD prevention programs, regular physical activity should be promoted as vigorously as blood pressure control, dietary modification to lower serum cholesterol, and smoking cessation" (21).

Threshold for Protection

How much physical activity is needed to provide protection from coronary artery disease? Paffenbarger's longshoremen needed to expend at least 8500 kcal over a 42-hour work week, at a minimum effort intensity of 5 kcal/min (15). Morris's bus conductors, running up and down the double-decker bus stairs 60–70 times a day, in addition to walking to collect fares, used at least that much energy, with peak expenditure of between 6 and 10 kcal/min during stair climbing (8).

In the workplace, we have seen increasing replacement of muscle by machine, and so we now must study recreational habits in order to compare active with inactive. Morris et al. (17) found that civil servants who regularly carried out "dynamic aerobic activity involving free movement of large muscle groups, and above the energy required for a training effect" had significantly fewer heart attacks. Swimming, jogging, brisk walking, and hill climbing were some of the activities cited; all require peak expenditures of 7.5 kcal/min. University graduates studied by Paffenbarger et al. (16) began to develop significant protection at total caloric expenditures of 7000 kcal over a 42-hour work week, of which at least 2000 kcal were spent in a vigorous sport ("vigorous" being defined as more than 5 kcal/min and closer to 10 kcal/min). Jogging, mountaineering, cross-country skiing, swimming, and tennis were given as examples.

The Multiple Risk Factor Intervention Trial (MRFIT), studying a group of some 12,000 men at high risk for coronary artery disease (smokers with hypertension and hypercholesterolemia) over a 7-year period, compared the effect of light (2–4 kcal/min), moderate (4.5–5.5 kcal/min), and heavy (equal or greater than 6 kcal per minute) physical exercise on coronary heart disease mortality and sudden cardiac death. The conclusions were that "the moderately active as compared with the least active men had 63% the age-adjusted rates for CHD mortality and sudden death" (22). The moderately active averaged 47 minutes of exercise daily, to burn 224 kcals or 4.8 kcal/min (equivalent to a daily brisk 2½ mile walk). There appeared to be no particular benefit, in this group at least, to higher levels of activity. Presumably, individuals who exercised less frequently than seven times per week would be required to increase the distance and/or intensity to achieve the same result.

Suggested Mechanisms of Protection

A number of exercise training effects can explain the mechanisms by which regular exercise protects against coronary heart disease.

Animal models have demonstrated that chronic exercise can significantly increase coronary artery diameter, the extent of myocardial capillarization

(23,24), and, in the presence of coronary stenosis, coronary collateral growth (25–27). Heightened resistance of the ischemic heart to ventricular fibrillation has also been demonstrated in treadmill-trained rats and dogs (28,29). Non-trained Macaca monkeys fed an atherosclerotic diet developed severe coronary atherosclerosis and fatal myocardial infarctions, whereas their treadmill-trained counterparts, fed the same diet, were found to have large caliber coronary arteries, totally free from atherosclerosis (30).

In man, it has been shown that regular endurance training increases end-diastolic volume, and that this is associated with an enhanced stroke volume and a resting and exercising bradycardia (31). Indeed, the bradycardia is a hallmark of the trained state, and is due to a variation in the influence of the autonomic nerve supply to the heart. The parasympathetic, or vagal, tone is increased at rest, and the sympathetic tone decreased during exercise (32). This makes for a more efficient pump, less likely to labor during intense and unexpected episodes of physical effort.

The demonstration of coronary collateralization as a result of training has proved to be difficult in man, possibly because these collateral vessels are frequently quite small (100–200 μM) are usually located intramurally, and are frequently undetectable by clinical coronary angiography. However, there is circumstantial evidence for collateralization from studies which show higher rate pressure products (heart rate multiplied by systolic blood pressure) after training, for equivalent levels of myocardial ischemia (as measured by the onset of angina or amount of ST segmental depression) (Fig. 20.1) (33,34). Recently, exercise scintigraphy has been used to detect the development of exercise-induced collateralization in man, and favorable reports are already beginning to appear in the literature (35,36).

A number of peripheral changes brought about by exercise training, by affecting the established risk factors, could explain the CHD protective effect. Blood pressure is reduced as a result of increased skeletal muscle vascularity and consequent drop in peripheral resistance (37). This, together with the training bradycardia, makes for a reduction in rate-pressure product, and thus myocardial oxygen demand, at equivalent levels of effort (38). Plasma triglyceride levels are lowered. There is an increase in levels of HDL cholesterol and

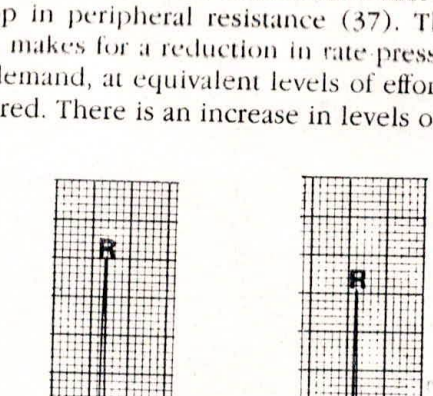

Figure 20.1. The S-T segment response to exercise. *A*, Normal isoelectric ST-segment seen at rest. *B*, Ischaemic changes with exercise; 3.5 mm of "horizontal" ST-segmental depression.

a decrease in LDL cholesterol (39–42). The former is inversely related to CHD risk, while the latter is directly related. The exercising Macaca monkeys mentioned above, who withstood the adverse effects of an atherosclerotic diet, developed higher HDL cholesterol than their nonexercising counterparts (30). Training enhances fibrinolytic response to intravascular clotting (43,44), improves glucose tolerance and increases insulin sensitivity (45,46), reduces stress-induced levels of circulating epinephrine and norepinephrine (47,48), and increases levels of circulating β-endorphins (49,50). On a simpler level, the regular exerciser is more health conscious and seems more ready, or at least most capable, of leading a healthful life-style, free from such CHD risk factors as obesity, cigarette smoking, and a highly saturated fat "junk food" diet. Altogether, this is an imposing list of explanations for the clinical observation that exercise protects against cardiovascular disease.

EXERCISE IN POSTCORONARY REHABILITATION

Although Levine and Lown (51) pioneered the early mobilization of cardiac patients as early as 1952, it was not until the 1970s that the practice became widely accepted throughout the United States and Canada. Contrary to previous beliefs, this aggressive approach is not associated with an increased risk of cardiac rupture, of left ventricular aneurysm formation, or of sudden death. On the contrary, the benefits are considerable. The patient equates early mobilization with recovery, a powerful psychological boost. Severe deconditioning is avoided, with consequent earlier return to work and everyday physical activities. Today, we even see reports of medically supervised submaximal exercise testing being safely carried out in a matter of days after acute myocardial infarction, affording the physician important prognostic information and the patient additional psychological benefit.

Since the early 1960s, there has been a proliferation of exercise rehabilitation programs for patients recovering from an acute myocardial infarction or aortocoronary artery bypass surgery. The results indicate that, compared with nonexercising cardiac patients, those who participate in an exercise program adjust better to their disease, have improved cardiovascular function and physical working capacity, and are more likely to return to active employment (52). All of the benefits of physical training described in connection with primary prevention can apply equally to the vast majority of myocardial infarction survivors. In particular, there is the reduction in the rate-pressure product at a given workload, which decreases myocardial ozygen demand. The training bradycardia also increases the period of diastole, and since coronary blood flow occurs during this phase of the cardiac cycle, the prolongation helps to reduce myocardial ischemia. Both these mechanisms are the likeliest explanations for the considerable alleviation and even abolition of anginal symptoms so frequently reported as a result of exercise training.

Other exercise-related benefits pertinent to the postMI state include: (a) decreased depression and anxiety (53,54); (b) greater adherence to the tenets of healthy living, i.e., diet, no smoking, etc.; (c) reduction in the frequency of ventricular ectopic beats (55); and (d) possibly stabilization or regression of the coronary atherosclerotic process (56).

Few would now disagree with the claim that exercise rehabilitation after acute myocardial infarction or aortocoronary artery bypass graft surgery greatly

enhances the patient's quality of life, improves functional capacity, counteracts CHD risk factors, and encourages return to work. For these reasons, postMI exercise therapy is firmly advocated by such bodies as the World Health Organization (57), as well as by many international and national organizations involved in the primary and secondary prevention of atherosclerotic heart disease.

A number of prospective randomized controlled trials showing the effect of postcoronary exercise on cardiovascular mortality and morbidity have now been published. Like many other secondary intervention trials after myocardial infarction, e.g., β-blockers, aspirin, the results have been unclear. Some studies show a statistically significant beneficial effect; others fail to do so. Often the reason for this has been methodological, e.g., limited patient entry, insufficient follow-up, high dropout rate, or contamination between control and intervention groups. In order to overcome this problem, the method of pooling the results of similar trials and then analyzing them as a whole has been introduced. Known as meta-analysis, this technique has been increasingly applied in situations where it is suspected that the trials, because of the problems mentioned above, have lacked the statistical power to successfully demonstrate the real benefit of a treatment.

May (58) was one of the first to review a number of long-term trials of secondary prevention after myocardial infarction. With regard to physical exercise studies, he found that "although none of the exercise trials showed a statistically significant reduction in total mortality, all but one had a positive trend favoring the physical training group that varied from 21% to 32%." On pooling of the results, he found a statistically significant 19% reduction in total mortality in the exercising group. He went on to say that "pooling of the results from these (i.e., exercise) studies may be more acceptable than for other categories of intervention, as one does not have to account for unknown pharmacological factors. The differences in exercise schedules between studies are minor, and the programs were all started at approximately the same time after the acute event" (58).

Subsequently, others have employed the same technique, the most recent being Oldridge and his associates (59), who subjected the 10 major randomized prospective trials to meta-analysis, and found a highly significant reduction of 25% in recurrent fatal myocardial infarction in the exercising group. This is as beneficial an effect as has been reported for β-blockade therapy after acute MI, a form of intervention now widely accepted clinically.

EXERCISE TESTING

Exercise testing is now a rapidly growing subject in its own right and there are a number of excellent texts which deal with the topic in its entirety. Only the essentials will be dealt with here.

Methodology

Currently, an exercise test is carried out primarily on a treadmill or a cycle ergometer. The latter is cheaper, quieter, and occupies less space. It allows for easier blood pressure readings and artifact-free electrocardiogram tracings. If the test includes a collection of expired gas and/or blood sampling, this can also be carried out with more facility during upright cycling. A drawback of the

cycle ergometer is that older individuals with weak quadriceps may find it harder to reach desired heart rates before the onset of quadriceps fatigue. Stationary cycling does not result in as high a maximum oxygen consumption as treadmill walking, but the difference is small; ventilation and lactate are slightly higher.

The treadmill employs the more natural walking action, and possibly for this reason, has become the principal choice of cardiologists in the clinical setting. Cycle ergometers tend to be used more by those involved in respiratory physiology, large-scale cardiac rehabilitation programs, and cardiorespiratory fitness testing.

The purpose of the test is to study the subject's cardiorespiratory responses to increasing levels of physical effort. The noninvasive parameters usually monitored are heart rate, blood pressure, and the exercise electrocardiogram. Less often, we collect and analyze expired air in order to calculate ventilation, oxygen consumption, and carbon dioxide production. Occasionally, blood gases, pH, and lactate are also measured. Exercise thallium scintigraphy is a diagnostic rather than an assessment procedure, and is outside the scope of this chapter.

Exercise Test Protocols

Starting from rest, the workload is increased in a stepwise manner until the patient is exhausted. This is known as a maximal test, and its completion is confirmed by the fact that, despite a further increase in the workload, the heart rate and oxygen uptake do not show a concomitant rise. If any untoward symptoms or signs appear before this physiological maximum is reached, then the test is terminated, and is referred to as a "symptom-limited" maximal test.

A submaximal test is one carried out to a predetermined target heart rate, usually 85% of maximum. Maximum heart rates, which decrease with age, can be estimated from age-related tables (60) or by using the formula (61):

$$\text{HR Max} = 210 - 0.65 \times \text{age (years)}$$

Cycle ergometer tests can be divided into two types, *progressive multistage* and *steady state*. In the former, the power output is increased by a constant value, usually 100 kilopond meters per minute (KPM), or 16.7 watts, every minute (16 watts) until maximal, or target, heart rate is reached. Measurements are made in the final 15 seconds of each minute. This test is particularly valuable when the ventilatory anaerobic threshold (see below) is being calculated from analysis of expired air.

The *steady state test* employs three power outputs, each of 3–5 minutes' duration, the intensity being usually 25%, 50%, and 75% of estimated maximal effort. Measurements are made during the last minute of each stage, when the variables are judged to have reached a constant steady state.

The maximum power output for healthy adults (on the cycle ergometer) can be estimated from the following equations (62):

Male

$$\text{Maximum Power Output (KPM)} = \frac{[4200 - (\text{age in yr} \times 32.0)] + 3.5 \times \text{body wt (kg)}}{2}$$

Female

$$\text{Maximum Power Output (KPM)} = \frac{[2600 - (\text{age in yr} \times 14.0)] + 3.5 \times \text{body wt (kg)}}{2}$$

Cardiac patients may have a reduced work capacity, and this has to be taken into account. In practice, the healthy sedentary individual's initial steady state test is usually 300 KPM (50 watts), 600 KPM (100 watts), and 750 KPM (125 watts). A fitter subject might be given a third power output of 900 KPM (150 watts). At initial assessment, cardiac patients are usually given power outputs of 150 KPM (25 watts), 300 KPM (50 watts), and 450 KPM (75 watts).

Treadmill testing can be carried out to maximum, or to a target heart rate, and the common protocols in current use differ only in the time it takes for the subject to reach either of these goals. The Balke and Naughton protocols are probably best suited to the early postMI patient. The Bruce (probably the most popular in use today) and the Ellestad protocols are slightly more demanding, but are less time-consuming (Tables 20.2, 20.3).

Table 20.2. Protocols for Treadmill Exercise Test.

A. Balke[a]

Stage	Speed 3.3 mph	Grade (%)	Duration (min)
1	Constant	2	2
2	Constant	6	4
3	Constant	10	6
4	Constant	14	8
5	Constant	18	10
6	Constant	22	12

B. Naughton[a]

Stage	2.0 mph Grade (%)	3.0 Grade (%)	3.4 mph Grade (%)	Duration (min)
1	—	—	—	2
2	0.0	—	—	2
3	3.5	0.0	—	2
4	7.0	2.5	2.0	2
5	10.5	5.0	4.0	2
6	14.0	7.5	6.0	2
7	17.5	10.0	8.0	2
8	—	12.5	10.0	2
9	—	15.0	12.0	2
10	—	17.5	14.0	2
11	—	20.0	16.0	2
12	—	22.5	18.0	2
13	—	25.0	20.0	2
14	—	27.5	22.0	2
15	—	30.0	24.0	2
16	—	32.5	26.0	2

[a]Lower speeds suitable for cardiac patients and those with low tolerance.

Table 20.3. Protocols for Treadmill Exercise Test.

A. Bruce			
Stage	Speed (mph)	Grade (%)	Duration (min)
1	1.7	10	3
2	2.5	12	3
3	3.4	14	3
4	4.2	16	3
5	5.0	18	3
6	5.5	20	3
7	6.0	22	3

B. Ellstad			
Stage	Speed (mph)	Grade (%)	Duration (min)
1	1.7	10	3
2	3.0	10	2
3	4.0	10	2
4	5.0	10	3
5	5.0	15	2
6	6.0	15	3

In the absence of metabolic measurements, and where treadmill performance is being expressed with reference to energy cost tables, the use of the grab-rails for support can give spuriously high readings. Apart from providing very slight and occasional support to the very apprehensive subject, the rails should not be touched during the test, and this exclusion may make cycle ergometry the choice for older and more disabled subjects.

OBSERVATIONS MADE DURING TEST

Heart Rate

The heart rate, which is read from the exercise electrocardiogram (ECG), increases linearly with workload and oxygen consumption. However, it should be noted that maximum heart rate (HR max) is reached a minute or so before maximum oxygen uptake (VO_2 max); this asymptote leads to an apparent discrepancy when comparable levels are expressed as percentages, e.g., 50% VO_2 max = 65% HR max.

Physicians should be thoroughly familiar with the normal heart rate responses to each stage of the protocol being used, since sluggish response to increasing effort or, less commonly, failure of the heart rate to rise (termed "chronotropic incompetence" by Ellestad) may be a feature of ischemic heart disease (63). There can also be profound reductions in resting and exercise heart rates as a result of treatment with β-blocking agents.

Blood Pressure

Systolic blood pressure increases linearly with exercise, rising in the average healthy middle-aged subject to 200–300 mm Hg. A normal response indicates good left ventricular function, while a sluggish or inadequate response, so-called "inotropic incompetence," suggests left ventricular dysfunction (usu-

ally in association with severe coronary artery disease) or aortic outflow obstruction. Again, the physician should be familiar with the range of expected increases in systolic blood pressure for each work-stage of the protocol chosen.

The rate-pressure product correlates very well with myocardial oxygen consumption during exercise, and can be used to identify a threshold for angina from test to test.

Diastolic pressure usually remains steady, or may decrease slightly during exercise. It should be noted that sometimes in testing young subjects, the Korotkoff sounds can be heard down to 0 pressure.

Electrocardiogram

The system of leads and electrode placement used to obtain the exercise ECG will depend on the testing laboratory's preference, but the following points should be kept in mind:

1. The most commonly sought exercise-induced electrocardiographic finding is depression of the ST segment (Fig. 20.1). It has been convincingly demonstrated that changes in ST-T amplitude and direction are most readily observed in the bipolar CM_5 lead, in which the positive electrode is placed at the V_5 position and the negative electrode on the manubrium. The configuration of the tracing obtained from this placement exaggerates the S wave, and allows one to pick up 89% of ST-segment abnormalities present in the full 12-lead record (64).

2. Addition of two other leads, e.g., V_1 and III, increases the sensitivity and allows easier analysis of ectopic beats.

3. While a 12-lead resting electrocardiogram should be carried out before and after an exercise test, a full 12-lead system of exercise monitoring is probably unnecessary. It will pick up very little abnormality not seen in a suitable 3-lead configuration, and is more time-consuming and expensive. But if the full 12-lead electrocardiogram is used for exercise, artifact can be avoided by placing the limb lead electrodes at the shoulders and iliac crests. Provided they do not advance too much onto the torso, the ECG tracing will closely resemble the orthodox resting configuration.

Computer analysis of the exercise electrocardiogram is now available, particularly with regard to mathematical evaluation of the ST-segment depression. However, despite the advances made in this area in recent years, skilled human interpretation still remains indispensable.

Irrespective of the lead system used, Bayes's theorem will apply (65). The predictive value of a positive test (i.e., the percentage of subjects with an exercise-induced ECG abnormality who ultimately prove to have coronary artery disease) is an expression of the prevalence of the disease in the population being tested. Thus, there are more false-positive responses encountered when testing a group of asymptomatic healthy young people than when evaluating a high-risk group or those with a prior history of myocardial infarction.

The classical exercise electrocardiographic changes commonly associated with an abnormal test are as follows:

1. Horizontal or downward sloping depression of the ST segment of 1 mm or more (measured 80 msec from the "J point") in any one lead, generally indicates myocardial ischemia. However, note that there are a number of nonischemic conditions in which this can occur, e.g., hypokalemia, bundle branch

block, WPW syndrome,
hypoxemia from other c

2. Elevation of the
with areas of ventricular
ant angina (coronary art

3. Frequent compl
often associated with m
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4. Increase in R v
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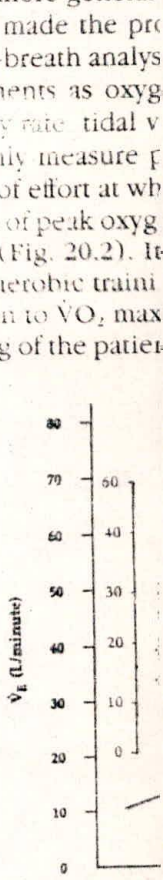

Figure 20.2. Determinat
tilatory equivalent ($\dot{V}_E/\dot{V}$
and the nadir of the $\dot{V}_E/$
min., approximately 60%
Kavanagh T, Yacoub MH
tives in Cardiology 4:21–

block, WPW syndrome, effect of various pharmaceutical agents (e.g., digitalis), hypoxemia from other causes, etc.

2. Elevation of the ST segment, 1 mm or more, may be seen in association with areas of ventricular dyskinesia or akinesia, ventricular aneurysms, and variant angina (coronary artery spasm).

3. Frequent complex ventricular arrhythmias (three or more in 10), are often associated with myocardial ischemia, although this finding is not as specific as ST segmental changes.

4. Increase in R wave amplitude, 25% or more above resting, is held by some to indicate ischemia, but more validation is required (63).

Analysis of Expired Gases

In the past edition of this chapter, the use of respiratory gas analysis during the testing of cardiac patients was advocated at some length. Since then, there has been more general acceptance of this approach. Modern, automated equipment has made the procedure relatively simple. A metabolic cart can provide breath-by-breath analysis, with graphic display and subsequent printout of such measurements as oxygen uptake, carbon dioxide output, minute ventilation, respiratory rate, tidal volume, and respiratory exchange ratio. From these, one cannot only measure peak oxygen uptake ($\dot{V}O_2$ max), but can also determine the level of effort at which work begins to be performed anaerobically, (usually 50%–60% of peak oxygen uptake). This point is known as the ventilatory threshold (66) (Fig. 20.2). It approximates closely the level of intensity required for effective aerobic training, occurs before maximal effort is reached, increases in proportion to $\dot{V}O_2$ max with training, and thus can be used to advantage in the evaluating of the patient with cardiac disease. Unlike heart rate, the submaximal

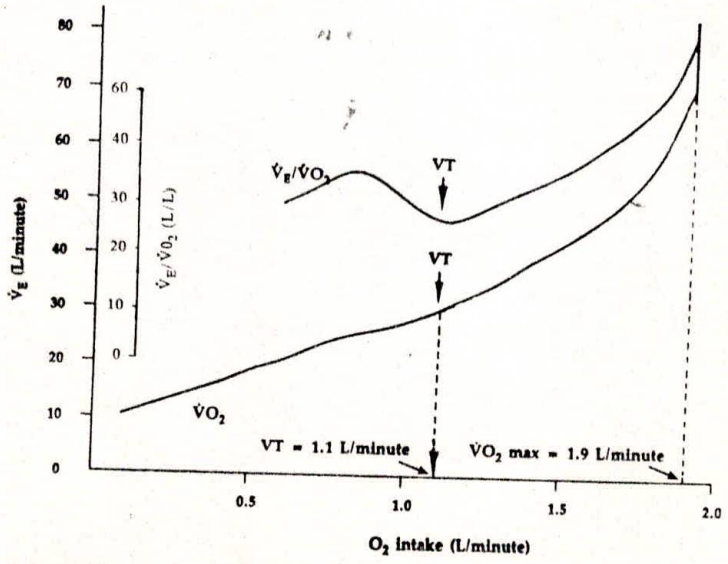

Figure 20.2. Determination of ventilatory threshold from plot of ventilation ($\dot{V}_E$) and ventilatory equivalent ($\dot{V}_E/\dot{V}O_2$) against oxygen intake ($\dot{V}O_2$). At the inflection of the $\dot{V}_E$ line, and the nadir of the $\dot{V}_E/\dot{V}O_2$ line, we read the ventilatory threshold. In this case, it is 1.1 L/min., approximately 60% of the measured peak oxygen intake of 1.9 L/min. (Adapted from Kavanagh T, Yacoub MH: The benefits of exercise for heart transplant patients. *Perspectives in Cardiology* 4:21–37, 1988.)

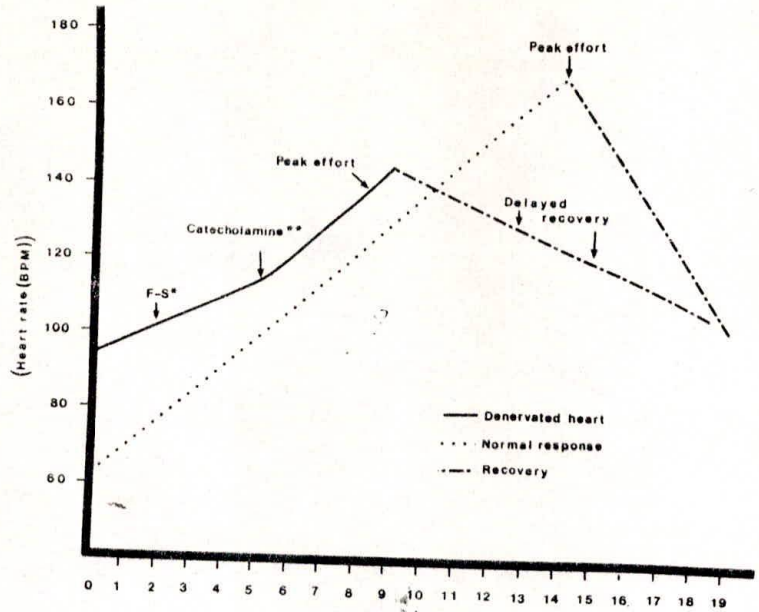

Figure 20.3. Typical transplanted denervated heart rate response to increasing effort, compared with the rate response of a healthy subject matched for donor age. Note the high resting rate, the delayed rate acceleration during effort, the delayed deceleration during recovery, and the tendency for the rate to continue to rise after the termination of exercise (peak effort). (Adapted from Kavanagh T, Yacoub MH: The benefits of exercise for heart transplant patients. *Perspectives in Cardiology* 4:21–37, 1988.)

oxygen uptake (and thus the ventilatory threshold), is relatively unaffected by β-blockade or calcium channel antagonists, noteworthy in light of current cardiac therapy. Cardiopulmonary exercise testing is increasingly employed in assessing the functional capacity of patients with congestive heart failure (67,68). This appears to give a more objective measurement than the New York Heart Association classification, or duration time on an exercise test. Another application is in the exercise rehabilitation of cardiac transplantation patients. The denervated heart fails to respond in a linear fashion to increases in power output (Fig. 20.3), thus completely invalidating the use in these patients of tables which relate heart rate to power output and/or oxygen uptake. Direct gas analysis allows one to offer clear advice on training intensity (69,70).

Thus, knowledge of both cardiac and pulmonary responses to effort permits more precise prescribing of a safe and effective training level. In addition, we can utilize pulmonary gas measurements to calculate stroke volume and cardiac output noninvasively (62).

INDICATIONS, CONTRAINDICATIONS, AND REASONS FOR TERMINATING AN EXERCISE TEST

In the context of this chapter, the major purpose of an exercise test is to establish a safe and effective level of physical training for the patient with ischemic heart disease. However, there are other indications, some of which are listed below.

Indications

Some of the indications include:

1. Diagnose where the occurrence of chest pain or other cardiac symptoms suggest the presence of coronary artery disease;
2. Evaluate the results of surgical or medical therapy in ischemic heart disease;
3. Assess prognosis after an acute myocardial infarction;
4. Screen for latent coronary artery disease;
5. Determine level of cardiovascular fitness before entering an exercise program; and
6. Quantitate functional status in congestive heart failure, and assess response to therapy.

Contraindications

Contraindications include:

1. Within 6 weeks of an acute myocardial infarction—exercise tests carried out during the very early recovery phase are usually low-level, the heart rate often not being allowed to rise above 120 beats per minute;
2. Acute myocarditis or pericarditis;
3. Unstable angina;
4. Complex ventricular arrhythmias;
5. Second- or third-degree heart block;
6. Severe aortic outflow obstruction, as in aortic stenosis or hypertrophic obstructive cardiomyopathy (HOCM);
7. Severe systematic hypertension that is not responding to medication; and
8. Acute infections.

Reasons for Terminating the Test

Among the reasons for terminating the test are:

1. A failure of heart rate or systolic blood pressure to rise, or a fall, with increasing effort;
2. Systolic blood pressure exceeding 260 mm Hg, or diastolic blood pressure 120 mm Hg;
3. Frequent (3 in 10 or more) complex ventricular premature beats, ventricular tachycardia;
4. Sustained supraventricular tachycardia or atrial fibrillation;
5. Development of second- or third-degree heart block;
6. ST-segment depression in excess of 2 mm, horizontal or downsloping;
7. Increasing anginal symptoms; and
8. Any adverse change in the patient's appearance or attitude, e.g., pallor, excessive sweating, confusion, etc.

THE PRESCRIPTION OF ENDURANCE EXERCISE

An exercise prescription requires four components. They are: (a) type of activity; (b) intensity of effort; (c) duration; and (d) frequency of workout. Each

of these is defined below, with specific reference to the coronary artery disease patient.

Type of Activity

This should involve repetitive movement of large muscle masses. *Endurance* or *aerobic* are now the descriptive terms most commonly used. Examples are brisk walking, slow jogging (12 minute per mile pace), relaxed swimming, long-distance cycling, cross-country skiing, orienteering, circuit training, etc. There are doubtless more possibilities, depending on one's ingenuity and the climatic environment. It should be mentioned that flexibility and muscle strengthening regimens, while valuable and even essential in their own right, are not included in the category of cardiovascular conditioning activities.

The more complex the training activity chosen, the more motor skill it will require and, therefore, the fewer patients will be able to participate. In addition, since the ability to perform a particular sport will vary widely, it is difficult to prescribe the effort intensity with any accuracy. Choose something that most people can do. The author has used walking and jogging in the Toronto Rehabilitation Centre for the past 20 years and has found it to be an ideal application for this purpose (71,72).

Patients with coronary artery disease cannot afford to use sports or games to get fit. They must be fit in order to play games! Healthy young adults will get a training effect from vigorous competitive sports such as tennis, squash, basketball, and soccer, but the patient with ischemic heart disease (or the apparently healthy but sedentary middle-aged male) is often unable to attain the levels of effort required. Furthermore, it may be highly dangerous to attempt to do so without medical clearance.

Intensity

This should be between 50–60% of peak oxygen uptake, and/or the level of the ventilatory threshold, and/or 65–80% of maximum heart rate. When dealing with coronary artery disease patients, one should err on the side of caution, choosing the lower intensities and compensating for this by increasing the duration of the workouts so as to achieve the desired training effect. Obviously, the intensity should never be greater than that attained during the exercise test. Patients should be exercised below their threshold for angina or ST segmental ischemic changes, and never in the presence of known complex arrhythmias. Telemetry and Holter monitoring should be utilized as indicated.

Duration

Ideally, at 50–70% of aerobic power, the workout should be steady, continuous, and last for at least 30 minutes. The intensity chosen should be such as to allow for this duration without causing excessive fatigue.

Frequency

A minimum of three training sessions a week is needed to gain any benefit. The author advocates five sessions weekly. More frequently than this will yield gains that are not commensurate with the additional encroachments on one's spare time. However, there will always be weeks when a session has to be missed, providing some leeway.

Fitness cannot be stored, and within weeks of discontinuing training, a decline is apparent.

Other Aspects

Training sessions should include a warm-up and a cool-down, and flexibility routines should be practiced in order to reduce the incidence of injuries. Patients should be instructed in pulse taking, recognition and interpretation of symptoms, effect of the various medications on exercise tolerance, how to cope with climatic conditions, and the choice of suitable footwear and clothing (73,71).

All exercise supervisory staff should be in possession of at least the basic certificate in cardiopulmonary resuscitation, and a defibrillator should always be immediately available in the exercise area. Ideally, facilities for telemetry and Holter monitoring should also be provided.

CONCLUSIONS

In recent years, a greater proportion of the population has become involved in the type of aerobic activities shown to be associated with cardiovascular health. The public is seeking medical guidance with regard to the advisability and safety of such endeavors. This chapter has outlined the rationale for advising a physically active life, and has provided guidelines in the areas of assessment for and prescription of exercise, particularly in those patients who have proven coronary artery disease.

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Exercise for Low Back Pain

David A. McCune and Robert B. Sprague

Despite recent advances in spinal imaging and diagnostics for clarification of the medical diagnosis, the conservative treatment of spinal disorders has held exercise as its cornerstone for decades. This chapter presents various objectives of exercise and possible mechanisms used in the treatment. Exercises, with variations, are presented in the Appendix to this chapter to demonstrate their application to spinal disorders. Unlike in years past when clinicians prescribed "standard" back exercises, today's clinician must apply exercise in a specific and judicious fashion when treating spinal disorders. The use of exercise has now been expanded to aid in clarifying the medical diagnosis, as well as in identifying a specific pathology. Exercise is an essential part of the treatment of acute back pain, chronic back pain, and in prophylaxis.

MEDICAL DIAGNOSIS

The specific pathology causing spinal pain frequently eludes even the most astute clinician. Quantification of structures at fault in back pain often must rely on a clinical diagnosis. Often, this is determined by assessing the patient's response to exercise. Although this chapter is not intended to present diagnostics, appreciation of the medical diagnosis is necessary for appropriate application of exercise. In general, there are three categories of spinal pain: chemical or inflammatory, mechanical, and organic. Patients often present with a combination of two, or even three of these categories. McKenzie (1) has outlined two general categories of spinal pain, referring to them as chemical or inflammatory pain and mechanical pain.

Chemical (Inflammatory) Pain

Chemical back pain arises from a local or systemic inflammatory process. The presence of inflammation causes the area to be associated with decreased and referred pain. Clinicians are aware of an inflammatory response in the patient's report that symptoms do not move, nor do they change with specific spinal movements. Generally, if the symptoms associated with an inflammatory process are to change, they worsen secondary to exercise. Though less effective for this type of pain, exercise may be helpful if appropriately prescribed. Wyke (2) states that "burning" is the most common description of chemical pain.

Mechanical Pain

Mechanical back pain represents the largest number of patient complaints (1). Mechanical pain is viewed as any stress that adversely affects the physiological function of the intervertebral disc, the apophyseal joints, or the surrounding contractile or noncontractile soft tissues. Disagreement as to the prevalence of any of these pathologies persists. However, there is agreement that the vast majority of spinal disorders falls into this category, and that exercises are essential for proper treatment of mechanical back pain.

Mechanical pain is altered by movement or posture, and is either intermittent or more variable than chemical pain. Wyke (2) states that pressing, prickling, bursting, stabbing, and throbbing are the most common descriptions of mechanical pain.

Organic spinal disorders represent those visceral abnormalities and disease processes that may manifest themselves as spinal pain. Also included in this category are congenital spinal abnormalities. Though specific knowledge of these disorders is essential, it is beyond the scope of this chapter. Exercise is not thought to be helpful in the treatment of visceral-related problems, but is often essential in the treatment of congenital spinal abnormalities.

PATHOLOGY CLARIFICATION

A thorough physical examination is required to determine appropriate exercises for spinal disorders. Assessment and documentation of active movements include the patient's responses to exercise both during and following single and repeated prescribed movements. It is essential that assessment not be limited to single movements, as much can be learned about the patient's pathology by assessing symptom responses to repeated movements. Cyriax stressed the efficacy of assessing passive as well as resistive movements (3). He has outlined a specific method to differentiate the source of the patient's complaints, as summarized in Table 15.1.

Table 15.1. Summary of Cyriax's Soft Tissue Evaluation (3)

A. *Active movement*—tests all anatomical structures
B. *Passive movements*—tests all inert structures (nerves, ligaments, capsule, bursas, bone, blood vessels, connective tissue)

Findings	Indicate
Active and passive motion is restricted and/or painful in the *same* direction	Arthrogenic lesion
Active and passive motion is restricted and/or painful in the *opposite* direction	Soft tissue lesion
Relative restriction of passive motion in *various* directions	Capsular pattern

C. *Resisted movements*—test all contractile structures (muscle, tendon, periosteum)

Findings	Indicate
Painful and strong	Minor lesion
Painful and weak	Major lesion
Painless and weak	Neurological or complete rupture
Painless and strong	Normal

Particular note should also be taken as to whether the patient's symptoms are reproduced during the test movement (in range) or only at the end range. This symptom-range relationship is helpful in differentiating between apophyseal/disc symptoms and soft tissue symptoms (4). McKenzie states that pain during movement is indicative of mechanical derangements in the disc, while others state that the apophyseal joints are at fault (1,5,6). Symptoms reproduced only at extremes of motion are felt to arise from adaptive shortening of soft tissues.

Once the source of the symptoms is clarified through history, physical exam, and test movements, the prescription of appropriate exercise designed to favorably alter these specific structures can follow. Even if a particular structure is not identified, exercises may be prescribed and modified based on desirable symptom changes.

OBJECTIVES OF EXERCISE

The use of exercise in the evaluative stage is essential in the process of clarifying the potential source of the pathology. In the treatment process, three major objectives exist: (1) pain reduction; (2) restoration of normal function; and (3) prevention of future recurrence.

PAIN REDUCTION

Exercise for reduction of pain has long been an accepted clinical goal. Various mechanisms for pain reduction and differing guidelines for the determination of appropriate exercises have been offered. When using exercise for pain reduction, three clinical symptoms should be evaluated in determining the appropriate exercise, and in assessing patient progress. If the exercise is appropriate, the patient will report one or more of the following: centralization of the pain, a decrease in frequency of the pain, and/or a decrease in intensity of the pain.

Mechanoreceptors

The mechanisms of pain reduction relate to the effect of exercise on the mechanoreceptors, muscle spasm, inflammation, and the resting anatomical state of the involved structure.

Extensive work done by Wyke (7) revealed that pain reduction is greatly enhanced through appropriate stimulation of joint mechanoreceptors. In general, relief of pain is perceived through prolonged end-range stretch-stimulating type I mechanoreceptors and through midrange oscillation frequency of .5/sec., which has its effect by stimulating type II receptors. Stimulation of each of these receptors through exercise has been found to function in pain inhibition.

Muscle Spasm

The presence of localized muscle spasm has also long been accepted as a source of pain. Many authors refer to the pain-spasm hypothesis to serve as a theoretical model, i.e., if the muscle guarding is prolonged, the altered local environment will result in further irritation to free nerve endings. The presence of this continual chemical irritation is believed to perpetuate the muscular spasm. Muscle guarding or spasm serves its immediate function by reinforcing immobilization for the involved injured structures. Whether the source of the

pathology is bone, joint, or connective tissue, muscle spasm may be present to prevent further injury.

Relief of the muscle spasm can be effected through two mechanisms. The first is the localized treatment of the spasm itself. This treatment may include modalities, but must also include a lengthening stretch to the involved muscles. Lengthening of tissues allows for dilation of capillaries and results in increased blood flow to the muscle cells. Removal of metabolic wastes and increase in local oxygen also result. Though this mechanism may be effective in immediate relief of muscle pain, it is not effective if other structures persist as the underlying cause of the protective spasm. In this instance, treatment of the muscle spasm only does not address the problem properly.

An alternative means of treating muscle spasm is through affecting the actual source of the spasm. Obviously, if traumatic bony fracture or gross dislocation is present, immobilization will ultimately assist in relief of local muscle spasm. In the absence of trauma, treatment requires clarification of the offending source of the muscle spasm. Williams (8) felt that the primary source of low back pain is from paravertebral muscle spasm and loading the apophyseal joints. If this is so, why do most patients with acute low back pain present with lumbar flexion deformities? Clinically, we have observed marked reduction in local muscle spasm through active or passive lumbar movements other than flexion. We must assume, then, that pain reduction in these instances is through mechanisms other than muscular stretch. Quite possibly, we have removed the offending stress from pain-producing structures other than muscle.

Chemical Irritation

Pain generated by chemical inflammatory irritation of the nociceptive nerve endings may be reduced or eliminated by two means: (1) physically reducing the chemical irritants; or (2) neurologically reducing the activity in the nociceptive receptor system. In the former, improved circulation results in a reduction of lactic acid, histamine, hydrogen ions, and kinens in the affected tissues. Cellular membranes may also become more permeable, resulting in decreased tissue tension. The latter mechanism (neurophysiological) will be discussed later in this chapter.

Mixed Causes of Pain

Maitland (9) implies that patients often present with not only mechanical or chemical pain, but with an assortment of both types of pain. He further implies that the chemical component of the patient's pain may be partly or wholly caused by mechanical stress. For example, chronic microtrauma to the lumbar spine created by adaptively shortened structures in the hip joint may provoke symptoms, both chemical and mechanical in nature, in either the hip or adjacent lumbar spine. Reduction and subsequent elimination of the mechanical stress in the hip indirectly reduces the related spinal pain. Likewise, reduction and subsequent elimination of any mechanical stress in the lumbar spine produces a positive effect on the chemical pain. Reduction of the chemical component, through the use of physical agents, provides only temporary relief of symptoms, as the clinician probably failed to address the underlying mechanical component.

Probably in some cases, both chemical and mechanical components of

pain are present. Overemphasis on treating the chemical component either with medications alone or in some combination with physical agents may actually prolong the patient's problems. Further consequences of not addressing the mechanical component include failure of the patient to fully recover from his ailment, and advancing the chronicity of the problem.

Gentle exercises may be used to reduce inflammation and edema, and once the inflammatory component is reduced or eliminated, the mechanical component may be identified and dealt with appropriately.

Mechanical Stress

The final proposed mechanism for pain reduction relates directly to mechanical stress. All spinal structures—the apophyseal joints, the intervertebral discs, and the associated soft tissue—have anatomical resting states. McKenzie (1) has postulated that appropriate application of exercise actively alters the state and position of the nucleus of the intervertebral disc. This has been confirmed by others (11). He feels that it is possible, through exercise, to remove abnormal stress from the disc and restore the normal anatomical relationship to the intervertebral junction. Reduction of mechanical deformation, when the intervertebral disc is at fault, is best accomplished by following the principle of centralization described by McKenzie (1) and further documented by Donaldson (12). Reduction of mechanical deformation, when adaptively shortened structures are at fault, is best accomplished by temporarily reproducing the pain of stretching the deformed tissues without permanently increasing the level of pain. In describing his "postural syndrome," McKenzie (1) also cites the *reproduction* of pain in normal soft tissue simply due to excessive mechanical stress. Others report that abnormal mechanical stress adversely affects the apophyseal joints (5,6). Whether it concerns the disc, soft tissue, or apophyseal joint, there is clinical evidence that removal of excessive mechanical stress from any or all of these structures will result in the reduction of perceived patient pain.

Using knowledge of neurology, physiology, and biomechanics, the clinician can prescribe appropriate exercises for low back pain. Direction of movement, starting position, frequency, and vigor are all coupled to reduce and eliminate pain.

RESTORATION OF NORMAL FUNCTION

Once pain has been reduced or eliminated, the process is directed toward restoration of normal gross and segmental spinal mobility, muscle coordination, and periarticular soft tissue length. Exercise is essential in the restoration of normal gross spinal motion and posture. Apparent normal gross mobility may hide an abnormal segmental movement. Though passive manual techniques are most effective for restoration of segmental mobility, exercises are essential in retaining this mobility. There is little evidence that exercise can produce a specific desired effect at only one segmental level. It is reasonable, however, to assume that with appropriate stabilization of superior and inferior segments, the desired effects of the exercise can be localized to within two to three sequential levels. When restoring segmental mobility, emphasis is usually placed on connective tissue and muscle.

Stretching

Connective tissue such as tendon, ligament, joint capsule cartilage, and fascia is thought by many authors to be the primary factor in the loss of mobility (10,13,14). The response of these structures to stretch is dependent upon the structural orientation of the collagen fibers, the properties of collagenous and elastic fibers, and the ratio of collagenous and elastic fibers (15). Collagenous fibers are the most prominent in fascia, ligament, and tendon. These fibers are relatively inextensible and are resistant to high tensile loads. Fewer in number, elastic fibers respond to stretch by lengthening momentarily and returning to their resting position with the removal of the load (14). Connective tissue reorganizes itself, responding to stretch with lengthening while responding to immobilization with shortening and thickening. To overcome the progressive shortening of connective tissue, daily repeated movement through a full and normal range of movement is essential.

Optimum stretch parameters affecting connective tissue are not clear. Recommendations for stretching duration range from 15–120 seconds, though specific times are unsubstantiated. Lehmann et al. (16) have demonstrated an increase in tissue extensibility and residual length with the presence of heat and a sustained stretch of 20 minutes. Numerous clinical studies have reported soft tissue length gains with variable parameters of duration and frequency (17–21). It also appears that if a stretch is applied within a duration and range of 15–120 seconds, that frequency may in fact be more significant in long-term flexibility (22).

The extensibility of muscle is dependent on many factors. Stolov and Weilepp (23) state that the length-tension characteristics of muscle are dependent on the presence of nonpathologic intermuscular adhesions, the sarcolemma, the contractile elements (actin and myosin), and the associated tendons. The relative effect of each of these factors on contractile element extensibility is unknown. DeVries (24) and Cumming (25) have shown that at the extreme ranges of motion, muscle is the primary limiting factor to further motion.

The presence of pathological scar tissue must also be taken into account when attempting to restore normal function. Kottke et al. (26) state that exercise can decrease the number of collagen cross-links by increasing the collagen turnover rate. Collagen turnover rate is essentially the process of simultaneous collagen breakdown and synthesis. If, through exercise, the rate of breakdown exceeds the rate of production, the resultant scar mass is more flexible and less bulky. The opposite may also occur, resulting in inflexible debilitating scar masses. In stretching immature scar tissue, one must be aware that excessive force has the potential to disrupt the vascular bed with resultant new injury and inflammation (27–29).

Neurophysiologic Approaches

In addition to the mechanical mechanisms, there are also neurophysiological means of producing tissue elongation. Proprioceptive neuromuscular facilitation (PNF) has been stated by Knott and Voss to affect the neuromuscular mechanism through stimulation of proprioceptors (30). PNF is based on the neurophysiological principles of facilitation and inhibition, resistance, irradiation, successive induction, and reflexes. The use of facilitatory stimuli decrease the threshold of motor neurons or enhances the recruitment of additional motor

neurons. Any inhibitory stimuli act conversely and essentially decrease excitability. Specifically, PNF techniques are the source of stimuli that raises the threshold of motor neurons or results in a decrease in number of actively discharging motor neurons (30,31). Though utilization of these principles may produce both increased strength and flexibility, we refer here only to their effect on tissue elongation.

The primary reason for PNF effectiveness in tissue elongation lies in the manipulation of the stretch reflex. This reflex involves two types of receptors: muscle spindles, which are sensitive to length changes as well as to the rate of length changes in the muscle fiber, and Golgi tendor organs (GTOs), which detect changes in overall tissue tension. Both of these receptors have been found to assist in muscle relaxation. Numerous authors (32–34) have hypothesized that isometric contraction followed by active relaxation results in an inhibition of the alpha motor neuron supplying the muscle, resulting in further relaxation and elongation. The mechanism for this relaxation is thought to be through the GTOs.

A second method of inducing relaxation is through the contraction of antagonist muscles to relax agonist muscles. This action facilitates relaxation through the Sherringtonian reciprocal inhibition reflex (35).

Deep rotator muscles, thought to be responsible for joint stabilization, are believed to be strengthened or retrained using high repetition, low resistance, midrange exercises done frequently with an emphasis on restoring coordinated movement. Muscle imbalances are also believed to contribute to the loss of function. Weak muscles require strengthening, tight muscles require stretching, and inactive muscles require retraining. Principles described by Sahrmann (36) provide the fundamental base for addressing these imbalances to reduce or eliminate the chronic microtrauma present during faulty movement. Strengthening of weak muscles only, using the most sophisticated equipment, may result in only partial recovery of function or absolutely no gain whatsoever.

Though it is still unclear what structures are at fault in limited spinal mobility, normal range of motion is essential to healing of new collagen and elongation of existing connective tissues.

PROPHYLAXIS

Complete success in the treatment of spinal disorders is assessed by more than relief of pain and restoration of motion. One must prevent future recurrence to be successful. The objectives for prevention are to restore: soft tissue length and balance (agonist vs. antagonist); coordination and endurance of tonic spinal stabilizers; phasic muscle strength; and proper body mechanics and posture. Posture must be addressed from the initial visit to discharge.

Achieving a balance of soft tissue length between agonist to antagonist is essential in the treatment of back disorders. The most commonly shortened muscles are the hip flexors, hamstrings, gluteal muscles, and paraspinal muscles. Specific stretching techniques are mentioned later using the rationale stated for soft tissue elongation.

Spinal Muscle Deconditioning Syndrome

Recent advanced techniques for quantification of physical function of the spine have become commercially available (37–42). Research resulting from

the quantification of muscle function has pointed to a marked deficit in physical function in patients with chronic back disorders. The role of this deconditioning syndrome is becoming more clearly evident (43–45). Weak muscles have long been considered a contributory factor in back disorders. Many authors therefore have advocated the use of strengthening programs (40,44,47). Improvement in one's physical conditioning has been shown to aid in restoration of normal life-styles following back disorders (31). Isokinetic strength quantification reveals that normal trunk extension-flexion strength ratios range from 2.7:1 to 1.1:1 (37), but little has been done to quantify the strength and endurance role of the smaller deep muscles of the back. Chronic fatigue in these deep muscles has been hypothesized to produce low back pain (48, 49).

Much has been written about strengthening exercises for low back pain. These exercises are generally directed to the muscles of the trunk and pelvis. Despite the importance placed on strengthening, relatively little has been reported regarding the appropriate use of exercise based on muscle fiber type and function. The paravertebral muscles are predominantly red fiber type and function in high endurance, low force activities. Muscles such as the abdominal and gluteal muscles have greater amounts of white fibers. Respecting these differences, it is then logical to also rehabilitate the paravertebrals for their specific functions in relation to the spine.

The deep paravertebral muscles (rotators and multifidi) have been found by inserted electrodes to contract moderately and bilaterally symmetrically during spinal rotation and during extension (50). During sitting and standing, they are slightly active (51). Due to their proximity to the apophyseal joints a corollary function may be coordination and guidance of the apophyseal joints during most movements. With this in mind, the clinician initiates a muscular training program with appropriate endurance training for these muscles. Once segmental movements are well coordinated muscularly, recruitment of more powerful muscles (larger paraspinals) should not disrupt normal joint mechanics. Clinically, those patients who demonstrate no segmental strength or range of motion deficits but complain of a "catch" in their back may be suffering from transient symptoms from apophyseal incoordination and subsequent joint stress. Muscular retraining includes the motion of rotation through the mid-range using little or no resistance. These motions should be performed with at least 30 repetitions to take account of the endurance nature of the fiber type of the deep muscles.

Increases in muscle strength are generally accomplished developing tension in involved muscles against a large amount of resistance for relatively few repetitions. In general, the fiber type of abdominal and paravertebral muscles does not lend itself to this type of stressful training. These muscles must also be trained with high repetitions of movement against low loads (48).

Muscles that are phasic in nature should be trained for strength. Strength gains have been reported using variations on DeLorme's original progressive resistive exercise concept (52). Progressive strength gains are achieved through multiple sets (usually three) of 10 or fewer repetitions.

The final approach to prophylaxis is the functionally specific exercise. These exercises must be designed by the clinician to simulate the patient's functional environment. The application of proper body mechanics in this stage is the basis for exercise design. For example, if the patient frequently bends and lifts heavy crates at work, weighted boxes will be lifted repetitively to strengthen needed muscles and reinforce proper body mechanics and posture.

PREVENTION OF RECURRENT LOW BACK PAIN

Objective

In view of the episodic and self-limiting nature of low back pain, the success of any treatment program cannot be judged on the achievement of pain relief or on the rapidity of return to work, but on the abolition of future low back pain. If successfully treated, a patient will never again be seen in the clinic for back pain. A comprehensive program of low back exercises never ends, as strength, endurance, coordination, balance, good body mechanics, and proper posture are not innately self-perpetuating.

Preventive Management

To maintain a healthy back, the patient must continue to exercise, use good body mechanics, and retain a balanced posture. Exercises most often used to retain the benefits of the successful treatment program are those that: (1) initially eliminate the pain; (2) restore normal function; and (3) are general fitness exercises such as walking, swimming, and/or sports. Thus, a successful preventive program has its genesis in a successful treatment program. Exercises must be individualized and perpetuated.

It should be noted here that our lack of emphasis on posture does not truly reflect our concerns. Proper exercises—the subject of this chapter—performed diligently can easily be negated by poor posture. Proper spinal treatment must include both proper posture and specific exercises.

RECOMMENDED EXERCISES

Exercises presented below are chosen because they are frequently used in the clinic. Each may be modified to function in pain reduction, function restoration, and prophylaxis. Exercises on pages 311–321 are given with basic directions. In the text below, exercises are grouped according to objectives, namely, pain reduction; restoration of normal function and coordination; and prophylaxis. There will be obvious duplications because some exercises may be used to meet all three objectives. These exercises are neither inclusive nor exclusive, but offer a representative sampling of frequently used exercises. The choices of active exercises, like passive exercises or mobilizations, are endless—the main limitation being the creativity of the practitioner.

Once more, we emphasize that exercises without proper assessment and modification are only partial treatment, and may be harmful. Also, the objective of the exercise must be satisfied and verified by subjective and objective assessment at the initial and subsequent treatment sessions. Appropriate deletions, modifications, and additions will depend on the patient's response to exercise. With few, if any, "correct" exercises for certain sets of clinical symptoms, general guidelines and principles guide the skilled clinician. For example (in oversimplified terms), exercises for the reduction of pain must produce a reduction of pain, and although exercises for restoration of function may produce a temporary increase in pain, they must produce an improvement in function over a reasonable period of time.

Objective: Pain Reduction—Suggested Exercises

Exercises suggested for pain reduction and/or pain elimination are supine lumbar flexion (Fig. 15.1), prone lumbar extension (Fig. 15.2), side-lying rota-

tion (Fig. 15.3), lateral glides (Fig. 15.4), and prone-lying oscillations (Fig. 15.5).

Midrange oscillation affects type II mechanoreceptors and end-range stretch affects type I mechanoreceptors. Muscle spasm is reduced by stretching the involved muscles or by reducing the mechanical deformation of other non-muscular tissues. Each of these exercises reduces pain by apparently decreasing the concentration of chemicals causing the inflammation. This is most effectively accomplished by exercising in the pain-free range initially without increasing existing symptoms. Progression is determined by accurate assessment. When the patient is generally able to perform each of these movements through a full range of motion without pain, emphasis then moves to restoration of normal function.

Objective: Restoration of Function—Suggested Exercises

Exercises suggested for restoration of function are supine lumbar flexion (Fig. 15.1), prone lumbar extension (Fig. 15.2), hamstring stretches (Fig. 15.6), hip flexion stretch (Fig. 15.7), sitting rotations (Fig. 15.8), side-lying rotations (Fig. 15.3), and lateral glides (Fig. 15.4).

These exercises are designed to restore full-range movement by stressing end-range stretch in each of their respective physiological motions. If the desired effect is stimulation and regeneration of collagen in an injured area, the stretch should be repeated 10 times and held for 2–5 seconds. For long-range tissue elongation and improved range of motion, stretches should be maintained for 15–30 seconds.

Objective: Prophylaxis—Suggested Exercises

Exercises suggested for prophylaxis are supine flexion (Fig. 15.1), prone extension (Fig. 15.2), hamstring stretches (Fig. 15.3), hip flexor stretches (Fig. 15.4), prone rotations (Fig. 15.5), abdominal strength exercises (Fig. 15.6), paraspinal strength exercises (Fig. 15.7), and gluteal strength exercises (Fig. 15.9).

Prophylactic exercises are designed to maintain range of motion and provide muscular strength and coordination throughout the full range of motion. For *tonic* muscles (paraspinals), exercises should be performed as tolerated with an ultimate goal of 30 or more repetitions. *Phasic* muscle exercises will best be performed against resistance. Suggested intensity is two to three sets of 10–15 repetitions.

CONCLUSION

Clinical experience has confirmed the beneficial use of exercise programs for the treatment of low back pain. In this chapter, we have outlined specific exercises that have been found to benefit the patient suffering from low back pain. Though many patients lack specific pathological changes, the clinician must rely on careful assessment of signs and symptoms as well as available objective findings to determine appropriate guidelines for individualized exercises. Where diagnostic precision is demonstrable or probable, the clinician can proceed with greater assurance to provide relief. The application of therapeutic exercise to low back pain remains the cornerstone of conservative treatment and prevention.

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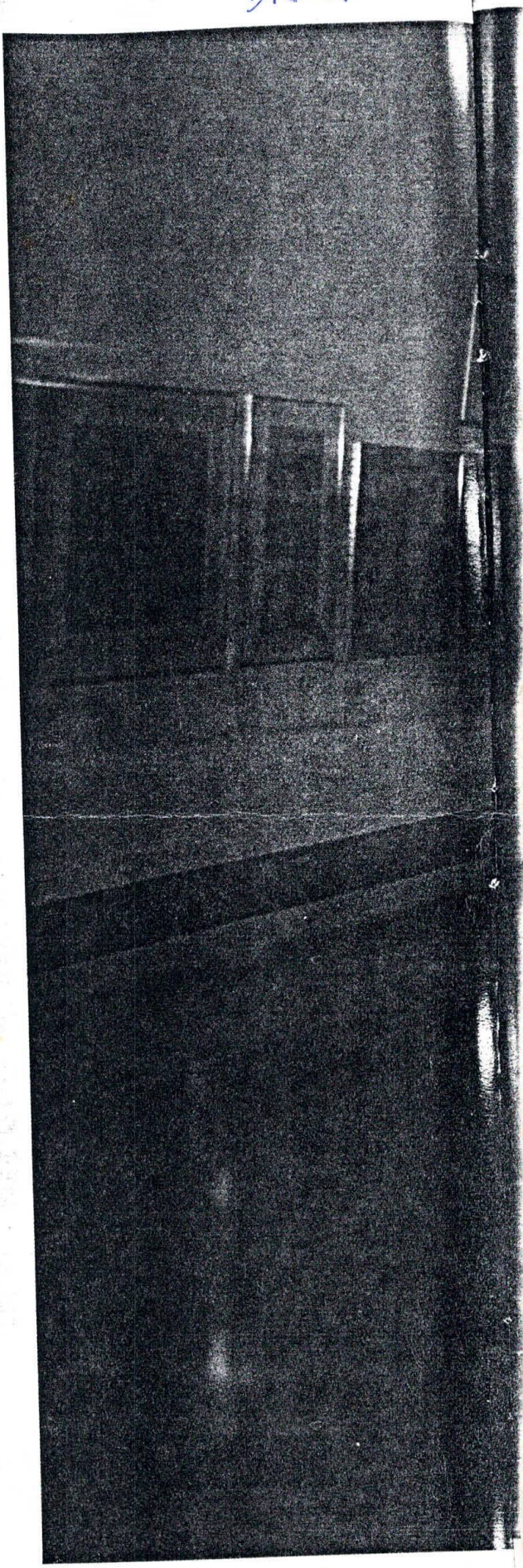
THY WILL BE DONE

By Emily Benedek



Mo Udall perseveres against the ravages of Parkinson's disease, the memory of his wife, and time itself.

In its way, Capitol Hill is not unlike high school. Bells ring, the men and women of Congress rise from their leather chairs and file out of their offices toward the chambers of the Senate and the House of Representatives. They rattle about the hallways, chat with colleagues, exchange jokes, pass along rumors, vote. Then they return until the next set of bells summons them back.

The bells ring again and Morris King Udall, U.S. Representative from Arizona's 2nd District, lumbers down a marble hallway of the Cannon House Office Building. Udall's 6-foot-5-inch frame, once the robust body of a professional athlete, is stooped by arthritis and the ravages of Parkinson's disease. He has become frail and thin, especially in the last year. His pants, too big for him now, are hitched up over his waist with suspenders, and the cuffs dangle inches above his ankles. Yet this day the tall

PAUL FETTERS PHOTOGRAPHS

Udall is indignant about his capacity being questioned. He told a colleague, "The man who can replace me hasn't yet been born."

man with the unassuming manner is in a hurry. He's got his one good eye set on the Capitol (the other was removed at age 6 when a childhood pal accidently hit it with a penknife) and he's got to get there in time to vote. He walks fast, very fast.

The long legs that served him well as a member of the Denver Nuggets in the old National Basketball League are set on cruising speed. The shoes, size 13, pound like paddle wheels beneath the high-water pants. The athlete's discipline propels him forward. According to Udall's doctor, anybody else with Parkinson's disease of the same severity would be in a wheelchair or bedridden. Says an aide, "If the team needs you, you play. That's how he thinks."

Udall is in a good humor this morning. It is primary day in Arizona and the "Mechamites" have just defeated the two most powerful Republican legislators in the state, throwing the party into further disarray. Beneath the furrowed brow and the gray hair, within the face that is rendered implacable by his disease, Udall's gaze turns mischievous. "Udall's first rule," he says. "Don't interfere while your enemies are self-destructing."

Actually, Udall does not find the situation so funny. The Republican turmoil may cost Arizona the $4.4 billion superconducting supercollider. The Arizona leaders defeated in their primary races, House Speaker Joe Lane and Senate President Carl Kunasek, had planned to offer state funding for roads, sewers and other requirements. Now those promises carry no weight.

"I used to be asked how Arizona could produce so many influential Americans," says Udall, stepping into the members' elevator in the Capitol building, "including a minority leader, a president of the Senate, two of nine Supreme Court justices, a secretary of the Interior, Barry Goldwater and me. I said well, I thought the reason was we had civilized politics. We could keep our differences on the high road."

The elevator stops on the second floor and Udall steps out. "Maybe we've had our day in the sun," he says, heading for the floor of the House, "and now we're slipping back."

Mo Udall has had a few of his own days in the sun, including a substantial run at the Democratic presidential nomination in 1976. In Congress, he led the vanguard of reformers who opposed the ossified seniority system in the House, reorganized the committee structure and the civil service, and instituted campaign reform. He has been Congress' most dedicated protector of wilderness areas, earning the moniker "Mr. Environmentalist." And he has been a vigorous advocate for Arizona; he has ensured, for instance, that funding for the Central Arizona Project Canal—a massive public works undertaking essential to Arizona's future—continues until completion.

For 27 years, Udall has waged these and other battles with humor, grace and affection, winning a reputation as a statesman in the grand old sense: funny, erudite, quick. Now he's dug in for his toughest battle, one that requires all his considerable resources. And the stakes couldn't be higher. Mo Udall is fighting for his life. Every moment, he battles with the unrelenting adversary of Parkinson's disease. He battles with the memory of his late wife, Ella. He battles with time itself.

The toll of Parkinson's, an ugly and chronic neurological disorder, has led some, publicly and privately, to suggest that Udall step down. No matter: Despite the ceaseless aches and pains of osteoarthritis and despite the confounding of his muscles and sometimes his memory, Mo Udall is running again, and on Nov. 8 he will almost certainly be returned to a 15th consecutive term in Congress.

For most of his career, Udall has run virtually unopposed. This time, he faces a Republican challenger in Joseph Sweeney, a one-time Democrat and perpetual candidate who mounted his campaign with less than $5,000. Udall barely bothered to campaign back in his Southwest Arizona district, waiting until Congress adjourned before making an appearance. In 1986, Udall was challenged in the primary by Luis Gonzales, who contended that Udall's poor health was preventing him from fulfilling his duties. Gonzales, who was defeated by Udall and who just lost a primary bid for a seat on the Pima County Board of Supervisors, today says, "He's slipped. The time is here for him to consider stepping aside and letting other people have the opportunity to be elected."

Udall's physical deterioration has not been lost on his congressional colleagues. Observes a political reporter in Washington, "For about three years, people have been referring to Udall in the past tense."

Yet those who work closely with Udall insist that his work is still top-notch. Says Sen. Edward M. Kennedy of Massachusetts, "He's always led the way to a higher standard. My brothers recognized this. He's a very, very important congressman, a very powerful and courageous individual. He's better than 95% of his colleagues, and the only appropriate comparison of his abilities is against himself."

Says Rep. Ben Nighthorse Campbell of Colorado, who serves on Udall's Interior Committee, "When you find somebody like Mo Udall, you hang onto him. Every Democrat would rather have a chairman who wields the power he does rather than have a rank beginner."

Udall himself is indignant about his capacity being questioned. "The man who can replace me," he once told Campbell, "hasn't yet been born."

Udall would prefer to ignore the disease. The man he sees in the mirror is not the man in his mind's eye.

Mo and Ella Udall at the Democratic National Convention in New York City in 1976.

That man is athletic, healthy, a Westerner, an outdoorsman. "I've always pictured him as a masked man who rides into town on a white horse," says a friend. "He shoots with silver bullets, never killing opponents, only wounding them. When he leaves, the townspeople ask, 'Who was that masked man?' And I tell them, 'That's the tall Udall.'"

"You can talk a great, optimistic game, like I do," Udall says of his condition, "or you can sit around and say 'I can't stand it, I'll hurt the rest of my life,' and you probably would. I've stretched this thing out 14 years now, and I figure I can go on a few more." Udall is determined to beat this beast. He has subjected himself to experimental medications, and he adopted a new diet with such rigor that he lost far too much weight.

Truth be told, his closest friends and relatives believe that his work in Congress is what keeps Udall fighting. Says Arizona Sen. John McCain, "Mo is a man whose every fiber is devoted to public service. It's in his heritage, in his blood, and it is his sustaining force."

His physician, Dr. Jerry Targovnick of Phoenix, says, "If he didn't do what he did, he'd lie down and die."

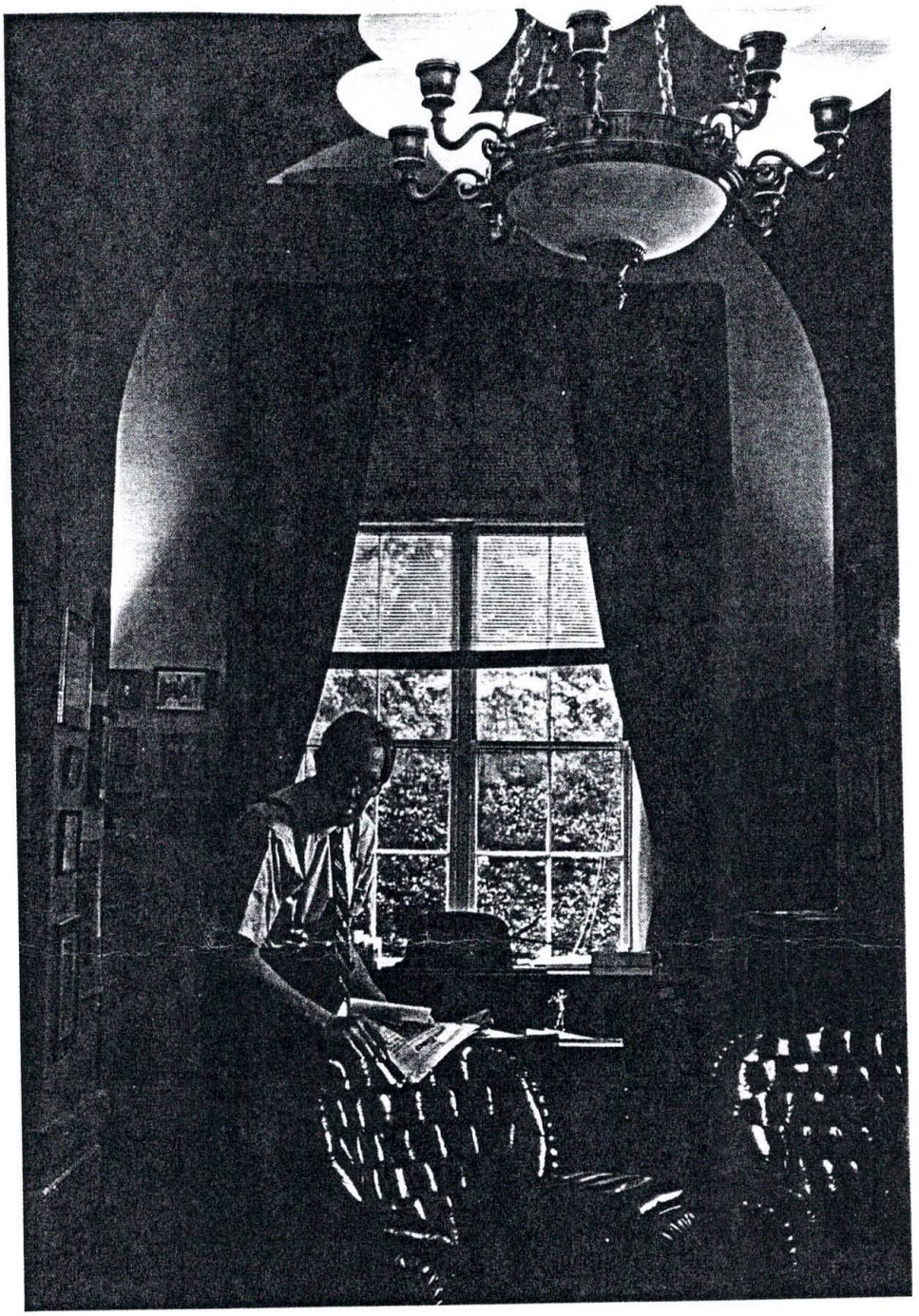
Certainly, Udall's disease sometimes leaves him depressed. And since his wife's suicide in August, he has been grim, even sullen, according to an aide. Udall is 66 years old. He once told Ella that he wouldn't live to 70. His family worries that the prediction will prove true. "I think Mo wants to go out in Congress," says the aide. "It's almost the only way for him to go."

A couple from Arizona waits to pay a courtesy call on their congressman. The man is a mechanic who used to service an airplane that Udall flew around his district. (Udall prides himself on having been an able pilot for 20 years despite his visual impairment.)

Udall returns from a vote and enters his office suite, head raised, with a slightly quizzical expression on his face. He walks past his secretary and into his private office. He needs time these days to get organized, to take his medicine. He takes five different medications and vitamins six times a day in an experimental program for Parkinson's run by the National Institutes of Health. Every three hours, every day, he takes his pills, which his staffers cut and place in piles for him. Because his illness prevents him from setting an alarm on his wristwatch, an aide reminds him to take his medicine—in much the same way that staffers leave knotted ties for him at home, drive him to and from work and fetch chocolate milkshakes in the hope that he'll put on weight.

Ready at last, Udall emerges to greet the couple. "So you're the man who rendered those planes useless at any speed?" he teases, breaking the tension a bit. But Udall is tired. His head is starting to roll, and he hasn't complete control over his facial muscles. The couple enter his office. Mo reaches down to turn his swivel chair. He can't quite get it to move. No one offers to help him; this is his struggle, this is what keeps him going, pushing that unresponding muscle, willing that nerve to transmit its

COURTESY OF M. K. UDALL



To keep his joints from stiffening and his arthritic back from aching, Udall tends to stay on his feet and in motion.

message. It is agonizing to watch. Finally, he positions the chair, puts his hand down on the seat and lowers his body onto it. His guests are outwardly calm, but their knuckles are white from gripping the arms of their chairs.

Udall notices it all. He offers a few pleasantries and a story. He tells the couple about the time he was flying into Dulles Airport and ran out of fuel nine miles out. "Congressman," his passenger suddenly asked, "are both those dials supposed to be on zero?"

The guests laugh more heartily than is necessary. Mo Udall will never fly an airplane again. After a few more minutes of catching up on old times, Udall is ready to conclude the meeting. The visitors don't pick up on his cues. At last he says, "OK, gang. It's time. School's out."

Mo Udall has distinguished himself as a man who can change votes through the power of affection. He is a master of the art of likability. Says Udall, "John Dingell [a representative from Michigan] keeps black books of people who don't vote with him. Others win things because of love and respect. I chose to go that way. I had to do it my way. I couldn't be mean. You can be just as effective using persuasion and affection as the more traditional games of hardball."

Young liberals regard Udall as a folk hero, and "Western congressmen look up to Udall regardless of their party," says Colorado's Campbell. "A suggestion from Mo is like a mandate from anybody else. He never says, 'I want you to do this.' He offers suggestions. He's

"I once tried to oppose the Udall machine," says a California congressman. "And I still have the tire tracks on me to prove it."

suggested a few things that I've listened to very carefully."

Adds Terry Bracy, who ran Udall's presidential campaign, "When was the last time Udall lost a vote?"

"Udall is his best when weighing in on the most difficult issues," says George Miller, a Democratic representative from California. "When an issue gets stuck, the Udall network in Congress is what moves things. He is a man of principle. When Mo puts his name to the paper, it's on the right side of the issue. Congressmen view him as a national figure."

Sen. Kennedy watched Udall chair an October meeting of the Office of Technology Assessment, a bipartisan board of heavy hitters, and observed, "He knows when to press, when not to press. He knows when to listen. He declared that the yeas had it in a vote that was very close, and no one challenged him to a roll call. People have a sense that if Mo wants it, it's probably right."

While Dingell kept enemy lists, Udall kept jokes. For 30 years, Udall has collected gags and political humor in his own black notebooks. He is frequently asked to provide a joke or story for his colleagues to use in a speech. One recent day, a staffer for vice presidential candidate Lloyd Bentsen called for a joke. "Those bastards have been stealing jokes from me for years," he kids. "Now they can buy my book." Last year, Udall published *Too Funny to Be President*, a long-awaited memoir and book of stories. It has sold 60,000 copies.

But Udall is more substantial than a soapbox funnyman. He is an intellectual and a legal scholar. He wrote the seminal lawyer's handbook, *Arizona Law of Evidence*, and two guides for lawmakers, *The Job of the Congressman* and *Education of a Congressman*. In 1984, he was voted the most respected and most effective member of Congress by all his peers.

Even before the onset of disease 14 years ago, Udall was prone to moods, sometimes dark moods, but he's never apologized for them. When an aide tells him he has been criticized in a newspaper story for brooding too much, Udall shoots back, "So was Abraham Lincoln."

A former top Udall aide, now a lobbyist, enters Udall's office with clients from a small Western town. They want to block an environmental bill that would prevent them from building a hydroelectric plant. Udall listens to them. He gets up from his chair, walks around the room. After a few minutes in any stationary position, Udall's joints stiffen and his arthritic back pains him.

The presentation continues. Udall paces, shuttles around his burrow. When the discussion is almost over, the charts still held in mid-air, Udall asks, "How much power will you get from the dam?" A man in cowboy boots and a blazer with decorative stitching says, "200 megawatts." Udall nods. It is a low number. The group is quiet.

Udall advises them to find a committee member who will support their changes. He doesn't say outright that he will not fight for them, but that becomes clear.

The delegation collects its maps and departs. Later, the lobbyist says, "Mo asked one question. He asked about the power output of the dam. If one thing will defeat this project, it's that low number. Goddamn, his mind is sharp. He went right to the heart of the matter."

For bringing his clients to the powerful chairman of the Interior Committee, the lobbyist doubtless earned a handsome sum. Udall told an aide later, "I did him a pretty good favor. He probably earned $25,000 for that meeting." But this is the name of the game, access to power and influence. These are things Udall possesses.

And sympathy is not the source of his power, either. "People are distressed to see Mo sick," says California's Miller, who also sits on the Interior Committee, "but sympathy won't get him down the road. You don't go to Congress or Jesuits for mercy. You don't go to the well as many times as Mo has and win because people feel badly for you. His illness means very little around here because of who he is and the fact that he shows up for work every day. He carries around a huge bag of assets."

Miller, who is itching to assume the Interior chairmanship from Udall, continues, "Mo Udall is a tough son of a bitch. He runs things his way. I once tried to oppose the Udall machine. And I still have the tire tracks on me to prove it."

On the paneled walls of the House Interior Committee are paintings of Indian scenes. Ben Nighthorse Campbell, the only Indian House member, requested that one of the paintings—*Death Whoop*, which depicted an Indian scalping a white man—be taken down. Udall arranged for its removal and called a news conference. "My esteemed colleague here," he told the press, "objects to the surgical operation this Indian gentleman is performing on this white gentleman. And if he's offended, then I'm offended."

"It used to be," says Udall's brother Stewart, who was secretary of the Interior under John Kennedy, "that you could read transcripts of the meetings Mo chaired and they were as good as literature. They were humorous and quick and absolutely entertaining."

Today the Udall wit, while plain to see, is less sparkling as he chairs a full Interior Committee meeting; much of his energy is consumed simply dealing with the pain. Across the room, over a fireplace, hangs a portrait of Udall, coat slung casually over one shoulder, a charismatic Western congressman. It was painted only four years ago, but today he looks 20 years older, thanks to Parkinson's disease.

Parkinson's is a degenerative disorder of the central

> Ella Udall's nickname was Tiger. She was outspoken, irreverent, quick-witted—and, says a friend, "terribly, terribly lonely."

nervous system. In its victims, neurons no longer produce enough dopamine, a neurotransmitter that helps smooth passage of nerve impulses. There is no known cure; victims usually experience motor problems, slurring of speech and, in some, a shuffling gait. The disease takes different courses. In some patients, it gets very bad very quickly, leaving them bedridden. In others, the degeneration is slow. Dr. Targovnick says Udall's disease developed slowly and is in its final phase, meaning it probably won't get worse. Parkinson's is not fatal. Though it can affect the mental capacity of some sufferers, Targovnick says it does not affect Udall's.

Mo Udall first noticed telltale signs of the disease during his run for the presidency. He explained to his doctor that it felt like his "motor was running too fast." Within two years, the disease was diagnosed at Bethesda Naval Hospital. Udall was so disturbed by the diagnosis that for six months he told no one, not even Targovnick. Eventually, he faced the disease head-on, trying different treatments, exercising. He is so determined to beat it that he followed, far too religiously, a special diet thought to help the absorption of dopamine in his brain.

One frustration of dealing with the disease is the dependence on medication. Udall takes a variety of pills, the most important ingredient of which is L-Dopa, which is metabolized by the body into dopamine. Udall must maintain the strict medication schedule, or the frightening Parkinson's symptoms reappear. "It's like an old monkey on your back," he explains. "You never quite get away from it. When the medication begins to wear off after three or four hours, you're like an addict. You need your next fix."

Another typical result of severe Parkinson's is an increasing and burdensome dependence on family, for even the most menial things. For years, Ella Udall stoically, even courageously, dealt with Mo's disease. Because his arthritic back makes sleeping prone so difficult, Udall would often doze off in his chair at home at 11 p.m. Ella would wake him at midnight for his medication. He'd struggle to fall asleep again, typically dropping off by 3 a.m., only to be awakened again at 6 by Ella to take more pills. "He'd be groggy and yell at her," says an aide.

Ella was also called upon to cook for him, lay out his clothes and, at times, help him dress. But increasingly, friends say, she was resentful of the demands. They became a wedge between them.

On the morning of August 13, Ella Udall entered her husband's bedroom at 6 o'clock and gave him his medication: one-half tablet of CR-IV, one-half tablet of Sinemet, one Symmetrel, Vitamin E and Motrin. Then she went into the kitchen and put her dog's food on the stove to warm. At some point, she walked out the kitchen door to the garage, stepped into her Cadillac and turned on the engine.

Mo Udall, who rarely is able to sleep mornings, awoke at 10 a.m. He smelled exhaust fumes and, fearing that something was wrong, walked downstairs. He found Ella dead in the car. He phoned the neighbors and asked their sons to come over. They lifted Ella out of the car and brought her into the house. Udall called for an ambulance. The death was ruled a suicide.

One recent morning, while walking to a vote, Mo Udall is asked about the ebullient, contrary woman whose nickname was Tiger. After her death, he went into seclusion with his children for two weeks, and the thought still torments him. "I don't want to talk about it now," he says softly. "Maybe in a few months."

Ella's many friends are not so reticent. Their reactions to her life and death involve anger, compassion, but mostly sorrow—for Ella *and* Mo.

"She was terribly, terribly lonely," says a friend of Ella's. "She wanted him to resign so they could have some time to themselves. It's awfully hard to watch someone you love deteriorate.

"All the time she asked him to quit," continues the friend, who as a former congressman's wife knows first-hand that politicians can't always make time for their families. "They don't hear. Maybe to him it sounded like a broken record and it would be better tomorrow.

"Ella was 59," she continues. "At that age, women need more reassurance; you're getting older, you don't look like you did at 25 or 35. You need more attention from your husband." However, she concludes, "You can't blame anybody for this. Many wives go through it and most survive."

Two and a half years ago, Ella kicked her husband out of the house; she said she wanted to establish a life of her own. They reconciled, but Ella found the burden of caring for her husband ever more difficult, and she blamed Udall's staff for encouraging him to push on. "I think she was fearful about the future," says Rosemary Cribben, who worked for Udall and was a friend of the family.

Indeed, for some years Ella's relationship with her husband's staff had been strained. Says one of her friends, "She felt tolerated by the staff—just tolerated—and that's a terrible feeling. It's common that staffs look on wives as meddling, interfering, bothersome objects."

It's not that Ella didn't know how the Hill operated. She had worked for several congressmen and had served as staff assistant of the Postal Service Subcommittee of the House Committee on Post Office and Civil Service. Udall was chairman of that subcommittee. When they met, Udall was divorced from his first wife, Pat, with whom he had six children. Ella had a son, Vincent, from a previous marriage. Mo and Ella married in 1968.

From the time he was a child, Mo Udall has battled adversity and turned misfortune to his advantage.

Problems first surfaced after Udall's 1976 presidential try. "Ella came back and thought she was going to run the office," says a staffer. "Finally, Udall told her it was his office, that he appreciated her input on certain matters. On personnel matters, for example, he'd say 'I'll ask Ella.' She was very astute. But he made it clear that he had to have the final word."

"Ella made the staff uneasy," says Erik Barnett, Udall's press aide, "because it put them in the position of having to please Mo and his wife. It almost seemed worse to displease her." In the end, Ella stayed away from the office. "She maintained a home, she got a poodle and she shopped," says a staffer.

Ella Udall was outspoken, irreverent, quick-witted, mercurial. "She was a very electric person, a spontaneous person," says Cribben. "She loved to play games." Ella spoke her mind and eventually tired of social dinners, with their demands of politesse and diplomacy.

"We thought she'd write the great American novel," says Udall's current secretary, Joan Shycoff. "She read voraciously, she was eloquent, but not well-educated. The skills she had she could never put in the right place."

"I think Ella was a woman of extremes," says Cribben. "She had swing moods. Sometimes she liked to be out socializing. Other times she stayed home for months.

"Nevertheless," Cribben continues, "she enjoyed the role of Mo Udall's wife—having influential friends, enjoying the perks of power. It was a real coup for her. But it's hard to accept the good and take the bad, too."

If Ella was the fire, than Mo was the ice. Says Stanley Kurz, who has been Udall's friend since they served together in World War II, "People find Mo cold. It's hard to be intimate. He's kind and he's thoughtful and helpful, but on a personal basis, you don't swap details of your personal life. I think it's his strength."

Udall also maintains that distance from his staff. Says press aide Barnett, who drives Udall to and from home and has the most access to him, "I've always tried to become a friend he could turn to, but he's never let me be one. I realized it's probably for the best."

Still, by all accounts Mo and Ella were devoted to each other. "He shared things with Ella that he never shared with us," says Barnett. Watching her husband's deterioration distressed her. "She felt that he was not well enough to do some of the things he did," says a family friend. Ella was particularly disturbed when Udall returned exhausted from the Democratic National Convention in Atlanta.

In the end, says one of Ella's friends, "she didn't have anything to look forward to." Says Cribben, "I think Ella's expectations in life were never met. There was probably not enough give-and-take from both parties. It might have been that Ella was the least yielding."

In the days before she died, Ella called many of her friends and relatives. In retrospect, some realized she was bidding them farewell. But others can't believe she intended to die. "She was an inveterate note writer," says Cribben. "She always wrote notes to Mo. She adored her son Vince. She would have written him a note."

No note was found. Ella had left the dog's food warming on the stove. "She loved that dog," says a friend. "Had she intended to go, she would have fed it first." The last thing she did remember to do was give Mo his medicine.

In a way, struggling against Parkinson's every day, every moment—just to walk, speak, sit, think—and succeeding beyond reasonable expectations is pure Udall. His life has been marked by setbacks that he battled, and eventually turned to his advantage. He lost an eye as a child, yet became a star athlete. He was kept out of the Army because of the disability, yet eventually served and was discharged with the rank of captain.

In 1954, he deferred to Stewart and decided not to run for the House seat from the 2nd District; he ran for a county judgeship instead and lost. But he replaced his brother in 1961 when Stewart became secretary of the Interior. Udall launched a symbolic challenge against Speaker of the House John McCormack in 1969. He lost, but became an obvious candidiate for majority leader in 1971. He lost that, too, to the late Hale Boggs, but gained enough prominence that he was pushed as a Democratic presidential hopeful in 1976. This characteristic Udall himself calls "succeeding by losing. Losing and bettering your prospects."

Now it's Parkinson's to battle while trying to oversee the final stages of the Central Arizona Project, to make final determination of water rights along the upper Colorado River, and to fight for the Arizona Wilderness bill. "It's a losing fight and he knows it," says his brother Stewart about the disease. "But he won't admit it. He keeps on fighting."

And laughing even as he fights. One day recently, Udall told the story of a hard-working, God-fearing man. The man was blessed with a lovely wife and several children. But one day things began to go wrong. First, his wife ran off with his best friend. In his humility, he said to God, "Thy will be done." Then his daughter took a shiftless husband who ran the family business into the ground. "Thy will be done," he repeated. By this time, he was reduced to working a small plot of land. He suffered through droughts and crop failures, yet he remained faithful. "Thy will be done," he would tell God. Finally, while out plowing under the stalks of his dead crops, he slipped and fell into the dirt, and his mule kicked him in the head. The man turned his gaze skyward and said, "God, Thy will be done. But this shit's got to stop." □

GOITRE CAN BE PREVENTED

Goitre prevalent all along the sub-Himalayan belt. It is also seen in the Chhotanagpur plateau, Aravalli range and the Eastern and Western Ghat ranges. About ₿ 90 million people live in these areas and 25 million may be suffering from goitre. Given below are a few tips on the causes and prevention of goitre.

Enlargement of the thyroid gland, which is situated in the neck of a person, is known as goitre.

Goitre is essentially a deficiency disease associated with lack of iodine in soil or water.

Goitre is prevalent in the Himalayan belt, from Jammu and Kashmir along the Southern slopes of the Himalayas to Arunachal Pradesh, Nagaland and Manipur. It is also seen in the Chhotanagpur plateau, Aravalli range and the Eastern and Western Ghat ranges.

Nearly ninety million people are living in these areas and about 25 million people may be suffering from the disease.

How do people develop goitre?

People develop the disease when sufficient amount of iodine is not available for their thyroid gland to maintain its normal function. Normally, the thyroid gland draws iodine from the blood and converts it into the hormone called thyroxin. This hormone is essential for the functioning of all body tissues.

How is goitre identified?

Goitre produces enlargement of the thyroid glands causing swelling in the neck. These may be large enough to be seen or palpable or can be felt by the hand. The gland may also not necessarily be large enough to be visible or palpable.

Who gets goitre?

Anybody can be afflicted by goitre. People of all ages and both sexes can fall a victim. But goitre affects children most. It is also more common in females than in males.

The size of the thyroid gland normally increases a little as children grow up. But in goitre, this growth is progressive and the gland keeps on increasing in size with age.

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Pregnant women are particularly at risk to get afflicted with goitre, since the demand for iodine is greatly increased during this period. In areas (villages and towns) lacking iodine in water and soil, the iodine deficiency continues to increase in the body of women with each pregnancy. This results in further enlargement of the thyroid gland.

Effects of goitre

Goitre leads to physical deformity. A person with large goitre presents an ugly appearance. In some cases, the enlarged glands may be large enough to cause respiratory difficulties, because of the pressure on the windpipe. In such cases, surgery may be necessary.

Goitre may reduce the physical strength of an individual. In pregnant women, insufficiency of iodine can affect the foetus. Children born on women affected by goitre are more prone to iodine deficiency than others.

Goitre may also lead to deaf mutism and varying degrees of mental deficiency in the offspring.

Prevention is possible

Goitre can be prevented. Consumption of iodized salt regularly is the best preventive measure against goitre. It supplies the iodine necessary for the thyroid gland to do its normal function.

Iodized salt is available in plenty from any local shopkeeper, and it costs just just as much as ordinary salt.

Take iodized salt and prevent goitre.

Remember

* Iodine deficiency is the main cause of goitre.
** Goitre can appear in both males and females and at any age.
*** Regular use of iodized salt in iodine deficiency areas ensures prevention of the disease.

Source: Swasth hind - May 1980

JAPANESE ENCEPHALITIS

JAPANESE encephalitis, which has been much in the news till recently, is a disease of short duration. It is a disease of the brain caused by a tiny germ called Japanese-B-encephalitis virus. The virus affects the brain and its meninges (covering of the brain) and spinal cord.

Signs and symptoms

How does one recognize a case of Japanese encephalitis? There are some definite symptoms. The victim experiences sudden rise of temperature. This is moderate to high. There are also signs of headache, backache and neck rigidity. The patient may also show symptoms like loss of consciousness of various grades, such as, confusion, convulsions, coma and paralysis.

How does it spread?

Japanese encephalitis, as has been stated earlier, is caused by a tiny germ. This diseased germ is transmitted to man by a particular type of mosquito. Usually, the infection is confined to birds, pigs and cattle, Interestingly enough, these birds and animals, when infected, do not show the disease. Man normally does not harbour the germ but can get infected if a germ carrying mosquito bites him. But it should be remembered that not every person bitten by an intected mosquito will suffer from the disease. According to estimates, the disease has been found to occur only in a vety few infected persons. It has been found that the disease has occurred in less than one person in one lakh of people.

Another matter to be noted is that Japanese encephalitis is not contagious, viz., it does not spread from man to man. Or, in other words, a diseased persons is not of any risk to any other person. Therefore, there is no need to keep a patient isolated.

The disease also is not spread by eating food, including meat or drinking of water or milk i.e., food articles do not act as 'carrier' of the disease.

Who gets the disease?

It should be remembered that Japanese encephalitis does not have affinity to any age group of population, or to any sex. It can attack people of all age groups and both males and females are equally prone to it.

Preventive measures important

Although Japanese encephalitis is a disease of short duration and occurs in a very few infected persons, it can often prove fatal, if not managed properly in time. Hence, preventive measures are of extreme importance in keeping this disease away.

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As the disease is caused only by the bite of the germ-carrying mosquitoes, all possible measures should be taken to eliminate chances of mosquito-breeding or getting bitten by mosquitoes. These measures should be followed:

i) Prevent breeding of mosquitoes by taking care to see that there is no stagnant water in and around houses.

ii) If mosquitoes are seen to be breeding in large pools of water like ponds, etc., the anti-malaria workers should be contacted and asked to take remedial measures.

iii) Get rooms and verandah, where mosquitoes rest, sprayed by the malaria workers.

iv) Use mosquito nets while sleeping.

v) If the residence is near the places, where cattle and pigs are kept, ensure that these places are thoroughly sprayed by anti-malaria team.

It should be remembered that Japanese-B-encephalitis often resembles malaria, meningitis, and other diseases with fever. It is, therefore, essential to make a proper diagnosis, Hence call for a doctor or health worker whenever there is a case of high fever, alongwith unconsciousness, or headache or neck rigidity. Early diagnosis and treatment can save a life.

Source: Swasth Hind - July 1979.

DIS 1-1

MESSAGE FROM DR HIROSHI NAKAJIMA
DIRECTOR-GENERAL OF WHO
WORLD HEALTH DAY 1997

UNTIL quite recently there was a widespread feeling that the struggle against infectious diseases was almost won. The means of controlling most of them seemed either available or discoverable without undue difficulty. Spectacular progress has indeed been made: smallpox has been eradicated and six other diseases will be eradicated or eliminated soon. But tragically, with optimism came a false sense of security, which has helped many diseases to spread with alarming rapidity.

Major diseases such as malaria and tuberculosis are making a deadly comeback in many parts of the world. At the same time, diseases such as plague, diphtheria, dengue, meningococcal meningitis, yellow fever, and cholera have reappeared as public health threats in many countries, after many years of decline.

In addition, previously unknown infectious diseases are emerging at an unprecedented rate. In the last 20 years, more than 30 new and highly infectious diseases have been identified. They include the virulent Ebola-type haemorrhagic fever, HIV/AIDS and hepatitis C. For many of these diseases there is no treatment, cure or vaccine.

Antibiotic resistance is another important threat to human health which has emerged during the last 20 years. Drugs which once could be counted on for protection against many infectious diseases are becoming less and less useful as resistance to them spreads. In addition, fewer new antibiotics are being produced, owing partly to the high costs of development and licensing. As the treatment of communicable diseases becomes less effective, more people need hospitalization, illnesses last longer, treatment costs more and absenteeism from school and work increases.

There are many reasons for the appearance of new diseases and the resurgence of communicable diseases once thought to be well under control. These include the rapid increase in international air travel and the growth of mega-cities with high population densities and inadequate safe water and sanitation. The risk of foodborne diseases has been heightened by the globalization of trade and changes in the production, handling and processing of food. Environmental factors can lead to the exposure of humans to previously unknown diseases. For example, man is destroying forests and moving into previously remote animal and insect habitats which carry high risks of exposure to disease.

Meanwhile, in rich and poor countries alike, resources for public health are being reduced as limited funds are spent on other priorities. As a result, the appearance of new diseases, the re-emergence of known diseases, or the development of antibiotic resistance, may go unnoticed until it is too late. A recent striking example is the human immunodeficiency virus (HIV) which was recognized only after it had already infected large numbers of people in many countries. If diseases of epidemic potential are detected early enough, epidemics and pandemics can be prevented in some cases, in others minimized.

For these very pressing reasons, the theme «Emerging Infectious Diseases - Global alert, Global response» has been chosen for World Health Day 1997. It is my hope that, by using World Health Day as a catalyst, countries will be able to take a realistic look at these problems and concentrate on rebuilding the foundations of disease surveillance and disease control. Both the public and the private sectors must be encouraged to research and develop better techniques for surveillance and control, and new antibiotics to replace those which are no longer effective.

We have to face the fact that infectious diseases are a common threat which demands urgent attention, especially at a time when people all over the world are being brought closer together by international travel and trade. Communicable diseases respect no frontiers. We must work together globally to control them.

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Emerging Infectious Diseases

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EMERGING INFECTIOUS DISEASES

What are **emerging and re-emerging infectious diseases?**

Emerging infectious diseases are those due to newly identified and previously unknown infections which cause public health problems either locally or internationally.

Recent emerging diseases include a highly fatal respiratory disease caused by a virus called sin nombre; a variant of Creutzfeldt-Jakob disease, a disease of the central nervous system which is suspected, though not proven, to be associated with a similar disease in cattle called bovine spongiform encephalopathy; HIV infection which causes AIDS, with its sequelae of human suffering and economic burden; and diseases such as Ebola haemorrhagic fever with a potential for international spread. Other examples of new or newly detected infectious diseases of global concern include a new form of cholera , a haemolytic uraemic syndrome , hepatitis C and hepatitis E, Legionnaires' disease, and Lyme disease. Although it is not always possible to know if these diseases are new in humans, or whether they have been present but unrecognized throughout the years, many emerging diseases are thought to be due to a closer contact of man with their reservoirs in nature, with a successful «jump» of the infectious agent from animal to man across the species barrier.

Re-emerging infectious diseases are those due to the reappearance and increase of infections which are known, but had formerly fallen to levels so low that they were no longer considered a public health problem.

Re-emerging infectious diseases often reappear in epidemic proportions. Tuberculosis is increasing worldwide due in part to its close association with HIV infection; cholera has been re-introduced into countries and continents where it had previously disappeared, and where it can spread because water and sanitation systems have deteriorated; dengue or «breakbone» fever has started to occur in urban areas where mosquito control has broken down.

Microorganisms resistant to antibiotic drugs emerged and spread soon after the introduction of these drugs and in parallel with their use. Many well-known antibiotics are no longer effective to treat common infections such as otitis, pneumonia, gonorrhoea and tuberculosis. At the same time, fewer new antibiotics are released on the market, partly because of the high cost of developing and licensing them and because the development of resistance reduces the «useful life» of antibiotics. If the arsenal of drugs against infectious diseases loses its power, the future for patients with even a banal ear infection will become bleak.

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Emerging Infectious Diseases

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WWW.WHO.CH - the home of WHO on the Internet

How to navigate your way around the WHO home pages

Using the WHO site

Once you have contacted the WHO via the Internet (www.who.ch) the main menu page should appear quite quickly. The layout of the WHO Web pages will be familiar to anyone who has used the net because they follow a pattern used by many other users and institutions. You will see the WHO logo and a picture of WHO HQ in Geneva but few other graphics as the site has been designed to allow the fastest possible downloading of information*.

The main menu is linked to other pages in the site by key words or phrases highlighted in blue and underlined. By clicking on the highlighted section, the desired pages are called up. For example, if you click on the light blue **WHO**, you access the page which gives you background information on WHO and a list of addresses, phone and fax numbers, and e-mail addresses regarding WHO HQ and the six Regional Offices. It might help to think of our web site as a book. The main menu page is the cover with the contents listed on it. By clicking on a particular subject on the cover (highlighted and underlined in blue), you will go to the chapter on that subject. Then by clicking on a highlighted topic in the chapter menu, you will see the individual pages of information, and so on.

So, if you want more detailed information on the topic of this year's World Health Day, Emerging and Communicable Diseases, click on WHO Headquarters' Major **Programmes** (light blue underlined) in the main menu. This will take you to another menu listing the major programmes including the **Division of Emerging and other Communicable Diseases Surveillance and Control (EMC)**. By clicking on this you will see another menu listing various aspects of the work of EMC such as **News of diseases reported** to EMC, **Cholera and Epidemic Dysentery** or **Haemorrhagic Fevers (including Ebola, dengue...)** If you click on any of the highlighted areas, you will find the latest information on that subject.

If you have a special interest in a topic and know you will visit the page frequently, you may like to bookmark that particular page to save time. How you bookmark a page will vary depending on which Internet browser you are using. For example, if you are using Netscape and want to bookmark a page simply click on **Bookmarks** and then on **Add Bookmarks** in the box which appears. The page will automatically be called up every time you select the page from your list of bookmarks.

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As well as information about WHO programmes, the site also gives you access to all of the Organization's Public Information materials in most cases both in French and English. These include Press Releases and Fact Sheets. To reach this information click on **Public-Information-Publique** on the WHO main page, there under Headquarters choose the language in which you want to view the information: either **English** or **Francais**. Then choose **Press releases** or **Factsheets** or **Backgrounders** or **Notes to the Press** and so on.

From the main page you may also view electronic versions of 10 WHO **Newsletters** on topics ranging from chemical safety and noncommunicable disease to changes in medical education and practice.

The WHO web site is big and getting bigger all the time, but don't be put off! There is a search engine installed at the top of the main menu page and on many of the inside pages, such as Public Information, which will help you find what you are looking for either by key word or concept. This is particularly useful in the WHO **Statistical Information System (WHOSIS)** page where there is a great deal of health and health-related data and information. Also, WHOSIS and some other Programmes have hypertext links to other non-WHO sources of information such as the **Centers for Disease Control and Prevention (CDC)** in the USA and the **Global Health Network** which also has versions in Japanese, Portuguese and Spanish.

In addition to the web site at WHO HQ there are links to web sites or e-mail addresses in the six WHO Regional Offices. These sites will contain information specific to the region. You can link to these sites or find the e-mail address by clicking on **Regional and other offices**.

What causes emergence or re-emergence of infectious diseases?

Several factors contribute to the emergence and re-emergence of infectious diseases, but most can be linked with the increasing number of people living and moving on earth: rapid and intense international travel; overcrowding in cities with poor sanitation; changes in handling and processing of large quantities of food; and increased exposure of humans to disease vectors and reservoirs in nature. Other factors include a deteriorating public health infrastructure which is unable to cope with population demands, and the emergence of resistance to antibiotics linked to their increased misuse.

Travel has always been a vehicle to spread disease across the world, and the central protective legislation edicted in the 14th century by the City-state of Venice has evolved, over the centuries, into the current *International Health Regulations*. The volume of travel has dramatically increased in recent years: presently well over 50 million people use international air transport each year. The speed of travel has similarly increased: whereas cases of cholera, plague and smallpox were slowly transported from one continent to another by ship and could be recognized during the voyage, it is now possible and quite likely that an infected traveller will only develop signs of the disease several days after arrival.

Emerging and re-emerging infections reflect the constant struggle of microorganisms to survive. One of the ways microorganisms have found of surviving is to overcome the barriers which normally protect humans from infections. This may follow deforestation, which forces forest animals closer to man in search of food, or failure to control mosquitoes and other carriers of disease to humans, or a breakdown in water and sanitation systems, or failure to detect diseases early, or failure of immunization programmes, or high risk human behaviour.

All of these have been observed within the past decades, together with a waning concern – and decreasing resources – for infectious disease control. During the first half of the 20th century deaths from infectious diseases declined steadily because of improved hygiene and nutrition. This trend was strengthened with the advent of vaccines and antibiotics during the 1940s and culminated in the late 1970s in the eradication of one infectious disease, smallpox. Because at that time infectious diseases appeared to be a decreasing threat, funds for their control were channelled to other problems, experts on infectious disease retired or left the field and students turned to more rewarding subjects than viruses and bacteria - the infrastructure for communicable disease control began to crumble.

The global response

Since 1992 alarm over emerging and re-emerging diseases has resulted in a number of national and international initiatives to restore and improve surveillance and control of communicable diseases. The Member States of WHO expressed their concern in a resolution of the World Health Assembly in 1995, urging all Member States to strengthen surveillance for infectious diseases in order to promptly detect re-emerging diseases and identify new infectious diseases. The World Health Assembly recognized that the success of this resolution depends on the ability to obtain information on infectious diseases and the willingness to communicate this information nationally and internationally. This resolution has been translated by WHO into the establishment of the Division of Emerging and other Communicable Diseases Surveillance and Control (EMC), whose mission is to strengthen national and international capacity in the surveillance and control of communicable diseases, including those that represent new, emerging and re-emerging public health problems, for which it ensures a timely and effective response.

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BSE

Bovine Spongiform Encephalopathy (BSE) was first described in the United Kingdom in November 1986 and up to mid-1996, approximately 160 000 cases had been confirmed. By mid-1996, BSE had been reported from 10 other countries and areas; in one group of countries the disease occurred in native cattle, while in another group cases were only identified in cattle imported from the United Kingdom.

This fatal neurological disease of cattle is associated with a transmissible agent, the nature of which is not yet fully understood.

It was known that similar transmissible agents caused brain disease in humans, including kuru, and the various forms of Creutzfeldt-Jakob Disease (CJD). The latter can be sporadic, familial, or occur accidentally as the result of a medical procedure (injection or graft of infected human material).

On 20 March 1996, the United Kingdom announced the existence of a cluster of 10 persons identified with what appeared to be a variant of CJD. Full investigation of these cases led to the conclusion that exposure to BSE was the most likely hypothesis. By late 1996, a total of 14 cases of the variant form of CJD have been reported in the United Kingdom and one confirmed in France.

The suspicion of a link between BSE, and the new variant form of CJD through the satisfaction of an essential need such as nutrition, has had important implications for public health and a devastating impact on consumer's confidence in beef safety and thereby the cattle industry. It has forced us to think through the links between public health, industrial development, technology, economic constraints, market and trade practices, public information and consumer safety.

In the case of BSE and the new variant form of CJD, advancement of our scientific knowledge should permit policy-makers to ensure both the continuation of economic activities dependent on the cattle industry and the safeguard of public health.

Hepatitis C

Viral hepatitis is a major global public health problem. The discovery of the hepatitis C virus (HCV) in 1989 ended a period of intensive international research efforts aimed at the elusive «Non-A, Non-B» virus, which was well known as a cause of post-transfusion hepatitis. Although HCV is not as infectious as hepatitis B or HIV, as many as 80% of infected people can become chronically infected and risk serious long term effects such as liver cancer which places HCV among pathogens of primary concern to humanity.

As with all recently discovered diseases, there is considerable controversy within the scientific community regarding prevalence, incidence, natural course, patho-biological implications, socio-economic burden and management of acute and chronic hepatitis C. However, the route of transmission through transfusion with unscreened blood, through the use of inadequately sterilized equipment or through needle-sharing among drug-users is well documented. Sexual and perinatal transmission have been reported but are uncommon. Additional studies are needed on possible alternative transmission modes.

Based on prevalence rates ranging from 0.1% to 33% in different countries, WHO estimates today that as many as 3% of the world's population could be infected with HCV and that there may be some 200 million chronic carriers who are at risk of developing liver cirrhosis and/or liver cancer.

Although the socio-economic impact of chronic hepatitis C has only been partly studied, the costs are likely to be high, as was found in studies dealing with chronic hepatitis B. Treatment with interferon is effective in about 20% of patients. For the remaining 80%, international research efforts should focus on combined antiviral therapy. It is clear that 90% of patients who are in need of treatment today cannot afford it.

No vaccine is available, but most HCV infections can be prevented by:

- Screening of blood and blood products worldwide.
- Destruction of disposable medical material and adequate sterilization of reusable medical material.
- Promotion of public education about the risks of using inadequately sterilized material.
- At a time when traditional public health activities are weakened and when conditions in public health laboratories are deteriorating, the challenge of a new disease places extensive pressure on the medical community and additional financial burdens upon society.

TUBERCULOSIS-a global emergency

Alarming outbreaks of tuberculosis caused by multidrug-resistant strains in the United States have lately stirred public interest. In Minneapolis, a person with tuberculosis infected 41 people in a neighbourhood bar. In Western Canada, a health care worker infected 100 other people. In recent years, outbreaks of tuberculosis in wealthy countries have been investigated in discotheques, churches, subways, schools, airplanes, court rooms, and even on a riverboat casino.

Tuberculosis is easily transmitted from person to person. One-third of the world's population – nearly two thousand million people, from New York City to New Delhi – has already become infected. The infection with the tuberculosis bacillus may lie dormant for many years; some people may not even progress to the disease at all. Active tuberculosis has a better chance of developing when the person's immune resistance is weakened, as is the case for women suffering from hormonal and nutritional stresses of pregnancy or for people living with HIV/AIDS. People dually infected with the tuberculosis bacillus and with HIV are 30 times more likely than HIV-negative individuals to become seriously ill with tuberculosis.

In 1993, the World Health Organization declared tuberculosis a global emergency. Tuberculosis is now the leading infectious killer of adults, and will have killed at least 30 million people within the next ten years if current trends continue. It is likely that no other infectious disease is creating as many orphans and devastating as many families as TB. This huge toll is the price the world is paying for complacency.

A cost-effective and proven drug treatment exists, but careless tuberculosis treatment practices are triggering bacilli that are resistant to once-effective drugs. Multidrug-resistant tuberculosis develops when doctors or other health workers prescribe the wrong drugs or the wrong combination of drugs. It also occurs if the right anti-tuberculosis drugs are not taken on a consistent basis, or are not taken for the entire six months of treatment. Powerful tuberculosis drugs should not be prescribed without ensuring that they are taken correctly.

That is why the Global Tuberculosis Programme of WHO is urging all countries to adopt the DOTS (directly observed treatment, short-course) strategy, in which health workers or volunteers watch tuberculosis patients under their care swallow each dose of the medicine for at least the first two months of treatment and monitor their progress toward cure. The strategy is already showing remarkable success in many countries.

WHO is vigorously promoting DOTS: it trains key health workers, assists governments and health ministries worldwide, promotes research into effective ways to cure tuberculosis, contributes to the cure of tuberculosis patients, and mobilizes funds and political commitment to address the pandemic adequately.

The existing BCG vaccine prevents severe tuberculosis in children, but it does not have much impact on the disease in adolescents and adults. Research to develop a new and more efficient tuberculosis vaccine is under way. A range of candidate vaccines is now available. for clinical evaluation studies.

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EMERGING AND OTHER INFECTIOUS DISEASES: PARTNERSHIPS TO MEET A CHALLENGE

THE LOGO

A worldwide partnership of countries, non-governmental organizations, international organizations, and individuals is required to respond to the threat of emerging and re-emerging diseases by ensuring rapid detection and effective containment. The logo selected for the Division of Emerging and other Communicable Diseases - Surveillance and Control illustrates this partnership. The arrow on the logo begins with a point or points on earth which signal a global alert - the re-appearance of a known disease such as yellow fever, cholera, meningitis or plague, or the appearance of a newly identified disease such as hepatitis C, AIDS or Ebola, or a disease resistant to usual antibiotic treatment. The arrow then increases in width and extends to encircle the earth, as do the increasing number of partners required to ensure a global response of maximal containment for communicable diseases, with minimal disruption.

The World Health Organization, as one of the partners in this global effort, is strengthening global monitoring systems to serve as part of the overall detection system. Three independent systems cover the globe, bringing together specialized laboratories and disease surveillance systems from all countries, and feed information electronically to the World Wide Web and other international electronic and printed media.

WHO COLLABORATING CENTRES

The first global monitoring system is that of the WHO Collaborating Centres, specialized laboratories and institutions with expertise in infectious disease diagnosis and epidemiology. During recent epidemics it has become clear that the WHO system of Collaborating Centres could no longer fully respond to global needs. Some centres, for example, had failed to keep up with changes in technology and were unable to provide the diagnostic support necessary to confirm the etiology of disease outbreaks. Some of the centres specializing in infectious disease epidemiology had failed to develop expertise in some of the newer infectious disease challenges. There are not enough Collaborating Centres in developing countries to ensure regional self-sufficiency. WHO is asking governments to provide the resources necessary to bring the WHO Collaborating Centres up-to-date. WHO is also facilitating exchange of information and reagents among Centres, increasing the number of Centres in developing countries, and ensuring that all centres are linked electronically and regularly exchange information.

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ANTIMICROBIAL RESISTANCE MONITORING

The second global monitoring system includes the WHO networks for monitoring and containing antimicrobial resistance: WHONET for the monitoring of antimicrobial resistance in general, and the programme for monitoring gonococcal antibiotic susceptibility (GASP). Antimicrobial resistance is rapidly increasing worldwide, facilitated by inappropriate prescribing by health workers, poor compliance by patients to prescribed dosage, and failure to control the availability of antibiotics by limiting them to pharmacies and health facilities. Antimicrobial resistance results in higher costs due to the use of more expensive combinations of antibiotics, to increased rates of hospitalization for infections once easily treated on an outpatient basis, and to time lost from work or school until cure. At the same time pharmaceutical companies are less willing to take the risk of developing new antibiotics, because the high cost of research and development and the potential of rapidly developing resistance jeopardize the recovery of investments made in research and development. Through WHONET and GASP, WHO regularly obtains standardized information of known quality on the current state of antimicrobial resistance, helps countries use this information nationally for sound drug policies, and internationally uses the information to identify problems and advocate research and development on antibiotics.

INTERNATIONAL HEALTH REGULATIONS

The third system is represented by the *International Health Regulations* (IHR), currently the only international public health legislation which requires mandatory reporting of infectious diseases. Three diseases are covered by the IHR - cholera, plague and yellow fever. Reporting these diseases, however, is often associated with negative repercussions such as restrictions to trade and travel. Some countries therefore do not report and WHO has no legal mandate to force reporting. In addition diseases such as haemorrhagic fevers and pulmonary disease are not included in the IHR. To turn the IHR into a working global alert system, where reporting will be encouraged and all globally important diseases will be reported, WHO is rewriting the IHR. This will eventually require an initial reporting of clinical syndromes of potential worldwide importance to ensure an immediate and appropriate international response, followed by causal reporting once the diagnosis is known, when modifications in the response may be made as necessary. Clear and concise guidelines for countries are also being developed, describing both appropriate and inappropriate responses once a syndrome is reported.

In addition to partnership in global monitoring, WHO is working in countries to strengthen national disease detection and response through improved surveillance systems and specialized training in epidemic preparedness and response. In this partnership WHO provides overall technical guidance through its international consensus policies on surveillance and control strategies; it facilitates bilateral or multilateral activities of governments and non-governmental organizations in enlarging the critical mass of epidemiologists and public health laboratory specialists, and its advocates for government commitment to provide the resources necessary.

A final role of WHO in this partnership is to help ensure a coordinated global response to infectious diseases of international importance, often with the technical expertise of the WHO Collaborating Centres or other centres of excellence. At other times the WHO response requires involvement of WHO staff at the field site to begin surveillance and containment activities while facilitating the arrival of technical expertise from other international partners, and to remain after containment to plan and implement activities for the prevention of future outbreaks.

To enter the 21st century and meet tomorrow's challenges of new, emerging, re-emerging infectious diseases, or even to meet the challenge of well-known diseases, WHO will continue to participate in and synergise global partnerships by ensuring strong national disease surveillance and control programmes, global networks to monitor and alert the world to infectious disease and related public health problems, rapid information exchange through electronic links, and rapid response to contain epidemics of international importance.

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PROTECTION WE TAKE FOR GRANTED

The routine immunization activities of WHO prevent an estimated 3 million deaths per year. In addition, at least 750,000 children are protected from blindness, mental retardation, or other disabilities. In 1995, almost 80% of children throughout the world were immunized against six vaccine-preventable diseases – diphtheria, tetanus, whooping cough, measles, polio, and tuberculosis. This achievement involves over 500 million immunization contacts throughout the year; at the same time, immunization activities provided opportunities for other primary health care interventions, such as health education for mothers, growth monitoring, administration of vitamin and mineral supplements to children in need/deficiency, child spacing and routine health checks. This again helps prevent diseases, disability, suffering and deaths.

An important key to the success of this ongoing preventive activity is the promotion of good disease surveillance and monitoring. As high immunization coverage is attained and the number of cases declines, disease surveillance becomes critical to monitor the changing patterns of vaccine-preventable diseases and to guide changes in immunization strategies. Disease surveillance is also critical to pinpoint pockets of poor performances and high risk so that public health action can be enhanced in these areas. For instance, incidence and immunization coverage data can help identify areas at high risk for neonatal tetanus and ensure that resources are channelled to these areas. Surveillance data can also be used as an early warning system to monitor trends in the number of new cases of a disease and predict where and when epidemics may occur. Specific action can thus be taken in time to prevent an epidemic. Surveillance systems also help detect and prevent the re-emergence of vaccine-preventable diseases such as yellow fever and diphtheria by identifying sub-populations and certain age groups at high risk.

Monitoring systems determine ways to boost immunization coverage rates and improve service delivery and related costs. For example, for vaccines to be effective, it is crucial that they be kept cool at all times of the supply chain (cold chain). By improving and developing good surveillance and monitoring systems, poor programme performance can be detected and corrected before public confidence in immunization is undermined.

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Control of influenza

Unlike other acute respiratory diseases, influenza can cause severe illness complicated by pneumonia. Elderly persons or persons with underlying health problems are at increased risk for these complications. The severity of influenza is reflected during major epidemics by large increases in the number of cases admitted to hospital and in the number of deaths from influenza; the increase in deaths during influenza seasons is in some countries used as a measure of the impact of influenza epidemics.

Influenza occurs globally and epidemics are registered in regions of temperate climates every year. Three to four times per century a new influenza virus appears which causes worldwide epidemics (pandemics) and some of them have been associated with extremely high mortality rates. The most severe pandemic this century occurred in 1918-1919 and killed at least 20 million. The last influenza pandemic started in 1968 with the appeareance of the A/Hong Kong influenza strain. It is clear that new pandemics will occur and it is equally evident that the preparation for this global threat has been insufficient.

Two measures can reduce the impact of influenza: vaccination and treatment with anti-viral drugs. Because of the cost, side effects and limited availability, drug treatment is not applicable on a global scale. Vaccination of persons at high risk therefore remains the most effective measure to reduce the impact of influenza. As the virus mutates continuously, vaccination must be repeated annually before each influenza season with an updated vaccine to assure a good match with the circulating influenza strains. Influenza vaccine can prevent severe influenza and deaths and it is therefore strongly recommended for persons aged more than 65 and those at risk to develop severe complications - especially those over 6 months of age with underlying conditions such as chronic heart or lung disease, renal or metabolic disorders.

WHO coordinates the global influenza surveillance which is built on a network of 110 national influenza centres in 80 countries and four WHO Collaborating Centres for Reference and Research on Influenza in Atlanta, London, Melbourne and Tokyo. The surveillance ensures the collection of epidemiological data and of viral isolates for rapid characterization and international comparisons. The annual recommendations for the influenza vaccine are based on the information obtained through this surveillance system. This regular and continuing influenza surveillance programme will also most likely detect a pandemic threat.

To prepare for the forthcoming pandemic, national and regional plans should be developed now. These plans should take into account that in case of a pandemic a vaccine might not be available or available only in insufficient quantities. The plans should set priorities and objectives to guide control strategies, operative decisions and allocation of resources at the national, regional and district levels

Emerging Infectious Diseases

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EXAMPLES OF SUCCESSFUL PREVENTION AND OUTBREAK CONTROL

THE PAST

Smallpox

One of mankind's greatest triumphs is the eradication of smallpox. Under the leadership of WHO, all the countries of the world united to destroy the killer virus.

Although a vaccine to fight smallpox had already been discovered 200 years ago, the disease was still endemic in the 1960s. In 1967, WHO launched a global smallpox eradication campaign, systematically vaccinating entire populations in endemic countries – an enormous and complex exercise. The strategy soon became «surveillance and containment»: every time a new case was discovered, it was isolated and contacts of the patient traced and vaccinated. Where cases were detected, local immunization was intensified. The last case of naturally acquired smallpox was reported from Somalia in 1977, and in 1980, WHO declared the world free from the scourge. In its 1996 session, the World Health Assembly recommended that the last smallpox stocks would be destroyed in 1999.

THE FUTURE

Just as they eradicated smallpox, WHO and its partners are optimistic that they are on the right track to eradicate or eliminate other infectious diseases by the year 2000, in particular poliomyelitis, leprosy and guinea-worm disease (dracunculiasis).

Poliomyelitis

Poliomyelitis is an infectious viral disease that attacks the central nervous system, causing permanent paralysis of the muscles and frequently death. It mainly affects young children. In 1988, WHO established a target to eradicate polio by the year 2000. The strategy used rests on two basic activities: surveillance and immunization. Surveillance data are used to gear immunization activities towards populations at higher risk for polio. Worldwide, almost half of the children under 5 were immunized against the polio virus in 1995 in the course of National Immunization Days.

An estimated US$700 million are needed to reach the target of eradicating polio by the year 2000, to save many lives and avoid much human suffering. The projected savings of more than US$1 500 million a year thereafter far outweigh this expenditure. WHO is confident that the drive for the eradication of poliomyelitis is on target.

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Leprosy

Leprosy is a disfiguring but curable disease. It is caused by an organism which mainly affects nerves and skin and is spread from person to person by droplets from the nose of an infected individual.

In 1996, the number of registered cases of leprosy in the world has fallen below one million. This offers striking evidence that WHO's strategy for eliminating leprosy as a public health problem is on course for success. There were an estimated 1.8 million people with leprosy compared with 5.5 million in 1991 and 12 million in 1985.

WHO pursues a two-fold strategy against leprosy: treating patients with a combination of three drugs (multidrug therapy – MDT) combined with case-finding. There is evidence that the elimination strategy has already had a significant impact in terms of a dramatic and constant reduction in morbidity. This approach has also increased the priority accorded to leprosy control activities in highly endemic countries; it has also improved case detection through better coverage with MDT (a free supply of drugs was provided through WHO to countries in need), and focused attention on difficult-to-reach populations.

Guinea-worm disease (dracunculiasis)

This is caused by the parasite Dracunculus medinensis, commonly known as the guinea-worm, which is transmitted by drinking water infested with the intermediate host of the parasite. The worm, ingested with drinking water, migrates through the body and eventually emerges slowly through the skin causing fever, nausea and vomiting, frequently for several months.

Although there are no drugs to treat the disease nor a vaccine to prevent it, dracunculiasis may be totally eradicated from the world in the near future. The strategy advocated by WHO combines a variety of interventions and approaches but emphasizes two primary measures: the strengthening of surveillance, which implies establishing or strengthening case-containment activities in all endemic villages with intensified community participation, and the mobilization of decision-makers, including village chiefs to improve community awareness and participation in making drinking water supplies safe and other eradication efforts. Campaigns to control guinea-worm disease have been instituted by most of the 18 endemic countries, mainly in Africa.

Proven strategies exist to reach the targets for all three diseases; their implementation requires more political commitment and financial resources. Together with WHO and UNICEF, Rotary International, for example, is raising funds to advance the polio eradication initiative. Global 2000, UNICEF, bilateral agencies, several non-governmental organizations, WHO and countries themselves are furthering guinea-worm eradication activities. More such expanded partnerships are needed for investments to be rewarded by significant economic, social and human benefits of eradicating these diseases.

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WHD 97.5

EMERGING INFECTIOUS DISEASES - CHALLENGES AND SOLUTIONS AHEAD

Vision for the 21st Century

A world on the alert, able to contain communicable diseases through:

- strong national disease surveillance and control programmes
- global networks of centres, organizations and individuals to monitor diseases
- rapid information exchange through electronic links to guide policies, international collaboration, trade and travel
- effective national and international preparedness, and rapid response to contain
- epidemics of international importance

Between the world of today and this vision for the 21st Century lies a huge gap. The likelihood of bridging this gap depends on how well committed partnerships can be forged between individuals and countries, with the backing of WHO and other agencies within and outside the UN family.

Recent outbreaks of Ebola haemorrhagic fever, meningitis, plague, and yellow fever illustrate the challenges to making both the global alert and the global response a reality.

CHALLENGE: EARLY DETECTION OF EPIDEMICS

In a poor public health environment an unusual disease event may not be detected until it has become a major threat to the population and cannot be contained with national resources. Public health laboratories, even if they exist, are often poorly equipped or unable to diagnose common diseases and assess their impact on the community.

International response required:

Improve the national infrastructure for routine surveillance of common diseases. Assess national surveillance systems, strengthen public health laboratory services, support training in epidemiology and laboratory techniques to increase the pool of staff capable of maintaining routine surveillance on a national scale. Surveillance will provide the background data against which uncommon events can be identified.

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CHALLENGE: RAPID NATIONAL RESPONSE TO UNUSUAL DISEASE EVENTS OR OUTBREAKS

An unusual disease event or outbreak may have been reported to local or national health authorities but may not trigger a response, or only trigger an inadequate or late reaction.

International response required:

Train key national staff, assess surveillance systems and prepare plans to contain future outbreaks before they become international emergencies. In addition to these long-term activities, WHO may be required to play an active role in the management of outbreaks with its partners through the provision of expert advice, diagnostic reagents, vaccines and drugs, an international response team if needed, within 24 hours. Once the outbreak is brought under control, WHO and its partners assist countries in evaluating the outbreak and the way it was handled, to improve future performance.

CHALLENGE: EFFICIENT AND VIABLE NATIONAL SURVEILLANCE SYSTEMS

Many countries lack a national, uniform surveillance system for the routine monitoring of communicable diseases. There may be a surveillance system dedicated to monitor one disease or a series of uncoordinated systems for different diseases. Data and information from a fractioned and poorly integrated system do not provide for disease alerts and for the global monitoring of communicable diseases, nor do they help national authorities in setting public health policies.

International response required:

Develop surveillance guidelines with internationally accepted case definitions; stimulate the use of these guidelines through workshops for regional and national key staff. Facilitate and coordinate the flow of information to and from national surveillance systems within a global network. Collaborate with international initiatives for communicable disease surveillance to ensure an efficient and cost-effective collection of data that can be compared internationally.

CHALLENGE: TIMELY HEALTH INFORMATION

Outbreaks of communicable diseases have become news; the media are often the first, and sometimes the only source of information on outbreaks. In the absence of official information from the country concerned, inaccurate reports have triggered panic situations which made it difficult to evaluate the true situation and the need for intervention. Official information, which could temper exaggerated or inaccurate reports, has sometimes been difficult to obtain, either because it does not exist or because it could not be cleared for release.

International response required:

Advocate an open, responsible exchange of information and facilitate national reporting of outbreaks. Make available reliable and relevant information on diseases and outbreaks to the world community through electronic and conventional media. Supplement this with appropriate advice to people living in or going to affected areas.

CHALLENGE: SOUND INTERNATIONAL REACTIONS TO OUTBREAKS

The international community sometimes reacts with panic to outbreaks of cholera, Ebola haemorrhagic fever, and plague in recent years. Extraordinary and inappropriate measures have been instituted, and barriers set up against travel and trade, including quarantine at airports. These measures cause heavy losses in tourism and export without providing much real protection against the potential import of the disease into the country. Quarantine is a poor protection against the import of a disease. Travel time is short and an infected person can board a plane in apparent good health and arrive at a new destination days, if not weeks, before symptoms appear.

International response required:

Revise the International Health Regulations to provide an internationally-agreed code of practice and control of the international spread of potentially dangerous infectious diseases, according to today's epidemiological and economic realities. Provide guidelines on the application of the Regulations to minimize the disruption of travel and trade which has been a strong disincentive to give alert in the past.

CHALLENGE: CRUMBLING INTERNATIONAL INFRASTRUCTURE

As public health priorities changed in the 1970s and 1980s, resources for communicable diseases became scarce and the necessary infrastructure weakened.

International response required:

WHO's network of Collaborating Centres is an important component in this infrastructure. The Centres are laboratories selected for their degree of excellence and willingness to cooperate internationally. Together they make a network which can handle a broad range of communicable diseases with a high degree of specialization. Strengthening of the WHO Collaborating Centres is required to provide high quality reference service for diagnosis, training and intervention in outbreaks. Identifying new laboratories to extend the network to new areas (subject and geographical), and establishing electronic links to facilitate the flow of data and information within, to, and from the network are also required.

CHALLENGE: SPREADING ANTIMICROBIAL RESISTANCE

Antibiotic-resistant bacteria appeared almost as soon as antibiotics began to be used. The emergence of resistant bacteria has accelerated in the past two decades and some infections have become difficult and expensive to treat. The problem is compounded by the slow appearance of new antibio-tics on the market. They cost much to develop and license and the problems of resistance gives manufacturers only a short time to recuperate these costs. A major cause is a massive misuse of antibiotics in humans and animals. The result is increasing health care costs and longer hospitalizations.

International response required:

Extend the use of WHO-developed programmes and others that accurately monitor the frequency and geographical distribution of antimicrobial resistance. Link users of the programmes in an international surveillance network to generate the data needed to develop national and global strategies and guidelines for the appropriate use of antimicrobials in humans and animals. Stimulate and support research to improve the number of drugs available on the market and to develop alternative ways of preventing and treating infections.

CHALLENGE: DISEASE EMERGENCE THROUGH CONTACTS WITH ANIMALS

Animal farming and food production has intensified and increased the risks that diseases in the animals are transmitted to humans through the food chain. Another reason why new infectious diseases have emerged in the past two decades is that more humans risk coming in contact with animals carrying diseases, for example when forest areas are cut and destroyed and animals living there seek other habitats closer to human populations, or when humans penetrate deeper into the remaining forest areas for leisure or work.

International response required:

Strengthen surveillance of communicable and zoonotic diseases, seek international consensus on policies to prevent and contain transmission of animal diseases to humans and prepare guidelines for the use and management of animals reared for human consumption.

Emerging Infectious Diseases

WORLD HEALTH DAY

WHD 97.6

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WORKING TOGETHER TO FIGHT DISEASE: THE RED CROSS AND WHO

EBOLA
Kikwit, Zaire 1995

In May 1995, joint action by the Red Cross, the World Health Organization, Médecins sans Frontières (Belgium), Institutes of Tropical Medicine (Belgium), Sweden, South-Africa, and Centers for Disease Control and Prevention (USA) teams and local non-governmental organizations proved quick and effective in containing a deadly epidemic of haemorrhagic fever caused by an outbreak of the Ebola virus in the town of Kikwit, Zaire.

The combination of medical advice from WHO and its partners and the capacity of the Red Cross Society of the Republic of Zaire (National Society) to access all levels in the community through its thousands of volunteers proved particularly efficient in stopping the spread to the rest of Zaire of a disease which left 245 people dead in and around Kikwit. National Society volunteers were on the front line, transporting the sick to quarantined sectors of hospitals, collecting the bodies of victims and burying them. Five Zairian Red Cross volunteers became infected and died in the line of duty.

With support from the International Federation of Red Cross and Red Crescent Societies (the Federation), the Zairian Red Cross mounted a vast public information campaign. Posters and leaflets in the four national languages of Zaire and in French explained how to avoid infection. One poster recommended avoiding contact with blood or other bodily fluids of a patient. A second advised people against washing the bodies of the dead, which is a traditional part of burial rites. A third warned that used syringes must be burned. A fourth recommended that patients' clothes be handled only with gloves on and that they be boiled before being washed.

All activities were coordinated by an international monitoring and surveillance team which was set up as soon as the disease was diagnosed. It included representatives from the Zairian Red Cross, the Federation, WHO and its partners, the Government of Zaire and other non governmental organizations. Research also began in order to identify the natural host of the Ebola virus.

After the epidemic, the National Society helped families who had lost members to the disease, and who were shunned by neighbours afraid of contagion. Volunteers distributed short term material assistance (such as food) to the affected families. They also informed neighbours that there was no risk in allowing these people to go about their ordinary business and that they should be re integrated into the community.

Mayibout, Gabon 1996

The Federation and WHO joined forces again together with the French government to help the Gabonese national authorities and the Red Cross fight an outbreak of the Ebola virus in February 1996. A massive information campaign included information sheets on how to fight Ebola, designed for medical personnel and produced by the Federation and WHO. Protective wear for all those in contact with patients (gloves, aprons, masks and goggles) as well as disinfectant was immediately shipped to Gabon. The epidemic was quickly stemmed, but left 16 people dead.

At the beginning of March 1996, at an international conference on Ebola convened by WHO in the Zairian capital of Kinshasa, some 140 medical specialists and representatives of NGOs discussed ways to combat future outbreaks of the fatal disease. The Zairian Red Cross received a special citation of gratitude for its work from WHO and the memory of the five Red Cross workers who lost their lives after contracting the disease was honoured. It was also decided to begin studying the usefulness of blood from survivors of the Ebola outbreak at Kikwit (some 60 people survived) in treating others with the disease. WHO has so far collected 13 samples which are being tested for antibodies to the disease. Plans are under way to have the Zairian Red Cross collect blood from those who still have high antibody levels.

DIPHTHERIA in the former Soviet Union 1995

For decades, diphtheria, thanks to widespread immunization, had become a controlled, almost forgotten disease. The sense of control changed abruptly in the early 1990s, as a diphtheria epidemic broke out in the Russian Federation and Ukraine. This was linked to the destruction of the Former Soviet Union, to heavy population movements and to social and economic stress. Diphtheria rapidly spread to all other Newly Independent States (NIS); by the end of 1994, a total of 47 802 reported cases and 1 746 deaths had been reported. Worse seemed in store for 1995. Only mass immunization efforts could slow and finally did control the epidemic.

In 1995, Estonia reported 19 cases of diphtheria, Latvia 369 cases, Lithuania 43 cases, Belarus 322 cases and Ukraine 5336 cases. In June 1995, the Federation launched a combined appeal with WHO and UNICEF calling for resources to control the diphtheria epidemic. The funds requested for this appeal were as high as US$ 33 million.

Under the strategy drawn up by the three organizations, the Federation has taken on operational responsibility for the three Baltic States of Estonia, Latvia and Lithuania, and for Belarus and Ukraine, by providing vaccines, syringes and needles, cold chain equipment, antibiotics, antitoxin and human resources for implementing and monitoring the programme.

Under the responsibility of the Federation, with funding from ECHO (European Community Humanitarian Office) and other donors, approximately 31 million doses of vaccines were shipped into the countries and mass vaccination campaigns took place in autumn 1995 and spring 1996. As an effect of these mass vaccination campaigns, the case load and mortality are stabilizing in some countries and decreasing in others.

The whole programme was planned in close collaboration with the National Red Cross Societies and the Ministries of Health. The Red Cross Societies were responsible in particular for social mobilization efforts, for training seminars for health staff, for printing posters, leaflets and other information material about diphtheria, vaccination places and dates. The national and local media got involved throughout the whole programme. Other institutions, such as churches, schools, transport companies, big enterprises and police were also mobilized by the Red Cross for spreading out information to the public. Vaccination rooms were established in all polyclinics, and medical personnel was trained and instructed on the Federation's requirements in reporting and data collection.

A big challenge for the Red Cross Societies was how to contact the so-called hard-to-reach groups, such as the unemployed, homeless, gypsies, and alcoholics. Mr George Weber, Secretary General of the Federation said, "infectious diseases have become the biggest killer these days, and poor and vulnerable people are more affected than others. We in the Federation have therefore given high priority to the control of epidemics, particularly in those groups which are hard to reach. This is possible through the widespread network of Red Cross volunteers". For the vulnerable groups, soup kitchens and secondhand clothes distributions were organized, market places and dormitories were visited and many home-bound and disabled persons were vaccinated in their homes. These efforts increased vaccination coverage by at least 20%.

WHO acts as the secretariat for the Interagency Immunization Co-ordinating Committee (IICC) which is addressing the problem of diphtheria in the former Soviet Union and coordinates the implementation of the programme. UNICEF has taken on responsibility for carrying out the programme in other countries of the NIS. The partnership between these organizations and the Federation is very close and well functioning. Much has been learnt on how to combine different institutional cultures and management styles, and future plans for controlling the epidemic are jointly discussed. This big operation is now well under way, the epidemic is under control in the Baltic States and Belarus, and vaccinations are continuing in all six countries.

Emerging Infectious Diseases

WORLD HEALTH DAY

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PERSONAL ACCOUNTS

The control of the outbreak of Ebola haemorrhagic fever1: the account of a WHO medical officer

On 9 April 1995, a 35 year-old male laboratory worker from Kikwit II hospital was transferred to Kikwit General Hospital with severe bloating and high fever. Surgery was performed the next day and abnormal bleeding was diagnosed. Unfortunately, and despite a second operation, the patient died three days later, on 14 April. Although this could have been the end of an unfortunate medical concern, it was in fact, for most health workers, nurses and physicians involved in the operation, the silent beginning of an epidemic.

On 7 May 1995, rumours about a possible outbreak of Ebola haemorrhagic fever in Zaire, together with a request for assistance reached WHO, Geneva. The diagnosis was rapidly confirmed by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, a WHO collaborating centre. On 9 and 10 May an international team with members from WHO and WHO collaborating centres assembled in Kinshasa and flew to Kikwit, where the national experts were fighting the outbreak under difficult conditions.

The WHO team led and coordinated the international response, working closely with the local authorities and Non-Governmental Organizations (NGOs) such as Médecins sans Frontières (MSF), the Red Cross, and the local Catholic Mission. Additional expertise for laboratory diagnosis, viral diseases, epidemiology, clinical management, public education, information, engineering, disaster relief, arrived in Kikwit from CDC, WHO, MSF, the International Federation of Red Cross and Red Crescent Societies, Sweden, South Africa, Belgium and Zaire. A strict isolation ward was set up; an agreed definition of an Ebola case was approved and used to sort patients and provide them with appropriate care. After a few days, the management of cases was under control.

It was then time for a more thorough investigation, to collect information from the population. The international team investigated reported deaths, suspected cases, unusual events or anything which could clarify the complex chains of transmission of the disease and lead to the source of the epidemic. Every day, special investigation teams checked rumours, by foot, on bicycle, driving miles in a 4-wheel drive vehicle. Daily radio contact with remote villages outside Kikwit was needed to monitor the entire region. This effort led to the identification of a 35 year-old charcoal maker who had died on 13 January 1996 in Kikwit General Hospital and who, retrospectively, seemed to be the first in a series of cases which had occurred over four months until the dramatic outbreak in the hospital.

Excerpt from *World Health*, January-February 1997

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Operational support from WHO headquarters in Geneva to the field operations faced complex logistical problems, because of the geographic inaccessibility of the outbreak zone, the poor state of the local infrastructure, particularly in telecommunications and transport, the high turnover of field staff; the high-level media interest in the epidemic intensified some of these problems. A satellite link with WHO headquarters in Geneva maintained the communication flow.

By late May, about two weeks after the alert, the epidemic was under control, although additional waves of patients were still expected. The last case occurred on 14 July 1995. A regional surveillance system for Ebola haemorrhagic disease was fully functional and the emergency phase was over. The epidemic command post, from which the international team of physicians and scientists had successfully controlled the outbreak, remained in place until October 1995.

The epidemic was declared over after 24 August 1995, once 42 days (twice the maximum incubation period of the disease) had passed without a case. The epidemic toll was 316 cases, of whom 124 women and 121 men lost their lives. A long-term surveillance system was set up in the Kikwit area, looking for any suspected case, particularly of haemorrhagic disease, or any unexplained death.

Dr Guenaël Rodier
Division of Emerging and other Communicable Diseases Surveillance and Control

Meningitis: the epidemic of the century in Nigeria
The account of a physician working for Médecins Sans Frontières

Nigeria: the states of Kano, Katsina, Bauchi... Three million people vaccinated, 30000 people treated. We did it! We would never have imagined we could carry out such a massive vaccination campaign in two months.

Since the beginning of 1996, Nigeria has been dogged by a meningitis epidemic of unprecedented scale. It is the first time that we in *Médecins Sans Frontières* have had to deal with an epidemic situation in such a densely populated region. There are two million inhabitants in Kano, the country's economic nerve centre, which we chose for our first mission.

When we arrived at Kano, the situation in the big 650-bed hospital was catastrophic: people with meningitis were laid out on mats, some people who were lying on the bare ground were in convulsions. The most serious cases were usually children. In mid-February 1996, when the situation deteriorated suddenly, 120 patients were arriving at the hospital every day. The staff were run off their feet and medicines and vaccinations had dwindled to nil.

There were too many cases in a very short space of time for the Nigerian health system to cope with the epidemic without outside help. Health structures were in place and the staff were qualified, but material resources were limited. Very soon, effective cooperation between Nigerian health teams and the international team from *Médecins Sans Frontières* helped provide suitable treatment and launch the vaccination campaign.

The challenge in Nigeria was, quite simply, enormous. In the three states of Bauchi, Kano and Katsina, with a total of 15 million inhabitants, several million people needed to be immunized. The race against time began on 7 March when 30000 vaccinations were given in one day at 20 centres. Armed with megaphones, we went round markets and places of worship in an effort to mobilize the population, and carried out a comprehensive information campaign.

Despite the operation's success, with 3 million people vaccinated and 30000 patients treated we are still slightly disappointed: of the eight Nigerian states that were particularly affected by the epidemic, we were able to help only three. Slow international mobilization, both in the media and at an operational level, more than likely deprived tens of thousands of patients of treatment*.

Elisabeth Le Saout

Meningococcal meningitis is found right across the world. It is the only form of bacterial meningitis that causes epidemics, with the most serious of which occur in sub-Saharan Africa. The disease is caused by a bacteria which is transmitted mainly through contact with the droplets given off by the respiratory tracts of persons infected. Meningitis is characterized by the sudden onset of headache, with fever, nausea, vomiting, photophobia and stiffness of the neck. Other symptoms of the disease are lethargy, delirium, coma and/or convulsions.

*Recognizing these difficulties, WHO and its partners launched an African meningitis initiative in 1996 with the objective of strenthening surveillance and response to prevent future epidemics of this size.

Emerging Infectious Diseases

WORLD HEALTH DAY

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7 April 1997

WHO NETWORK ON ANTIMICROBIAL RESISTANCE MONITORING

WHO is establishing a global network of laboratories that generate standardized, quantitative data on antimicrobial susceptibility testing. Data are used locally for containment of resistance and internationally to develop better drug policies and advocacy for new antibiotic development.

The long-term goals are to:

- encourage policies and practices that will ensure better infection control and patient care at local level
- prolong the useful life of available antimicrobials
- support rational selection of regional essential drug lists
- detect and contain the emergence of new and major multidrug resistant bacteria
- standardize interpretation of antimicrobial resistance tests
- support those involved in antimicrobial drug research, development and advocacy.

1.BACKGROUND

WHO headquarters, in close collaboration with the Regional Offices and WHO Collaborating Centres, is establishing a global network of laboratories to monitor antimicrobial resistance.

WHO is also developing a global data bank to help identify antimicrobial resistance problems of local, regional and global priority, seek consensus on how to tackle these problems, and initiate and coordinate appropriate control and containment measures.

The establishment of this Network represents a new stage in the global surveillance of antimicrobial resistance. Funds from both WHO regular budget and external sources are being made available and the first laboratories have been enrolled.

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WHO will support laboratories which:

- participate in an initial Quality Control pilot project
- routinely conduct quality control tests and process their test results in a computer database
- use standardized susceptibility tests (pre-ferably as outlined by WHO guidelines) and process quantitative measurements
- process test results with a software compa-tible to WHONET (WHO supports provision of interfaces)
- participate in routine proficiency testing

In order for the Network to generate data which are of regional and global significance, core network laboratories are applying standardized laboratory techniques so that the data are accurate.

The Network will:

- be temporally and geographically representative
- be flexible enough to react to changing trends
- be open to both hospital and community laboratories
- include important bacteria and antimicrobial drugs
- become sustainable.

2. CHARACTERISTICS OF THE NETWORK

Network laboratories are in command of the skills required to conduct standardized and quality controlled antimicrobial susceptibility tests.

Through training courses, external quality control and proficiency testing, local support.

Results of antimicrobial susceptibility testing are locally processed and analysed and data are routinely submitted to WHO for incorporation in the WHO data bank. Laboratories participate in a quality assurance programme.

Through local quality control, on-site evaluation, data bank and report monitoring, periodic proficiency testing.

Fifty laboratories will provide standardized, quantitative antimicrobial susceptibility testing data to WHO by the end of 1997. The Network will be expanded to 60% of WHO Member States in 1998 and to 80% in 1999.

WHO manages its data collation ensuring, feed-back and publication of information. It expands the Network with its partners and establishes national WHO working groups on antimicrobial resistance monitoring for identification of priority areas for research and development and policy formulation.

3. INSTITUTIONAL FRAMEWORK

External quality control and proficiency testing is conducted by the Centers for Disease Control and Prevention, Atlanta, USA. A second centre is being identified for continuous external proficiency testing, which will be able to support a growing network of laboratories.

Training courses are conducted by WHO teams using training material developed in collaboration with WHO partners.

On-site quality control, local advice and training are provided by WHO consultants.

The **WHO data bank** is managed within WHO.

Overall management and coordination of the WHO Network and routine publication of results are the responsibility of the Division of Emerging and other Communicable Diseases Surveillance and Control (EMC) in WHO. EMC liaises with national authorities, the pharmaceutical industry and other interested parties.

Emerging Infectious Diseases

WORLD HEALTH DAY

WHD 97.9

7 April 1997

THE INTERNATIONAL HEALTH REGULATIONS: MAXIMUM PROTECTION, MINIMUM RESTRICTION

INTRODUCTION

In 1377, Venice wrote the first recorded quarantine legislation to protect itself from rats on ships arriving from foreign ports. Later legislation in Europe and elsewhere led to the Paris inter-national sanitary conference in 1851, which laid down the basic tenet protection against the international spread of infectious diseases: *maximum protection with minimum restriction,* a tenet still valid today. A full century lapsed before the International Sanitary Rules were adopted, in 1951; these were amended in 1969 to become the International Health Regulations (IHR).

Three communicable diseases – cholera, plague, yellow fever – must currently be reported under the IHR. International enforcement of reporting is not a feasible proposition under the IHR, however, and reporting is far from complete. Countries fear economic consequences when they report (see below); for new diseases with potential for international spread, the IHR do not apply (see box).

In 1995, the World Health Assembly called for a revision and updating of the IHR to make them more applicable to infection control in the 21st century. Over the years, the policing sense of the Regulations, reflected in the emphasis on quarantining of cases and contacts, has given way to public health measures in order to minimize the risk that an imported infection establish a new focus. The application of the IHR has been affected by changes in the global health situation and the increase in international travel. The control of infectious disease at the international level through improved surveillance and intervention strategies is more effective than the application of quarantine practices. The basic principle of the revised IHR should continue to be to ensure maximum security against the international spread of diseases with minimum interference with world traffic and trade. The IHR will be revised along the lines shown in the following box:

Immediate reporting for only three diseases should be replaced by immediate reporting to WHO of defined syndromes representing disease occurrence of international importance and of the basic epidemiological information that will be useful in control of disease. The IHR should be accompanied by a practical handbook facilitating their use and defining the requirements for international reporting. The revised IHR should be integrated into all epidemic surveillance and control activities at global, regional and national level. The IHR should include a mention of inappropriate or unnecessary interventions and provide clear indications as to why their actions are not required.

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The IHR also describe health facilities and personnel that should be available in ports, and what maximum measures national health authorities should institute to protect their territories. The IHR allow national authorities to dispense with those measures which are not appropriate in the national context.

The revised draft will be submitted to the World Health Assembly for ratification in 1998, and widely diffused along with its operational handbook; these documents have great potential to serve as a global alert system for diseases of international importance, and to ensure maximum protection with minimum restriction.

Examples of misapplication of the IHR

Cholera in Latin America. When cholera was identified in 1991, Peru notified the disease at once, as specified by the IHR. Help was immediately forthcoming, but during that year alone cholera infected over 300 000 persons and caused 3000 deaths in Peru. In addition to its public health impact, the epidemic led to losses in trade and travel estimated at US$ 700 million at least due to excessive measures imposed by other countries.

Plague in India. In 1994 an outbreak of presumptive plague occurred in India. India reported the outbreak to WHO after information had been diffused by the international press. The outbreak led to much economic disruption and concern worldwide: in some countries airports were closed to aeroplanes arriving from India, and Indian guest workers were forced to return even though some had not lived in India for several years. Imports of foodstuffs from India plummeted; the overall loss was estimated at nearly US$2000 million.

Examples of irrelevance of the IHR in new diseases

Ebola in Zaire. In 1995 an outbreak of Ebola haemorrhagic fever occurred in Zaire (316 cases and 245 deaths). The immediate official reaction was to close the road leading to Kinshasa, the capital city 500 kilometres away, but the airport near the outbreak site was not part of the quarantine and a case of Ebola did arrive in the capital city by air. Strengthened disease surveillance in Kinshasa, however, immediately detected the case and no local spread occurred. Even if this case of Ebola had boarded an international flight in Kinshasa, the IHR would have had no application since the disease does not fit under their mandate.

Hantavirus Pulmonary Syndrome in the United States. In 1993 an outbreak of a disease characterized by fever, muscle aches and intestinal complaints followed by of shortness of breath and rapid progression to death was first identified in the southwestern United States, then in other states. The cause was found to be a newly identified virus in the Hantavirus family. The deer mouse is now known to be the reservoir of this virus. Despite national alarm as a result of this outbreak and concern about the possibility of cross-border transmission, the IHR again were not applicable.

The revision of the IHR is being undertaken with such scenarios in mind in order to ensure an orderly and appropriate response to outbreaks of infectious disease of global importance.

DIS-1

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Dental Caries in Underdeveloped Countries

Aubrey Sheiham

The London Hospital Medical College, London, England

Dental caries is a sugar-dependent infectious disease. Therefore any discussion of the changing patterns of dental caries in underdeveloped countries must consider the changes in sugar consumption. Sugar consumption in all underdeveloped countries is rising. By 1984 their consumption is predicted to exceed the use in industrialized countries, where sugar consumption is falling [27]. Industrialized countries can absorb little more sugar so underdeveloped countries are consuming four-fifths of what they produce. 50 years ago they exported four-fifths of production [31]. In addition to home production, in some underdeveloped countries, sugar is the second largest food item imported. Sugar is one of the first foods to respond to a rise in income in low-income countries and the percentage of sugar consumed in hidden forms rises progressively with rising income and increasing total sugar consumption [28].

The greatest percentage increases in consumption are anticipated in countries which had a per caput consumption of less than 20 kg/year [29]. The biggest users of sugar in underdeveloped countries are the subsidiaries of large multinational food and drink processing companies and include cake and biscuit manufacturers and the soft drink industry. Soft drinks are probably the most important factor in the sharp increase in sugar consumption in countries as diverse as Iran and Venezuela. In Mexico, nearly five bottles of soft drinks are consumed per man, woman and child every week [9].

Increases in Dental Caries

Deteriorating dental health is seen as a necessary consequence of economic growth which in itself is assumed to be a desirable goal for

everyone. Yet the extent of the deterioration will reflect the priorities of the society and of policy-makers.

There is no doubt that the prevalence and severity of dental caries is increasing rapidly in underdeveloped countries; of 20 countries where two surveys have been conducted on 12-year-olds some years apart, 15 have recorded marked increases, two (Ghana and China) showed no change and three (Sri Lanka, Argentina, Cuba) have had a decrease in caries [32]. In those countries which have reported increases, the increases in DMFT were from 0.4 to 1.5 between 1966 and 1982 in Uganda, 2.8 to 6.3 in 18 years in Chile, 2.7 to 5.3 in 4 years in Mexico, 0.2 to 2.7 in 19 years in Jordan and 1.2 to 3.6 in 13 years in Lebanon [32]. Further evidence of the increase in caries have been reported by *Barmes* [2] and *Sardo Infirri and Barmes* [17]. *Barmes* [2] described the increased rate of caries in underdeveloped countries as 'absolutely frightening'. He reported changes of 0.1 to 1.7 in 21 years in Kenya, 0.2 to 1.6 in 17 years in Ethiopia and 0.7 to 4.5 in 15 years in Thailand. These changes are frightening when the DMF is converted into treatment needs. *Barmes* [3] estimated that a dentist:population ratio of 1:4,200 would be needed to treat 12-year-olds with a DMF of 3.0. If one dentist and two operating auxiliaries were used the dentist:population ratio would be 1:12,500. A difference in DMF of 0.7 to 3.5 would require an extra 700 dental operators per million children [2]. A level of dental manpower which is impossible to achieve in countries in which the annual per capita expenditure on health is less than 5 US$ the cost of one restoration per child would exhaust the majority of the health budget. What chance is there of treating children in Fiji, for example, where the dental needs are 'At six years of age only 11.4% of children did not need treatment, whilst 48% required one-surface fillings, 73% required two-surface fillings, 16% needed three-surface fillings and 0.5% fillings involving more than three surfaces. 29% of children required extraction of deciduous teeth because of caries' [24].

Sugar and Dental Caries

What is the cause of this frightening increase in dental caries in underdeveloped countries? The consensus view is that refined sugars and in particular sucrose is the principal dietary cause [13, 19, 25]. *Sreebny* [25] found a strong association between the quantity of sugar

consumed per person per day on the one hand and the DMF on the other. He found that at levels above 50 g/day the intensity of the caries attack increased. *Schulerud* [18] in Norway and *Takeuchi* [26] and *Shimamura* [21] in Japan had previously shown that the caries pattern changed with increases in sugar consumption. *Takeuchi* [26] found that at a given level of sugar consumption specific teeth were affected differentially.

In underdeveloped countries the first change in the pattern of caries with rising sugar consumption is an increase in the primary teeth [16]. In the permanent teeth pits and fissures are mainly affected at low sugar levels [10]; the second molar being more frequently carious than first molars [1]. With increases in sugar consumption the ratio of first to second molars affected is one – similar to that found in high sugar consuming countries [6]. At the higher sugar levels proximal surface caries becomes more common. These patterns of disease indicate that environmental factors are more important than genetic predisposing factors. They cast further doubt on Jacksons' theory of caries aetiology [22].

In some underdeveloped countries dental caries is a disease of the very young and the middle-aged [20], coronal caries occurring in the young and root caries in the older group [15].

Socio-Demographic Variables

In underdeveloped countries the distribution of caries varies with social class and acculturation, level of urbanization, gender, ethnic group and level of fluoride consumption.

The influence of social class is strong [5]. *Olsson* [14] found that Ethiopian children from more affluent high social class families had four times more caries in primary teeth than poorer children and twice as many permanent teeth with caries. She found that the caries pattern differed by class. Upper class children had more anterior teeth affected and a higher number of both proximal and smooth surface lesions. This pattern of caries was associated with the increased availability of sugar to high income families since the establishment of a national sugar company.

Urbanized populations in underdeveloped countries are more likely to consume refined sugars than those in rural areas. Therefore it is

not surprising that caries rates are higher in urban populations. In the Sudan, *Emslie* [4] found seven times more caries in 15- to 19-year-old urban children, where the annual per capita sugar consumption was over 100 lb, than in rural children living in an area where the sugar consumption was below 5 lb/year/person. Similar trends were found in Mozambique [7], Swaziland [8] and South Africa [3].

Females usually had a higher caries rate than males [10]. And there are differences in caries rates in different ethnic groups within a country. In Malaysia, Chinese children had a much higher caries rate than Malays and Indians [11]. Similar trends existed in Singapore despite water fluoridation [12]. In Fiji, Indians also had lower caries rates than Fijians. This difference was mainly due to the differences in the ages of exfoliation of primary teeth and eruption of the permanent teeth [24].

Fluoride levels in water and foods have been shown to be related to caries rates. Studies in underdeveloped countries, some with low levels of sugar consumption, offer an opportunity to assess the effect of fluoride with differing levels of sugar consumption. In an extensive study of populations living on 14 South Pacific islands, *Speake* et al. [23] did not find a clear relationship between enamel fluoride levels and caries prevalence when comparisons were made between islands, yet a significant relationship did exist within island populations. This suggests that where environmental factors were similar, fluoride did have an effect. They found that where sugar levels were high, the influences of fluoride were outweighed by dietary factors. It was possible to develop a predictor chart of caries rates from enamel fluoride levels and sugar consumption levels [23].

Public Health Aspects

The increases in caries in many underdeveloped countries are very rapid. The principal reason for the increase is the increase in consumption of sugar-containing foods, drinks and confections. The conventional methods of preventing caries used in industrialized countries are not appropriate for underdeveloped countries. The cost of fluoride toothpaste, paper cups for fluoride rinses and toothbrushes are beyond the means of the vast majority. Therefore the logical public health strategy is primordial prevention; preventing the emergence of patterns of eating that are known to contribute to caries [33]. The strategy

should include a national food and agriculture policy, controls on imports and alternative useful uses of sugar.

To summarize, dental caries is rapidly becoming a severe puplic health problem in underdeveloped countries. In some countries such as Swaziland, the dental caries rate is as high as in Denmark but the resources are hopelessly inadequate to cope with the treatment of the disease [8]. The increases in dental caries may not appear to be great when compared to the caries rates in industrialized countries but it should be remembered that every increase of 1 in the DMF would require about 200 dental operators per million children. The cost of training and employing such an increase in the dental workforce is considerable and beyond the educational or financial capabilities of many underdeveloped countries.

Increases in dental caries appear to have a well-defined pattern; as the intensity of the disease increases different teeth and tooth sites are affected.

The major factor associated with the increase in dental caries is refined sugar. Therefore if worthwhile efforts are going to be made to control the rising epidemic of dental caries in underdeveloped countries, primordial prevention aimed at controlling the availability of refined sugars and sugar-containing foods, drinks and confections, is needed.

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Dr. Aubrey Sheiham, Department of Community Dental Health,
The London Hospital Medical College, Turner Street, London E1 2AD (England)

Routine Medical Management of Acute Myocardial Infarction

Lessons From Overviews of Recent Randomized Controlled Trials

Salim Yusuf, MB, DPhil, MRCP, Peter Sleight, DM, FRCP,
Peter Held, MD, PhD, and Stephen McMahon, PhD, MPH

In recent years, several large randomized trials have clarified the role of various interventions in acute myocardial infarction. There is clear evidence that thrombolytic therapy, aspirin, and β-blockers reduce mortality. Both aspirin and β-blockers also reduce reinfarction and stroke. Of the thrombolytic agents, comparative trials have established that tissue plasminogen activator and streptokinase have similar effects on mortality, morbidity, and left ventricular function. There appears to be an increased risk of cerebral hemorrhage with tissue plasminogen activator. The benefits of heparin in conjunction with aspirin and a thrombolytic agent are unclear and, at best, are likely to be modest. Heparin increases the risk of hemorrhagic complications twofold. Although trials of vasodilators conducted before the widespread use of thrombolytic therapy and aspirin have been promising, newer trials are needed to evaluate their effects among patients receiving these agents. The aggregate of all trials of the routine use of calcium antagonists or antiarrhythmic agents indicates that these agents do not improve survival. (*Circulation* 1990;82(suppl II):II-117–II-134)

During the last decade, emphasis on the management of patients with acute myocardial infarction (AMI) has shifted from approaches focused largely on the prevention or management of malignant arrhythmia to strategies aimed at reducing the extent of infarction, preventing reinfarction, and promoting myocardial healing. This change in emphasis has been due, in part, to better understanding of the factors influencing the course of experimental and clinical infarction and, in part, to our increasing ability to evaluate reliably the benefit–risk ratio of new interventions in large well-designed randomized clinical trials. This article reviews pharmacological interventions in AMI and does not review the trials of percutaneous transluminal coronary angioplasty (PTCA). Despite its theoretical appeal, all the trials of routine PTCA have consistently failed to demonstrate benefit; in fact, there is a trend toward increased mortality and morbidity in several trials of routine PTCA.[1–3] The results of these trials have been reviewed by Ryan[4] in this supplement.

Rationale for Interventions in Acute Myocardial Infarction

Deaths in patients after AMI are usually due to one or more of the following causes: 1) Large infarcts that lead to deteriorating pump function and secondary arrhythmias, 2) primary or drug-induced ventricular tachyarrhythmias or asystole, 3) cardiac rupture, 4) reinfarction, and 5) infarct expansion and ventricular dilatation.

Deaths after AMI might therefore be reduced by any one of a number of potential interventions. The size of an infarct can be reduced by improving the balance between oxygen supply and demand through increasing myocardial blood flow (dissolving an obstructing clot or improving collateral blood flow) or by reducing oxygen demand by reducing cardiac work. Antiarrhythmic drugs could be used to decrease the risk of death due to arrhythmias although these drugs may themselves confer an increased risk of asystole and heart block. Some antiarrhythmic agents are known to have a negative inotropic effect and may even exacerbate arrhythmias. Cardiac rupture and arrhythmias might be

From the Clinical Trials Branch, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute Bethesda, Md (S.Y., P.H.), the Cardiac Department, John Radcliffe Hospital, Oxford, England (P.S.), and the Clinical Trials Research Unit, Department of Medicine, University of Auckland, New Zealand (P.S.).

Address for correspondence: Salim Yusuf, MB, DPhil, MRCP, Clinical Trials Branch, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, Bethesda, MD 20892.

prevented by reducing myocardial wall stress. Reinfarction could be prevented by preventing reocclusion or by reducing oxygen demand. Infarct expansion and ventricular dilatation may be prevented by reductions in afterload and preload or by promotion of infarct healing by preserving blood supply to the infarcted area. In this article, we review the data from randomized trials of a number of commonly available interventions and discuss their results in the context of their mechanisms of action.

In the last few decades, there has been a growing acceptance of the randomized controlled trial as the preferred method to evaluate most treatments. It has also become apparent that most successful or adverse treatments in cardiovascular diseases typically have only moderately sized effects (10%, 15%, or 20%) on such major outcomes as death or myocardial infarction. To detect such differences reliably (10% mortality reduced to 9% or 8.5%), studies with a few *thousand* events are usually required. Individual small trials of a few hundred patients often show misleading and conflicting results. When only one of a number of similar trials testing a treatment shows statistical significance while others are unpromising or equivocal, the reader should not base judgment on a single "positive" trial. An unbiased and more representative estimate of the effect of treatment can be obtained by a formal overview (or meta-analysis) of all relevant trials. This approach requires a meticulous search for the relevant data on all randomized patients in all trials, careful and unbiased extraction of data, and use of valid statistical techniques that preserve the randomized comparisons. Such analyses have sometimes found convincing evidence of an effect of treatment or the lack of effect, even when the separate trials have appeared to be contradictory. The significance levels from a trial or from an overview should be interpreted cautiously unless they are dramatic (say, $p<0.001$). Details of the general and statistical methods and the advantages and limitations of meta-analyses are outlined elsewhere.[5]

Thrombolytic Therapy

Among patients with the early clinical signs suggestive of acute transmural MI, about 80% have thrombotic occlusion of the coronary arteries.[6,7] About three fourths of these occlusions can be dissolved by intracoronary infusion of a thrombolytic agent.[7] If the obstruction is cleared early enough, some salvage of ischemic myocardium, and, hence, improvement in ventricular function is likely. Only about 1,000 patients have been studied in all trials of intracoronary thrombolysis.[8] These trials appear superficially conflicting, but pooling these results suggests a non-significant 18% lower mortality among the treatment group.

Even if intracoronary thrombolysis were effective, its widespread use would be impractical and expensive. The delays caused by the need for angiography may further limit its value. Most efforts at thrombolysis have therefore focused on rapid intravenous infusion of a high dose of streptokinase (SK) or, more recently, of the second-generation agents such as tissue-plasminogen activator (t-PA) or anisoylated plasminogen-streptokinase activator complex (APSAC).

In addition to salvaging ischemic myocardium, thrombolytic agents may reduce mortality by a number of additional mechanisms. For example, in experimental infarction, reopening of the ligated coronary artery several hours after myocardial salvage is possible, prevents infarct expansion, and promotes healing.[9] SK and APSAC markedly reduce circulating fibrinogen levels.[10] This reduces plasma viscosity and blood pressure.[11] These mechanisms may increase myocardial blood flow through collaterals and may also decrease myocardial oxygen demand. In addition, circulation of anticoagulant fibrin degradation products may prevent rethrombosis.

Effect on Mortality

Although the newer agents appear to be more effective than SK for rapidly recanalizing coronary thrombi,[12,13] their effects on mortality and major morbidity have been evaluated much less extensively than for SK. During the past 25 years, at least 31 randomized trials involving about 41,000 patients with suspected AMI have compared the effects of intravenous SK with those of standard treatment. In 1985, we reviewed data from 20 of the earlier trials, which included about 5,300 patients.[8] These analyses showed that treatment reduced mortality by 24% (95% confidence interval [CI] from −34% to −12%, $p<0.001$). In addition, these analyses suggested that the reduction in mortality occurred regardless of routine anticoagulant use and occurred even among patients treated 6–12 hours and 12–24 hours after the onset of symptoms. Subsequently, two very large trials, Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI)[14] and the Second International Study of Infarct Survival (ISIS-2),[15] each demonstrated significant reductions in mortality of about 20–25% (at 21 days, 628 deaths among 5,860 patients in the SK group compared with 758 deaths in 5,852 controls, $p<0.001$ in GISSI; and at 35 days, 791 deaths among 8,592 treated patients compared with 1,029 deaths among 8,595 controls, $p<0.001$ in ISIS-2; Figure 1). In addition, the collective data available from several small or moderately sized trials show a significant reduction in mortality.[16–24] An overview of all the available studies indicates that early (≈2–5-week) mortality was 12.8% (2,614 of 20,371) in the control group and only 10.0% (2,062 of 20,634) in the SK group. The estimated 24% reduction in the risk of death has a relatively narrow 95% CI (−20% to −29%) and is highly significant ($p<0.0001$). Long-term follow-up of patients entering the two largest trials demonstrates that the short-term reduction in mortality is maintained for at least about 1–2 years.[15,25]

Recently, data on the effects of t-PA and APSAC on mortality have become available. The Anglo-Scandinavian Study of Early Thrombolysis

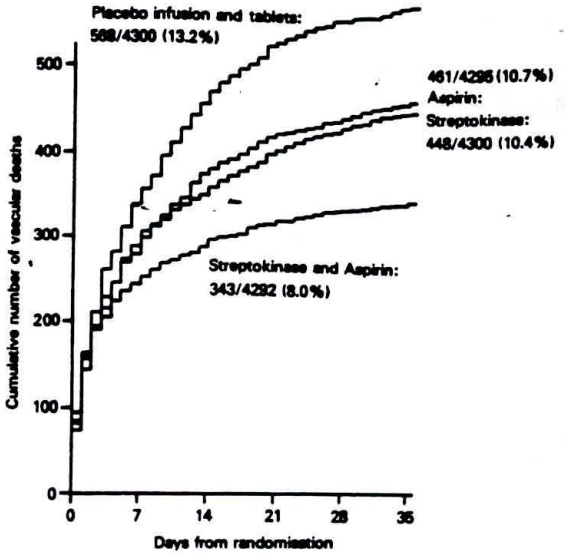

FIGURE 1. *Vascular mortality curves at 5 weeks in ISIS-2. There were similar numbers of nonvascular deaths in the streptokinase group compared with placebo but fewer nonvascular deaths among those allocated to aspirin. Since the number of nonvascular deaths are very few (about 1%), the data for total mortality are essentially unchanged. See text for explanation of trial name abbreviation. (Reprinted with permission from Reference 15.)*

(ASSET),[26] a trial of 5,000 patients, studied the effects of intravenous t-PA or placebo given within 5 hours of onset of pain. All patients received intravenous heparin for over 24 hours. In this study, t-PA reduced mortality by 26% (95% CI, −11% to −39%; $p<0.001$). A similar trend has been observed in an overview of seven small trials of t-PA in a total of 1,700 patients (33% reduction; 95% CI, −54% to −3%).[27-33] A British study of APSAC (APSAC In Myocardial infarction Study [AIMS]) given within 6 hours was terminated prematurely, after randomizing 1,200 patients, because of an apparent 50% reduction in mortality ($p<0.001$).[34] Combining data from all available APSAC trials involving a total of about 2,000 patients suggests a 52% reduction in mortality (95% CI, −33% to −65%; $p<0.001$).[35] The available data (Table 1) from the trials of t-PA and APSAC should be interpreted cautiously and should not be used to assess the relative efficacy of the agents because the apparent effect sizes observed with SK, t-PA, and APSAC in different trials might be influenced by differences in patient selection, timing of treatment, and co-interventions. The effect of patient selection is illustrated by the relatively large effect of similar magnitude in the subset of patients in ISIS-2 that were selected by the entry criteria for the AIMS trial (Table 1). Moreover, the CIs of the overall estimates with each agent overlap, such that it would be prudent to await the results of trials that directly compare these agents. (For example, ISIS-3 will compare SK, t-PA, and APSAC, and preliminary data from GISSI-2 comparing t-PA with SK will be discussed later.) Thus, at present, the available data are more useful in showing that thrombolysis is effective, rather than providing reliable information as to which agent, if any, is most effective.

Effect on Left Ventricular Function

Table 2 summarizes the data from 20 randomized trials of intravenous SK,[16,17,19-24,36] t-PA,[27,29-32] and APSAC[37-41] compared with placebo regarding the effects of early treatment on left ventricular ejection fraction measured by contrast angiograms. In most trials, an improvement in left ventricular ejection fraction of about 2–6% (absolute units) has been observed with each agent. Only one small study examined the effects of intracoronary SK on left ventricular ejection fraction when treatment was started late.[46] This study reported a significant improvement in left ventricular ejection fraction in patients treated with intracoronary SK who had preexisting collaterals. However, the results of this study should be interpreted cautiously until confirmatory evidence from other studies is obtained. t-PA has been directly compared with SK in four trials[42,43,45,47] and with urokinase in one trial.[44] In none of these trials was ejection fraction significantly different in patients treated with t-PA compared with those treated with SK or urokinase. Of these studies, the most data are available from the Italian component of the second GISSI trial, which included more than 12,000 patients.[47] There was no difference in the proportion of patients who had an ejection fraction less than 35%, who developed left ventricular failure, or who had a QRS score greater than 10 (an indirect electrocardiographic measure of the extent of infarction). These data conclusively prove that there is no appreciable difference in the effects of these agents on ejection fraction.

Expanding Indications for Fibrinolytic Therapy

There is consensus that treatment with any one of the available fibrinolytic agents in patients presenting within 6 hours of symptom onset, with ST-segment elevation on the electrocardiogram, and less than 70 years of age will reduce mortality by about 25–30%. However, such patients represent only about 20–30% of patients presenting with suspected MI.[26] If thrombolytic therapy can be shown to have a similar or even a smaller (e.g., 15–20% reduction in the risk of death) but worthwhile net benefit in other categories of patients (e.g., those presenting late or in older high-risk patients), then the clinical and public health value of such treatment would be considerably greater. In this context, it should be emphasized that trials designed to assess the effects of a treatment in the overall population rarely have adequate power to detect a benefit in every subgroup that really benefits. Moreover, the larger the number of subgroups examined, the greater the likelihood of finding spurious effects in one or the other subgroup simply by chance. Therefore, it is usually worth placing greater reliance on the overall results of the trial, and

TABLE 1. Effect of Intravenous Thrombolytic Agents on Short-term Mortality When Administered Within 6 Hours of Onset of Symptoms

Reference	Deaths (*n*)/patients (*n*) Active	Control	Odds ratio	O−E	V
Streptokinase					
Yusuf et al[8]	105/622	115/564	0.80	−9.8	44.1
GISSI[14]	495/4,865	623/4,878	0.77	−63.2	247.4
ISIS-2[15]	471/5,350	648/5,360	0.70	−88.0	250.5
Nine small to moderately sized trials[16–24]	113/1,730	131/1,525	0.72	−18.5	55.3
Subtotal streptokinase	1,184/12,567 (9.4%)	1,517/12,327 (12.3%)	0.74	−179.5	597.3
	95% confidence interval of 0.68 to 0.80, $p<0.0001$				
t-PA					
ASSET[26]	182/2,516[26]	245/2,495	0.72	−32.4	97.7
Seven small trials[27–33]	48/874	70/870	0.67	−11.2	27.5
Subtotal t-PA	230/3,390 (6.8%)	315/3,365 (9.4%)	0.71	−43.6	125.5
	95% confidence interval of 0.59 to 0.84, $p<0.001$				
APSAC					
AIMS[34]	40/625	77/630	0.50	−18.3	26.5
11 small trials[35]	33/583	55/536	0.55	−12.1	20.2
Subtotal APSAC	73/1,208 (6.0%)	132/1,166 (11.3%)	0.52	−30.4	46.7
	95% confidence interval of 0.39 to 0.69, $p<0.001$				
ISIS-2 "AIMS" Cohort*	180/2,745 (6.6%)	310/2,783 (11.1%)	0.57	−63.3	111.6
	95% confidence interval of 0.47 to 0.68				
Total all agents (streptokinase+t-PA +APSAC)	1,487/17,165 (8.7%)	1,964/16,858 (11.7%)		−253.5	770.0
	95% confidence interval of 0.67 to 0.77, $p<0.0001$				

O−E, observed minus expected; V, variance; t-PA, tissue plasminogen activator; APSAC, anisoylated plasminogen-streptokinase activator complex. See text for explanation of abbreviations of trial names.

*Consists of patients who presented with ST-segment elevation <6 hours after onset of symptoms and who were <75 years old.

accepting that this result tends to provide the best estimate of the direction of the effect within each subgroup, rather than trying to scrutinize the results of each subgroup separately. In the next few sections, we will examine the effects of treatment on a number of important subgroups and demonstrate the general consistency of the data.

Time from onset of pain. An overview of the randomized trials conducted before 1984 demonstrated that intravenous SK reduced mortality by about 25% and that the reduction in mortality observed was approximately similar among patients starting treatment within 6 hours, 6–12 hours, or 12–24 hours after onset of symptoms.[8] This conclusion seemed controversial, especially since GISSI demonstrated steeply diminishing benefit with increasing delay from onset of pain, with little apparent benefit after 6 hours.[14] However, GISSI randomized only about 2,000 patients after 6 hours (17% of all patients randomized), so that the statistical power to detect even a 20% difference after 6 hours was low, and the 95% CIs of the actual result included fairly sizable benefits (e.g., a 15–20% reduction). The ISIS-2 study[15] tested the effect of late treatment by deliberately randomizing about 10,000 patients after 4 hours (58% of all patients randomized) and observed benefit in patients treated both early and late. However, the benefit decreased with increasing delay to treatment from the onset of symptoms (odds reductions of 35±6% [mean±SD] at 0–4 hours [$p<0.0001$], 16±7% [$p=0.01$] at 5–12 hours, and 21±12% [$p=0.04$] at 12–24 hours). The mortality reduction

TABLE 2. Left Ventricular Ejection Fraction After Intravenous Thrombolytic Therapy

Reference	Patients randomized (*n*)	Patients with angiograms (*n*)	Time window (hr)	Ejection fraction (%)		
				Active	Control	Δ
Streptokinase vs. control						
Heikkila et al[22]	?	130	<3	59	49	+10*
Durand et al[24]	64	45	<3	57	49	+8*
White et al[17]	219	194	<4	55	50	+5*‖
Schreiber et al[21]	38	24	<5	47	42	+5
ISAM[18]	1,741	848	<6	57	54	+3‡
Kennedy et al[19]	368	170	<6	54	51	+3
Wisenberg et al[23]	66	59	<6	54	47	+7
Binaghi et al[36]	251	206	<12	57	54	+3
Olson et al[20]	52	46	<12	44	43	+1§
t-PA vs. control						
O'Rourke et al[30]	145	126	<2½	61	54	+7†¶
Holmberg et al[32]	352	295	<3	59	55	+4*
Armstrong et al[33]	118	105	<3¾	54	48	+6*
Guerci et al[27]	138	117	<4	53	46	+7*
Australian Heart Foundation[29]	144	103	<4	58	52	+6*
Van der Werf et al[31]	721	577	<5	51	49	+2*
APSAC vs. control						
Been et al[37]	32	22	<3	41	33	+8
Buchalter et al[38]	43	?	<3	35	29	+6
Meinertz et al[39]**	313	256	<4	55	56	−1††
Taeymans and Materne[40]**	82	68	<4	55	54	+1
Bassand et al[41]**	230	?	<5	52	47	+5‡
Comparison of agents				*t-PA*	*SK/UK*	
White et al[42]	270	240	<3	58	58	0
PAIMS[43]	171	152	<3	55	53	+2‡‡
Neuhaus et al[44]	246	239	<6	55	55	0
Sheehan et al[45]	290	145	<7	50	49	+1
GISSI-2[47]	12,381	?	<6	Similar		0§§

Δ, Active minus control ejection fraction; t-PA, tissue plasminogen activator; APSAC, anisoylated plasminogen-streptokinase activator complex; SK, streptokinase; UK, urokinase. See text for explanation of abbreviations of trial names.

*$p<0.05$, †$p<0.01$, ‡$p<0.001$.

§Radionuclide left ventricular ejection fraction.

‖Data for all patients randomized were derived from the data on those with and without previous myocardial infarction provided separately in the article.

¶Ejection fraction was also measured using radionuclide angiography. There was a 4% higher ejection fraction in treated patients (p=NS).

**Control group received heparin.

††Mean ejection fraction for each group derived from data provided in article by site of myocardial infarction.

‡‡A subset of patients (116 of 171, or 68%) had echocardiographic ejection fraction measured. The left ventricular ejection fraction was 56% in the t-PA group compared with 51% in the SK group.

§§The Italian part of GISSI-2 studied 12,381 patients with two-dimensional echocardiograms. The proportion of patients with an ejection fraction<0.35 was 2.5% in the t-PA group compared with 2.2% in the SK group.

for patients entered between 6 and 24 hours was highly significant overall (18±7%, p=0.01) and was also observed among patients with initial ST-segment elevation (22±10%, $p<0.025$). The mortality data from all trials of intravenous SK in which treatment was given later than 6 hours are summarized in Table 3 and indicate that the combined results of the old trials, GISSI, and the ISIS-2 pilot are almost identical to the ISIS-2 results (17±5%, $p<0.001$).

The evidence for benefit in patients entered late is reinforced by the data from the APSAC and t-PA trials. Although none of the trials of intravenous t-PA or APSAC randomized patients 6 hours after the onset of pain, the "slope" relating mortality reduction to treatment delay within the early period provides clues that later treatment might still be beneficial. For example, if a steeply diminishing effect were observed within 4 or 6 hours, it would be logical to

TABLE 3. Short-term Mortality in Patients Treated >6 Hours From Onset of Symptoms With Intravenous Thrombolytic Agents

Reference	Time window (hr)	Deaths (*n*)/patients (*n*) SK	Control	Odds ratio	O−E	V	*p*
Streptokinase							
Yusuf et al[8]	6–24	109/712	154/724	0.67	−19.5	51.1	0.01
GISSI[14]	6–12	133/985	134/961	0.96	−2.1	57.6	NS
ISIS-2 pilot[18]	6–24	19/146	9/67	0.96	−0.2	5.3	NS
Subtotal		261/1,843	297/1,752	0.83	−21.8	114.0	0.05
ISIS-2[15]	6–24	318/3,241	375/3,235	0.83	−28.8	155.0	0.01
TOTAL	>6	579/5,084	672/4,987	0.83	−50.6	269.0	0.001

Typical odds ratio of 0.83; 95% confidence interval of 0.73 to 0.93.
No data are available for tissue plasminogen activator or anisoylated plasminogen-streptokinase activator complex.
Note that both ISIS-2 and the pool of previous trials each indicate a 17% reduction in mortality, so that these two sets of data reinforce each other.
See text for explanation of abbreviations of trial names.

assume that after 8 or 9 hours, there could be little benefit. On the other hand, if there is no such slope or only a gradually diminishing effect in patients treated within 6 hours, it would be reasonable to expect that treatment a few hours later might provide some benefit. Therefore, we examined the effects of treatment by time in the two largest trials (other than those in Table 3). In ASSET, t-PA reduced mortality by 26% when given within 3 hours (81 of 992, or 8.1%, vs. 107 of 979, or 10.9%) and by 24% when given at 3–5 hours (99 of 1,504, or 6.5%, vs. 129 of 1,488, or 8.6%).[26] In AIMS, APSAC reduced short-term mortality to a similar extent when given within 4 hours (18 of 334, or 5.4%, vs. 30 of 326, or 9.2%; 41% risk reduction) and when given 4–6 hours (14 of 168, or 8.3%, vs. 31 of 176, or 17.6%; 53% risk reduction).[33] These data from ASSET and AIMS show little evidence of a slope within 6 hours and strongly imply, therefore, that treatment even after 6 hours is likely to reduce mortality (Figure 2). This is consistent with the data from the intravenous SK trials, which provide clear evidence that treatment with a thrombolytic agent more than 6 hours after the onset of symptoms will lead to a worthwhile reduction in mortality. Although a few small trials like the Western Washington trial[19] or the European Cooperative trial[31] appear to contradict this, the number of deaths in these studies were too few to reliably assess the overall benefits of treatment, let alone the effects in various subgroups.

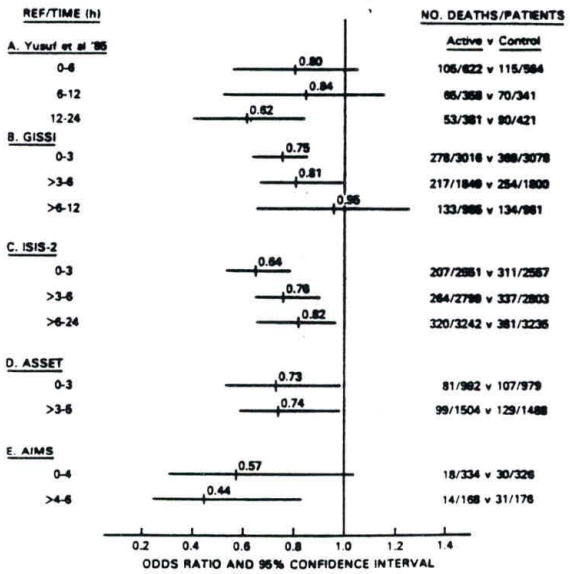

FIGURE 2. *Chart showing mortality reduction (odds ratio with 95% confidence interval) in four large recent trials of thrombolytic agents and the overview of old trials subdivided by the time to treatment from onset of symptoms. See text for explanation of abbreviations of trial names.*

Although in experimental infarction, myocardial salvage may be possible only if reperfusion is achieved within a few hours of coronary ligation, there may be important dissimilarities in human infarction, so that benefit may be achieved by a number of additional mechanisms: 1) Late reperfusion may prevent infarct expansion and promote healing.[9] 2) Coronary occlusion has been shown to be intermittent in humans; this may prolong the period of myocardial viability.[48] 3) In patients with collaterals, it is possible that the period of myocardial viability is prolonged. 4) The onset of symptoms in humans is difficult to time, and it is possible that a period of subtotal obstruction that causes ischemia and severe pain (unstable angina) may precede total obstruction and infarction. (In the ISIS-3 study, although 70% of patients were admitted >3 hours after *onset* of pain, 94% of patients were entered within 3 hours of the *cessation* of pain, indicating that most patients had repeated episodes of pain and, presumably, ischemia.)

Age of the patient. In all four large trials, older patients still benefitted from thrombolysis. These data are summarized in Table 4. Although ASSET and AIMS included only patients less than 75 years old, both the relative and absolute risk reductions were greater in older patients. Moreover, ISIS-2 randomized about 3,400 patients older than 70 years

TABLE 4. Effect of Thrombolytic Therapy on Short-term Mortality by Age Groups in Four Large Randomized Trials

Reference/ age group (yr)	Deaths (*n*)/patients (*n*)		Odds ratio	Deaths (*n*) prevented by treating 100 patients
	Active	Control		
Streptokinase				
GISSI				
≤65	217/3,824 (5.7%)	291/3,784 (7.7%)	0.72	2
65–75	240/1,444 (16.6%)	261/1,442 (18.1%)	0.90	1.5
>75	171/592 (28.9%)	206/623 (33.1%)	0.82	4.2
ISIS-2				
<60	162/3,864 (4.2%)	224/3,856 (5.8%)	0.71	1.6
60–69	320/3,033 (10.6%)	435/3,023 (14.4%)	0.70	3.8
≥70	309/1,695 (18.2%)	370/1,716 (21.6%)	0.81	3.3
t-PA				
ASSET				
≤55	29/748 (3.8%)	33/745 (4.4%)	0.87	0.6
56–65	63/963 (6.5%)	71/896 (7.9%)	0.81	1.4
66–75	90/827 (10.8%)	140/852 (16.4%)	0.62	5.5
APSAC				
AIMS				
<65	21/405 (5.2%)	35/411 (8.5%)	0.59	3.3
≥65	11/90 (12.2%)	26/86 (30.2%)	0.34	18*

This table shows that the percent risk reduction is independent of age and that there is benefit in all age groups in these trials. However, the absolute numbers of lives saved increases substantially with increasing age.

t-PA, tissue plasminogen activator; APSAC, anisoylated plasminogen-streptokinase activator complex. See text for explanation of abbreviations of trial names.

*Since the number of patients within each subgroup tends to be quite small, especially in AIMS, care should be taken in interpreting the precise "degree" of benefit.

and observed a highly significant reduction in mortality among them (309 of 1,695, or 18.2%, vs. 370 of 1,716, or 21.6%; $p<0.01$). In this trial, the benefits of SK were additive to those of aspirin (in the whole population and among the elderly), so that with their combination, the absolute mortality reduction was substantial (135 of 854, or 15.8%, vs. 203 of 852, or 23.8%; $p<0.001$ among those >70 years; Figure 3).

Other subgroups. Several studies have shown reductions or improvement in left ventricular function or mortality in patients with anterior or inferior MI, those with and without previous MI, and those with and without ST-segment elevation.[15,26,34] Although it is possible that the relative and absolute risk reductions in certain subgroups of patients, such as those with an inferior MI or those without ST-segment elevation, may be somewhat smaller, it is still likely that these patients may experience a worthwhile benefit from treatment.

Therefore, it appears that the categories of patients that might benefit from fibrinolytic therapy are fairly broad and probably include about 70–80% of patients presenting with suspected AMI. Several trials (e.g., Estudio Miocardio Estreptoquinasa Republic Americas Sul [EMERAS], Late Assessment of Thrombolytic Therapy [LATE], and ISIS-3) are currently seeking further evidence of the value of treatment in a number of subgroups in which the effects of treatment are less well accepted (e.g., patients presenting 6–24 hours after onset of symptoms or with no ST-segment elevation on the electrocardiogram.

Adverse Effects of Fibrinolytic Therapy

Reocclusion and reinfarction. In the recent trials of short-duration, high-dose infusions of SK, lysis of intracoronary thrombus has been observed to produce an excess risk of reinfarction. In cases where

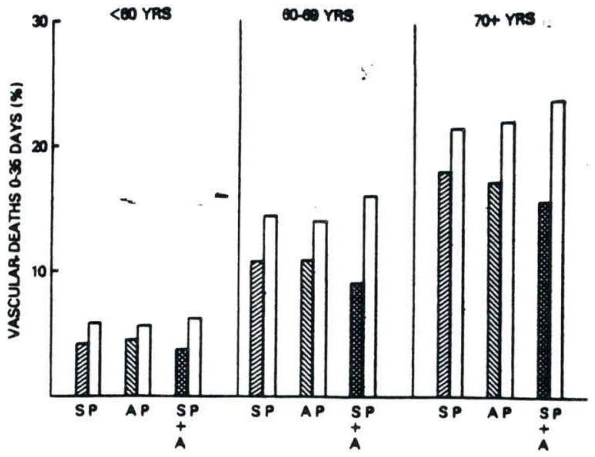

FIGURE 3. *Bar graph showing percent mortality reduction by streptokinase (S), aspirin (A), and their combination in ISIS-2 by different age groups (yrs, years). Note that the absolute numbers of lives saved by any one of the three treatments increase substantially with increasing patient age. P, placebo.*

treatment was prolonged for 24–48 hours (as in the old trials), significantly fewer patients suffered reinfarction, whether or not anticoagulants were routinely used.[8] These data, however, do not indicate that anticoagulants are without value. Data on reinfarction are available from seven of the eight trials of t-PA. Surprisingly, these data indicate only a small excess in reinfarction (321 of 3,317 among treated patients compared with 299 of 3,298 among the patients receiving placebo; 9.7% vs. 9.1%). No data on reinfarction are available from the trials of APSAC. In ISIS-2, which employed a 2×2 factorial design (one fourth of patients received SK; one fourth, aspirin; one fourth, both; and one fourth, neither), aspirin prevented the excess reinfarction observed with SK (reinfarction rates: placebo, 3%; aspirin, 2%; SK, 4%; and aspirin+SK, 2%).[15] In the Thrombolysis in Myocardial Infarction (TIMI)-IIb trial, immediate administration of β-blockers was found to reduce the incidence of reinfarction among patients treated with t=PA (6-day reinfarction: 2.3% among 696 patients allocated to immediate β-blockade compared with 4.5% among 694 patients allocated to receive β-blockers after the sixth day; $p<0.02$).[2] No other intervention has been demonstrated to reduce the risk of reinfarction after thrombolytic therapy. In particular, several trials of immediate (at admission) PTCA or deferred PTCA (18–48 hours after thrombolytic therapy) versus usual care have each shown a trend toward excess mortality and excess reinfarction in those randomized to an "invasive" strategy.[1,2] Although heparin has been routinely used after a thrombolytic agent in some trials, little controlled data exist to support its use in conjunction with thrombolytic therapy and aspirin. Preliminary data from GISSI-2 indicate little additive benefit from the addition of heparin to a regimen consisting of a thrombolytic agent, aspirin, and β-blockers. (See also a following section on heparin.[47]) ISIS-3 is further evaluating this question.

Hemorrhage. In ISIS-2, minor bleeding occurred more commonly in the SK group (3.5% vs. 1.0%).[15] There was also a small excess in the number of patients with hemorrhage requiring transfusion (0.5% vs. 0.2%). The excess in bleeding was unrelated to the use of aspirin but was closely related to the use of heparin (absolute excesses in minor and major hemorrhagic episodes were 5.3% and 0.7% in the SK and control groups, respectively, with planned intravenous heparin; 2.6% and 0.4% with planned subcutaneous heparin; and 1.5% and 0.0% with no heparin use planned; also see the section on heparin). In ASSET, in which all patients received heparin for 21 hours, 6.3% of patients given t-PA and 0.8% of patients given placebo had a minor bleeding episode.[26] The proportion of patients developing a major bleeding episode was 1.4% and 0.4%, respectively. The incidence of bleeding in the various trials should not be used to compare the effects of the different agents because of differences between studies in definitions and ancillary drug use. Of note, no particular subgroup (e.g., the elderly) was at higher risk of suffering episodes of major bleeding in the treatment group compared with controls in ISIS-2.

Stroke. In ISIS-2,[15] GISSI,[14] and ASSET,[25] there was no overall excess in stroke. However, in all these trials, there was a significant excess of early and presumed hemorrhagic strokes, which was balanced by a similar decrease in late, presumably thrombotic strokes. No excess in stroke was observed among elderly patients treated with SK compared with those allocated to the control group in ISIS-2.

Hypotension. In ISIS-2, there was an excess of hypotension and/or bradycardia (10% SK vs. 2% placebo) and allergic reactions (4.4% vs. 0.9%).[15] None of the allergic reactions were considered to be due to anaphylactic shock. The bradycardia and hypotension may be the result of production of vasoactive kinins by the less-specific SK-based drugs and is therefore likely to also be seen with APSAC. This may not necessarily be harmful since in ISIS-2, there was no excess mortality in patients with this condition. The incidence was not reduced by the use of prophylactic steroids.[15] Similar results have been reported from GISSI.[14] The incidence of hypotension, bradycardia, and allergic reactions appears to be lower with t-PA.[42,47]

Cardiac rupture and arrhythmias. In almost all SK trials, there appears to be more deaths among the treated patients than controls during the first day. For example, in GISSI, there were 120 deaths in those allocated to receive SK compared with 76 deaths among those allocated to receive placebo within 6 hours of onset of symptoms.[48] Some deaths were due to arrhythmias, but a high proportion was reported to be due to electromechanical dissociation, raising the possibility that treatment might cause myocardial hemorrhage and cardiac rupture. Detailed analyses from ISIS-2, ASSET, and AIMS

are not yet available. In ISIS-2, there was a similar excess of deaths in the SK group in the first 24–36 hours. However, data from the discharge forms suggest that the numbers of patients who suffered cardiac rupture overall were similar in the two groups. In all four major trials[14,15,26,34] of thrombolytic agents, there was no excess in the incidence of ventricular fibrillation or cardiac arrest. On the contrary, in at least two trials, there was a significant reduction in nonfatal cardiac arrests.

Comparison of thrombolytic agents. Several studies have directly compared the effects of "clot-specific" thrombolytic agents (e.g.; t-PA, pro-urokinase) with the nonspecific agents (e.g.; SK, APSAC, or urokinase). In most studies, the proportion of patients demonstrating recanalization or patency 90 minutes after initiation of therapy was greater with the former class of agents.[12,13,50] However, angiograms performed at 24 hours or later did not reveal any significant differences in patency.[42,43,50] In one study comparing pro-urokinase with SK, while there was a difference in patency at 60 minutes, there was little difference at 90 minutes.[50] In the TIMI study, the differences in recanalization rates were more marked when treatment was initiated after 4 hours after the onset of symptoms, whereas with earlier treatment, the differences were only modest.[12] These data indicate that although clot-specific agents produce more rapid thrombolysis, especially with "old" clots, these differences narrow after about 90 minutes. The relevance of the early difference in recanalization to mortality or ejection fraction has been assessed in several studies.

There have been five randomized trials that compared the effects of t-PA with SK or urokinase on left ventricular function.[42–44,46,47] In none of the studies was there a difference in left ventricular ejection fraction. The GISSI-2 study,[47] along with its international counterpart, randomized 20,749 patients in a 2×2 factorial design to receive t-PA alone, SK alone, t-PA plus subcutaneous heparin (started 12 hours after randomization), and SK plus subcutaneous heparin. All patients presented within 6 hours of the onset of pain and had ST-segment elevation. All patients without contraindications received aspirin and intravenous β-blockers. There were 926 (8.9%) deaths in the t-PA group compared with 887 (8.5%) in the SK group. In the group receiving t-PA plus heparin, there were 475 (9.2%) deaths compared with 408 (7.9%) deaths among those receiving SK plus subcutaneous heparin (started 12 hours after randomization). While this difference in favor of SK is statistically significant ($Z=2.41, p<0.02$), this result may be due to the play of chance. However, it makes it unlikely that t-PA is superior to SK, even if a more intensive regimen of earlier and intravenous heparin is used in all patients. This conclusion is indirectly supported by 1) the similarity of effect on mortality of t-PA and SK compared with placebo in separate trials. (Most of these t-PA trials used an aggressive regimen of intravenous heparin.) and 2) the similarity of effect on left ventricular function in trials that directly compared the agents against a background of intensive intravenous heparin therapy.

In GISSI-2, the incidence of minor hemorrhagic episodes was significantly higher with t-PA compared with SK, whether or not heparin was used. In both groups, the risk of these minor hemorrhagic episodes was increased by the use of heparin. The incidence of major hemorrhagic episodes was significantly higher with SK, but this was largely due to an excess among those given heparin (0.8%, t-PA+heparin vs. 1.2%, SK+heparin). Among those not given heparin, there was little difference in major hemorrhagic episodes between the two groups (0.5%, t-PA alone vs. 0.6%, SK alone). There was a significant excess in stroke among those treated with t-PA (139 events, or 1.35%) compared with 99 events (0.95%) among those treated with SK ($p<0.01$). The excess in stroke in the t-PA group was due to those classified as hemorrhagic or undefined (82 with t-PA vs. 51 with SK), with no difference in the incidence of ischemic strokes (57 in both groups). Heparin did not appear to increase the risk of stroke in either group.

Therefore, it appears that both t-PA and SK have similar effects on ejection fraction and mortality. However, t-PA increases the risk of hemorrhagic stroke. The higher incidence of major bleeding episodes with SK is largely prevented by avoiding the use of heparin.

Aspirin and Other Antiplatelet Agents

ISIS-2 randomized about 18,000 patients not only to SK or placebo but also to relatively low-dose aspirin (160 mg given on the day of MI and continued for 4 weeks) or placebo in a 2×2 factorial design. Mortality was reduced by 23% (804 of 8,587 in the aspirin group compared with 1,016 of 8,600 in the control group; 95% CI, −15% to −30%; $p<0.0001$). In addition, there was a 44% reduction in nonfatal MI (83 vs. 170; 95% CI, −41% to −61%; $p<0.0001$) and a 46% reduction in nonfatal stroke (27 vs. 51; 95% CI, −26% to −65%; $p<0.01$). The combined benefits of SK and aspirin yielded considerably greater benefit than either treatment alone. Their combined use resulted in a 42% reduction in mortality (5-week mortality of 8.0% in those given SK and aspirin, 10.7% in those given aspirin alone, 10.4% in those given SK alone, and 13.2% in those given placebo) without any excess in major bleeding complications (Figure 1). The effect of aspirin, unlike that of SK, was independent of the delay from onset of symptoms to time of treatment (odds reduction at 0–4, 5–12, and 13–24 hours: 25±7%, 21±7%, and 21±12%, respectively). Aspirin added to the benefit of SK in all subgroups examined. In particular, in patients older than 70 years among whom these drugs might have been considered contraindicated, the combination markedly reduced mortality (135 of 854 [15.8%] vs. 203 of 852 [23.8%], $p<0.001$) without increasing the risk of hemorrhage or stroke (Figure 3). Thus, because older patients are at high risk of

death, the absolute numbers of lives saved by treating those older than 70 years is substantially greater than treating younger patients (based on ISIS-2, the number of deaths prevented for every 100 treated patients less than 60 years old is 2.5; for those 60–69 years, 7; and for those older than 70 years, 8).

The Antiplatelet Trialists Collaborative Group[51] recently reviewed all the long-term trials of antiplatelet agents in secondary prevention (including patients with unstable angina and cerebrovascular disease). Ten trials evaluated aspirin or other antiplatelet agents started some months or years after MI and continued for a year or two. Six trials evaluated aspirin and dipyridamole, and two evaluated sulfinpyrazone. In the 10 post-MI trials in a total of 18,441 patients, antiplatelet treatment reduced the risk of vascular death by 13% (7.9% in the active group compared with 8.8% in controls; $p<0.01$), of nonfatal MI by 31% (5.5% and 7.4%, respectively; $p<0.0001$), and of nonfatal stroke by 42% (1.1% and 1.9%, respectively; $p<0.0001$), with no effect on nonvascular deaths (0.8% and 0.9%, respectively). Overall, treatment reduced the risk of developing a major vascular event by 25% (95% CI, −19% to −31%; $p<0.0001$). This benefit was observed in all subgroups examined (e.g., by age, sex, blood pressure, and presence or absence of diabetes). This benefit in preventing major vascular events observed in both the early and late post-MI trials is consistent with the results of trials in patients with cerebrovascular diseases (22% risk reduction, $p<0.0001$) and unstable angina (36% risk reduction, $p<0.002$).

The data from an overview of the trials suggest that aspirin alone is just as effective as aspirin plus dipyridamole or sulfinpyrazone. The benefits of aspirin appear to be similar in the trials that evaluated doses of 160 mg/day, 300–325 mg/day, or 900–1,500 mg/day. Data from the UK trial[51] of transient ischemic attacks suggest that lower doses of aspirin were associated with two thirds fewer gastrointestinal side effects but were equally effective in reducing cardiovascular events. In conclusion, it is reasonable to recommend aspirin at 160–325 mg/day or 325 mg on alternate days to patients with AMI, starting early, and continuing for at least a year or two. The best dose is not precisely known, but this should be considered a minor issue compared with the decision to use aspirin.

Heparin

Until recently, there were only limited data on the use of heparin in conjunction with thrombolytic therapy and aspirin. Before the recent results from ISIS-2 clearly indicated benefit from aspirin, many investigators had routinely used intravenous heparin during or after fibrinolytic therapy with the expectation that reocclusion and reinfarction would be prevented. The pilot study to the ISIS-2 trial, in which about 600 patients were randomized to heparin or control, observed a trend toward less reinfarction among treated patients but found no difference in mortality.[18] Similar effects on mortality and excess reinfarction have been observed in the thrombolytic trials in which anticoagulants were routinely used and those in which they were not, indicating that it may not be absolutely essential to follow thrombolytic therapy with heparin. In ISIS-2, there was a trend toward greater mortality reduction by SK when more intense anticoagulation was planned (risk reductions of 31% when SK was used with intravenous heparin, 27% when used with subcutaneous heparin, and 12% with no heparin). However, as stated earlier, both major and minor bleeding episodes were more common with the more intense heparin regimen.[15]

There have been several trials of subcutaneous or intravenous heparin completed before the common use of aspirin and/or thrombolytic agents. These have been reviewed by MacMahon et al.[53] The odds of suffering death or subsequent infarction were reduced by 16±7% and 22±10%, respectively (both about $p=0.02$). In addition, there was a halving in the incidence of strokes, pulmonary emboli, and deep vein thromboses. These trials do not address whether these beneficial effects will be realized when heparin is given after fibrinolytic therapy and/or aspirin and whether the risks of bleeding will be a major problem.

Several small trials have evaluated the role of heparin in maintaining coronary artery patency after thrombolytic therapy. Topol et al[54] randomized 131 patients to receive t-PA only or t-PA plus heparin 90 minutes after initiation of therapy. The patency rates in the two groups were identical (79%). Bleich et al[55] randomized 93 patients 3 hours after initiation of t-PA therapy to receive heparin or no heparin. None of the patients received aspirin. Angiography performed at a mean of 57 hours later showed a trend toward greater patency with heparin (71% vs. 44%; two-tailed $p=0.08$). In an Australian study,[56] 195 patients received t-PA followed by heparin for 24 hours. Patients were randomized to continue heparin therapy or to receive aspirin for 7 days. Patency was the same in the two groups (80%). Ross et al[57] randomized patients to receive t-PA alone or t-PA plus heparin for 1 week. Angiography performed at a mean of 7 hours after randomization indicated higher patency in the latter group. However, aspirin was used in a dose of 80 mg daily orally. It is therefore possible that after a single dose of 80 mg aspirin orally (unlike the 160 mg aspirin chewed in ISIS-2), little immediate antiplatelet effect is observed. Consistent with this possibility, in this study there were fewer reocclusions in the aspirin group compared with the heparin group among patients who had an angiogram performed 1 week later.[57] The Studio Sulla Calciparina nell'angina e nella Trombosi ventricolare nell Infarto (SCATI) group randomized 360 patients to receive 12,500 units of calcium heparin subcutaneously twice daily and 351 patients to no heparin.[58] None of the patients received aspirin; 433 patients received prior thrombolytic therapy. There was no difference in reinfarction, but mortality was

significantly lower (21 of 360 vs. 35 of 351; $p<0.03$). Similar results were observed in the subgroup of patients who had previously received SK. The above data suggest that while heparin is likely to be valuable after thrombolytic therapy, heparin may not be superior to aspirin. Moreover, it is unclear whether heparin provides additional benefit when added to aspirin and thrombolytic agents.

The GISSI-2 study evaluated the role of subcutaneous heparin in addition to thrombolytic therapy and aspirin in 20,749 patients.[47] There were 883 deaths among the 10,353 patients allocated to receive heparin compared with 930 deaths among the 10,396 allocated to receive no heparin (odds ratio of 0.95, with a 95% CI of 0.86 to 1.04). While these results are still consistent with a 10% reduction in mortality, it definitely indicates that in the presence of aspirin, the benefits of heparin may be only modest. There was no effect on reinfarction (285 vs. 301) or stroke (118 vs. 120). However, there was a significant increase in patients experiencing minor and major hemorrhagic episodes (863 vs. 471 for minor episodes, $p<0.001$). These data do not rule out the possibility of a modest reduction in the risk of death of about 5–10%. For the moment, it would be prudent not to use heparin routinely, at least until the results of ISIS-3 become available in late 1990 or early 1991.

β-Adrenergic Blocking Agents

β-Blockers reduce oxygen demand by lowering heart rate and blood pressure; they also counter the direct adverse effects of catecholamines and also have antiarrhythmic properties. Thus, β-blockers may cause a reduction in infarct size, decrease myocardial wall stress, and prevent cardiac rupture. Reductions in indirect indexes of myocardial damage (such as enzyme or electrocardiographic changes) in humans have been observed in at least nine studies in which intravenous treatment with a β-blocker was started within 12 hours of onset of pain.

Data are available from at least 28 randomized trials including about 27,500 patients.[59,60] In the largest of these studies, ISIS-1,[60] vascular mortality was reduced by about 15% during the 7 days of treatment (3.9% in the β-blocker group, 4.6% among controls; $p<0.05$) (Figure 4). After 7 days, the difference in mortality between the treated and control groups increased slightly; this may be due, in part, to the modest excess of continued use of β-blockers after discharge in the treated group compared with controls. Almost identical mortality results were observed in another large trial, the Metoprolol In Acute Myocardial Infarction (MIAMI) study.[61] Pooling the results of all 27 available randomized trials indicates that such treatment reduces mortality by 13% (95% CI, −2% to −25%) in the first week ($p<0.02$). The mortality reduction when analyzed by separate time intervals was most marked in the first 2 days (≈25%), so that maximum benefit is likely to be obtained by initiating treatment early (Table 5). Data on nonfatal reinfarction and nonfatal cardiac arrests

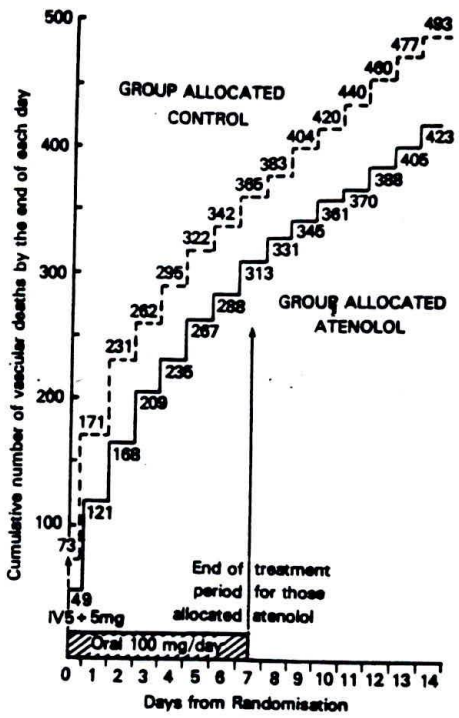

FIGURE 4. *Vascular mortality curve at 7 days (period of therapy randomized to control or atenolol) and for the next week in ISIS-1. Note that the mortality curves diverge early and then remain parallel. See text for explanation of trial name abbreviation. (Reprinted with permission from Reference 60.)*

in hospital suggest that early treatment reduces risk by about 19% ($p<0.01$; 95% CI, −5% to −33%) and 16% ($p<0.02$; 95% CI, −2% to −30%), respectively. The available data on all patients suffering death, nonfatal cardiac arrest, and nonfatal reinfarction indicate a 16% reduction in the risk of suffering one of these major events (1,110 vs. 1,298, $p<0.0001$) and provide strong evidence that treatment is indeed beneficial. Retrospective analyses of the causes of deaths in ISIS-1 suggest that the reduction in mortality is due chiefly to prevention of cardiac rupture and ventricular fibrillation.[62] A trend toward fewer deaths due to cardiac rupture was also observed in both the MIAMI trial and the earlier trial from Göteborg.[63] The benefit with early intravenous β-blockade was particularly apparent in the first 24–36 hours after drug administration, unlike thrombolytic therapy, where in both GISSI and ISIS-2 there was an excess number of deaths in this early period. These data suggest a complementary role for β-blockers after thrombolytic therapy.[2] There has been only one small trial of β-blockers given after thrombolytic therapy. In this trial, although the numbers of deaths were similar at 6 days with β-blocker and control groups (17 of 696 vs. 17 of 694), the 95% confidence interval is quite consistent with the previously observed reduction in mortality of about 15%. In this trial, there was a significant reduction in early nonfatal reinfarction (16 of 696 vs. 31 of 694, $p<0.05$) and in recurrent ischemic episodes (107 of 696 vs. 147

TABLE 5. Mortality in Trials of Early Intravenous β-Blocker Followed by Short-term Oral Treatment Divided by Time to Death After Myocardial Infarctions

	Deaths (*n*)							
	0–1 days		2–3 days		4–7 days		0–7 days	
Trial	BB	Con	BB	Con	BB	Con	BB	Con
ISIS-1	121	171	91	92	105	104	317	367
MIAMI	29	41	21	23	29	29	79	93
26 small trials	55	51	25	38	37	37	117	126
Total mortality (*n*)	205	263	137	153	171	170	513	586
Total patients (*n*)							13,815	13,721
Approximate percent change in odds (±SEM)	−23±8		−11±11		−1±11		−14±6	

BB, β-blocker; Con, control; SEM, standard error of the mean. See text for explanation of abbreviations of trial names. (Modified with permission from Reference 51.)

of 694, $p<0.005$), providing some direct evidence of additional benefit with β-blockers when added to thrombolytic therapy.

In addition to the short-term benefits of β-blockers, several independent trials have clearly demonstrated that long-term therapy with β-blockers for a year or two reduces mortality and reinfarction by about one fourth.[59] Examination of the results in various subgroups based on baseline characteristics such as MI location, Q- or non–Q-wave MI, age, heart rate, or blood pressure do not suggest any significant heterogeneity of effect. Therefore, a policy of starting β-blockers intravenously within the early hours of MI, followed by long-term oral treatment, should be considered in all patients who have no contraindications.

Calcium Channel Blockers

Calcium channel blockers reduce oxygen demand by lowering blood pressure and myocardial contractility. They dilate coronary vessels and prevent calcium overload of ischemic cells. While the above mechanisms may be expected to reduce the extent of myocardial injury, several of these drugs produce adverse effects that could potentially offset the benefit. For example, nifedipine can cause reflex tachycardia and coronary vasodilatation of vessels supplying nonischemic areas. This could lead to a diversion of blood from the ischemic zones ("steal"). Verapamil and diltiazem have the potential to cause sinoatrial and atrioventricular block and depression of myocardial contractility, thereby causing heart failure. Therefore, the net benefit of these agents can only be assessed in carefully controlled randomized trials.

In total, data are available from 21 randomized trials of varying sizes.[64] Altogether, these trials studied about 17,800 patients. Five trials included more than 1,000 patients each, while most studies had fewer than 200. This means that most trials were individually too small to be able to detect even large differences in mortality and major morbidity.

Only one large short-term trial has been reported,[58] while two other studies started treatment early and continued treatment for 6 months.[59,60] In the nifedipine study by Wilcox et al,[65] 4,491 patients with suspected MI were treated for 1 month. Almost 70% of patients were entered into the study within 8 hours of the onset of chest pain. A similar number of patients in each treatment group (64%) developed an MI, and the mortality was 6.3% in the placebo group and 6.7% in the nifedipine-treated group. Reinfarctions were slightly more common in the treated (2.2%) than in the control (1.5%) group (p=NS). The Secondary Prevention Reinfarction Israeli Nifedipine (SPRINT)-2 trial[66] was stopped early after randomizing 1,358 patients due to a trend toward increased early mortality in the nifedipine group. The 6-month mortality was 15% in the treated groups compared with 13% among controls. The number of patients developing MI in the nifedipine and control groups (84% compared with 87%) was similar. In the third large trial, verapamil or placebo was administered intravenously in 3,498 patients and continued orally long-term at a dose of 120 mg three times daily in patients who developed an MI and who could tolerate the study drug (42% of the patients in each group).[67] The withdrawal rate due to side effects during long-term treatment was high, 42% in the verapamil group and 34% in the placebo group. At the end of the 6-month treatment period, 8.6% of the verapamil-treated patients had died compared with 8.4% in the control group. There were 50 reinfarctions in the group randomized to verapamil compared with 60 in the placebo group (p=NS). Enzymatically estimated infarct size in a subgroup of 100 patients was not significantly different between the groups. A fourth study, the Multicenter Diltiazem Post-Infarction Trial (MDPIT), randomized patients to receive diltiazem or placebo starting 2–4 weeks after AMI for 2–3 years.[68] There was no significant difference in the proportion of patients who suffered death (166 active vs. 167 control) or reinfarction (99 vs. 116, p=NS). Subgroup analyses suggested that treatment appeared to be significantly harmful for patients with large infarction, depressed left ventricular function, or pulmonary congestion, whereas there appeared to be a nonsignificant favorable trend in patients without pulmonary congestion or

non–Q-wave MI. The authors of this report wisely caution that their analyses do not provide conclusive results but only suggest hypotheses for future trials. A further small trial of diltiazem in patients with non–Q-wave infarcts demonstrated no effect on mortality but claimed that treatment reduced nonfatal reinfarction.[69] This result is not significant if a standard two-sided p value is used, which has been used in most trials. Moreover, there was an excess of adverse effects such as sinoatrial arrest and atrioventricular block. Similar excess occurrences of sinoatrial arrest and atrioventricular block were observed in the Danish verapamil study.[67]

In addition to the above four studies, 14 smaller studies in which treatment was started early included about 1,800 patients. An overview of the results from all 18 trials provides reliable estimates of the likely effects of treatment.[64] In the studies in which treatment was started within 24 hours, 3,258 of 5,352 (60.8%) patients treated with calcium channel blockers developed MI compared with 3,289 of 5,356 (61.4%) among controls (p=NS). An overview of the mortality results from trials in which treatment was started early indicates a nonsignificant increase in the calcium blocker–treated group. This adverse trend is observed in both the short-term studies (200 of 3,121 [6.4%] in the calcium-blocker group died compared with 185 of 3,150 [5.9%] among controls) and the studies in which treatment was started early and continued for several months (251 of 2,409 [10.4%] and 235 of 2,396 [9.8%], respectively). Because the various calcium antagonists differ in some of their pharmacological properties, we stratified the analyses by agent. With no agent was there a significant reduction in mortality or reinfarction. The trials with diltiazem suggest a trend toward fewer reinfarctions (113 of 1,557 among actively treated patients compared with 142 of 1,560 among controls; p=0.10). However, this trend is not significantly heterogeneous compared with the overall results (χ^2 for heterogeneity=NS). Moreover, there does not appear to be any reduction in mortality with diltiazem (180 of 1,574 vs. 181 of 1,577, respectively).

These data indicate that prophylactic use of calcium channel blockers during the early phase of MI is not likely to be beneficial and may well be potentially harmful in some high-risk patients.

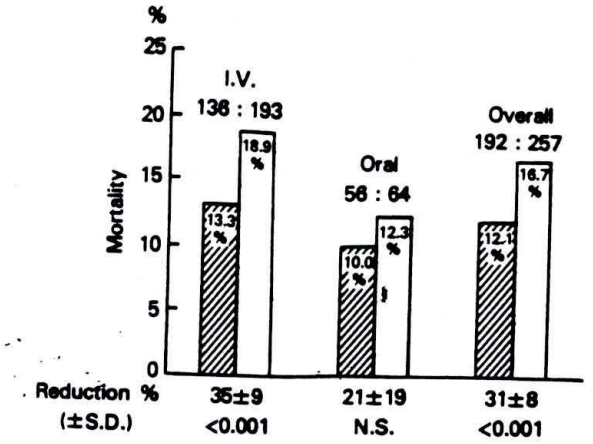

FIGURE 5. *Bar graph showing short-term mortality reduction (%) in randomized trials of intravenous (I.V.) or oral nitrates in acute myocardial infarction. Active, ▨; placebo, □; SD, standard deviation; NS, not significant.*

Nitrates

Intravenous Nitrates

Nitrates reduce oxygen demand and myocardial wall stress by reduction of both afterload and preload; nitroglycerin might additionally increase blood supply by relieving coronary spasm. Intravenous sodium nitroprusside has been evaluated in three trials and intravenous nitroglycerin in six trials in approximately 1,000 patients each.[70] Lower mortality was observed in all three trials of nitroprusside, with the difference being statistically significant in one trial. Lower mortality was observed in five of six trials with nitroglycerin; in two, the differences were statistically significant (p<0.05). Overall, the pooled data indicate a 12% mortality rate among the 1,009 treated patients compared with an 18% mortality rate among the 1,004 control subjects (p<0.001). This represents about a one third reduction in the risk of death (95% CI, −18% to −49%). The risk reduction in the six nitroglycerin trials (45%) appears somewhat greater than that in the three trials with

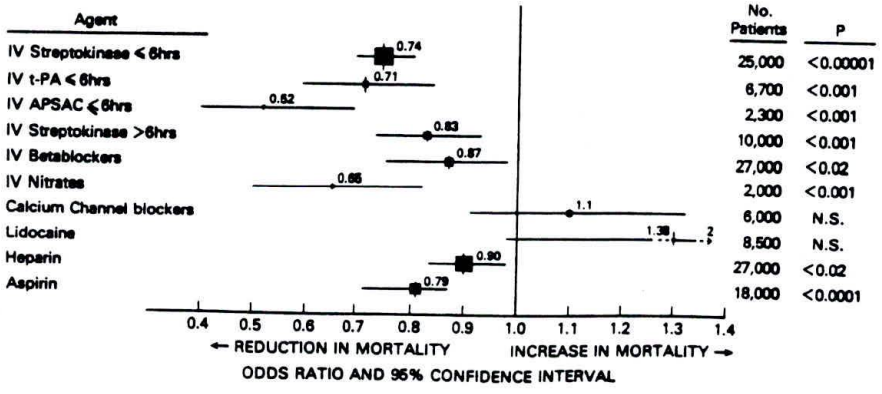

FIGURE 6. *Chart showing summary of effects of various treatments on mortality in acute myocardial infarction. Odds ratios and their 95% confidence intervals are plotted. The size of the square is related to the variance of the data. Larger squares reflect more data, and narrower confidence interval indicates more precise estimates of treatment effect. IV, intravenous; t-PA, tissue plasminogen activator; APSAC, anisoylated plasminogen-streptokinase activator complex; NS, not significant.*

sodium nitroprusside (23%). This difference, although not statistically significant by conventional criteria, is consistent with clinical and pharmacological data that suggest nitroglycerin is likely to be the more beneficial agent.

Oral Nitrates

At least five trials with oral nitrates have been published.[71] Overall, there was a 10% short-term mortality among 560 patients randomized to oral nitrates compared with 12.3% among 521 controls. This 21% risk reduction (95% CI, +16% to −46%) is not significantly different from the results of the intravenous nitrate trials.

Overall (oral and intravenous treatment), there were 192 (12.1%) deaths in nitrate-treated patients compared with 257 deaths among controls (16.7%) (31% risk reduction; 95% CI, −7% to −47%; Figure 5). Subgroup analyses of these trials by such variables as location of infarction and time from onset of pain did not consistently reveal benefit in any particular subgroup. These data suggest that intravenous nitrates (in particular, nitroglycerin) and probably oral nitrates reduce mortality when given early to patients with moderate or large MIs.

Lidocaine

In the early hours after an MI, death due to ventricular fibrillation is common. To prevent ventricular fibrillation and hence to reduce mortality, physicians often treat patients, especially those with complex ventricular arrhythmias, with a prophylactic antiarrhythmic agent such as lidocaine. At least 14 randomized trials with a total of 9,155 patients have studied lidocaine.[72] Nine trials evaluated intravenous lidocaine infusions in 2,194 patients during a 24- to 48-hour period, whereas five trials evaluated intramuscular lidocaine injections in 6,961 patients and followed them up for 1–4 hours. In the 14 trials, 89 nonfatal and 14 fatal cases of ventricular fibrillation were reported. In three trials no event was recorded, and in seven trials there were fewer cases of ventricular fibrillation in the treated group; in only one trial was this difference statistically significant. In the four remaining trials, there were more events among patients treated with lidocaine. Overall, the data from all trials indicate a 35% reduction in the odds of developing ventricular fibrillation (95% CI, −56% to −3%) but with only borderline statistical significance ($p<0.04$).

In the 14 trials, 137 deaths were reported. In neither the trials individually nor overall was there any significant difference in mortality. Indeed, early mortality was about one third greater among lidocaine-treated patients, but the 95% CIs include the possibility of no effect as well as the possibility of harm (38% excess risk; 95% CI, −2% to +95%; $p<0.10$). There was no heterogeneity in the results between the intravenous and intramuscular trials regarding the effects of lidocaine on ventricular fibrillation and mortality. Data on fatal or nonfatal asystole were available from only seven trials. There was an excess of fatal asystole (10 vs. 5, p=NS), fatal asystole plus asystole requiring resuscitation (34 vs. 13, $p<0.01$), and total asystole (54 vs. 25, $p<0.01$). However, because of the incompleteness of the data on asystole, biases in end-point ascertainment cannot be ruled out. However, if prophylactic treatment were to double the number of early deaths from asystole (given a rate of three asystolic deaths per 1,000 observed among controls in the trials), then this could outweigh the benefits of a one third reduction in ventricular fibrillation, especially among patients at low risk for this event and when so few cases of ventricular fibrillation are fatal (one per 1,000 among controls in the trials). Therefore, routine use of prophylactic lidocaine in patients with suspected MI should be avoided in situations where facilities for resuscitation are available.

The need for caution in routinely using antiarrhythmic drugs is further emphasized by the results of the Cardiac Arrhythmia Suppression Trial (CAST),[73] which demonstrated that among post-MI patients with frequent ventricular arrhythmias, survival was significantly shortened by the use of two class-Ic antiarrhythmic agents despite excellent suppression of ventricular arrhythmias (encainide and flecainide: 56 of 730 [7.7%] deaths or cardiac arrests among actively treated patients compared with 22 of 725 [3%] in the placebo group; $p<0.001$). The two large trials of mexiletine also demonstrate a trend toward an increase in mortality.[74,75]

It is possible that in certain types of patients (e.g., those with prolonged ventricular tachycardia or those resuscitated from ventricular fibrillation) or in certain situations where facilities for resuscitation are limited, the benefits of preventing ventricular fibrillation by lidocaine might outweigh the potential for harm. However, routine use of antiarrhythmic drugs in other situations could potentially result in excess mortality.

Discussion

During the last 5–10 years, the emphasis in the treatment of AMI has moved from the era of monitoring, arrhythmia management, and circulatory support to a new and very promising approach based on reperfusion and damage limitation. In the past, recommendations for therapy have been based largely on either a presumption of benefit by extrapolating from experimental work or the effect of an intervention on certain mechanisms or surrogate end points. Instead, current recommendations are based on direct evidence of the effects on clinically important outcomes after careful evaluation in large well-designed randomized controlled trials (Figure 6). Such trials have been made possible by the selfless collaboration of hundreds of investigators in common protocols around the world. These trials have provided clear proof of benefit for some agents and lack of benefit or even evidence of harm with other interventions. Often, the results of these trials could

TABLE 6. Description of Major Trials of Acute Myocardial Infarction Being Conducted or in Advanced Planning Stages

Reference	Type of trial	Expected study size	Principal outcome of interest	Status of study as of April 1990	Expected report date
Value of thrombolysis among subgroups where there is no consensus					
EMERAS	> 6 hr after onset; SK vs. placebo	4,000–5,000	5-wk mortality	3,000 recruited	March 1991
LATE	> 6 hr after onset; t-PA vs. placebo	5,000	Short-term mortality	800 recruited	1992
ISIS-3	Patients who, in the opinion of their physicians, have no clear indications or contraindications to thrombolytic therapy (SK, t-PA, or APSAC vs. placebo)	12,000–15,000	5-wk mortality	20,000 overall (25% in this part of the study)	March 1991
TIMIT	Unstable angina, non–Q-wave MI	2,000	Combined end points of mortality, reinfarction, and ECG evidence of ischemia	?300	1992
Other trials					
ISIS-3	Comparison of t-PA vs. SK vs. APSAC; factorial: heparin vs. no heparin	50,000–60,000	5-wk mortality	20,000	March 1991
GUSTO	<6 hr; ST-segment elevation; comparison of t-PA vs. SK vs. t-PA+SK; all patients on i.v. heparin	30,000	Short-term mortality	Planning	1993
CONSENSUS-2	Enalapril vs. placebo	9,000	6-mo mortality	Recruitment underway	1991
Chinese study	Captopril vs. control	10,000	Short-term mortality	Recruitment underway	1992
SMILE	Zofenopril vs. placebo	3,000	Mortality or heart failure in hospital	Recruitment underway	1993
ISIS-4	2×2×2 factorial design of captopril vs. control, nitrates vs. control, magnesium vs. control	30,000	5-wk mortality	Pilot underway	1993
GISSI-3	Lisinopril vs. control	10,000–12,000	Short-term mortality	Planning	1993

TIMIT, Thrombolysis in Myocardial Ischemia Trial; GUSTO, Global Utilization of Streptokinase and T-PA on occluded coronary arteries; SMILE, Study of MI Late Evaluation; SK, streptokinase; t-PA, tissue plasminogen activator; APSAC, anisoylated plasminogen-streptokinase activator complex; MI, myocardial infarction; ECG, electrocardiographic. See text for explanation of abbreviations of other trial names.

not have been predicted from prior theories or study from data that focused solely on mechanisms.

Perhaps the most surprising result of the large trials is the remarkable efficacy of a simple inexpensive agent such as aspirin and that the substantial short-term gains of thrombolysis and aspirin therapy are maintained for at least 1–2 years, and probably longer, without large-scale intervention with coronary artery bypass graft surgery or PTCA. It may be that early thrombolysis gives time for the rapid development of collaterals, which then exert a protective effect, so that rethrombosis is less likely to lead to reinfarction. Moreover, the use of simple measures such as aspirin and β-blockers appear to substantially reduce the risk of reinfarction and recurrent ischemia.

It also appears that thrombolytic treatment is beneficial in many categories of patients who were previously excluded from some of the earlier trials, such as elderly patients, patients with shock or hypotension, patients with inferior infarction, and patients seen 4–6 hours after symptom onset. Reductions in mortality by SK among patients entered into treatment late after onset of MI or reductions in mortality by aspirin given in the acute phase were not predicted based on hypotheses, theories, or dogma prevalent a few years earlier. Subsequent to publication of the results from some recent trials, claims of mechanisms to explain the above findings are now being proposed! These experiences suggest that the approach to entering patients into trials, while recognizing existing theories, should not be unduly restrictive. Instead, investigators should be willing to test the validity of such opinion by randomizing a broader range of patients with the condition than has been the practice in some studies and among whom the effects of treatment are uncertain ("the uncertainty principle").[76] The safety of thrombolysis with modern regimens makes it plausible to consider its use in patients with other conventional contraindications, for example, hypertensive patients after control of blood pressure or those with a history of ulcer or stroke in the distant past, so long as the patient is considered to have a high risk of dying of the AMI. However, it should be emphasized that decisions should be taken in light of benefit–risk ratios for each individual patient based on reliable evidence from large clinical trials.

Finally, one should reemphasize the importance of general preventive measures after MI, such as stopping smoking, lowering cholesterol, controlling hypertension, reducing weight, and encouraging regular exercise.

Future Directions (Table 6)

Current trials such as ISIS-3 in conjunction with further analysis of GISSI-2 will resolve which of the three available thrombolytic agents (SK, t-PA, or APSAC) is preferred. ISIS-3, the South American EMERAS trial, and a trial of late thrombolysis with t-PA (LATE) will provide more information on those categories of patients (e.g., presentation with equivocal electrocardiograms or late entry into treatment after pain onset) in cases where there may still be some controversy about potential benefit. ISIS-3 will provide further information regarding the role of heparin after different thrombolytic agents. Several large trials studying the effect of angiotensin converting enzyme inhibitors and nitrates should provide further information on vasodilators and their role in preventing infarct expansion, ventricular dilatation, and death. Approaches to preventing reperfusion injury, such as free-radical scavengers, or to preventing reocclusion by blocking specific platelet receptor sites with monoclonal antibodies appear promising but are yet to be investigated in humans. The role of magnesium in prevention of arrhythmic deaths in AMI appears promising and deserves to be evaluated in large-scale trials.

Recommendations

Based on an overview of all available randomized trials in AMI, the following general strategies for the treatment of patients can be recommended, so long as there are no contraindications to the administration of a particular agent. A thrombolytic agent administered intravenously within 24 hours of onset of symptoms is likely to reduce mortality. Since the benefits appear to be greatest when thrombolytic agents are administered very early, every reasonable effort (such as minimizing the time of patient admission to a coronary care unit or administering therapy in the emergency room) should be made to initiate treatment promptly. If a patient presents 6–12 hours after onset of symptoms, thrombolytic therapy should still be considered if there is clinical evidence that the infarction is still evolving (repeated episodes of chest pain, presence of R waves on the electrocardiogram, etc.). The currently available data indicate that there is no appreciable difference between t-PA and SK although comparative data with APSAC are lacking. Therefore, it would be reasonable to administer any one of the three agents until the results of ISIS-3, which is expecting to randomize 50,000–60,000 patients, are available. The addition of aspirin to SK (or presumably to other thrombolytic agents) results in further reductions in mortality, reinfarction, and stroke without an excess of serious bleeding episodes. Intravenously administered β-blockers, when given to patients without contraindications, reduce mortality (probably by preventing cardiac rupture and fatal ventricular fibrillation), reinfarction, nonfatal cardiac arrests, and recurrent ischemic episodes. Both aspirin and β-blockers should be continued long term in appropriate patients since further reductions in mortality and reinfarction can be realized. Thrombolytic agents, β-blockers, and aspirin can be safely used together. They are thought to produce benefits by quite different mechanisms, and because the available data suggest no appreciable adverse but probably beneficial interactions, using them in combination is likely to be more beneficial than any one used alone. Vasodilators (intravenous or oral nitrates) may benefit patients, especially if they have large MIs and pulmonary congestion. Based on the available data indicating little benefit and possibly an increase in mortality with calcium channel blockers, lidocaine, other antiarrhythmic drugs, and PTCA, these interventions should not be used routinely.

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DIS-1.

26

Traumatic Paraplegia and Quadriplegia

DONALD A. NAGEL, M.D.

The word *paraplegia*, according to *Dorland's Medical Dictionary* means "paralysis of the legs and lower part of the body, both motion and sensation being affected." *Quadriplegia* means paralysis of all four limbs. These conditions, broadly speaking, could be caused by congenital abnormalities, infections, tumors, or chemicals, as well as by injury (trauma). Traumatic paraplegia and quadriplegia are the subject of this chapter.

There are many causes of traumatic paraplegia and quadriplegia. Birth injuries can produce it; accidents about the home or school, which would include falls from a height, can produce it; and bullet wounds, sports injuries, and injuries from motor vehicle accidents can produce it. Of all of these, motor vehicle accidents are perhaps the most frequent cause. As younger people are increasing their exposure with high-speed bicycles, motor-driven bicycles, motorcycles, and sports cars, it is anticipated that the number of children who have traumatic paraplegia and quadriplegia will increase.

From ancient times this injury has been noted as one of the most devastating. It is frequently associated with fractures of the bones of the spinal column—but not always; the spinal cord can also be damaged by dislocation of one bone upon the other, without any signs of fracture (Fig. 26-1); and there also are many fractures of the back (spine) that do not damage the spinal cord. The paralysis is caused by an interruption of the nerves and pathways going from the brain to the involved limbs. These pathways are located in the spinal cord, which passes through the bones (vertebrae) that comprise the spinal column (Fig. 26-2). The function of

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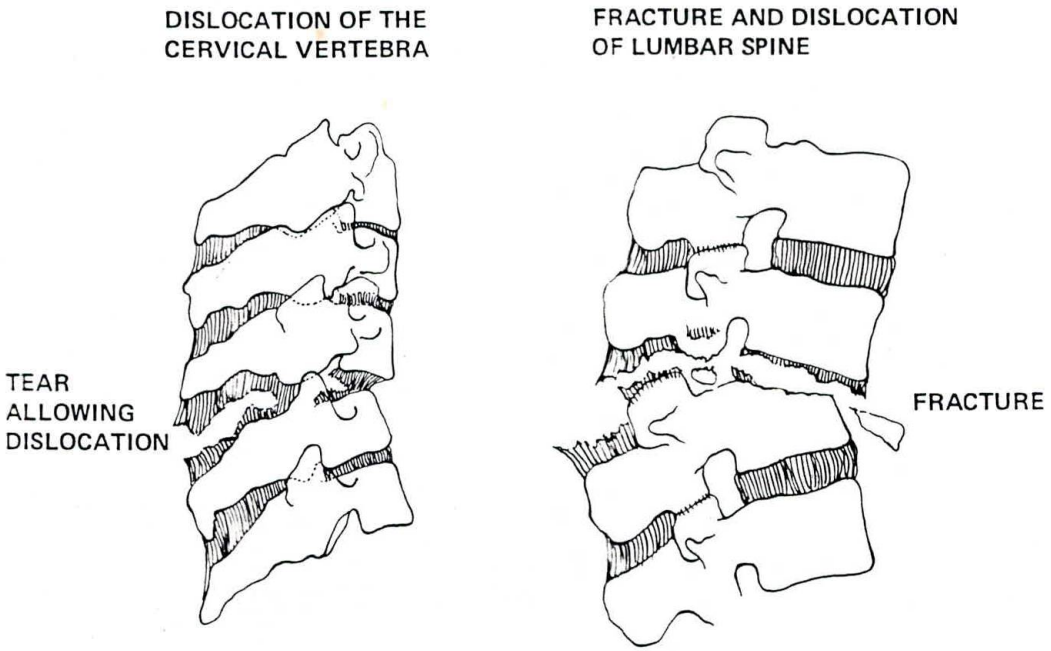

Fig. 26-1. Injuries to the spinal column. Dislocation and fracture dislocation of the spinal column may or may not cause serious injury to the spinal cord.

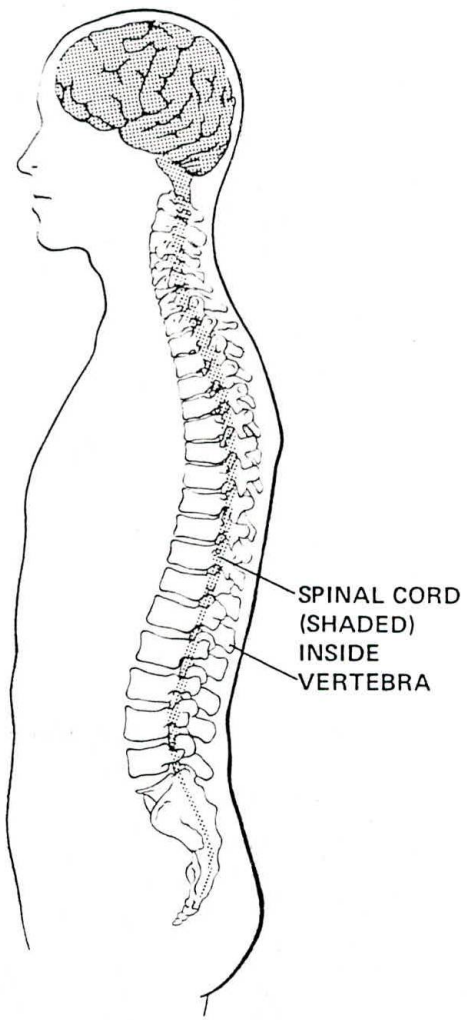

Fig. 26-2. Normal spinal column and spinal cord. The spinal column is composed of 7 cervical, 12 thoracic, 5 lumbar, and 5 fused sacral vertebrae through which the spinal cord and its branches pass.

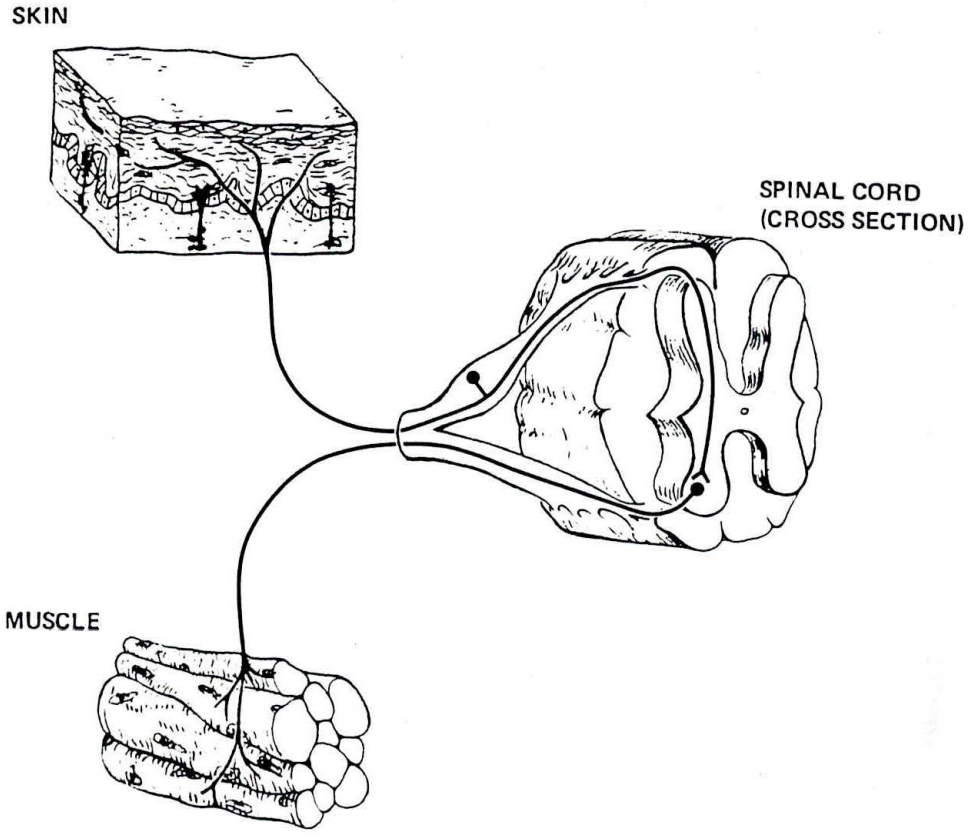

Fig. 26-3. Nerve pathway. Sensory nerves bring impulses into the cord, where they can be transmitted to the brain, and motor nerves carry impulses from the cord (and brain) to various muscles.

these pathways may be disturbed because of pressure exerted on the spinal cord by bony fragments or, in rare instances, soft tissue from the cushions (discs) between the vertebrae. If the pressure can be removed quickly enough and the blood supply to this area restored, then occasionally the nerves will begin to function again. Spinal cord pathways that have been completely torn apart by the injury will not regrow with our present repair techniques, however, and the resulting paralysis will be permanent. Research is ongoing in this area, and hopefully the future will hold discoveries that will allow us to repair these injuries successfully. Nerves located *outside* the spinal cord, which either bring impulses from the skin or carry impulses to muscles from the spinal cord, can be successfully repaired (Fig. 26-3).

ACUTE CARE

The handling of the patient with an injured spinal cord immediately following the injury can, in some cases, make the difference between an incomplete injury, which may recover, and a complete injury, which will not. Injured athletes or persons injured in a motor vehicle accident who are conscious but complain of being unable to move their limbs very well, or note an electric type of pain shooting into their limbs, should *not* be moved until they can be moved by people who have been trained to take care of such injuries. Such patients should be moved on a board that has attachments to fasten the head and body so that the head will not rotate in the process of moving. These patients must not be allowed to sit or to

have their heads elevated to take a drink, and they must not be allowed to walk, even though they desire to. If transportation cannot be arranged quickly, patients who have little or no sensation and no motion in their extremities should be protected from shock.

Once these patients have reached a hospital, they should be placed in the hands of a physician knowledgeable in the care of such injuries. The patient's injured spine should be protected during the process of obtaining x-rays. Treatment will be based on the history, physical examination, and the x-ray findings. In injuries to the neck, tongs are usually placed into the skull so that traction can be applied to bring about a reduction or a realignment of the fractured bones. Injuries to the spine at the chest and at the abdominal level are usually cared for in special beds. Rubber tubes (catheters) are inserted into the bladder to allow drainage of urine, and care is given to see that the patient continues to have bowel movements. Of special importance is frequent turning so that the skin does not break down. There is some disagreement as to whether or not operations should be done on patients who have complete paralysis and loss of all nervous functions below the level of the injury. There is uniform agreement, however, that if the patient has some neurologic function, and if this diminishes during observation, the patient should have an operation. The operation usually consists of a decompression of the spinal cord, and may, in addition, be accompanied by a spine fusion. Depending upon the type of spine fusion, the patient will have to be immobilized in some type of device while the fusion becomes firm. This will take 6 weeks or longer.

REHABILITATION

Rehabilitation should begin shortly after injury. Perhaps the most important aspect of this is the patient's morale. Generally speaking, patients who develop traumatic paraplegia and quadriplegia have been active individuals. They should be encouraged to continue in their active approach to life. The seriousness of their injuries should not be ignored, but the fact that the personality of the individual and his or her mind are more important than any physical loss should be stressed. Patients should be encouraged to set goals for themselves, such as self-care and locomotion. If they can be treated in a spinal cord injury unit, where the personnel are geared to handling the problems of this type of patient and where the patients can see other people with problems as serious as theirs who are making progress towards their goals, then they will be encouraged.

Patients who are quadriplegic will have to set lower goals for themselves than patients who have the use of their arms. Nevertheless, such patients should be able to feed themselves with the assistance of various special devices, and locomotion should be possible, at least with a motorized wheelchair.

Paraplegic patients, in addition to being able to feed themselves, should learn to take care of their bladder and bowel functions. Many paraplegic patients develop some control of their bladder without the insertion of a tube. This involves the use of their hands on their abdomen to push out the urine. Male paraplegic patients will require the use of a urinal, and females generally use pads with special types of pants. The bowels are usually easier to regulate than the bladder; this is accomplished by means of suppositories or enemas. Even when the level of the spinal cord injury is high, paraplegic patients should at least be instructed in the use of crutches for ambulation. They may later choose to use the wheelchair as their primary means of locomotion, but if they have

the option of using crutches in particularly difficult situations, they will be better able to cope with their environment. Paraplegic patients will be taught a swing-to or a swing-through type of crutch walking and will be fitted with long-leg braces.

A major step in patients' rehabilitation occurs when they leave the hospital to return home; yet another occurs when they return to school. Patients must be accepted in each of these situations as individuals, and at times this will be quite awkward for patients, as well as family, teachers, and friends. They must be encouraged to take the positive approach—to seek out new friends and experiences and to develop their minds to the fullest so that they can become self-supporting in the future. Literature is available for these young people (some is listed at the end of this chapter), and, in many areas, associations of patients who are paraplegic and quadriplegic have been formed. There are, in fact, international wheelchair olympic games (Fig. 26-4), and young athletes might be encouraged to join organizations that participate in such activities.

There are problems to be faced and adjustments for family and teachers to make. Specifically, patients will need more time than the average for self-care and for attention to their bladder, bowels, and skin. They will probably need a special bed, wheelchair, and braces. Other assistant devices will be necessary. Patients should be encouraged to care for themselves as much as is physically possible and should not allow themselves to become dependent and depressed. They should seek guidance in vocational planning and training so that the employment that they plan for is obtainable for them. They should remain in close contact with the physician, who understands their problems completely. Urinalysis should be performed at least monthly, and x-rays should be taken yearly to evaluate the possibility of kidney-stone formation. In contradis-

Fig. 26-4. Wheelchair games. Games are important to some paraplegic patients.

tinction to adults, younger patients may develop deformities in the spine and in the extremities if they have asymmetrical muscle pull. Many patients with quadriplegia and paraplegia develop pain and muscle spasm. Various new medications are becoming available almost monthly. If these do not solve the problem, then neurosurgical consultation should be obtained to evaluate the possibilities of removal of scar from around the traumatized area or of other neurosurgical procedures to eliminate the pain.

One of the most important decisions that patients will make is what vocation to pursue. Patients who can become self-supporting are well on the way to an independent, fruitful life. It is recommended that each individual work closely with a vocational counselor and read the *Handbook for Paraplegics and Quadriplegics*. The following is quoted from the Handbook with the author's permission:

> Among some of the jobs or businesses that paraplegics and quadriplegics have successfully had are as follows: switchboard operator, secretary, salesman, teacher, watch repairer, jewelry designer and repairer, woodworkers, artist, bookstore operator, accountant, office manager, lawyer, doctor, physical therapist, architect, publicity man, actors, disk jockey, book reviewers, copy readers, writers, mail order businesses, stationery and greeting-card store, gift store, magazine agency, florist, weaving, hydroponic farming, statistician, IBM operator, Comptometer operator, plastics manufacturer, electrical assemblers, radio and TV repair, wheelchair repair, civil service, sewing machine operator, embroidery, leathercraft, photography, bookbinding, hobby shop, philatelist, real estate, phone solicitation, answering service, addressing envelopes, advertising, taxidermist, research worker, clipping service, designers, draftsman, and many others. These jobs and businesses are not conjecture, in each case at least one paraplegic or quadriplegic has worked or is working in the classification. If anything about them should impress you, it should be the variety of employment.

Setting realistic vocational goals and then setting about their achievement with determination should make living a successful adventure.

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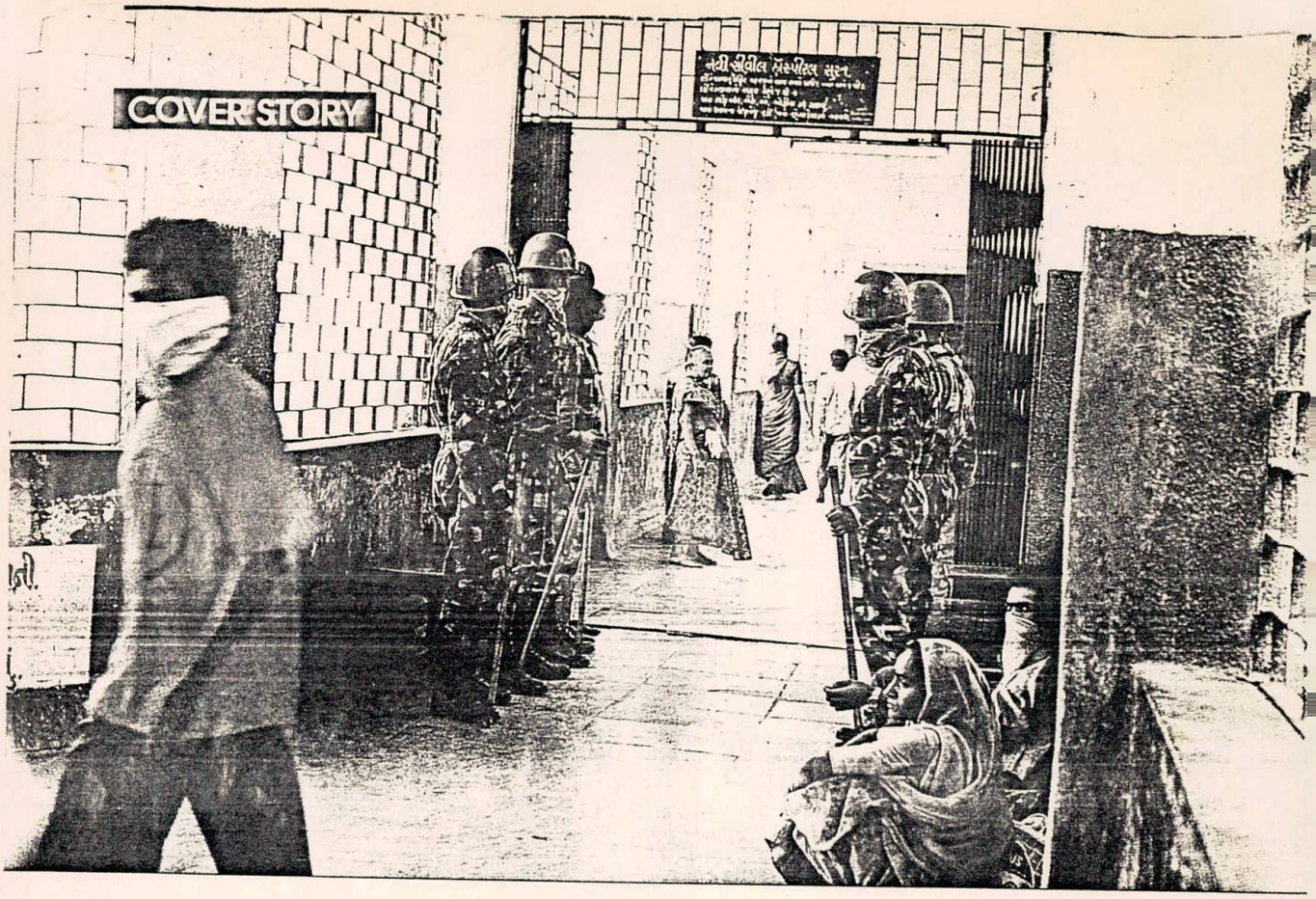


THE SCOURGE

The Indian plague epidemic of 1994

V. K. RAMACHANDRAN
in Bombay

IN the first week of September 1994, the first laboratory-confirmed cases of human plague in India since 1966 were reported in Beed district in Maharashtra. By September 29, according to official reports, there were 328 suspected cases of plague in an area with a radius of 30 km in Beed, and there were 325 suspected plague cases in no less than 23 out of 29 districts in the State. On September 22, an epidemic of pneumonic plague spread rapidly in the city of Surat in Gujarat. By September 30, according to official figures, there were 752 plague patients in Surat, and 44 persons were killed by plague. Surat remains the worst-affected centre of the current epidemic.

From Surat, the disease spread to Maharashtra, and, in addition, by September 29, 62 cases were reported from West Bengal, 21 confirmed cases and 43 suspected cases from Delhi, five cases from Varanasi (Uttar Pradesh), three from Haryana and one each from Punjab and Kerala. Three suspected cases were reported in Bangalore on September 30. On October 1, it was reported that there were more than 2,800 suspected cases countrywide, and more than 4,000 on October 2. Putting together evidence from press reports of officials figures, by October 1, the total plague-related mortality was 54 persons in Gujarat, and, on September 25, Maharashtra's Health Secretary Ramanand Tiwari told *Frontline* that there had been one plague death in Dhule district. Two persons died of plague in Delhi on September 30, and, on the same day, a youth from Khar in Bombay died in the isolation ward of the Kasturba hospital.

The plague epidemic has had international repercussions. By September 30, the Gulf Cooperation Council had banned flights to and from India; the United Arab Emirates had stopped the import of foodstuff from India and the berthing of ships from India at its ports; Russia had declared a six-day quarantine on passengers from India; and Air Lanka, Emirates, Pakistan International Airlines, Bangladesh Biman, and Aeroflot had suspended services to India (some airlines have since resumed some flights). On September 30, European airlines decided not to suspend flights to India. The United States State Department announced that the risk of international travellers being infected by plague in India was low, and the British Foreign Office said there was no cause for concern in the major tourist destinations, while advising people not to visit plague-affected areas. Some European countries have introduced limited controls at airports.

On September 29, plague cases were still spreading, although cases were being cured, and plague mortality had fallen sharply in Surat. In New Delhi on September 28, Union Health Secretary M. S. Dayal said that mortality had been controlled (two plague-related deaths occurred in New Delhi the next day), that the infective stage of the outbreak would end in a week, and that treatment of affected persons could take another three weeks or so.

(Facing page) In a hospital corridor in Surat, alert with personnel of the Rapid Action Force: removing a body.

Pictures: By special arrangement

At the same press briefing, the representative of the World Health Organisation (WHO) in India, N. K. Shah (who is a citizen of Nepal), expressed confidence in the Government of India's estimate that the number of plague-affected persons was about 1,100, and said that, barring a fresh outbreak of plague, the current one will be over in three weeks.

The epidemic began in Beed district. There were some tremors in the district during the earthquake in the Latur-Osmanabad region in 1993. Although outside the main earthquake area, many people left their homes and old houses were used to store grain. Reporters have been told that these storage-places became infested with rats. Early in August, Sonaji Kashinath Lange, sarpanch of Mamala village, Majalgaon taluk, informed the Kuppa health centre that a swarm of fleas flew out of a house that was unlocked after being closed for a long time (subsequent reports confirm significant rat-falls in the village). On August 26, the first suspected human plague case appeared in Beed. On September 2, the National Institute of Communicable Diseases (NICD) was called in by local authorities. On September 15, a front-page piece in *The Times of India* by Kalpana Jain and Subhas Kirpekar reported four cases of plague from Beed. (Asked to comment, Maharashtra Chief Minister Sharad Pawar said he was unaware of the news.)

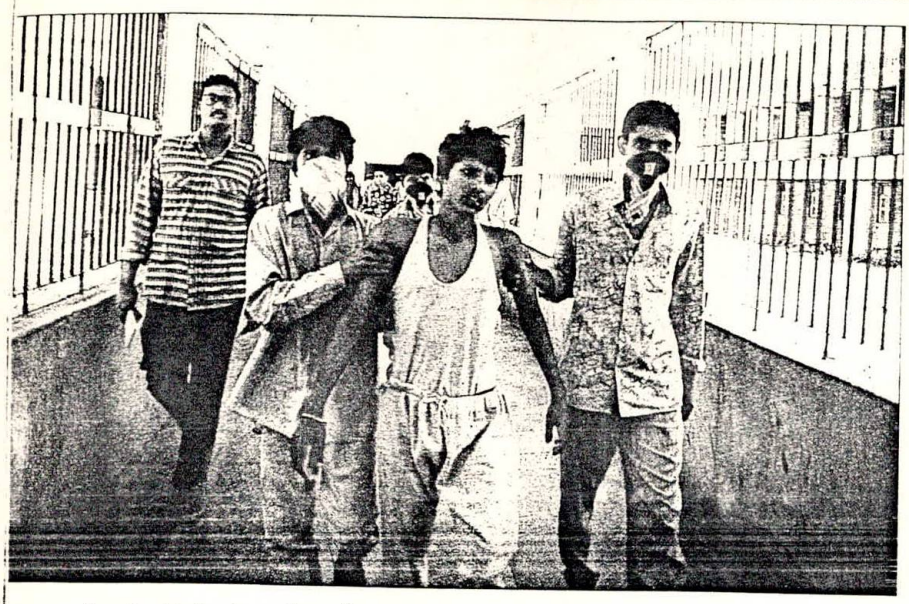
Although no deaths have been reported, the number of cases of bubonic plague in Beed and Sholapur continues to rise. One case of pneumonic plague has also been reported from the Beed civil hospital.

On September 22, after a day on which rumours went through Surat city that the public water supply was poisoned, an epidemic of pneumonic plague began. Reports of the number of deaths on the first day – even from official sources – varied: *The Times of India* cited an official report that 24 people died; another "official figure" cited was 45; and the Chief Secretary to the Government of Gujarat said 17 deaths had been reported by the evening of September 22. Two prominent persons, however, differed; Union Health Minister B. Shankaranand said that until a team of the NICD submitted its report, "it could not be said that the deaths were caused by plague," and Gujarat Chief Minister Chhabildas Mehta declared that the virulence in Surat was "not plague at all." In Bombay, Doordarshan's Marathi news telecast made no mention of the Surat epidemic.

In Surat, nevertheless, officials confirmed an epidemic of plague on September 22, and by September 24, six cases were reported from Ahmedabad, six from Baroda (Vadodara), four from Bhuj, and one each from Gandhinagar, Palanpur and Cambay in Gujarat. By Sunday, September 25, Ahmedabad, Baroda, Amreli, Bharuch, Ankleshwar, Jamnagar and Bulsar were declared plague-threatened. The areas worst affected in Surat were Katargam and Ved Road. Cases were also reported from the Ghodod, Mithikhadi and Chimini Tekra areas, from Sanjaynagar and Rajivnagar of the Udhna industrial suburb, from slums around the Elbee Cinema, from the working-class Limbayat and Ruderpura areas, and from the commercial areas of Chowk Bazar and from a centre of the diamond cutting industry in Varachha. Although the epidemic is one of pneumonic plague, three cases of bubonic plague were reported on September 24.

Epidemiologists suggest that plague could have been brought to Surat by migrant workers from Maharashtra (Biswaroop Das's study of Surat slums shows migration to Surat of workers from Jalgaon, Nashik, Dhule, Nagpur, Buldana, Bhandara, Raigad, Aurangabad, Akola, Ahmednagar and Beed districts in Maharashtra) or could have originated in Surat after the floods, when carcasses were left to rot in the streets, or by a combination of these two lines of transmission.

For at least three days, the health and general administrations in Surat



A patient being brought to hospital.

were in chaos. Large numbers of private doctors fled the city, the coordination between public health authorities and health personnel in hospitals was poor, supplies of antibiotics were attacked and looted, and spokesmen of the Government spoke in different voices. A large-scale exodus of persons from Surat began. One newspaper calculated that 270,000 persons left Surat in the three days between September 23 and 25; others have estimated that 400,000 persons, or about one-quarter of the city's population, left the city. Buses and trains were packed and tickets were sold at very inflated rates; a friend from *Economic and Political Weekly* reported that the price of a bus ticket from Surat to Bombay was Rs. 1,500 on September 25.

A lesson from the first four days of the epidemic in Surat was that where a fear-stricken population has little faith in the public health system, isolating patients is difficult. More than 100 patients ran away from hospitals in Surat in the early days of the epidemic.

On September 25, the Rapid Action Force was deployed in Surat, and the Government announced an eight-point "action plan" to control the epidemic. In practice, hospitalisation and the provision of antibiotics are the most important measures of control at present. After September 25, the number of deaths declined, although the disease continued to spread.

Although many doctors, particularly doctors with private practice, fled the city, many stayed on, particularly in public hospitals. At least five doctors and three nurses from the Surat civil hospital were infected by plague; among those on the honour-roll of persons infected while treating others were Avinash Dave, S. Sharma, Kalpesh Bavsar and Sudeep Nair.

Index of real per capita public health expenditure in India on public health and on the prevention and control of diseases, 1984-85 = 100

Year	Index	
		Public prevention and health control of diseases
1984-85	100	100
1985-86	101	94
1986-87	100	94
1987-88	95	98
1988-89	97	100
1989-90	103	103
1990-91	100	94
1991-92*	95	87
1992-93**	94	83

* revised estimates
** budget estimates

Source : V.B. Tulasidhar, "Expenditure Compression and Health Sector Outlays", Economic and Political Weekly, November 6, 1993.

The epidemic in Surat is a special threat to Bombay. There is enormous traffic between Surat and Maharashtra and between Surat and Bombay (according to one official estimate, more than 55,000 persons migrated from Surat to various parts of the State during the present crisis). Bombay is rodent-ridden, and one-half of its population is homeless or slum-resident, and lives in conditions of bad sanitation, congestion and general deprivation that are conducive to the rapid spread of infectious disease.

Measures to control plague have been taken in Bombay in response to the crisis in Surat; the administration in Bombay did not consider it necessary to take public health security measures in the city in response to the outbreak of plague in Beed.

An attempt is being made to screen entrants to Bombay from Surat and to fumigate incoming trucks, but given the volume of traffic and the diversity of modes of transport, these cannot be even remotely comprehensive. The Bombay Municipal Corporation and the Government of Maharashtra have discussed the possibility of invoking the law to seal the city from entrants from Surat; this too is unlikely to be successful. (It is of some interest that a similar measure failed in the last century as well. On October 19, 1897, a telegram from the Government ordered that all third-class railway passengers from the plague-affected areas of Surat and surrounding areas be stopped. The Plague Committee noted that the order did not work mainly because they were evaded "(1) by passengers booking second class and (2) passengers travelling down the line from Surat, and buying tickets to Bombay from Broach and other uninfected stations.") The Corporation has announced that it would increase rodent-killing in the city and that more garbage-collecting trips were being organised. It also announced that, by September 26, two million people had been surveyed and that 600 "contact" persons – that is, in contact with immigrants from Surat – had been identified.

Of the different methods of plague control, Bombay's administration appears to be concentrating on three sets of measures: first, large-scale public announcements; secondly, identifying patients, organising hospital beds and hospitalising patients; and, thirdly, stocking up on antibiotics, particularly tetracycline and especially for prophylaxis (there was panic buying of tetracycline in Bombay as soon as news of the Surat crisis appeared: as in Surat, the price of tetracycline rose sharply, to prices the poor cannot afford). Bombay's Deputy Municipal Commissioner in charge of health, Sudha Bhave, expressed confidence that the supply of hospital beds and drugs would be adequate. At present, the public mood in Bombay can be described as tense, but there is no panic.

It has been noted that the real per capita public expenditure in India on public health and disease-control programmes has been cut back in recent years (see Table). V. B. Tulasidhar, an economist at the National Institute of Public Finance and Policy, has noted

that "real expenditure on disease control programmes remained virtually stagnant during 1985-91 and fell steeply during the adjustment period".

Tulasidhar considers the overall impact of adjustment programmes on medical and public health budgets to have been marginal; at the same time, "due to cuts in specific-purpose health sector grants to States, the burden of compression was mainly on preventive-type disease-control measures... mainly meant for controlling infectious diseases which afflict mainly the poor."

In addition to general cutbacks in expenditure on public health and the control of infectious diseases, in 1987 the Government of Maharashtra began explicitly to dismantle the institutions of plague prevention and control in the State. The plague control unit under the Department of Public Health was abolished. Despite repeated advice, despite warnings regarding the possibility of rodent-borne infections after the earthquake, and despite having agreed in principle to re-establish the unit, the Government did not re-establish the unit. (After the epidemic in Surat, Ramanand Tiwari told *Frontline* it would be revived.)

In 1989, the Government-run Haffkine Bio-Pharmaceutical Corporation ceased production of anti-plague vaccine. On September 25, Tiwari told *Frontline* that a remaining batch of 14,000 vaccines, with an expiry date of November 1994, were being tested for their potency (the first batch of 10,000 vaccines was presented by the chairman of the Haffkine Bio-Pharmaceutical Corporation to the Mayor of Bombay on September 30). The Health Secretary said a lead time of "about a month" was required to begin production of the vaccine. It has since been announced that the first 100,000 doses of fresh vaccine would be ready by October 30. Asked to comment on the cutbacks and on the abolition of the plague control unit, the Health Secretary told *Frontline* that, given the conditions at the time, "investment in plague was like investment in dinosaurs."

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Plague can be prevented, controlled and cured. The prevention, control and cure of plague are basic tasks of the public health authorities, and the occurrence of an epidemic of plague in the late 20th century represents a fundamental failure of a health system in modern society. The Indian plague epidemic of 1994 must be controlled and ended, and health policy and investment must ensure the prevention and control of avoidable infectious disease among the people of India. ■

COVER STORY

Shocked, shattered Surat

ARUNKUMAR BHATT
in Surat

THIS time round, the people of Surat panicked. Nearly half of the 22-lakh population in this industry-rich city in Gujarat fled their homes – by road, rail, air – in the last week of September. They ran from pneumonic plague and carried with them the infection to other parts of the State, and other States. The plague became an epidemic.

Officially, 48 persons have died of pneumonic plague in Surat and 55 per cent of 600-odd cases admitted with its symptoms in the local hospitals tested positive for it.

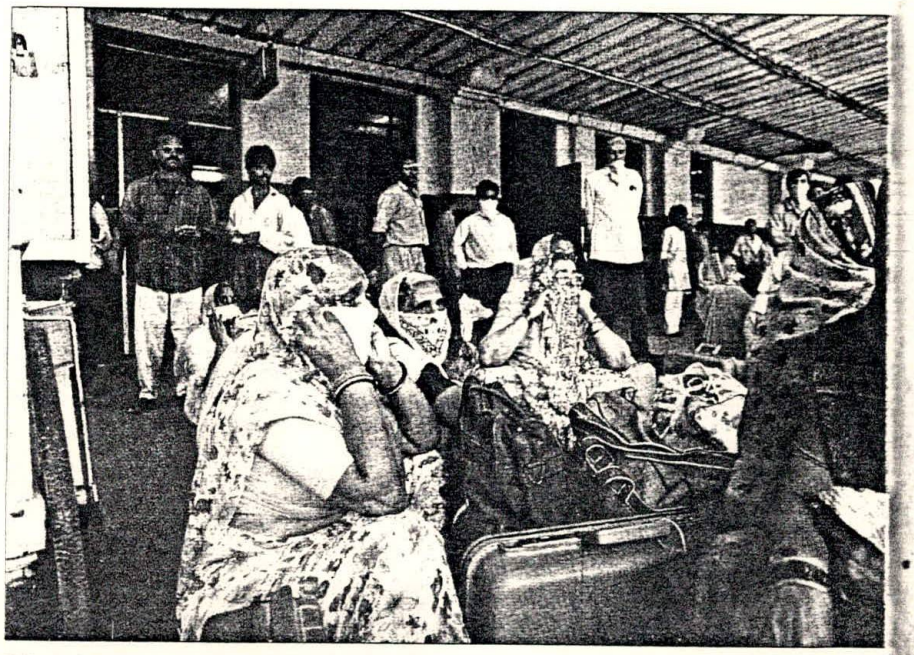
The normally resilient Suratis, who took in their stride an outbreak of cholera in 1988 which claimed 102 lives and an outbreak of hepatitis B in 1989 which claimed 129 lives, were devastated this time by the very name – plague. The Government's inability to tackle the problem, its attempts to underplay the gravity of the situation, and the media's exaggerated reports of death, compounded their fears.

Among the first to leave were doctors, particularly those with a roaring practice, executives and businessmen. A Government given to imposing curfew at the slightest provocation did not bother to impose restrictions on entry to and exit from the city; the question of putting Surat in quarantine was not even considered.

The civic authorities and a local newspaper, *Nav Gujarat Times*, undertook a campaign telling the people that pneumonic plague was curable and advising them not to leave. But no one was willing to listen.

"How can you stop people running for their lives when you do not provide either medicines or treatment, or even clear the filth?" asked a civic official in Ahmedabad. Besides, said a police officer, if the people had been prevented from leaving Surat, it would have led to a law and order problem. So, the Government opted to allow the epidemic to spread.

Traditionally a centre for business, Surat is also among the filthiest cities in India, largely the result of rapid industrialisation and haphazard growth. When the waters of the river Tapti,



When the exodus began, a scene at a railway station.

which had inundated the city in the second week of September, finally receded barely 10 days before the disease broke out, it left behind stinking puddles, slush, garbage, sewage and carcasses, ideal conditions for an outbreak of diseases. However, in spite of protests from residents demanding that the city be cleaned up, neither the municipal authorities nor the Government took any notice, let alone initiate action.

The pneumonic plague was first reported from Ved Road, where seven persons believed to have been suffering from dengue fever for three days, died within hours of one another on September 21. Three of them were from Maharashtra. Suresh Bokade, 20, of the Lakshminagar Housing Society, was perhaps the first victim – he died on the way to hospital after passing blood in his sputum.

By September 22, 17 people had died in quick succession. The symptoms were the same: high fever, blood in the sputum, cough, lung congestion and severe body pain. The municipal corporation's Chief Medical Officer, Dr. R. P. Sinh, and Deputy Municipal Commissioner (health) Dr. Mohanty suspected it was pneumonic plague.

But in the capital, Gandhinagar, the entire matter was kept under wraps. A senior Minister, not from the Health Ministry, told the bureau chief of a news agency under cover of anonymity the toll in Surat was 200. Immediately, the news was wired and was picked up by the national and international media. In Surat, the people panicked further.

As far as they were concerned, the fact that even the BBC had reported this figure was enough. Given the administration's abysmal record in providing sanitation facilities, fearful memories of plague kept alive through fact and folk tale, and the ravages of the flood and the Government's tardy response, the non-availability of medicines, the lack of infrastructure to identify quickly those affected, and the unhygienic conditions in public hospitals resulted in the exodus from Surat.

Gandhinagar made things worse by withholding information. Often its version contradicted the information emanating from Surat. As the official death toll went up from 17 to 27, Chief Minister Chhabildas Mehta told the press in Ahmedabad that the killer disease was possibly viral pneumonia. He quoted a research paper published by Dr. Saraljit Sehgal and Dr. Rajesh Bhatia of the National Institute of Communicable Diseases (NICD) saying, "The preliminary circumstantial evidence suggests that it cannot be the plague."

The Chief Minister's argument was that plague first attacked the rodent population which then died *en masse*. What he did not reveal, which the research paper did, was the fact that these deaths could occur elsewhere, not necessarily in the affected area. His second argument was that the incidence was typically confined to a particular neighbourhood and did not occur in the scattered manner it struck in Surat. This, however, is more typical of bubonic, not pneumonic plague spread by inter-human transmission. Besides, it had been confined to Ved Road, Katargam and Chhatrabhata. The third point was that the family members of victims had not been infected.

However, before his arguments could reach Surat, two local pathologists had done blood cultures and established that it was pneumonic plague. As Mehta prevaricated; the NICD confirmed the finding. Dr. A. K. Mukherjee, Director-General of Health Services, and Union Health Secretary M. S. Dayal also put the toll in Surat at 44.

Thus when Mehta finally announced that 35 lakh capsules of tetracycline had been rushed to Surat and 34 lakh capsules of tetracycline and 8,000 injections of streptomycin were being airlifted from Ahmedabad, there was anger among the people. The drugs were in short supply and their prices had risen three to four times; a strip of 10 cost Rs. 80. Many thought the disease was water-borne; as a result even mineral water, at Rs. 25 a bottle, cost more than double.

For five days, confusion reigned in

The starting point

SANJEEV UNHALE

THE Government of India, and the people in general, had by and large ignored the threat from plague in the comforting belief that the killer disease had become extinct in the subcontinent way back in 1966. Even the detection of a significant, though isolated, case which indicated the presence of the *Yersinia pest* is bacteria in 1976 by the Beed district health authorities had no effect on the government machinery. The Rip Van Winkle-like slumber continued till the pestilence claimed its first batch of victims in Mamala village of the same district in Maharashtra, in August this year. However, it took one more month for the authorities to acknowledge the existence of a plague epidemic.

For the first time, 38 persons were identified as showing positive symptoms of plague in Mamala, a hamlet with 53 houses, in Majalgaon tehsil. Last year, during the September 30 earthquake in the Marathwada region, the village had received tremors and the entire population was rehabilitated in makeshift shelters away from their houses which were since used to store grain and fodder. One theory put forward on the emergence of plague is that the rodent population in the fields migrated to human habitats on account of the destruction of their holes in the subterranean upheavals and passed on the epidemic to humans through house rats. The rodent population had increased manifold in the entire Marathwada region after the earthquake.

When this correspondent visited the plague-affected villages, including Mamala, Salimba and Laxmipur, the pungent smell of pesticides hung in the air. Walls and houses were covered with graffiti and posters appealing to the people to eliminate rats. A number of dead rats had pea-sized nodules on them, indicating that they were infected with plague. Villagers said some cats and dogs which had eaten the rats had died.

Village sarpanch Sanaji Kashinatha Langhe recalled that the first sign of danger was noticed by one Vashitha Langhe in the first week of August. The moment he opened his house which had remained locked for a long time, a swarm of fleas covered him and soon spread in the area surrounding the house.

The sarpanch said he had informed the Kuppa health centre of this on August 5. Only when a doctor, who visited the place 10 days later, was covered with fleas did the authorities realise the seriousness of the problem. The villagers were unaware of plague though they were showing symptoms of lymph adenitis in their armpits. The district administration started spraying DDT in the last week of August. By that time, 38 persons had been affected in Mamala. On Sepetmber 1, their blood samples were sent to Pune and Bangalore for

testing. The samples tested positive.

All this was over in the first week of September, but the officials of the Central Government pressured the State machinery not to announce the return of plague, to avoid panic. The State health officials were confused though they had started distributing tetracycline tablets. The situation went out of control after September 15.

Half a century ago, the spread of any epidemic used to be restricted to a particular town and could be contained there by controlling the entry and exit of people. Considering this, the administration launched an intensive plague prevention drive in 50 villages falling within a radius of 15 km. However, this time, because of the increase in the population and speedier means of communication, their task was difficult and the disease was transmitted to seven adjoining districts.

By September-end 200 cases of bubonic plague were identified in Beed district, 35 in Parabhani, 33 in the quake-affected Latur district, 29 in Nanded, 16 in Aurangabad and four in Jalna. But the severity of the calamity was felt by the authorities only when the disease took a heavy toll in Surat. The return of more than 1,000 labourers to Marathwada, who were working in Surat, intensified the panic.

A red alert was now sounded. Teams of doctors were deployed at entry points such as railway and bus stations. Civic bodies and the Public Health Department were geared up to spray pesticides in vulnerable areas like slums. Regular garbage removal from the streets and bylanes was ordered. Non-governmental organisations such as the Janarth in Aurangabad and the Manavlok in Beed have initiated, among other things, mass campaigns to educate the public.

However, these had an unexpected response: people started buying and using tetracycline tablets. In a tragic case in Malegaon town, an infant died after it was administered tetracycline by panic-stricken parents. Many people are consuming tetracycline as a preventive measure, which is dangerous. Surprisingly, the Government, some experts say, is giving out misleading advertisements regarding preventive measures. A prominent advertisement given by the National Institute of Communicable Diseases, published through the Directorate of Advertising and Visual Publicity (DAVP, 94/352) in almost all the newspapers, suggests a preventive dose of 500 mg of tetracycline every six hours for five days. This has been contradicted by experienced physicians, who say this dose is too high and the medicine is curative. Likewise, a syrup suggested for children was banned a decade ago, they point out.

Amidst all this, the common man feels the health and local authorities do something only when a crisis, like the present plague, presents itself; otherwise they pay scant attention to the need to maintain the environment clean, which is their immediate responsibility. Once the epidemic recedes, and the hue and cry raised through the media subsides, "Rip Van Winkle" will go back to sleep. ■

the city. One Surati, fleeing for his life, was virtually looted by transporters, druggists and roadside dhaba-owners. Families even refused to give shelter to relatives from Surat. In some villages in Saurashtra, lathi-wielding patrols were organised to keep out Suratis until they took the plague test at district health centres and reported negative. Urfortunately, none of these centres is equipped to carry out these tests.

If the Suratis who fled to their native villages became outcasts there, in the city they were dubbed traitors. The original Suratis reviled them for encroaching upon the city's services and comforts, for ruining the environment, for engendering disease and, finally, when called upon to lend a hand, for turning tail. According to Kashiram Ran, a Lok Sabha member from Surat, "The social relations within Surati society will perhaps not be the same anymore."

As the plague moves elsewhere and the city struggles to overcome the residue infection by swallowing tetracycline and shovelling filth, the people are hard put to get their economy together. The city's trade, commerce and industry have invested in Rs. 40,000 crore worth of art silk, textile processing, diamond, dyes and chemicals and support engineering units. Most of them are now closed. Workers fled on the eve of pay-day, September 22, leaving behind pay-packets totalling Rs. 100 crore. Factory owners have fled to Bombay; some diamond merchants have gone abroad. Doctors' suggestion that factories be shut down to prevent the spread of the epidemic was read as an official order. And although by September-end some people were returning to Surat, it will take a month at least before activities are on an even keel.

The president of the Southern Gujarat Chamber of Commerce and Industry estimated that the daily losses in Surat's industries amounted to Rs. 51.65 crore, including an export earning of Rs. 2.5 crore. The largest industry, art silk and fabric, is losing Rs. 25 crore a day, the diamond industry Rs. 15 crore, dyes and chemicals Rs. 5 crore and engineering Rs. 3.85 crore. Trade turnover loss is estimated at Rs. 20 crore. The exchequer is losing Rs. 3.35 crore daily – Rs. 2.10 crore by way of excise, Rs. 25 lakh by way of octroi and Rs. 1 lakh by way of sales tax.

The total loss suffered by various industries and trades is estimated at a staggering Rs. 1,200 crore, a major blow for the thriving but small economy. The diamond industry, for instance, has piled up stocks of rough stones (raw material) worth Rs. 3,000 crore. Delayed processing and export would add to the interest burden. Many units in all the sectors are small-scale and the apprehension is that their working capital may have been wiped out. In fact, the Rs. 30 to 50 crore annual turnover of private couriers (angadia) between Surat and Bombay is a fair gauge of the volume and pace of commerce in the city.

But, of course, the heaviest blow has fallen on the workers, who comprise about 10 lakh of Surat's population. While the 2.5 lakh diamond cutters and polishers are losing Rs. 1.25 crore in wages daily, about 4.5 lakh textile workers are losing, daily, Rs. 2.25 crore. They earned between Rs. 80 and Rs. 250 a day in Surat; now in their native villages most of them are unemployed. The current financial crisis is bound to erode the wage structure considerably.

The tragedy is that the epidemic and its aftermath could have been avoided had timely measures been taken. The plague has not yet been eradicated. Doctors Sehgal and Bhatia recall the experience when "a disease simulating pneumonic plague hit Tangnu village in Himachal Pradesh in 1983. The suspected human pneumonic plague with well-defined inter-human transmission involved 22 cases and 17 deaths. The outbreak lasted three weeks and abruptly stopped after the suspect cases and contacts were effectively treated and control measures initiated." If this was possible in an obscure village nestling 3,000 metres high in the mountains, there is no excuse for a bustling city like Surat to have gone the way it did.■

COVER STORY

Filth and decay

Pictures: By special arrangement

(Top) A common sight in Surat: (above) Municipal employees with insecticides on a street after the outbreak of plague.

V. K. RAMACHANDRAN

SURAT is a major centre of industrial growth in Western India, and is a metropolis that has grown very rapidly. The growth of industrial production has been, on a substantial scale, by means of small industry, carried on in workshops, rough sheds, manufactories and households in different parts of the city. Among the important industries that are either wholly or partly in the small and less-regulated or "informal" sector are textiles – including the production of artificial silk (Surat produces 60 per cent of India's artificial silk) and *zari*, textile processing and the production of parts for textile and garment-making machinery – diamond-cutting (30 per cent of India's turnover in this sector is from Surat), plastics, engineering, and chemicals and dyes. There has also been growth in the high-investment organised sector, notably chemicals and petrochemicals, and in the financial service and transport sectors.

The growth of Surat's population has been extraordinary: it

increased from 317,519 at the Census of 1961 to an estimated 1.7 million at the beginning of 1993. A study by Biswaroop Das of the Centre for Social Studies in Surat published this year estimates that 28 per cent of Surat's population lives in slums. Migrant labour is a most striking feature of Surat's labour force, and according to one recent newspaper estimate, migrants form close to 75 per cent of Surat's population; in Das's study, there were migrants from Gujarat, Maharashtra, Uttar Pradesh, Orissa, Andhra Pradesh, Himachal Pradesh, Rajasthan, Bihar and other States. Jan Breman of the Centre for Asian Studies, Amsterdam, who has worked in Surat and other parts of Gujarat over the last 30 years, describes Surat as "one big transit camp" of workers. "We have here a reserve army of labour moving around in an economic jungle; a predominantly male force of aliens with no or meagre skills... forever kept on the run and worn out in a ruthless work regime."

The growth of urban living facilities and civic amenities remains far behind the growth of Surat's population. Breman writes: "The roads remain unpaved in the new neighbourhoods, all surface water is thoroughly polluted, plants and trees are nowhere to be seen, power failure is the order of the day and night, sanitation and drainage are in a dismal state and... malaria has come back to the urban milieu with a vengeance. Even a longer list would fall short of conveying the overwhelming impression of filth, ugliness and decrepitude that meets the eye of the newcomer on leaving the railway station. Surat is said to be the dirtiest city of its size in the whole country... Nevertheless, the municipal authorities boast that real estate prices are nearly as high as in Bombay, hardly less expensive than in the most prosperous parts of the world." A municipal official has been cited as saying that the city generates 1,000 tonnes of garbage a day, of which 500 tonnes is collected by municipal staff.

According to Biswaroop Das's survey, about 80 per cent of the slum households used open spaces, canal and river banks, roads and rail tracks and other places other than latrines for defecation. "The attention is now focussed on the plague, as well it should be," Breman told *Frontline*. "But we must also remember that malaria and hepatitis may have claimed more casualties this year than the plague."

Early in September floodwaters were in the town, and, in the Ved Road area – one of the main areas of plague – water rose about 60 cm. Carcasses were left to rot in open spaces after the water receded. According to a newspaper report, at a recent (before the plague epidemic) meeting between Surat's Deputy Municipal Commissioner in charge of health and hospitals and 250 doctors and journalists, doctors warned the municipal official "that epdemics of cholera and possibly even plague were imminent."

Speaking to *Frontline*, Jan Breman emphasised repeatedly the connection between the current economic policies of the Government of India and Gujarat and the current public health crisis: "The epidemics have to do with the retreat of the state and the absence of a public sphere," he said. Public housing and public health were not municipal priorities at all and "the state has given up any pretence of being an arbiter between capital and the poor."■

A ghost town

A SPECIAL CORRESPONDENT

"WE are individually clean and communally dirty," Gandhiji had said. When I was in Surat a few days back, it occurred to me that he probably got that insight when he was visiting Surat. As you approach the town, from 5 km away itself there are hillocks of garbage on either side of the road. The river Tapti has been turned into one vast sewer and along both banks are sprawling slums. Of all the cities I have seen, this is easily the filthiest, much worse than Varansai or Kanpur. If at all plague had to break out, it had to be here.

When I visited Surat on September 25, the fourth day of the epidemic, it was like a ghost town. The shops were all closed though some autorickshaws were on the road. Remarkably, the State transport buses were plying, ferrying people out of the city.

The railways, the telecom and the postal services were functioning. Most of the private doctors had fled the city and the government doctors of Surat and some from other parts of the State were working round the clock. These are the lowly government servants who are often remembered only for their faults. There were no voluntary agencies at work except some Bajrang Dal workers who were cleaning up some streets and the Church's Auxiliary for Social Action (CASA) from Delhi that was distributing medicines in the slums.

Surat has a tradition of business and it was here that the British established their first trading post in A.D. 1813 and the Dutch in A.D. 1820. Though the city has one of the oldest municipalities, set up in 1852 and made a corporation in 1966, in recent decades it had grown out of control. The textile factories and the diamond-cutting industry have attracted migrant workers from other States, Oriyas forming the single largest group.

Not governed by labour laws and badly organised, these people are exploited and work under miserable conditions. They live in shanty colonies along the canals and the river. A large percentage of the city's 2.2 million people live in slums. One estimate says that just on Ring Road there are 5,000 slums and that huts spring up in these settlements at the rate of 100 a day.

The urban influx, coupled with the newly-found wealth, has given rise to a number of housing colonies around the city, many of them unauthorised. So they lack basic civic amenities. The drainage system covers only a small area of the town. Garbage is just thrown by the roadside and sewage flows into the streets. Basic facilities needed for a decent life get a short shrift in all the cities of Gujarat, but this is much more pronounced in Surat.

Piles of garbage, rotting carcasses and cesspools of sewage can be seen on the main thoroughfares. Rats and bandicoots multiply in this situation. They were all flushed out of their holes by the recent floods. Cattle and donkeys roam the thoroughfares.

If the disparity between the rich and the poor is the highest in India, within the country it is the highest in Surat. Side by side with those who take a flight to Bombay in a private aircraft to have lunch and get back, there are children who, without a stitch on, are raised along the railway lines.

As we were leaving the city, I saw a group of children frolicking in water, at the edge of the Tapti. They have nowhere to go, plague or no plague. They are from the shanty-town on the bank. ■

Paying the price

A long history of apathy

PRAVEEN SWAMI
in New Delhi

"THE only good business to be in," one Delhi businessman recently said, "is the the tetracycline business." Weeks after the first reports of a plague outbreak came in, the national costs of India's worst recent public health disaster are becoming evident. Reports indicate that the plague may have an abiding impact not only on its victims and their families, but on a spectrum of Indian domestic and international business activity. If the Central Government believed the suffering of plague victims in Gujarat, Maharashtra and Delhi would, like other national calamities, soon be erased from collective memory, that smug assumption has been shattered.

The first sign that the outbreaks in Beed and then Surat would have national implications came days after cases of suspected plague, later confirmed, were reported in Delhi on September 24. Within a week, the number of cases was to cross 120. The outbreak was, perhaps, predictable. Thousands of people from Gujarat had come to the city, and little effort had been made to identify or monitor them. No surveillance infrastructure was in place, either, for Delhi residents who had returned from business trips to Surat or other plague-affected cities: nor was an epidemic control plan in place.

On September 25, United States Ambassador Frank Weisner called on Union Health Minister B. Shankaranand and told him Indians travelling from plague-affected areas to the U.S. would have to fill up special forms on their arrival. Tour operators read this as an advance warning of impending curbs on travel, particularly if the plague hit Delhi or Bombay, the major traffic hubs, in a big way.

Over the next two days, as the number of reported cases grew, several countries announced plague-related restrictions on Indian travellers. From September 25, aircraft from India were fumigated on arrival at airports in Rome and Milan, and passengers were subjected to special health checks. In Frankfurt, doctors checked passengers before being allowed to disembark. Similar restrictions were announced by the Bangladesh Government.

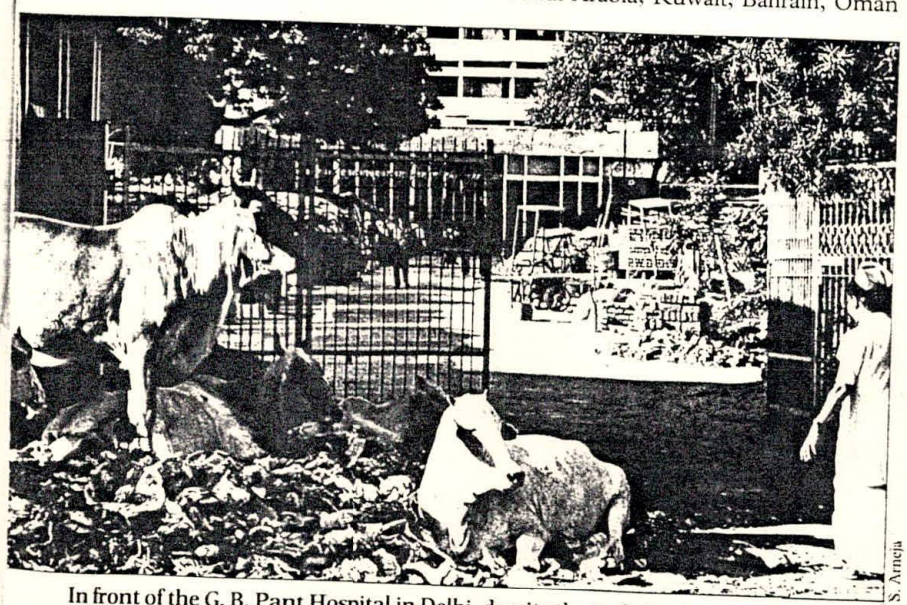
Other countries reacted in a more drastic manner. When on September 28 an international alert was declared against air passengers from India, Saudi Arabia, Kuwait, Bahrain, Oman and Qatar suspended all flights between their countries and India. One Air-India flight to Jeddah, with 240 passengers on board, had to be recalled after take-off, and pandemonium resulted at the international airports when thousands of passengers were told their flights had been cancelled. Dubai, Abu Dhabi and Pakistan soon followed suit. Malaysian Airlines stopped operations to India, and recalled staff working for Jet Airways.

The implications of these actions soon became evident. Though most European and Asian countries did not stop traffic, media coverage had its inevitable impact: tourists in Delhi could be seen walking around with surgical masks on. One major German tour operator, Der, cancelled a tour of India. Major British tour operators like Thomas Cook and Lunn Polly, too, are offering refunds to anxious travellers. "At the moment," says one representative of the Indian travel agent Sita World Travel, "there is no major drop, and charter flights to Goa, for example, are arriving on schedule. But if this plague scare continues, particularly in Delhi, which is the hub for trips to Jaipur and Agra, it will be disastrous."

The September 29 decision by the United Arab Emirates to suspend all cargo transhipment from India has put trade with one of India's major markets in jeopardy. The principal victim so far has been Air-India, which has been losing Rs. 2 crore a day. Indian Airlines also has reported massive losses, which have been initially estimated to run into "several crores", and domestic operators like East West, too, have reported declining traffic.

The domino-effect provoked by the breakdown in Gulf transhipments has been enormous. Union Finance Secretary Tejendra Khanna has said the "panic reaction" may retard Indian exports by as much as 2 per cent, or Rs. 1,400 crore. Agri-exporters have been sharply hit by the loss of their principal market, the Gulf, and their scrips have been steadily plunging. A spectrum of commodities, ranging from frozen meat to fruit and basmati rice, can no longer be shipped to West Asia. Bilateral trade with the United Arab Emirates alone is estimated at 3 billion a year: Qatar alone imports over five lakh tonnes of Indian fruit daily.

Similarly, remittances from the Gulf to Kerala have been hit (see box). Alternatively, several Indians have been standed in the Gulf, though visa extentions have been granted. While Emirate nationals whose visas were



S. Ameja

In front of the G. B. Pant Hospital in Delhi, despite the 'red alert'... hygiene gets low priority.

expiring have been evacuated from India on a special flight, Indians wishing to return to work in the Gulf or join new jobs there have not been able to go.

Two thirds of India's oil imports come from the Gulf, and no one is certain whether Indian tankers will be allowed to dock at Gulf ports. While a Shipping Corporation of India tanker arriving from Korea was allowed to pick up oil and proceed to India, other tanker operators have been warned their ships will not be allowed into the territorial waters of the Gulf Cooperation Council. If the situation persists, India will be forced to dip into its buffer oil stocks, which can only last 45 days.

These losses are likely to be compounded by a loss of international investor confidence. In London, Indian Global Depository Receipts (GDRs) crashed after the BBC and CNN began carrying regular reports on the plague situation in Gujarat and Maharashtra. The Japanese trading giant Mitsui is evacuating its staff from Bombay and Delhi; Israeli software expert Ayelet Rosenweig has cancelled a high profile visit to Bombay; a tour by the Mauritian Minister for Tourism has been postponed, and foreign experts at the Essar Gujarat steel plant in Hazira have left the country.

Is this international reaction hysterical? Union Petroleum Minister Satish Sharma told journalists in London the plague threat had been handled irresponsibly by the international media. This argument, however, misses the key point: that the international response merely mirrors the breakdown of public confidence within India. The problem has been that State governments have shown little clarity of purpose. As late as September 20, when bubonic plague spread from Mamala to several adjacent villages, Maharashtra Deputy Health Minister Paban Ghatowar made the incredible claim that the outbreak was minor, since it was "of the bubonic variety, not the fatal pneumonic variety." Similarly, on September 26 after cases had been reported from around Gujarat and two deaths recorded in Vadodara, the Chief Minister insisted that "not a single case of pneumonic plague was registered anywhere in Gujarat except Surat."

Why did the State governments respond in this way? One possible reason is that they had no infrastructure to deal with the crisis they were facing. Critics, however, argue that the response was entirely consistent with official attitudes to health and urban development policy issues. The Director of the National Institute of Urban Affairs, Dr. Dinesh Mehta, has argued that the central problem in Surat was that revenues from high-value businesses had been pumped into land rather than infrastructure. High land prices and poor infrastructure resulted in overcrowding and poor sanitation. Surat, Dr. Mehta argues, was a disaster waiting to happen.

The Central Government's intervention, when it came, was also limited. Initially, no effort was made to limit the exodus from Surat: only after the outbreak in Delhi did trains bypass the city. "Health is a state subject," argues National Institute of Communicable Diseases (NICD) Director K. K. Datta, "so our role could only be advisory." The Central Government instead used financial aid and drug availability programmes as its instruments. On September 24, the Union Health Ministry set up a central control room under the supervision of the Prime Minister.

More positive action decisions, when made, were clearly firefighting measures devoid of any direction other than ensuring drug availability. By late-September it was decided to despatch 10 million tetracycline capsules and 2,000 tonnes of the powerful insecticide Gammexane to Maharashtra and Gujarat. Total duty exemption was granted for tetracycline imports to ensure availability at reasonable prices, and the Finance Minister announced that Rs. 20 crore would be kept aside to meet plague-related expenditure.

Could this situation have been avoided? As Dr. Saraljit Singh, a plague expert and adviser to the World Health Organisation, points out, "plague breaks out fairly regularly around the world." Exactly 13,366 plague cases were reported globally between 1980 and 1992, 206 of these in an advanced country like the United States. What went wrong in both Beed and Surat was the absence of a containment apparatus. "It is true the warnings were not heeded," argues Dutta. "It is true that Maharashtra shut down its plague monitoring facility in 1987. But please remember, there are other demands. Polio, cholera, malaria, people die of all of these. And resources are few."

"Today", admits Delhi Health Minister Dr. Harsh Vardhan, "there is no epidemic control or disaster management masterplan either in this city or nationally. We deal with situations as and when they emerge."

The capital city's response to its near-700 cases of suspected plague has been chaotic. Figures given out by various authorites were often at odds. Until recently, hospitals like the All

Kerala concerns

BINDU BHASKAR

THE Gulf ban on air landings has heaped losses amounting to several crores of rupees on the aviation, travel and export sectors operating through Kerala. Flights of six airlines ferrying 8,000 passengers on the Gulf route and generating a daily business of Rs. 3.75 crore have ground to a halt. A drop of Rs. 2 crore a day in customs revenue has also been estimated.

Caught in the grip of a severe cash shortage owing to flight cancellations, travel agents and tour operators, employing roughly 40,000 people, have requested airlines to defer demands for payment and to refund unused tickets. October-March is their peak season and all the major agencies are in the throes of a 'zero-revenue' situation.

At least 25 per cent of the passenger traffic to the Gulf consists of job-seekers. As Gulf employers are unlikely to wait indefinitely, there is concern that recruits from Pakistan, Bangladesh and the Philippines would fill up vacancies. Many who came home for the Onam festival, are worried about not being able to return before their visas expire.

Remittances from expatriates have come under a shadow. Thousands of households are affected as postal links are cut off.

Canara Bank, which manages Rs. 880 crore of non-resident Indian remittances from the Gulf every month, has tied up with three exchange companies in Dubai, Doha and Bahrain to facilitate financial transactions electronically.

With ships from South-East Asia skipping the port, tonnes of tea, coffee and foodstuff remain in storage in Kochi. Garments from Tirupur, Tamil Nadu, sent to various destinations through a sea-air link via Dubai, have also piled up in Kochi. There is also a setback to the horticulture trade. Nearly 40 tonnes of vegetables and fruits worth Rs. 30 to Rs. 40 a kg routinely find their way to the Gulf. ■

India Institute of Medical Sciences were not even reporting cases to the monitoring authority. More critically, no proper information on the plague was put out by the authorites, leading to a mad rush for surgical masks, tetracycline and even quack remedies.

At the central Infectious Diseases Hospital, patients walked in and out freely, unrestricted by nervous policemen sitting a safe distance away from the building. The hospital itself is a decrepit, rat-ridden colonial building, with an irritable and overworked staff: in one case, the body of a patient abandoned by his family was allowed to lie on a bed for five hours before it was removed.

Once schools and public entertainment facilities were closed, complete panic ensued, with commuters disappearing off buses and shoppers walking around with surgical masks. The official cleanliness drive failed to improve conditions for the urban poor, particularly in East Delhi's sprawling slums. "Do you know," says Delhi Chief Minister M. L. Khurana, "that until recently, garbage was not even cleared out of slums because they were illegal colonies?"

This story of chaos, confusion and apathy has been mirrored at all levels. Union Health Minister B. Shankaranand has been holed up in silence since the plague broke, and repeated attempts to contact him proved unsuccessful. The Minister has not, so far, seen it fit to hold a press conference. Similarly, the Prime Minister has not seen any need to address the nation to calm the widespread panic, justified or otherwise. Foreign journalists and tour operators have been offered free travel and hospitality to "see the situation for themselves," but there appears to be few takers.

If there is one lesson from the plague outbreak, it is that a coherent system of preventive medicine, urban planning and disaster management would have proved less expensive than containing the epidemic. Delhi is now spending Rs. 2 crore for a rapid urban clean-up programme, an expenditure rendered necessary by the decades-old degeneration of the city's urban infrastructure.

Critically, the plague is not the only problem confronting the public health system: over 1,200 people are believed to have died in the last four months of cholera in Bihar, Uttar Pradesh, Himachal Pradesh and Jammu and Kashmir, an epidemic that rages largely unreported. If the lives lost are not adequate reason to address these issues, the crores of rupees wasted will hopefully provide an added incentive. ■

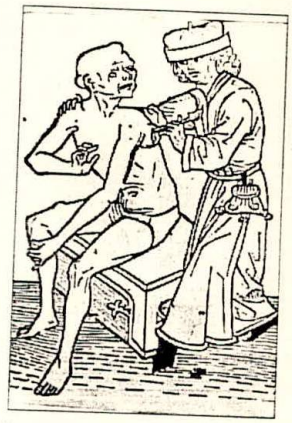
A disease of rodents

V. K. RAMACHANDRAN

PLAGUE is an infectious fever caused by the bacillus *Yersinia pestis* (the information here on the etiology, prevention and control of plague draws mainly on J. E. Park and K. Park, *Textbook of Preventive and Social Medicine* (1991). It is primarily a disease of rodents, transmitted by the rat flea, in which human beings become involved. In India, the wild rodent *Tatera indica* has been identified as the main reservoir of plague.

There are three main clinical forms of plague in human beings: bubonic, pubonic pneumonic and septicaemic plague. In bubonic plague, the patient suffers a sudden fever, chills, headache and prostration, and enlarged lymph nodes (buboes) appear, particularly in the groin and the neck. Pneumonic plague, which affects the lungs, is highly infectious and spreads by droplet infection; it generally follows as a complication of bubonic-septicaemic plague. Plague bacilli exist in a pneumonic plague patient's sputum.

There are at least five types of transmission of plague to human beings: commensal rats-rat fleas-humans; wild rodents-wild rodent fleas or direct contact-humans; wild rodents-peridomestic rodents, commensal rodents-wild rodent fleas, peridomestic rodent fleas, commensal rodent fleas-humans; humans-human fleas-humans; and humans-humans (as in pneumonic plague). The incubation period of bubonic plague is two to seven days, of pneumonic plague one to three days and of septicaemic plague two to seven days.



Incising a bubo —1482, Nurenberg.

Courtesy: Dept. of Public Health & Preventive Medicine, Tamil Nadu

The prevention and control of plague involves the control of plague cases, the control of fleas, the control of rodents, vaccination, chemoprophylaxis, surveillance and health education. Measures to control plague cases include early diagnosis, notification, isolation, treatment and disinfection. Treatment is started without waiting for confirmation of the diagnosis. The drug of choice is streptomycin administered intramuscularly; tetracycline administered orally is an alternative. Sulphnomides are used when other drugs are not available and in certain other cases. Oral tetracycline is also the drug of choice for chemoprophylaxis; the alternative is sulphonamide. Immunisation with the plague vaccine (the vaccine was developed in India in 1897 by Haffkine and modified in the 20th century by Sokhey) is an important preventive measure.

Park and Park write that there is a great deal of evidence of plague remaining "silent" for periods of 10 years or more in respect of plague in certain areas, followed by "sudden explosive outbreaks of rodents or human plague." Mean temperatures between 20 deg. C. and 25 deg. C. and a relative humidity of 60 per cent are considered favourable for the spread of plague; these are roughly the climatic conditions that obtain in western India from November. ■

Definitions of plague

PLAGUE is an infectious fever caused by the bacillus *Yersinia pestis*, transmitted by the rat flea. It is a disease of rodents, and epidemics in human beings originate in contact with the fleas of infected rodents. In other words, plague is primarily a disease of rodents and man enters only incidentally into the cycle. The disease in humans has three clinical forms:

★ *Bubonic plague* is characterised by a swelling of the lymph nodes.

★ *Pneumonic plague* is one where the lungs are extensively involved.

★ *Septicaemic plague* is one in which the blood stream is so invaded by *Yersinia* that death occurs before the bubonic or pneumonic forms have had time to appear. ■

The route to humans

T. S. SUBRAMANIAN

PLAGUE took a very heavy toll of human life in the latter part of the 19th century and the early part of the 20th century. In India alone, more than 10 million people perished from plague between 1896 and 1918. There was a steady decline in the incidence of the disease from the middle of this century in India and human plague cases almost ceased in 1967. It has now erupted again, first at Mamala village in Beed district, Maharashtra, and a few days later in Surat, Gujarat. While victims at Mamala were hit by bubonic plague, the more virulent pneumonic plague has stalked Surat.

According to A. V. Sadanand, Vice-President of the Indian Academy of Entomology and retired Chief Entomologist, Tamil Nadu Government, plague first starts with wild rodents, that is, rats in the field. The flea gets it from the wild rodents but does not die. When the flea bites domestic rodents, the disease spreads among the latter. Thus "rat falls" occur. When rats fall and die, the fleas leave them and attack people. So it spreads from man to man. This is called bubonic plague, that is, produced as a rule by the bite of infected rodent fleas, and also called enzootic plague. Persons with bubonic plague suffer from a swelling in the neck, groin and axilla (arm-pits) and then from high fever. The incubation period for humans is two to six days.

Sadanand said: "After the bubonic stage, it becomes a pneumonic stage when the bacteria invade the lungs of man. Once that stage is reached, transmission can take place from man to man easily by droplets, that is, by spitting saliva. This transmission does not require fleas. Sometimes the human blood stream will be full of plague bacteria. That plague is called septicaemic plague. This again spreads through the flea (*Pulex irritans*)."

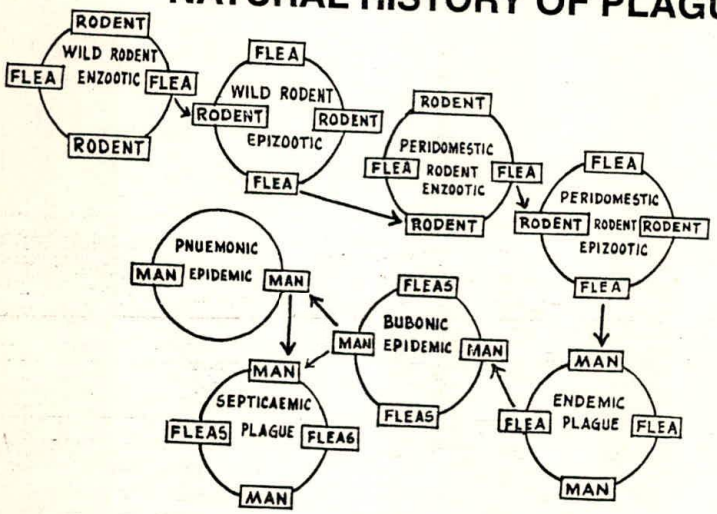
Although plague was considered a public health menace which had been eradicated, the risk of its spreading to domestic rodents has remained. This is essentially because plague organisms have been present in wild rodents. A public health problem could surface following natural clamities such as flood, earthquake or war. All these disturb the natural ecology, that is, the normal habitat of wild rodents. With these beginning to migrate to domestic or peri-domestic areas, there could be a sudden eruption of the disease.

Sadanand explains: "To prevent this, the wild rodent population should be kept under surveillance. Plague control units (in various States) do this by collecting wild rodents, taking out their blood and testing it in the laboratories. Once we find any wild foci, we perform anti-rodent and anti-flea measures. While rodent control is done by fumigation of rat burrows, flea control is done by spraying benzene hexachloride (BHC, Gammexane). That is why we have to continue the existence of plague control units. We are doing this in Tamil Nadu. We established the Institute of Vector Control and Zoonoses at Hosur in Tamil Nadu in 1984." (Zoonoses are animal diseases transmitted to man.)

"What is important is that people should be educated immediately to take precautionary steps and use drugs. If the treatment starts within 24 hours of the onset of the disease, nobody need die. In olden days, there were no antibiotics and people used to die like flies. Now we have potent drugs. People having fever, headache and swelling in the neck, groin, etc. should immediately take tetracycline. The second most important thing is that the medical profession should be alerted because most of them have forgotten what is plague. They should be educated to analyse the cases. Thirdly, in places like Madras, where the rodent population is very high, the municipal corporation should take rodent control measures. Once the rodent population is controlled, the flea population goes down automatically.

"Most important is that previously endemic areas such as Karnataka, Andhra Pradesh and Maharashtra should revive their plague control units. By watching the rat density and flea density and performing serological tests and rodent blood tests, we will be able to predict the onset of plague. Port-cities, where foodgrains come by ship, are at risk because along with the grain, rats also come in. The main thing is people should not panic and run away." ■

NATURAL HISTORY OF PLAGUE



COVER STORY

Plague, through the centuries

V. K. RAMACHANDRAN

PLAGUE has killed huge numbers of people at different periods in history, and has played an enormous role in human social and demographic history as well as in our language and collective memory. The 14th century plague epidemic in Europe, the Black Death, is estimated to have killed 25 million people, or one-fourth the population of Europe.

In a 1986 paper on plague in London in the 16th and 17th centuries, Paul Slack, a historian of plague in England, noted that plague was a "regular visitor" to London between the Black Death of 1348 and the epidemic of 1665-66. "Nearly a quarter of the city's inhabitants died in 1563," Slack writes. "In 1665 more than 80,000 people died: that is, equivalent to the total populations of contemporary Norwich, Bristol, Newcastle, York and Exeter... Nothing in the modern world, short of nuclear catastrophe, could match that. Yet these figures... understate the extent of those disasters."

In 1894, plague in Canton and Hong Kong killed 80,000 to 1,00,000 people, and was transmitted from south Chinese ports to different parts of the world. The epidemic of the 1890s and early 20th century of plague in India, particularly in west and south India, was part of this third pandemic of plague. David Arnold estimates that the plague epidemic that began in 1896 – "massive in scale and fraught with political, social and demographic consequences" – claimed, by 1930, more than 12 million lives.

According to the World Health Organisation (WHO), in 1992, nine countries recorded 1,582 cases of plague in humans, and there were 138 plague deaths. Brazil, Madagascar, Vietnam, Myanmar and the United States reported plague cases almost every year between 1983 and 1992. With respect to India, J.E. Park and K. Park (*Textbook of Preventive and Social Medicine*, 1991) state that there has been) no laboratory-confirmed human plague since 1966. In 1984, there were two "suspected outbreaks", in areas on the Tamil Nadu-Andhra Pradesh border and in Himachal Pradesh. Positive sera specimens from rodents "were observed in 1979 in Kolar and in 1976 in Maharashtra, where suspected human cases were reported earlier in Bhir (sic.) district."

THE WORST-HIT

Given the means by which plague is transmitted, it is inevitable that the poor, particularly those who are ill-housed and live in insanitary conditions, are affected worst by it. Paul Slack writes of the London epidemic of 1665-66: "Plague was not only concentrated in time. It was concentrated socially and geographically. Since the disease was carried by rats and fleas, people in the most dilapidated, overcrowded houses and with fewest changes of clothing were most vulnerable: the poor, in other words, who were 'pestered' together in those sheds, cellars and subdivided tenements which contemporaries recognised as the foci of infection."

In Bombay in the 1890s, too, the worst-off areas were those where people were "forced to live in miserable shanties, dark, low, small, and built on insanitary sites, without plinth, added to which... 16 to 20 persons will sleep, eat and work in a space hardly sufficient for the requirements of four" – which, although a description taken from the report of the Bombay Plague Committee of 1896-97, is a reasonably accurate description of the living conditions of about half of Bombay's current population.

Describing in 1993 some areas where plague broke out in 1994 in Surat, Jan Breman of the Centre for Asian Studies, Amsterdam, who has worked in Surat and other parts of Gujarat over the last 30 years, wrote: "On my wanderings through the slums of Katargam, Limbayat, Udhana and Pandesara, my eyes never fail to fill with tears and my nose does not stop running... Adjacent to workshops are labourers's hutments and dormitories owned and given out on rent by slumlords. The work-sites and sleeping places are not far apart and sometimes even coincide." ■

T. S. SUBRAMANIAN

PLAGUE is a disease of great antiquity: it existed several centuries before the birth of Christ. Central Asia is considered the cradle of plague.

The first recorded epidemic was among the Philistines in 1320 B. C. And the first reported pandemic was in A.D. 542.

"This pandemic appears to have originated from Pelusium in Egypt, and it lasted about 50 to 60 years and spread to all parts of the world. The next recorded pandemic, called the Black Death, started from Central Asia during the 14th century and its wave swept through Europe, India, China and other Asian countries," says a report published by the Directorate of Public Health and Preventive Medicine, Tamil Nadu, during the 15th All-India Inter-State Coordination Meeting on Plague held in Madras on August 27 and 28, 1982.

In India, there is a reference to plague in the ancient Sanskrit poetical work, *Bhagavath Purana*, which warned people to leave their homes as soon as rats fell from the roofs and died. Says the well-researched report: "The definite recorded history of introduction of the disease into India was in 1031-1032 A. D. from Middle Asia, following the invasion by Sultan Mohamed Ghazni. The first epidemic was in Calcutta in 1895 and in Bombay in 1896. The total number of deaths due to plague in India from 1896 to 1918 was more than ten million... The endemic centres in the South probably got established after the Bombay city epidemic of 1896. Andhra Pradesh got involved in 1898 and the Nilgiris in 1903."

Plague made its entry into Bombay city in August 1896. "At first, diffusion was comparatively gradual, but by the middle of 1898, the disease had spread over the greater part of the Bombay Presidency, where it had been the reported cause of some 90,000 deaths. Infection was also carried to Mysore," says the *Mysore Gazetteer* , Volume I, edited by C. Hayavadana Rao, printed at the Government Press, Bangalore, in 1927.

There is a vivid description of how plague swept through Bombay city and the havoc it wrought in a book entitled *A Tour Through the Famine Districts of India* by F. H. S. Merewether, Reuter's Famine Commissioner, published by A. D. Jones and Co., London, in 1898.

Merewether wrote:

"Bombay has earned another title to our respect, and may be justly called

The pandemics in Bombay, Mysore

Bombay the Busy... One of the first things that strikes the newcomer is the enormous mass of humanity which throngs the city; which crowd is intensified tenfold in the native quarters of the town... In the native quarters at night the footway is simply impassable, owing to the masses of shrouded natives who use it as their sleeping-place. In the vicinity of the Crawford markets and in the quarter of Cammatepura, they simply line the pavement and wrapped closely in their dirty-white chuddahs, look like bales of merchandise. But the destroying angel of plague altered all this. In streets where even towards midnight it was impossible, owing to the crowds, for a *ticcagharry* to proceed beyond a walking pace, a battery of artillery might have galloped in safety down the now-deserted thoroughfare. I went on a tour of inspection when the disease was at its height, and found whole streets in the busiest portion of the native town practically deserted. The shops were all closed, and the occupants had disappeared *en bloc*. It was calculated at that time that nearly two-thirds of the inhabitants had fled from the pest-stricken island to the mainland. This enormous exodus on the part of the people did incalculable harm to the Presidency, and without doubt caused the spread of the fell disease into the country districts of the province.

"At a later period on my tour, I found in one remote village of the Konkan that more than forty people had died of the plague which had been imported by a sufferer from Bombay..."

There is a striking similarity between what Merewether wrote in 1898 about Bombay and what has now happened in Surat and in Beed district, Maharashtra. He observed:

"In the earlier stages of the epidemic, the (Bombay) municipality attempted the disastrous plan of concealment; and it was mainly due to the fearless policy and tone of *The Times of India* in laying bare the actual facts of the case, and especially in tracing its abnormal mortality to its true cause, that the Government was forced to take the strenuous repressive measures it subsequently did. If from the first the nettle had been grasped firmly, and a cordon established round Bombay, the disease would not have attacked Kurrachee nor been so widespread as it eventually became. The Plague Committee which the Government too tardily formed, had it been in existence sooner, would doubtless have achieved at an earlier stage a still more brilliant success. With such popular and indomitable chiefs as General Gatacre and Dr. Pollen, the dread monster would have been sooner quelled."

The mortality caused by the "Angel of Death", as Merewether described the plague, was "enormous" in Bombay. He wrote:

"When a case occurred or proved fatal, a circle was placed on the door-post of the house, and in one house alone the number of rings shown up adds up to forty-three. There was also an *oart* or square where this number was exceeded... Hospitals sprung up on all sides like mushrooms in a single night. The wail of the mourners was heard on every side, and one could not pass down a street without meeting one or more funeral procession. The burning ghauts were strained to their utmost capacity, and the Mahommedan burial-grounds could not hide beneath the earth sufficiently fast the Moslem victims. On Mahim sands, if in ordinary times you ride out there in the early morning, you may generally find the dying embers of one fire. In the times of the plague, the whole sea-shore was clothed with the fires of innumerable funeral pyres..."

Just as the plague has now hit hard the textile and diamond industries in Surat, the plague in Bombay left its "indelible mark" on the city's "commerce and enterprise".

When the infection spread to Mysore, more than 2,24,476 people died in Mysore State between July 1898 and June 1918 – more than 11,000 deaths a year. "Formidable as this total is, it certainly falls short of the truth. It is probably a closer approximation to the actual number, however, than is common in the case of other diseases," says the *Mysore Gazetteer*.

"The State has been persistently affected with plague during the whole of the twenty-year period and no month has been completely free from plague since July 1898. Altogether 2,24,476 plague deaths were reported for twenty years, 2.1 per cent of the all-India mortality and equivalent to a death rate of 39.21, or a mean annual rate of 2. The climate of the Mysore plateau is more equable and uniform than that of any other part of India and perhaps as a result of this climatic peculiarity, the annual incidence of plague has presented a lesser degree of variability in the State than elsewhere," it adds.

To give an all-India break-up, while 60,32,693 people died of plague from 1896 to 1906, another 42,21,528 lost their lives between 1909 and 1918, and yet another 17,02,718 perished between 1919 and 1928.

The number of deaths went down by a quarter between 1929 and 1938 – it stood at 4,22,880. It went down further between 1939 and 1948, accounting for 2,17,970 lives. Between 1949 and 1958, 59,056 persons died of plague while only 678 fell to the disease betweem 1959 and 1968.

On a global level, though there was a drastic decline in the incidence of plague because of the introduction of rodent control by cyanogas fumigation in the 1930s and organochlorine insecticides for flea control in the late 1940s, about 30 countries were affected by plague between 1986 and 1979 with 46,987 human cases. In 1967, 6,004 cases were recorded, nearly 94 per cent of these from Vietnam. In 1953, 78 per cent of the human cases in the world were from India. However, India has been free from the human plague since 1967.

FOCI OF THE INFECTION

According to the report published by the Tamil Nadu Directorate of Public Health and Preventive Medicine, however, the natural foci of this infection remained entrenched in the following three areas: "(i) the sub-Himalayan focus comprising Punjab, Uttar Pradesh, Bihar and north of the Ganga; (ii) the central Indian focus comprising the water sheds of the Vindhya, Bhanrer and Maikal ranges and, the Mahadeo Hills; and (iii) the focus along the Deccan plateau of peninsular India consisting of three centres in the South as follows: (a) the water sheds of the Western Ghats in Maharashtra and Karnataka States; (b) the water sheds located in the districts of Periyar, Dharmapuri, Nilgiris and North Arcot in Tamil Nadu; and (c) Chittoor district of Andhra Pradesh."

At present, the focus in the South is believed to be confined to the southern half of the hilly Kolar district in south-eastern Karnataka, adjoining Dharmapuri and Periyar districts of Tamil Nadu and Chittoor district of Andhra Pradesh. ■

Less than vigilant

Plague surveillance in India

RAVI SHARMA
in Bangalore

PLAGUE surveillance in India exists only in its rudimentary form. The country's only surveillance unit is in Bangalore. Established in 1975, it works under the National Institute of Communicable Diseases (NICD), India's central plague laboratory and nodal centre for the control of the disease.

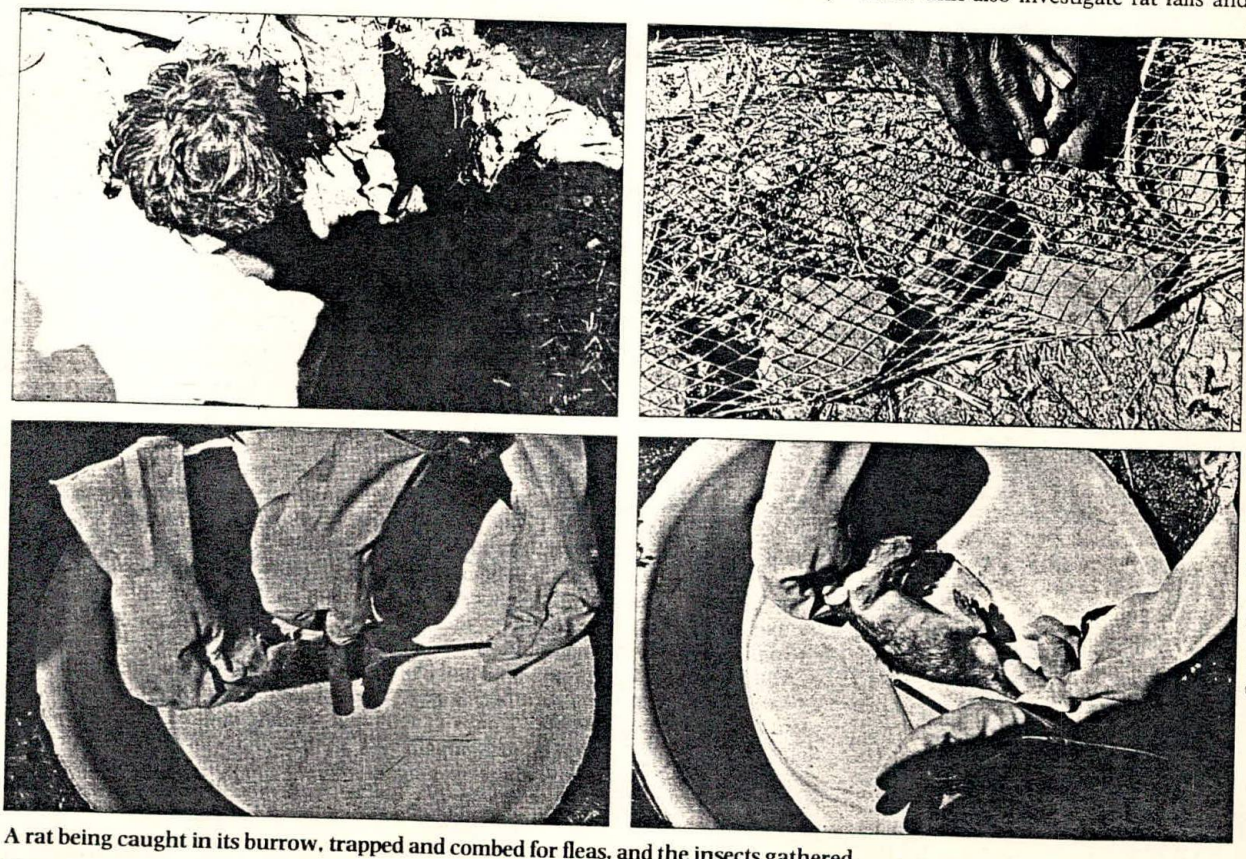
The Bangalore Plague Surveillance Unit carries out research in epidemiology and the detection of plague and other rodent-borne diseases like leptospirosis. A team of officials from this unit have gone to Mamla (the Maharashtra village where the first cases of the current epidemic were discovered) and also to Surat.

Its operation is restricted mainly to a geographic area located at the junction of Karnataka, Tamil Nadu and Andhra Pradesh, States which have been long perceived as the plague zone of India – especially the rocky delta districts of Kolar in Karnataka, Chittoor in Andhra Pradesh and Dharmapuri in Tamil Nadu.

The decision to position the unit in Bangalore was taken for two reasons. First, the last reported case of human or domestic plague (defined by the World Health Organisation, or the WHO, as "plague that is intimately associated with man and rodents living with man, and has a definite potential of producing epidemics") as opposed to sylvatic or wild plague (defined by the WHO as "plague that exists in nature independent of human populations and their activities") in India was reported in 1966 from Mulbagal taluk of Kolar district.

Secondly, sylvatic foci continued to be active in these three States and, according to experts like Dr. Saraljit Sehgal, Director, NICD, was till the recent outbreak, "the last known focus" of plague in India. He had cautioned at a workshop in Bangalore in November 1992 that the fact that plague persisted in rodents in these States meant plague was "simmering beneath the surface."

The Bangalore unit coordinates the activities of the State plague control units located in Kolar (Karnataka), Hosur (Tamil Nadu) and Palamner (Andhra Pradesh). These units are manned by around 600 personnel whose main job is to trap rodents, catch rat fleas, collect sera samples and dispatch them to the Bangalore Plague Surveillance Unit, from where, after bacteriological diagnosis, the positive samples are sent to the NCID's central laboratory for reconfirmation. The State units in tandem with the surveillance unit also investigate rat falls and



Courtesy: Dept. of Public Health & Preventive Medicine, Tamil Nadu

A rat being caught in its burrow, trapped and combed for fleas, and the insects gathered.

suspected cases of human plague. The Bangalore unit also trains health officers from all the States in measures to combat plague.

According to Dr. Shyamal Biswas, Assistant Director, NICD, currently heading the Plague Surveillance Unit, the unit regularly does random sampling of wild rodents for the plague bacilli and over the past few years there has been a "positive occurrence of sylvatic or rodent plague". Says Biswas, "We have been doing tests since 1976, but it was only in 1989 that we got the first positive samples (plague-infected rodents)."

In 1989, of 28,561 rodents tested three proved positive; in 1990, of 32,644 four tested positive; in 1991, of 45,301 rodents 50 tested positive, in 1992, of 54,626 rodents 135 were positive; and in 1993, of 51,427 tested five tested positive. In the first eight months of this year, of 30,000 rodents tested, 30 (20 from Tamil Nadu, two from Karnataka and eight from Andhra Pradesh) were positive for sylvatic plague.

Biswas, however, says emphasis should not be given to the numbers, since "even one positive case is bad enough, and it showed sylvatic plague activity was going on in the area".

But, as Biswas says, the incidence of rodent plague does not necessarily mean that an epidemic is just around the corner. It happens "only when an infected wild rodent (a permanent reservoir and a relatively resistant host) comes in contact with semi-domestic rodents, which in turn transmit the disease to commensal rodents (both of which are highly susceptible), and then to man." As Sehgal says, "Rat fall is the harbinger of the domestic rodent plague and a sign of imminent outbreak of the epidemic bubonic plague in humans."

Curiously, blood samples are not taken from States other than Karnataka, Tamil Nadu and Andhra Pradesh. An NICD unit, which was functioning in Maharashtra, was shut down in 1987 as it was considered expendable. As a doctor at the NICD says, that line of thinking could be a thing of the past now. Sources in the Plague Surveillance Unit aver that after the experience in Surat the Government might well decide to set up units similar to the one in Bangalore in other States.

The surveillance unit, as Biswas explains, only detects plague; it is not equipped or meant to control it. But, as Dr. M. T. Hema Reddy, Director, Health and Family Welfare Services, Karnataka, under whose directorate the plague units in Karnataka function, says, control of human plague never arose since plague was looked as more of an "academic problem". He says the State Government had brought down the staff strength in both the Bangalore and Kolar units to skeletal levels, but unlike other States had not abolished the units. "It is a question of economics. My field staff are full-time employees. Besides, we pay Rs. 200 for every rat caught."

As experts say, plague, like any epizootic disease, cannot be eradicated or controlled: "It can only be monitored". And India hardly has an effective surveillance network. ■

The first steps

JAYA SHREEDHAR

"IT was 1925, and we were in the Army station at Trimulgherry, near Hyderabad. The Army was always on the alert for suspicious incidents. The first evacuation order came following a rat fall in one of the houses. We immediately set about collecting our children and belongings and assembled at the maidan, disinfected and readied for us. We pitched our tents or built crude huts and stayed there, sometimes for as long as three months, till it was declared safe to return to our homes. Shops in the bazaar opened at 9 a.m. and were closed by 4 p.m. People had to be back in the maidan by evening and were not allowed out at night. Relatives or friends were not allowed to visit for months together. We were all given a single injection and our houses were sprayed with pesticides. This happened nearly six times, about every two years, till the rat falls stopped," said 88-year-old Saraswati Benegal, recalling the plague epidemics of the 1920s and 1930s.

Immediate evacuation to a controlled environment, inoculation with Haffkine's vaccine, rat destruction and sun or chemical disinfection were the temporary measures to be adopted in an infected locality, according to a memorandum on Plague Preventive Policy, dated April 30, 1934. Fumigation of rat burrows with cyanogas ensured the complete destruction of rats and fleas and this was extensively and successfully carried out in endemic areas like Cumbum in Madurai district, Tamil Nadu.

The memorandum, however, strongly deprecated the practice of "commencing rat destruction at the onset of plague and stopping it at the first signs of subsidence of plague cases."

It is considered dangerous to attempt rat-trapping in the midst of heavy infection because it will tend to disseminate infection and also hinder the progress of development of natural immunity to plague among the local rat population.

Today, as part of the Tamil Nadu Government's anti-plague measures, a plague surveillance and monitoring cell functions round the clock. All rat falls are to be immediately reported to this cell (phone 454269 in Madras) or to the Deputy Director of Health Services or the nearest primary health centre. Dead rodents are to be carefully packed in several layers of paper or in plastic bags. The neck of the bag should be tied to prevent the escape of fleas. The bag should then be placed in an empty box or tin and packed with cloth or cotton to prevent leakage of any fluids. The box should then be labelled giving details of when and where it was found and forwarded to the cell.

According to Dr. N. C. Appavoo, Additional Director, Department of Public Health and Preventive Medicine, "The prevailing chaos is due to the time lapse between the recognition of the problem and responding to it systematically. It will take a mere fortnight to get the epidemic under control with weapons like tetracycline at our disposal." Meanwhile, rats are being trapped and screened for plague antibodies and vehicles are being fogged with pesticides to eliminate fleas.

Rat flea surveys are carried out to assess flea indices which will indicate the effectiveness of spraying operations. The average number of *Xenopsylla cheopis* fleas per rat is used to foretell the potential explosiveness of the situation, during an outbreak.

It may be vital to desist from importing plague metaphors from the past if we are to deal effectively with this epidemic. Evoking bleak images and the odour of death and devastation may hamper sensible efforts to put a system in place to combat the epidemic. ■

Is your blood red enough?

A recent Health Ministry study shows that over a lakh Indian women die each year due to anaemia. **Dr SHANTI B. RANGWANI** provides a few tips on how to improve your energy levels

IN THE Third World, where female nutrition levels remain low, anaemia is one of the main causes of fatigue among women. In India, an estimated 83 per cent of the adult female population would qualify as anaemic. Anaemia or iron deficiency means that the blood does not have enough haemoglobin, the oxygen-carrying iron compound that gives human blood its characteristic red colour. With reduced oxygen availability, the body is unable to burn off sugar to produce enough energy, and a study has proved that on an average, anaemic women could stay on a treadmill for eight minutes less than normal women.

An unbalanced and low iron diet depletes iron reserves as does the consumption of devitalised refined foods and over-processed foods lacking in life-giving ingredients. Iron may have nothing to do with energy production directly, but it is a mineral crucial to the transport of nutrients and oxygen as it is one of the chief components of the haemoglobin molecule. Iron is difficult to absorb — a person can absorb no more than 2 mg a day. Thankfully, it is also difficult to eliminate.

Iron deficiency is generally found among young women with menstrual problems and among those who have been continuing with a faulty eyesight, poor memory, general body weakness, frequent dizziness, fatigue, shortness of breath on exertion, headache, and depression.

Except in the case of heavy bleeding, anaemia doesn't come about overnight. To overcome it, supplements are essential but so is a proper diet.

- Common foods rich in natural organic iron are wheat, brown rice (rice with husk), green leafy vegetables, cabbage, carrot, beet, tomatoes, and spinach. Apples, being rich in iron, arsenic and phosphorous are recommended. Other fruits rich in iron are bananas, grapes, dates and peaches.
- A small but essential amount of copper contained in apricots and almonds acts along with iron and vitamins as a catalyst in the synthesis of haemoglobin. Copper also boosts iron absorption.
- Supplements of trace elements, Vitamin B-12 and folic acid are necessary for the proper production of haemoglobin. Folic acid deserves a special mention. In a study in which women received either iron alone, or folate alone, or iron and folate together, only 26 per cent of those who received a single nutrient showed a rise in haemoglobin.
- Foods like mangoes, raisins, red beets, spinach and lettuce supply a good form of vegetable haemoglobin.
- One cup of freshly-sprout-

prove that on an average anaemic women could stay on a treadmill for eight minutes less than normal women.

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Iron deficiency is generally found among young women with menstrual problems and among those who have been continuing with a faulty diet for some months. Heavy blood loss due to serious injury, or ailments such as piles and heavy menstruation can also lead to anaemia. Even normal periods drain iron, pregnancies sap it, and weight-reducing diets cut down its intake.

Anaemia can also be a result of sustained emotional strain and anxiety, which affect the production of hydrochloric acid essential for the assimilation of proteins and iron. Again, a variety of drugs, such as aspirin and steroids, if taken in excess, can destroy beneficial intestinal flora and this in turn hampers the assimilation of certain vital vitamins and minerals, including iron. Vitamin E, especially, is very sensitive to the effect of drugs, and the absence of this vitamin leads to poor blood quality.

The normal level of haemoglobin in a person is 15 gm per 100 cc of blood. Since haemoglobin is the oxygen carrier of the body, adequate levels are vital for respiratory and metabolic efficiency. Lack of haemoglobin can make you look haggard and can also lead to premature wrinkles. The absence of a vital blood ingredient like haemoglobin also results in slow clotting and in slow healing of wounds, weak

in iron are bananas, grapes, dates and peaches.

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- Foods like mangoes, raisins, red beets, spinach and lettuce supply a good form of vegetable haemoglobin.
- One cup of freshly-sprouted *moong* seeds, taken early morning on an empty stomach, also helps. Alternatively, make an emulsion of black sesame seeds by grinding them and adding water. To this, add just a dash of milk and jaggery. Take half a cup on an empty stomach every day.
- Though many naturopaths ask anaemics to eschew fasting, microscopic examination of blood before and after fasting has shown an overall improvement in the quality of blood after fasting.
- Ayurveda offers the most comprehensive cure for anaemia. Special Ayurvedic iron preparations are humanised, non-toxic iron oxides, prepared by repeated incineration of iron, as well as by cooking it in various herbal substances. As iron supplements weaken the digestion, they should be taken with compensating herbs such as ginger and cinnamon to improve digestion. Good formulas are the famous *shatavari* and the *ashwagandha* compound. *Chyavanprash* has also been used for curing anaemia for thousands of years.
- Two glasses of carrot and spinach (*palak*) juice in the ratio 3:1 every day with breakfast are good for anaemics. ■

Annexure-III

List of sub-g[illegible]

1. Tuberculosis

Dr. S.P. Pamra, Hony.Advisor, TB Association of India, New Delhi.

Dr. G.A. Panse,
Joint Director (Planning, Development and Evaluation).
Dental College Building, BOMBAY

Director, N.T.I. Bangalore (Karnataka)

Dr. S.P. Gupta,
ADG(TB) Dte.GHS.,New Delhi.....CONVENOR

2. Malaria, Kala.azar, Japanese Encephalitis, Filariasis

1. Dr. A.N. Raichowdhuri, Director, NICD, Delhi

Dr. P.K. Rajagopalan, Director, VCRC, Pondicherry.

Dr. S.K. Sharma, Director of Health Services, Haryana

Dr. S.N. Saxena, Director, CRI, Kasauli (HP)

Dr. G.K. Sharma (*).....CONVENOR
Dr. C.K. Rao (**) .....CONVENOR

(*) Director, NMEP for MALARIA and
(**) Deputy Director(H) for other Diseases.

3. Diarrhoeal diseases

Dr. S.K. Sengupta, DDG(P), Dte.GHS, Nirman Bhavan, New Delhi

Dr. K.B. Banerjee, DADG(Diarrhoeal), Dte.GHS, New Delhi

Dr. K.C. Nandy, Asstt. Director of Health Services(Malaria)
Dte. of Health Services, Writers' Building Calcutta

Dr. S.C.Pal, Director, NIC α ED, P-33, CIT Road Scheme XM, Calcutta-700010.

4. Sexually Transmitted Diseases and Yaws

Dr. Dharam Pal, Advisor (STD), Dte.GHS, New Delhi

5. Guineaworm

NICD, Delhi.

6. Measles α Polimyelitis

Dr. T. Jacob John, Prof. α Head, Deptt.of Virology and Immunology, CMC Hospital, VELLORE-632004.

Dr. K.H. Dave, Director, Enterovirus Research Centre, Haffkine Institute, BOMBAY-400012.

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7. Rabies control

Dr. V.R. Kalayanaraman, Director, Pasteur Institute, Coonoor.

8. Vaccines, Production and requirement

Dr. K.H. Dave, Director, ERC, Bombay
Dr. V.R. Kalyanaraman, Director, Pasteur Instt. Coonoor
Dr. S.N. Saxena, CRI, Kasauli (HP)
Dr. T. Jacob John, Vellore.
Dr. Indra Bhargava, Dy. Commissioner(MCH) Min. of Health and F.W., Nirman Bhavan, New Delhi.

Dr. S.K. Sengupta, DDG(P), Dte. GHS..... CONVENOR.

9. Typhoic and Intestinal parasites

Prof. A.K. Chakravarti, Prof. of Epidemiology AIIαPH, Calcutta - 7000073.

10. Viral Hepatitis - NICD, Delhi

11. Epidemiological services

Dr. S.K. Sengupta, DDG(P), Dte.GHS, Nirman Bhavan, N.Delhi
Dr. Mahendra Singh, Director, CBHI -do-
Dr. Harcharan Singh/Dr. N.K. Sinha
(Jt. Advisor(H) (Dy. Advisor(H), Planning Commission New Delhi.
Dr. Rajyalakshmi, Director, Institute of Preventive Medicine and Lab. Services, HYDERABAD(AP)

Dr. G.A. Panse, Joint Director of Health Services (PDE) Bombay.
Dr. A.N. Raichowdhuri, Director, NICD, Delhi.

Dr. A.K. Chakrabarti, Professor of Epid. AIIαPH Calcutta.....CONVENOR

12. Environmental Sanitation and Industrial Health

Dr. B.B. Chatterjee, Director, National Institute of Occupational Health, AHMEDABAD(Gujarat)

Dr. B.B. Sunderesan, Director, NEERI, NAGPUR

Dr. K.J. Nath, Prof. of Environmental Sanitation, AIIαPH, Calcutta.....CONVENOR

13. Prevention of Blindness

Dr. Madan, Mohan, Advisor (Ophthalmology) Govt. of India, Dte. GHS, Nirman Bhavan, New Delhi.

14. Leprosy

Dr. K.C. Das, ADG(Leprosy) Dte.GHS
Nirman Bhavan, New Delhi-110011.

3. Financial inputs during sixth plan.

4. Results of evaluation.

5. Health Programmes which have made spectacular/ adequate progress.

6. Reasons of increasing or stable incidence/prevalence of some diseases and remedial measures suggested for improving the situation.

7. Changes in the strategies, if any, with justification (backed up by pilot trials, research studies or experience inside or outside the country).

8. Components that are required as vertical health programme(s) set up and those that can be integrated with horizontal health services.

9. Resources required for the seventh plan period commensurate with the performance and impact objectives.

10. Goals/targets that are related to control of communicable diseases as mentioned in the national health policy.

Indicators:

	Current level	1985	1990
Infant mortality	125(1978)	(105)	(87)
Crude death rate	(14)	(12)	(104)
Pre-school child (1-5) mortality:	(24)	(20-24)	(15-20)
Maternal Mortality rate	4-5	3-4	2-3
Leprosy: (% disease arrested cases out of those detected)	20	40	60
Tuberculosis (% disease arrested cases out of those detected)	50	60	75
Blindness (incidence %)	1.4	1.0	0.7

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Annexure-II

Guidelines for preparing Seventh Plan proposals in respect of control of communicable diseases and Blindness.

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The following facts be kept in mind

A. The National Health Policy accepted by the Government of India envisages to provide universal, comprehensive, primary health care services, relevant to the actual needs and priorities at a feasible cost.

B. The 20-point programme of the Prime Minister includes - Water supply, sanitation, tuberculosis, leprosy control and Blindness.

C. The Government of India isa signatory to the declaration 'Health for all by the year 2000 AD'.

D. Development of primary health care system in the country, so that the planning and implementation of health programmes where feasible is through the organised involvement and participation of the community.

Status Paper

1. Review of the infrastructure as will be existent at the end of the VI Plan period with a view to consider for their continuation during the VI Plan period.

2. Review of the existing health programmes in the light of mid-term appraisal of VI Plan.

3. Approach to VII Plan and identification of thrust areas for VII Plan.

4. Improvement of communicable diseases surveillance/ services.

5. Identification and initiation of new disease control/ eradication programmes.

6. Strengthening of institutions/organisations in order to

   a) develop trained manpower for the programmes
   b) undertake applied research based on feedback for the programme implementing agencies
   c) assist in problem solving :
   d) undertake periodic independent evaluation of the programme.

Sub-group reports may focus on the following:-

1. The problem as it exists today and before the implementation of disease control measures if any.

2. Year of commencement of disease control.

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7. Dr. K.H. Dave, Director, Enterovirus Research Centre, Haffkine Institute, Bombay.

8. Dr. T.Jacob John, Prof. & Head, Deptt. of Virology & Immunology, CMC Hospital, VELLORE-632004.

9. Dr. C.K. Rao, Deputy Director (H) NICD, Delhi.

10. Dr. C.M. Habibullah, Prof. of Gasteroenterotology, Institute of Medical Sciences, Osmania Medical College & Hospital, HYDERABAD-500012(AP).

11. Dr. B.B. Sunderesan, Director, National Environmental Engineering Research Institute, Nagpur-440020.

12. Dr. C.R. Krishna Murti, MADRAS (Tamilnadu)

13. Dr. S.C. Pal, Director, National Institute of Cholera & Enteric Diseases, Calcutta-700010.

14. Dr. S.K. Sharma, Director of Health Services, Haryana - CHANDIGARH

15. Dr. G.A. Panse, Joint Director of Health Services(PDE), Dental College Building, BOMBAY

16. Dr. B.B. Chatterjee, Director, National Institute of Occupational Health, Meghani Nagar, AHMEDABAD-380016.

17. Dr. Dharam Pal, Advisor, STD, Dte. GHS, New Delhi.

18. Dr. K.J. Nath, Professor of Environmental Sanitation, AIIH&PH, Calcutta

19. Dr. Harcharan Singh, Joint Advisor (Health), Planning Commission, New Delhi.

20. Dr. S. Sriramachari, Addl. DG, ICMR, New Delhi.

CO-OPTED MEMBERS

1. Dr. A.K. Chakraverty, Professor of Epid. AIIH&PH, Calcutta
2. Dr. Mahendra Singh, Director, CBHI, Dte.GHS, New Delhi.
3. Dr. V.R. Kalyanaraman, Director, Pasteur Institute,Coonoor.
4. Dr.(Miss) Jotna Sokhey,DADG(EPI),Dte.GHS, New Delhi
5. Dr. S.K.Sengupta,DDG(PH), Dte.GHS, New Delhi.
6. Mr. M.S. Madhava Rao, Senior Research Officer, Planning Commission, Yojana Bhawan, New Delhi.

Annexure-II

Terms of Reference of the Working Group on control of Communicable Diseases and control of Blindness

(i) To assess the present status regarding prevalence/ incidence of communicable diseases like malaria, filaria, tuberculosis, leprosy and diarrhoeal diseases and the arrangement for monitoring thereof:

(ii) To examine the strategies adopted in the 6th plan for control/eradication of these diseases and the operation thereof in the field situations and to advise how deficiencies, if any, in the strategies or operations could be rectified and the programmes made more result-oriented and cost effective, keeping in view the long term goals for the control/ eradication of these diseases in the health policy statement and to achieve Health for All by 2000 A.D.

(iii) To identify the additional manpower and training needs and advise to what extent they could be fitted into the ongoing health sectors programmes and to what extent additional training programmes would be necessary:

(iv) To identify the areas of research thrust and development of appropriate technologies and their application to strengthen the ongoing programmes towards the objective of health for all by the year 2000 A.D.

(v) To quantify the requirement in the 7th five year plan of financial and material resources for effective control/eradication of these diseases and define the respective roles in financing and implementing these programmes.

Members of Working Group

Chairperson - Shri P.K. Umashankar, Addl. Secretary (Health)

Convenor - Dr. A.N. Raichowdhuri, Director, NICD.

Members

1. Dr. Madan Mohan, Advisor (Ophthalmology) Govt. of India, Dte. G.H.S., Nirman Bhavan, New Delhi-110001
2. Dr. G.K. Sharma, Director, NMEP, 22-Sham Nath Marg,Delhi
3. Dr. S.P. Gupta, ADG(TB), Dte.GHS, Nirman Bhavn, New Delhi
4. Dr. S.P. Pamra, Hony. Technical Advisor, TB Association of India, New Delhi.
5. Dr. K.C. Das, ADG (Lep), Dte.GHS, Nirman Bhavan, New Delhi
6. Dr. M.S. Nilakantha Rao, Bangalore (Karnataka).

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DIS-1.

REPORT OF THE WORKING GROUP ON CONTROL OF COMMUNICABLE DISEASES AND CONTROL OF BLINDNESS

National Institute of Communicable Diseases,
22-Shamnath Marg, Delhi-110054.

Report of the Working Group on Control of Communicable Diseases and Control of Blindness.

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Foreword.....

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Foreword

The Planning Commission, vide their letter No.HLH. 2(2)/83, dated the 18th August,1983 constituted eight groups for the formulation of proposals for the 7th five year plan, which included the group on control of communicable diseases and control of blindness. The terms of reference and composition of this group are given in Annexure-I.

The members of the Working Group were requested to prepare the status papers on their specialities within the guidelines developed (Annexure-II) in accordance with the 20-point programme and the National Health Policy approved by Parliament.

These status papers were presented and discussed in detail in the first meeting of the working group held on 28th and 29th November,1983. On the basis of discussion, 14 sub-groups were formed to prepare draft proposals on the identified areas. In case of few subjects, single officer was assigned this task. The list of sub-groups is given in Annexure-III.

The second meeting of the working grcup was held on 17th and 18th January,1984 to review the draft proposals presented by the sub-groups/officers who were assigned the tasks. The proposals for the different programmes - ongoing and new were discussed in depth and suggestions were made by the members to further modify the proposals. A Drafting Committee was constituted to prepare a comprehensive document in the light of suggestions made submitted the draft report that was finally adopted in the meeting held on 29.2.84 and 1.3.1984. I must thank the members of the working group for their unstinted cooperation and involvement. A special word of thanks is due to Dr.A.N. Raichowdhuri, the convenor for his untiring efforts and hard work in giving a final shape to our proposals.

I have great pleasure in submitting the report of the working group for consideration of the Planning Commission.

P.K. UMASHANKAR
Additional Secretary (Health) and
Chairman of the Working Group on
Control of Communicable Diseases
and Control of Blindness.

I. Introduction

The Constitution of India envisages the raising of the level of health of the people as among its primary objectives by ensuring adequate opportunities and facilities.

The health infrastructure has been expanded through planned development during the previous plan periods and now a fairly extensive net work of primary health centres, sub-centres, dispensaries, hospitals etc. is functioning in the country. The problem of communicable diseases is a major public health problem. Some of the communicable Diseases that were controlled, for example, malaria, kala-azar, cutaneous leishmaniasis etc. are again posing a serious threat to the health of the people. The infant and child mortality rate in the country is still high compared to developed countries. Majority of these deaths are due to preventable communicable diseases.

In view of the Prime Minister's directive - "The need of many should prevail over the need of a few", it is imperative to make the health services responsive to the needs of many. The Prime Minister's new 20-point programme lays emphasis on control of communicable diseases which are sapping the vitality of the nation. The National Health Policy document rightly draws priority attention to nutrition, prevention of food adulteration, water supply and sanitation, environmental protection, immunization against preventable diseases etc. Indeed, attention to these areas will undoubtedly go towards effective control of communicable diseases and is in tune with the Nation's commitment to health for all by 2000 AD.

II. Current situation

Before the 6th plan period, the control programme was mainly directed against diseases like smallpox, malaria, tuberculosis, leprosy, filaria, venereal diseases, trachoma and cholera. The country has been able to achieve eradication of smallpox, substantial reduction in morbidity and mortality due to malaria and as a collateral benefit, virtual elimination of plague, kala-azar and cutaneous leishmaniasis. The reduction in mortality due to cholera and control of explosive epidemics was also achieved. This is reflected in the reduction of infant mortality rate (161 to 120), reduction of death rate (27.4 to 14.8) and increase in average life expectancy (30 to 54 years)

Encouraged by the results achieved, the disease control programmes were extended during the 6th plan period to cover other conditions as well as to expand the scope of the ongoing programmes. Accordingly, the cholera control programme was re-designated as diarrhoeal diseases control, trachoma control as prevention of blindness and venereal disease control as prevention of sexually transmitted diseases. The DPT and TT immunization were incorporated in the Expanded Programme on Immunization.

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The current situation regarding the five major National health programmes are reviewed below:-

1. Leprosy

About 400 million people live in areas where the prevalence of the disease is 5 and above per 1000 population. The estimated number of cases in the country is about 4 million, out of which 20% cases are of infectious type, 25% have some sort of physical deformities and about 20% belong to child age groups. About 0.4 million cases are detected additionally every year and about 0.3 million cases are discharged from the list as cured or dead. Till 1977, the programme was run as 100 per cent centrally sponsored scheme under category I. From 1978-79 to 1980-81, it was converted to category II scheme with financial responsibility being shared between centre and state on 50:50 basis. During this period it was observed that achievements and progress of the programme was tardy and slow. Hence, from 1981-82 onwards, it was reconverted to category I, i.e. 100 percent centrally sponsored scheme by the Planning Commission. The national leprosy control programme was also renamed as national leprosy eradication programme from April 1983 in pursuance of the recommendation of the Swaminathan Committee report.

During the 6th plan period, 15.18 lakh cases have been detected till December,1983 against the target of 17.20 lakhs, out of which 14.31 lakhs cases have been brought under treatment. During the same period, 8.87 lakhs cases have been discharged as disease arrested/cured against the target of 11.10 lakhs. During the same period, 17 leprosy control units have been set up against the target of 15; 202 urban leprosy centres have been set up against the target of 50; 865 survey-education-cum-treatment centres have been established against the target of 200. 64 temporary hospitalisation ward of 20 beds each have been started against the target of 50 and 65 district leprosy officers' unit have been established against the target of 50. 290 other units (reconstructive surgery units, sample survey-cum-assessment units, training centres etc.) have also been established against the target of 233. Figures show that the targets fixed for each of the components have been substantially exceeded as a result of concerted effort made to complete the accummulated backlog of earlier plan period.

The budget provision of Rs.40 crores was made for the entire 6th plan period. Out of this, an amount of Rs.24.07 crores have been utilised till December,1983 to meet the expenditure on plan components under the programme.

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2. Tuberculosis

Fully equipped and staffed district TB centres to undertake district-wise TB programmes in collaboration with General Health and Medical Institutions, have been established in 354 districts of the country. In addition, nearly 300 TB clinics are also functioning and about 45,000 TB beds are available for treatment of seriously sick TB patients.

During the 6th plan, the schemes of establishment of district TB centres and TB beds has been included in the state plan sector, while the schemes of supply of material and equipments/anti-TB drugs have been classified as a centrally sponsored scheme on 50:50 sharing basis between the centre and the states. The scheme of supply of material and equipment/anti-TB drugs to the TB clinics run by voluntary bodies has been classified as 100% centrally sponsored scheme. An amount of Rs.700 lakhs was initially provided for the implementation of these schemes during 6th plan. Upto the end of 1983-84, it is expected that about 1090 lakhs would be spent on the implementation of the schemes. A sum of Rs.1050 lakhs has been provided during 1984-85 and thus it is expected to spend about Rs.2100 lakhs for the implementation of the schemes during 6th plan period against the initial allocation of Rs.700 lakhs. With the inclusion of tuberculosis programme in the 20-point programme, a new thrust has been given for the expansion of the essential activities and targets were laid for the first time for detecting one million TB cases during 1982-83 which was fully achieved. During 1983-84 target has been laid for detection of 1.25 million new TB cases and for conduction of sputum examination of the new chest symptomatics at the primary health centres. During 1984-85, it is proposed to increase the target of detection of new TB cases to 1.375 million cases.

3. Malaria

The incidence of malaria was brought down to 0.1 million by 1965 as a result of malaria eradication programme activities. However, there was resurgence of malaria and in 1976, the incidence was 6.5 million cases which was again brought down to 2.1 million cases in 1982 as a result of implementation of modified plan of operation. During the above period, there was extended coverage of the community for detection of malaria cases as reflected by the increase in the number of blood smears examined from 55 million in 1976 to 62.64 million in 1982. The spread of P.falciparum infection which was posing a serious problem is being tackled with the introduction of a new strategy. There are, however, localised problem of P.falciparum to commonly used drugs. The resistance to DDT and BHC has also been recorded in vectors of malaria in different parts of the country. Against an outlay of Rs.224 crores, the anticipated expenditure is Rs.296 crores during the sixth plan.

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4. Filaria

Physical targets proposed under the programme includes establishment of 38 control units and 187 filaria clinics. Of these so far 21 control units and 57 clinics have been established. 31 million population have been protected under the programme, 26 million urban and 5 million rural, against an estimated of 304 million population (82 million urban and 222 million rural) living in areas known to be endemic.

The National Filaria Control Programme has an approved outlay of Rs.300 lakhs for the sixth plan period to meet the 50 per cent of the material and equipments required for urban filariasis activities and 50 per cent total cost of rural filariasis projects. A sum of Rs.200 lakhs is expected to be spent till the end of the year 1983-84.

5. Blindness

The National Programme for control of Blindness was launched in 1976. The programme envisaged immediate eye care relief to the needy by adopting camp approach and fast development of infrastructure at various levels. Since the inception of the programme the following infrastructure has been developed:-

	VIth plan target	Achievement upto 1983-84.	Expected achievement 1984-85
Mobile Units	80	78	2
Primary Health Centres	2000	1670	330
District hospitals	400	354	46
Medical colleges	60	42	18
Training schools for Ophthalmic assistants	37	35	2
Regional institutions	6	4	2

In 1982, the Govt.of India set up a working group under the chairmanship of Dr.M.S.Swaminathan. This group suggested speedy augmentation of services at various levels with an object to reduce the incidence of blindness from 1.4% in 1975 to 0.5 by 2000 AD. These recommendations included development of eye banks in each medical college, eye collection centres at each district centre, district mobile units, setting up of ophthalmic cells in major states and encouragement to voluntary sector both for eye camp and for augmentation of institutional eye care facilities.

During the 5th plan period, the financial allocation for the programme was Rs.5.6 crores and during the 6th plan Rs.22.0 crores. Sixth plan expenditure till 1983-84 has been Rs.16.60 crores. Allocation for the financial year 1984-85 is Rs.7.5 crs.

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Mid-term appraisal

The mid-term evaluation of the 6th plan programme with respect to malaria, tuberculosis, and control of blindness revealed the following trends -

a. The incidence of malaria declined from 6.5 million cases in 1976 to 2.1 million cases in 1982. The spread of P. falciparum infection which was posing a serious problem is being tackled with the introduction of P. falciparum containment programme as a new strategy.

b. The treatment regimens in respect of tuberculosis and leprosy were modified to reduce the duration of treatment through short-term chemotherapy and multi-drug regimen respectively.

c. With regard to control of blindness, ophthalmic facilities have been strengthened at various levels and 7.8 lakhs of cataract operations have been done in 1982.

III. Broad issues emerged

Based on the brief review attempted above and taking into consideration the mid-term appraisal of the Planning Commission as also the terms of reference, the broad issues that emerged during the working group discussions for consideration in the seventh plan proposals are as follows:-

a. The on-going disease control programmes, viz. Malaria, Filaria, Tuberculosis, Leprosy, Sexually Transmitted Diseases, Diarrhoeal Diseases and Poliomyelitis etc. be continued and strengthened to benefit the large segment of population who are affected mostly and scope of introducing innovative measures and appropriate technology should be considered.

b. Primary health care system should be optimally utilised for comprehensive health care and for better disease surveillance and control in view of the national health policy and the commitment of the nation to 'Health for All' by 2000 AD.

c. Diseases which could be eradicated or reduced to a great extent with the existing technological knowledge, namely yaws, guineaworm, rabies should be considered.

d. Emerging/re-emerging health problems like viral hepatitis, japanese B encephalitis, kala-azar, acute respiratory illness in children below 5 years' should receive attention.

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e. Necessary research infrastructural facilities should be developed/augmented to meet the challenge of future needs of control of communicable diseases.

f. For effective control/eradication programme, inter-sectoral collaboration should be ensured - (i) for development of modern bio-technology and (ii) improvement of environmental sanitation and industrial hygiene.

g. Self-reliance in respect of production of vaccines, drugs, chemicals and planned development of ancillary industries needed for the purpose should be achieved through inter-sectoral collaboration.

h. Effective implementation, monitoring and evaluation of various disease control programmes should be ensured through development of epidemiological services.

IV. Approach to issues

Keeping in view the broad issues outlined above, a rational approach should include -

a. Effective and efficient implementation and strengthening of multipurpose workers' scheme is essential pre-requisite for successful implementation of communicable disease control programmes in the 7th plan period.

b. On-going disease control programmes should be strengthened to produce impact on the disease incidence.

c. Identifying new and emerging health problems and working out strategies for their control/prevention through national/regional programmes.

d. Steps be taken to establish a permanent mechanism of the nature of cabinet sub-committee and also a health advisory committee for achieving 'Health for All' by 2000 AD with administrative authority for establishing inter-sectoral collaborations with other ministries such as works and housing, agriculture, irrigation, environment, social welfare, education, industry, science and technology, chemical and fertilizer and information and broadcasting.

e. Vaccine production and quality control should be taken as a major plan project in providing inputs (financial and material) to central and state institutes with a view to stabilise and diversify

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the production and quality control of diagnostic reagents and immunologicals for disease investigations and for expanded programme of immunization respectively.

f. Establishment of epidemiological services as an integral part of primary health care system for implementation, monitoring and evaluation of various health activities should be taken up as a national programme.

g. Mechanism should be developed for active involvement of the community, allied institutions, voluntary organisations, professional associations and the general medical practitioners in the health care delivery.

h. A built-in health education component in all the progr mmes utilizing all available media including mass media for proper motivation of the community should be incorporated. Each programme should provide not less than 5% of the total outlay for this purpose.

i. Facilities for continued education through pre-service and in-service job oriented training of health manpower should be provided on the job and through the existing institutions and by establishing new institutions. Training of the trainers, should receive due emphasis. Adequate provision should be made for this purpose in the plan programme.

j. Health services research for more effective implementation of the programmes should be taken up. Operational research technique should be adopted.

k. Newer technology including bio-technology need to be introduced for improving the current production technology for further improving the quality of immunodiagnostic immuno-biologicals, drugs etc.

V. Recommendations:-

In view of the issues raised and the approaches suggested, the recommendations of the Working Group with respect to identified areas are given below:-

a. On-going national health programmes, national malaria eradication programme, national filaria control programme, leprosy, tuberculosis, guineaworm eradication, sexually transmitted diseases, diarrhoeal diseases control, prevention of blindness have to be continued with augmented inputs so that the task which have been taken in the 6th plan period are carried forward and new targets set up in the 7th plan period. There

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will be significant reduction in the morbidity/mortality from the current level of malaria, tuberculosis, filaria, diarrhoeal diseases, sexually transmitted diseases during the 7th plan. Guineaworm will be eradicated and preparatory phase for eradication of leprosy will be completed. The production of different vaccine will be coordinated to meet the requirements of the national health programmes.

b. New efforts will be mounted to control and contain the following diseases which are of national and/or regional importance, namely japanese encephalitis, kala-azar, viral hepatitis, typhoid, intestinal parasitic diseases, yaws, measles and acute respiratory illess in children below five years.

c. Establishment of epidemiological services at all levels of health care would be necessary for proper implementation and monitoring. Every programmes should have an inbuilt provision independent evaluation.

d. Effective inter-sectoral coordination need to be established for potable water supply, sanitation, solid wastes, sullage and storm water disposal, water and air pollution control between the ministries of health, works and housing, department of environment and other related organisations. Such collaboration is absolutely essential to make a dent in the control of communicable diseases such as cholera and diarrhoeal diseases, typhoid and intestinal parasites, viral hepatitis, malaria, encephalitis, filariasis etc.

e. A permanent and continuous system of monitoring and evaluation of public water supply system including that in mass transport systems shouldbe introduced all over the country. This should preferably be carried out by the health services departments of the state in close coordination with local governments, public health engineering and other departments concerned with community water supply. This would go a long way in improving the quality of drinking water and would contribute significantly in controlling communicable diseases.

f. Health education component of all diseases control programmes should be given full attention to enlist individual as well as community support. Each programme should, therefore, make provision of not less than 5% of its total outlay for this purpose.

g. Mechanism should be evolved to ensure that the central assistance for implementation of the various national health programmes are utilised for the specific purpose for which the assistance is made.

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h. The 7th plan allocations for various identified programmes should be done as per priority given below:-

i) Leprosy, tuberculosis, malaria, filaria, diarrhoeal diseases and control of blindness should receive high priority;

ii) Development of epidemiological services as a national programme should be taken up in the 7th plan.

iii) Guineaworm and yaws eradication and kala-azar, poliomyelitis and sexually transmitted disease control programmes should be continued/started, where applicable.

iv) A national programme for vaccine production and quality control should be included in the 7th plan.

v) Beginning should be made towards development of new health programmes on viral hepatitis, acute respiratory diseases in children below 5 years, control of typhoid fever and intestinal helminthic infections, measles, rabies and japanese B encephalitis.

The brief description of the proposals in the identified areas, describing the current status, objectives and strategy in the 7th plan proposals and areas of research are given in the next few pages.

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1. National Leprosy Eradication Programme

1.1 Current status - Please refer to page 2.

1.2 Objective and strategy

During the 7th plan period, we expect to detect 1.5 million additional cases and treat about 4 million cases including old and new cases. At the same time about 2 million cases are expected to be discharged from the list so as to gain start towards negative balance. As a result it is expected that by the end of 7th plan, the total number of cases on record will be about 2 - 2.5 million achieving a substantial control of the disease in some districts. This is also expected to be reflected in the reduction in the prevalence rate, deformity rate and new case detection rate.

The strategy in broader aspect will remain unchanged but during the 7th plan emphasis will be given to wider coverage of multi-drug campaign trial in 100 high endemic leprosy districts, intensive health education through all types of mass communication media and community participation, inclusion of welfare and rehabilitation services, introduction of monitoring and concurrent evaluation with periodic and practical assessment of the programme, free supply of specific anti-leprotic drugs. introduction of new training courses for social welfare and managerial skill for senior non-medical supervisors and nursing staff, wider participation of voluntary organisations and international agencies and establishment of new training centres and regional institutes for augmentation of action oriented research both in the field and laboratory.

1.3 Seventh plan proposal

1.3.1 Manpower development

a) Strengthening of Directorate

The office of the programme officer at the centre will be strengthened by giving him additional technical, secretarial and statistical help.

Similarly staff in the office of the state leprosy officer and district leprosy officer will be adequately strengthened.

b) Strengthening of field organisation

To cover the high endemic areas where the prevalence rate of the disease is 5 and above per thousand it will be necessary to provide trained leprosy technicians at the rate of 1 for every 20-25 thousand population, 1 trained non-medical supervisor (NMS) for every 5 leprosy technicians, physio-technician and health educators - 1 each for every 4 such Non-medical supervisors covering a population of

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about 4 lakhs in rural areas and about 4-6 lakhs in urban areas. Other ancilliary staff for secretarial support, supervision, assessment will also be needed.

1.3.2 - Training - Training will be organised through regular and short orientation courses and also by conducting workshops and seminars. There are 41 leprosy training centres including one central and two regional institutes. Six weeks' training for medical officers, 4 months' training for NMS, 6 months' training for para-medical workers, 12 months' training for laboratory technicians, 9 months' for physio-technicians and 2 months' training for leprosy health educators and one year training for Assistant Leprosy Officers will be run during the plan period by providing stipends to the trainees. A few regional training-cum-referral institutes will also be established in the country. Training is multi-drug campaign will also be impacted through holding seminars at district and sub-district level before the district is taken under the campaign.

1.3.3 - Health education - Health education through mass communication and audio-visual aids to be introduced through a specific component to the scheme by involvement of Health education, mass communication and media experts. Specific funds provided at central and state levels for central directorate, state directorate and voluntary agencies can take up action straightway.

1.3.4 - Welfare and rehabilitation - Welfare and rehabilitation of patients will form a specific component of the 7th plan scheme and integrated with case detection and case treatment programme for a meaningful life to the patient in the context of repeal of Leprosy Act and correction of physical deformity. The existing socio-economically dislocated patients will be specially taken care of in addition to those the community.

1.3.5 - Multi-drug treatment - Multi-drug treatment in the form of a district-wise campaign for 3 years for a comprehensive case detection supervised treatment with a view to early cure, preventing deformities, preventing drug resistant germs and achieving interruption of transmission of the disease in the community will be introduced as the main thrust of the programme. 100 such districts having leprosy prevalence rate above 5/1000 prevalence rate will be covered. In addition the benefit of multi-drug treatment will also be provided to patients being treated in indoor institutions having trained medical and laboratory services.

1.3.6 - Monitoring and evaluation

a) The states will be advised to monitor the programme through their State Leprosy Eradication Board. The effective implementation of the programme and adjustments in operations, as necessary, in

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different areas of the state will be made by the State Board.

b) The concurrent evaluation of the programme will be made by the authority who is implementing the programme. This evaluation will be made at least twice a year.

c) Annual and more infrequent evaluation will be done by independent team who are not directly concerned with the implementation.

Attempts will be made to send a central evaluation team once in 2 years to hyper-endemic states for evaluation and making recommendations.

1.3.7 - Material and equipments

a) Equipments, vehicles, microscopes, calculators, projection equipment, duplicator and typewriters will be needed. Construction of clinic building, training centre, hospital wards will also be required.

b) Anti-leprotic drugs and drugs for treatment of reactions and associated complications or other diseases for treatment of leprosy patients will be needed. Laboratory reagents dressing materials, protective shoes and prosthetics will also be required. Drug like Refampicin, Clofazimine are not manufactured inside the country. Hence these have to be imported.

1.3.8 - Financial implications - Funds will be needed for full implementation of the units, established during the 5th plan period and for establishment of some more new units to complete coverage in high endemic areas and to provide technical and supervisory support to lesser endemic areas for introduction of multi-drug campaign. Funds will also be needed to meet operational cost, salary of the staff, supply of drugs, materials and equipment, transport and construction of buildings particularly of functional type and also for staff quarters in tribal, hilly and backward areas where houses are not available on rent.

1.3.9 - Areas of research

i) Vaccine
ii) Operational
iii) Chemotherapy
iv) Chemoprophylaxis
v) Investigation into drug resistance.

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2. National Tuberculosis Control Programme

2.1 Current status - Please refer to page 3.

2.2 - Objective and strategy

To achieve detection of 2.5 million cases per year which will approximately be equal to estimated incidence.

To augment and strengthen the treatment activity so that cure rate rises from 40 per cent to about 80 per cent.

2.3 Seventh plan proposal

The main objective during the 7th plan period would be to continue the expansion and strengthening of TB case finding activities at all levels and arranging supply of anti-TB drugs in sufficient quantities for treatment of diagnosed TB patients.

(a) The following schemes are suggested for implementation:-

i) Establishment of fully equipped and staff district TB centres in thickly populated districts and establishment of mini TB centres with basic minimum staff and equipment in thinly populated districts where there is no such centre;

ii) Establishment of additional district TB centres in 100 thickly populated districts having a population of over 1.5 million;

iii) Replacement of old sets of X-ray equipments with Odelca cameras which have outlived their utility and considered unserviceable or uneconomic for repairs;

iv) Provision of X-ray unit with Odelca cameras to the TB clinics run by voluntary bodies;

v) Replacement of 100 old vehicles at the district TB centres;

vi) Provision of miniature X-ray film rolls in sufficient quantities for use at the equipped district TB centres;

vii) Provision of additional laboratory technicians at the primary health centres where the workload is considered extremely heavy;

viii) Establishment of 2000 TB beds specially in those districts where they are not available or the existing number is insufficient;

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ix) Supply of standard anti-TB drugs to states/union territories/voluntary body run organisations.

x) Introduction of short course chemotherapy drugs regimens containing Rifampicin and Pyrazinamide in a phased manner - 75 districts each year so that by the end of 7th plan about 375 districts in the country are covered under these regimens.

The group recommended that the items at sub-paras (iii); (v); (vi); (ix) and (x) be taken up as 100% centrally sponsored schemes and the remaining may be taken up by the states/union territories under their own budget to quality for central assistance.

(b) The following activities will be taken up as purely central schemes :-

i) Production of health education material;

ii) strengthening of TB sections, Dte.GHS to undertake proper monitoring of the programme and for shouldering additional responsibilities involved.

iii) National TB institute, Bangalore - It is proposed to augment substantially the research and training activities of the institute during the 7th plan period. For this it would be essential to provide additional building blocks, machinery and equipments in various sections, replacement of old vehicles and manpower in various sections of the institute.

3. National Malaria Eradication Programme

3.1 Current status - Please refer to page 3.

3.2 Objectives and strategy

The objectives of the modified plan of operation - NMEP will remain unchanged during the seventh plan period. They are -

a) to prevent deaths due to malaria and reduction in the period of sickness.

b) maintenance of status of industrial development and green revolution due to freedom from malaria, deaths and reduction of morbidity.

c) to consolidate the achievements obtained so far.

To achieve the above objectives, the residual insecticides spray in rural areas as well as in peripheral areas of townships and anti-larval operations in urban areas will continue

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to be adopted. Similarly for detection and treatment of malaria cases, the periodic surveillance on fortnightly basis with microscopic examination of blood smears and administration of anti-malarial drugs will continue to be in force during this period. No major deviation in the technology of malaria control is envisaged during the seventh plan period. But research on operational aspect of Malaria control for developing alternate integrated methods of control will be given high priority.

Special programme for containment of Plasmodium falciparum namely P. falciparum Containment Programme, to prevent deaths and spread of resistant strain of Pl.falciparum to commonly used drugs in new areas will continue with the assistance from SIDA/WHO.

3.3 Seventh plan proposal

3.3.1 - Requirements - The spray and surveillance operation will be continued and the present pattern of assistance may be modified in view of the fact that the surveillance activities will be carried out through multipurpose workers and this should be reflected in the budget which will be earmarked for development of multipurpose workers scheme during the seventh plan period, whether it is decided to be centrally sponsored or the state liability. However, the component for spray operation, i.e. district level and the seasonal staff for spray operations, material and equipment (insecticides, pumps, vehicles and anti-malarial drugs) may be made 100 per cent centrally sponsored as was in force prior to 1979-80.

However, it will be necessary to strengthen the peripheral services by additional staff for supervision of delivery of services to the community, monitoring and reporting under NMEP will also be made more effective by strengthening the services with appropriate staff component. This is all- the more necessary, consequent to introduction of MPW scheme on a horizontal basis and increase in population.

For the above purpose, suitable augmentation of staff, at peripheral, district, state and central level will be effected.

3.3.2 Areas which need research are -

a. Research on operational aspect of malaria control; with a view to develop alternate integrated methods of control.
b. Ecological and control of vectors of malaria.
c. Chemotherapy of malaria.
d. Drug resistance in malaria parasite.
e. Serology of malaria.
f. Cultivation of malaria parasite.
g. Immunological aspect of malaria.

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4. National Filaria Control Programme

4.1 Current status - Please refer to page 4.

4.2 Objectives and strategies

a) To continue the ongoing antilarval measures and detection and treatment of mf. carriers in 177 control units located in the urban areas.

b) To extend filariasis control activities in the form of treatment of clinical cases through the village health guides to the total rural population at risk.

The strategies to be followed are given below:-

The main strategy of the programme in urban areas is to control vector mosquito breeding by carrying out recurrent antilarval measures with chemical larvicides at weekly intervals. These methods are envisaged to control also the vectors of malaria and other mosquitoes. To reduce the source of infection quickly 102 filariasis detection and treatment teams are operating in some control units to treat microfilaria carriers and filaria cases.

The present strategy of detection and treatment of mf. carriers with DEC is not cost effective. The only possible effective method for reducing the filaria disease is by making DEC available under the primary health care system for treatment of clinical cases of filariasis. DEC reduces the frequency of future acute attacks and thereby chronic disease. Pilot studies during the last one year in two endemic areas showed that the village health guides (VHGs) could make DEC available to suspected cases of filariasis without affecting their other activities.

4.3 Seventh plan proposal

4.3.1 - Requirements - Every village health guide or in his absence his equivalent or in their absence multipurpose workers in 158 filaria endemic districts in the country would be trained to detect and treat clinical cases of filariasis with DEC in their areas. Necessary addition would be made in the training manual for village health guides. DEC would be replenished to VHGs periodically. Posts of District Filaria Officers would be created where necessary to entrust coordination and guidance of the programme activities in endemic districts. Total cost of DEC would be borne by the Government of India. The existing NFCP units and detection-cum-treatment centres evolved in urban areas and survey units in endemic states would continue and their cost would be shared between centre and the states on 50:50 basis as for NMEP.

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4.3.2 - Areas for research

a) Operational aspects of control would continue to be identified and studied.

b) Medical social science research.

c) Integrated vector control measures.

5. Control of Diarrhoeal diseases programme

5.1.1 - Current status - Acute diarrhoeal disease is one of the major causes of morbidity and mortality in children below 5 years of age. In India, 13.8% of the total population, i.e. 94 million are in the age group of 0-4 years. Since the average number of diarrhoeal episode is two per child per year, about 188 million episodes of Diarrhoea takes place among the group. 10% of these patients, i.e. 18.8 million need rehydration therapy and 1% i.e. 1.8 million are in the grave risk zone facing mortality and require hospitalisation.

During the fourth five year plan, 46 cholera combat teams were set up in the cholera endemic states and laboratory facilities were augmented. During the fifth plan, the programme was transferred to the state sector. During 1983-84, a provision of Rs.3 lakhs exists for preparation of health education materials. In view of the magnitude of the problem, it is essential that the present diarrhoeal disease control programme should not only continue but requires to be further strengthened in all aspects.

5. .2 - Objectives and strategies - The short term objective is the reduction of mortality through effective implementation of oral rehydration therapy at the peripheral level. This includes production and distribution of the ORS packets, training of medical and para-meeidal health personnel as well as education of mothers and community and operational/ health services research for identification of suitable strategy of implementation. The long term objective of reduction in morbidity is envisaged through provision of safe water and sanitation facilities.

5.3 - Seventh plan proposal - Operational studies at community level have indicated the efficacy of ORS and training of adequate number of health workers, it will be possible to bring down the mortality rate during the seventh plan by 50%.

5.3.1 - Production of ORS packets - Present production of ORS packets is around 5 million per year. This need be increased to 10 million by 1984-85 and 40 million packets

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by the end of the 7th plan, so that atleast 100 packets could be distributed by each village health guide each year.

5.3.2 - Training - About 18,000 doctors working in the primary health centres are to be trained at the district level training courses. This can be achieved during the first two years of the 7th plan. The paramedical staff working at the primary health centres can be trained at the PHC level in batches by the doctors who have already been trained at district level. Training of the state level officers will be arranged at national level. The education of the mothers and the community members are to be arranged through the suitable audio-visual aids on proper feeding of the children, breast, feeding, weaning, personal hygiene etc.

5.3.3 Financial Outlay - Provision should have to be made for purchase of 40 million packets of ORS, development of supply system upto peripheral level, strengthening of diagnostic facilities and establishment of clinical management system in hospitals and other treatment centres plus educational materials and other treatment centres plus educational materials for the community.

5.3.4 - Areas for research

a) Etiology, pathophysiology, mode of transmission, role of safe water supply;

b) Operational research to determine the best means for successful implementation of the programme.

6. National Programme for control of Blindness Summary of VIIth plan proposals -

6.1 Current status - Please refer to page 4.

6.2 - The objective will be implementation of Swaminathan Committee's recommendations and reduce the incidence of blindness from 1.2% in 1985 to 1% by 1990. The strategy will be as recommended in the Swaminathan Committee's report.

6.3 Seventh plan proposals - The VIIth plan proposals are broadly based on the recommendations of the Working Group which aim at -

i) completing the infrastructure at PHC block, Taluka and district levels. It is envisaged that atleast one Ophthalmic surgeon and one ophthalmic assistant should be available for rendering eye care services to population of 50,000.

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ii) Adequate number of eye beds be provided at district hospitals and community health centres with a ratio of 1 eye bed for 20,000 population.

iii) All medical colleges be covered with specialised treatment and diagnostic facility for comprehensive eye care including the development of eye banks.

iv) Adequate training/research facility be created in all the medical colleges in the country.

v) Training facilities for training of Ophthalmic Assistants be augmented to meet the requirement of Ophthalmic Assistants to man all PHCs, Distt.Hospitals, Mobile Units etc.

vi) Voluntary sector be encouraged both for eye camps and for establishment of permanent eye care facilities.

vii) Management and monitoring component of the programme be adequately strengthened.

viii) Intensification of eye health education measures.

ix) Vision research and Bio-Ophthalmic Research for development of research in instrumentation and Bio-Ophthalmics.

x) Ten regional institutes including those already established be established for development and strengthening of sub-specialities, ophthalmic training and research.

xi) Dr.Rajendra Prasad Centre for Ophthalmic Sciences, New Delhi be developed as the National Institute of Ophthalmology to provide technical leadership for planning and implementation of the programme and for development of super specialities, operational and basic science research and manpower development.

xii) Mobile units be established at district level for strengthening preventive and promotive aspects of the programme including provision of services for children screened for ophthalmic care through ongoing school health scheme.

xiii) Ophthalmic instrument workshop be established to provide base for quality control, repairs maintenance of equipment and to provide training to the staff in maintenance and repairs of ophthalmic instruments/equipments.

xiv) Provision of spectacles to cataract operation cases.

6.4 <u>Areas of research.</u>

a. Epidemiological research on cataract, corneal ulcers and nutritional blindness.

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b. Basic science research on cataract and essential ophthalmic drugs.

c. Operational research on mobile ophthalmic health care delivery in rural areas including eye camps and school eye health.

d. Development of ophthalmic instrumentation and implements and corneal substitutes.

7. Development of Epidemiological Services

7.1 Current status - The integration of preventive and curative aspects of health care delivery as a national objective has been identified and acted upon during earlier plan period. It has made steady progress culminating into development of primary health care programme for providing comprehensive health care to the people. But development of epidemiological services as an integral part of primary health care has not been given serious consideration. Without any mechanism for epidemiological services it will not be possible to tackle the various disease problems in the country on horizontal basis.

7.2 Objectives and strategies - The objectives will be to establish the nation-wide epidemiological services where in the pivotal role will be played by the district, state and national levels with a strong organisational set up, with a view to implement, monitor and evaluate various health programmes being delivered through the primary health care system.

In evolving the strategy main considerations will be given to available health infrastructure. For implementing the programme, a two-fold strategy is required vis. administrative and technical.

The administrative strategies will be to a) launch a centrally sponsored scheme; b) appoint a programme officers at the national/and state levels; c) restructuring/reorganising/redefining the job requirements of functionaries at various levels.

The technical strategies will involve a) setting up an organisational structure to meet the requirements of disease surveillance, outbreak investigation and containment, monitoring and evaluation, feedback and health services research; b) ensuring prompt service and availability of rapid diagnostic facilities; c) training of personnel.

7.3 Seventh plan proposal

7.3.1 Organisation and structure - In suggesting the organisational pattern, full consideration should be given to

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the requirements of the epidemiological services at the various levels as defined under technical strategies. It is fully realised that in different disease control programmes, additional manpower has been provided. It is quite possible that the broad staffing structure required for establishment of the epidemiological services may possibly be made partly by suitably restructuring/reorganising and redefining job responsibilities of the various personnel already available at different levels.

(a) National level - As has been pointed out in the strategy, appointment of a programme officer at the national level with appropriate staff will have to be made.

(b) State level - Every state at the headquarters will have a composite epidemiological cell headed by a senior officer suitably trained in epidemiology and supported by statistical, laboratory and other ancilliary components. The state epidemiological cell will have facilities for data collection, processing, analysis and feed back.

(c) District level -

i) District is the implementing agency unit of all health programmes. Each district will, therefore, have an epidemiological wing with surveillance and disease investigation unit and a data processing unit with inbuilt facilities of feedback. This wing will be headed by a suitably trained person in epidemiology;

ii) Community health centre/PHC level - At this level, epidemiological services will be taken care of by imparting appropriate training to all health personnel in the principles and practice of epidemiology and disease control.

(d) Urban population - The Government of India is keen to strengthen the health care services in urban slums and the scheme in that regard has already been finalised. For corporation which have epidemiological wing, the same needs to be streamlined and in view of the government's decision to provide comprehensive health care to the urban slum population. Additional inputs may have to be provided after necessary appraisal of the situation. For corporations with limited epidemiological services, the same is to be organised on the same lines as envisaged for a district.

(e) Hospitals - Hospitals are an important source for morbidity and mortality data but these data are rarely available for analysis and thus valuable information is missed. It is, therefore, necessary to have medical record sections in all district hospitals. The medical

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record technician with the assistance of statistical assistant will compile and analyse the data and submit the report to the Medical Superintendent for onward transmission to district epidemiological wing.

7.3.3 Materials and equipment

Prompt services are the key to success for effective epidemiological service. Therefore, provision of transport facilities with POL, rapid data processing with the help of electronic computors, adequate stationeries, typewriters, duplicating machines, display boards etc. and rapid diagnostic kits for outbreak investigation should be given adequate budgetary support.

7.3.4 Training

Training requirements of the programme is categorised under two heads, viz. continued education through inservice training programme and continued education in improving professional skill by encouraging personnel to take professional examination, such as the one taken by the National Board of Examiners. Training is to be provided to three broad levels of health personnel, viz. managerial level, mid-level and lower level. To impart this training, national and state training institutions will be identified and strengthened.

7.3.5 Areas of research

One of the important functions of epidemiological services will be to conduct health services research for improving planning, better implementation, monitoring and evaluation of disease control programmes. It is obvious that the activity cannot be efficiently discharged without adequate research into the dynamics of health care delivery. Consequently resources will be required to foster and sustain this activity.

8. Guineaworm Eradication Programme

8.1 Current status - Dracunculiasis or guineaworm disease is endemic in seven states, namely Rajasthan, Madhya Pradesh, Maharashtra, Andhara Pradesh, Karnataka, Gujarat and Tamil Nadu in that order. The disease being rural in distribution occurs in drier areas with low rainfall and deep water table where step wells, ponds or tanks form drinking water sources. About 13 million people living in about 13,000 villages distributed in 85 districts are exposed to this disease. This disease is transmitted by drinking only contaminated water.

8.2 Objectives and strategies - The objective is to interrupt the transmission and ensuring disease free status for a continuous period of three years before eradication is declared.

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The current strategy of provision of protected drinking water, health education of communities, chemical treatment of unsafe water sources, surveillance and training would continue.

8.3 Seventh plan proposal.

8.3.1 Provision of safe water - Funds towards provision of safe water to guineaworm affected villages without such a source would continue to be a high priority programme under rural water supply programme. Chemical treatment of unsafe water sources, case searches and printing and distribution of health education material should also be provided for.

9. Yaws Eradication Programme

9.1 Current status - No reliable estimate of extent of yaws problem in the country is available. Anti-yaws teams are currently working in Orissa and Andhra Pradesh and resurgence of yaws has been reported from Madhya Pradesh. The problem needs attention as it is technically and administratively feasible to eradicate the disease. Yaws mainly affects the population living in tribal areas. In view of the Government's commitment to uplift the socio-economic dondition of the tribal people the programme should receive adequate support.

9.2 Objectives and strategies -

a) Active search operation be carried out in erstwhile endemic areas to delimit the problem and identify population at risk.

b) Training of medical and paramedical personnel in yaws case detection, diagnosis and treatment.

c) Strengthening of laboratory facilities where needed.

9.3 Seventh plan proposal

The essential requirements are provision of funds for undertaking the following activities:-

a) One mobile team will be established for 0.5 million population at risk.
b) Functional responsibilities of the organisational structure at each level. Arrangement for treatment with PA for each detected case has to be made.
c) Training of personnel.

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10. Kala-azar Control

10.1 Current status - Kala-azar was virtually eliminated from the country as a collateral benefit of insecticides spray under NMCP/NMEP. A large outbreak occurred with many deaths in several areas of Bihar in 1977. Number of cases and deaths reported from Bihar since 1977 is as follows:-

	Cases	Deaths
1977	18589	229
1978	41953	62
1979	25473	28
1980	12623	18
1981	13801	37
1982	9956	31
1983 (Upto Nov)	9986	91

Imported sporadic cases of kala-azar were also reported from Assam, J & K, Tamilnadu, Gujarat and Delhi during the recent years. Large number of indigenous cases are also reported from some districts of West Bengal during the last two years. From the trends seen it appears likely that disease may spread to other areas particularly in the eastern region unless special efforts are made to contain this.

10.2 - Objectives and strategies -

a) To reduce the incidence and level of transmission of kala-azar.

b) To prevent deaths.

c) To prevent the spread to adjoining unsprayed districts.

Strategies include -

a) Early detection and treatment of kala-azar cases by establishing good surveillance system.

b) Timely indoor residual spray of DDT in all the affected areas.

c) Training professionals and paramedicals in kala-azar control.

10.3 - Seventh plan proposal

10.3.1 Strengthening of NICD - The NICD would be strengthened to take up the additional responsibility of guiding this programme and research;

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10.3.2 Supply of materials - Timely supply of DDT in adequate quantity would be ensured to the states of Bihar and West Bengal. Adequate funds would be made available to the states to ensure appointment of spray staff and availability of drugs.

10.3.3 Areas of research

a) Role of PKDL in the spread of kala-azar.

b) Methods for predicting the areas that would be affected during the next one/two years.

c) Establish the presence and nature of animals involved in the spread of kala-azar, if any.

11. Poliomyelitis control programme

11.1 Current status - Polio vaccination programme has been introduced as a part of national immunization programme from 1979. During 1982-83, 37 lakh children benefitted with three doses of oral polio vaccine. The National Sample Survey carried out by the DirectorateGeneral of Health Services in 1981 and 1982 has estimated that every year, 1.5 lakh children get poliomyelitis in the absence of vaccination programme. The survey has also indicated that it is as serious a public health problem in rural areas as in the urban areas. 85% of the cases get the disease before three years of age.

11.2 Objectives and strategies - Considering the residual disability due to poliomyelitis, it is proposed to have faster expansion of the polio vaccination programme. It is proposed to cover 100% of the new-borns by 1987-88 as a part of the Expanded Programme for immunization. The proposed vaccination target, percentage of coverage of new-born and requirement of vaccine (including booster dose) year-wise during the 7th plan is given below:-

Year	No.of beneficiaries (in lakhs)	Percentage of new-born.	Requirement of vaccine (in lakh doses)
1985-86	140	60	500
1986-87	170	76	600
1987-88	228	100	800
1988-89	233	100	800
1989-90	238	100	800

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Three doses of oral poliovaccine at a minimum interval of one month starting at the age of 3rd month will be followed. A booster dose will be given 12 to 18 months after primary vaccination. In addition to the fixed centres strategy (clinics) annual outreach campaigns will be organised for wide coverage.

11.3 Seventh plan proposal

11.3.1 Augmentation of poliovaccine production in the country

The need of polio vaccine for the programme at present is met by importing bulk concentrate separately for type I, type II and type III. It is expected that the indigenous production of oral polio vaccine will start at Haffkine Biopharmaceutical corporation Ltd.(HBPC) Bombay from 1985, with an initial annual production capacity of 5 million doses, which will gradually increase to 20 million doses. Thus most of the requirements of the programme has to be met by importing bulk concentrate for the present. A second unit for blending and importing of imported oral poliovaccine will be organised to meet the expanding requirement of the programme. In the field, arrangements for maintenance of cold chain by providing not only equipments but also ensuring their maintenance has to be made. The staff has to be provided with mobility so that all the children get three doses of oral polio vaccine by first birth day. This will involve community participation to be achieved by large scale health education programme using various mass media. The financial outlay will be included in the MCH budget of Department of Family Welfare.

11.3.2 Research needs -

a) Usefulness of killed poliovaccines;
b) Blending of killed poliovaccine with DPT manufactured in India.

12. Sexually transmitted diseases (STD)

12.1 Current status - The number of cases of STD reported to Dte.General of Health Services during the last five years is given below:-

Year	Total number of STD cases
1978	4,79,687
1979	5,69,676
1980	7,12,262
1981	5,57,992
1982	4,60,939

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From the figures, it will be seen that for the years 1978-80, there has been a rising trend in the number of cases seen and treated at the various government run centres. For the years 1981-82, there has been a decline. This decline probably is due to the late submission of the statistics by the various centres.

12.1.2 A small fraction of the patients suffering from STD report at hospital/treatment centres and thus the above figures do not indicate the exact nature of the problems. The majority of STD cases are syphilis, chancroid, gonorrhoea, lymphogranuloma venerieum and granuloma inguinale.

12.2 Objectives and strategies - The objective of reducing the incidence of STD in the country is proposed to be achieved through -

a) serological screening of all pregnant women-attending, antenatal clinics run by states, union territories, voluntary organisations and civil bodies.
Equipments - V.D.R.L. testing are being provided to district hospitals and later to primary health centres.

b) Training of medical and para-medical personnel on STD in five regional training centres.

c) Training of laboratory technicians in five reference laboratories.

d) Provision of health education about STD, to the target group - students community, labour force, industrial workers, general public patients - patients attending family welfare clinics etc.

e) Establishment of a nodal centre - D.G.H.S. for monitoring coordination and dissemination of scientific information to various centres involved in the STD control programme.

f) Assess the magnitude of the problem of STD through f-our survey and mobile STD units - Evaluation of the programme.

12.3 Seventh plan proposal - It is envisaged to arrange for detection of more cases suffering from STD at PHCs, district hospitals, civil hospitals. The above will be achieved by strengthening the regional training centres, reference laboratories and survey-cum-mobile units.

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13. National Programme for Vaccine Production

13.1 Current situation - India is self sufficient in the production of DPT, DT, TT, BCG and typhoid vaccine. The need for polio vaccine is met by import of bulk concentrate of polio vaccine, separate for type I, type II and type III. It is then diluted, blended and empouled for distribution to the field. The working group on maternal and child health have worked out the year-wise tentative vaccination target and on that basis estimated the annual requirements of different vaccine.

13.2 Objectives and strategies - The objectives are to

a) make the country self-sufficient and self-reliant in its vaccine requirement for expanded programme of immunization;

b) induct modern biotechnology for production of better quality of existing vaccines and introduction of new vaccines which are epidemiologically necessary for the country;

c) establish an independent quality control laboratory at the national level;

The strategies will be to

a) start a national programme on the same line as national disease control programmes for vaccine production and quality control in order to develop and d-iversify the production in the state and central institutions;

b) channelise on a national basis the international aids available in this area;

c) separate the final quality control and certification for release of immunobiologicals from the production establishments;

d) augment training facilities for providing trained manpower at various levels in this field.

13.3 - Seventh plan proposal

13.3.1 DPT vaccines, DT and TT vaccines - The tables below present the likely availability of DPT, DT and TT vaccines from public sector institutes by providing additional inputs, during the various years of seventh plan.

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i) Likely availability of DPT vaccine from public sector institutes with additional inputs during 7th plan (in million doses).

Institutes	1985-86	86-87	87-88	88-89	89-90
CRI Kasauli	13.0	16.0	16.0	18.0	18.0
PII Coonoor	7.5	10.0	12.0	13.5	15.0
HBPC Bombay	7.0	will increases in phases			10.0
Shortfall	25.3	22.1	23.4	23.9	23.7

(This shortfall will be made up by private sector supplies. The production capacity of DPT from Bengal Immunity not known)

ii) Likely availability of DT vaccine from public sector institutes with additional inputs during 7th plan (in million doses).

Institutes	1985-86	86-87	87-88	88-89	89-90
CRI	16.0	16.0	13.0	13.0	13.0
PIIC	5.0	6.0	7.5	8.0	10.0
HBPC	6.0	6.0	6.0	6.0	6.0
Shortfall	2.7	2.8	-	-	-

(This shortfall will be made up by private sector institutes).

iii) Likely availability of TT vaccine from public sector institutes with additional inputs during 7th plan (in million doses).

Institutes	1985-86	86-87	87-88	88-89	89-90
CRI	22.0	22.0	22.0	22.0	22.0
PIIC	5.0	5.0	7.5	8.0	10.0
HBPC	8.0	Will increase in phases			14.0
State institutes	9.0	9.0	9.0	9.0	9.0
Shortfall	14.8	21.1	26.2	26.0	20.0

(Shortfall will be made up by private sector supply).

The production capacity of Bengal Immunity is not known.

13.3.2 - BCG Vaccine - The National requirements of the BCG vaccine during the 7th plan period can be met adequately by the BCG vaccine institute at Madras by providing extra facilities for filling and freeze-drying of vaccine.

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13.3.3 Poliomyelitis vaccine (oral) - This programme is of national importance and at present the oral poliovaccine is imported in bulk and blended by only one source (HBPC) in the country. It is highly desirable that an alternate source be organised at the earliest. At the same time, steps should be taken to augment the existing blending and bottling facilities in the BHPC to meet the need. Indigenous production of oral poliovaccine has commenced in HBPC and 5 million doses of oral poliovaccine is expected to be available by 1984-85. It is also expected that this unit will be able to step up the production during the 7th plan period to 20 million doses.

13.3.4 Measles vaccine - It is proposed during the 7th plan period to commence the immunisation against measles starting with a coverage of 27% and achieve atleast 73% coverage at the end of 7th plan.

At present the measles vaccine is not produced in the country and hence has to be imported. The approximate cost of measles vaccine is around Rs.16/- per 10 dose vial.

A measles vaccine production unit is being proposed with CRI Kasauli under the 7th plan and the project reported is under the preparation for envisaging a production of 2 million .

13.3.5 Rabies vaccine The Pasteur Institute Coonoor has submitted a project proposal for 7th plan to the Ministry of Health & FW. towards production of one million doses of the tissue culture vaccine in vero-cells per annum at a reasonable cost for the use of common man. This project should be provided with sufficient plan aid to go into production.

13.3.6 Japanese encephalitis vaccine - The unit has been established at the CRI Kasauli under Indo-Japanese collaboration for production of this vaccine during 7th plan period. The unit will produce 2 million doses per annum.

13.3.7 Quality control of vaccines - Immediate steps should be taken to set up an independent new institute for standardization and quality control of immunobiologicals in the country and also to meet the needs of providing trained manpower in this important field. A project report in this regard is being drawn up by the Vaccine Production Board.

13.3.8 Areas for research -

a. Towards production of newer vaccines like MMR vaccine, hepatitis vaccine, etc. for the future.

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b. Towards application of modern bio-technology in vaccine production.

c. In view of the trend towards alternative strategies in control of poliomyelitis using injectible poliovaccine particularly in combination with DPT vaccine for development of quadraple vaccines, steps need to be initiated to develop expertise and infrastructure towards such a goal in the public sector.

14. Viral hepatitis surveillance

14.1 Current situation - Viral hepatitis is one of the leading causes of morbidity and mortality in the country. Presently the diagnosis is mainly based on clinical information. According to the central bureau of health intelligence, 180974 cases and 228 deaths were reported in 1980. In view of the deficiency in reporting of cases, these figures are perhaps the tip of the iceberg of the real extent of the problem.

Based on epidemiological investigations conducted in different parts of the country, it has been observed that Viral hepatitis is expanding health problem and affect both urban and rural areas.

14.2 - Objectives and strategies - The objective is to begin a new health programme for broadly delimiting the problem viral hepatitis both in urban and rural areas through surveillance and laboratory confirmation.

In order to effectively tackle the problem, the following strategies will be ---- as under:-

a. identification of viral hepatitis surveillance centres in different parts of the country and providing them with diagnostic facilities. Such centres may be identified in the central as well as state sectors.

b. to develop laboratories at medical colleges and district level to act as sentinal centres for surveillance.

c. to make available suitably trained personnel to man these laboratories and centres.

d. strengthening of research capabilities of these centres to undertake research in the priority areas including surveillance and control activities.

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14.3 Seventh plan proposals.

. Resource allocation will be required for the following activities:-

14.31 Strengthening of viral hepatitis centres - At present 9 such centres have been identified in the country. But due to paucity of funds, adequate facilities could not be provided in these institutions and as such they have not been in a position to function as desired. During the 7th plan, it is proposed to augment the facilities in these centres with manpower and equipments for effective functioning. In addition it is also proposed to identify more centres for the purpose.

14.3.2 Expert committee meetings - An expert committee will be set up to develop/model training modules on viral hepatitis surveillance and laboratory diagnosis.

14.3.3 Training - Training courses will be organised and conducted to provide trained manpower to these centres.

14.3.4 Area of research -

a. delimination of hepatitis problem in urban and rural population;

b. Dynamics of three hepatitis virus transmission in the context of socio-economic and cultural settings.

c. Operational strategy for control of the disease.

15. Acute Respiratory Illness (ARI)

15.1 Current situation - ARI is a great killer particularly in early childhood. This constitutes a major cause of illness in infants and pre-school children. Very little is known about the current status of ARI. A number of viruses, bacteria, chlamydia and other agents are the causative agents. Of this expanded programme of immunisation takes care of Diphtheria and Pertusis and it also envisages some action against measles during seventh plan. For the remainer, practically nothing is being done. It is necessary for some specific remedial actions to be integrated with the primary health care programme.

15.2 - Objectives and strategies - The objective will be to reduce mortality and morbidity in children below 5 years of age.

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The strategy will be (a) training of medical and paramedical personnel for early detection of clinical cases and their domicillary treatment; (b) development of referral system for cases that cannot be attended at home; (c) immunisation of target population ; (d) strengthening of five regional laboratories for providing diagnostic laboratory services of acute respiratory illness and (e) health education of mother and the community.

15.3 Seventh plan proposal

15.3.1 Training - Training courses will be organised for medical and paramedical officers in case detection and treatment of service for patients and materials for laboratory diagnosis.

15.3.2 Drugs - Drugs required for the first line of treatment will be provided to all PHCs.

13.3.3 Laboratory services - Identification of five regional laboratories - Five regional laboratories, each one in central, eastern, western, northern and southern zones will be identified and strengthened with equipment, personnel and necessary reagents for laboratory diagnosis for acute respiratory illness. Rapid diagnostic kits will also be made available.

15.3.4 Health education - Health education material will be prepared and distributed to all concerned.

15.3.5 Research needs - (a) development of local rapid diagnostic kits for acute respiratory illness should be taken up with urgency. The micro organisms responsible for acute respiratory illness in the children below 5 years should be identified for better understanding of the transmission dynamics of these diseases; (b) Simple and cost effective treatment schedule for these diseases will be searched.

16. Typhoid control programme

16.1 Current status - In India, the incidence of typhoid fever is high due to inadequate provision of protected water supply and proper sanitation services. The exact incidence of typhoid fever in India is not known. Reports received by central bureau of health intelligence (CBHI) indicate occurrence of three lakh cases and eight hundred deaths every year. However, the acqual incidence is certainly much higher. Considering the public health importance control of typhoid fever has been included under the expanded programme of immunisation. Vaccination with bivalent typhoid vaccine is being carried out for primary school entrants.

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16.2 Objectives and strategies - The objective will be to (a) provide medical aid/relief to the needy through primary health care system; (b) protect by active immunization children, adolescents and young adults; (c) improvement of food and personal hygiene through extensive health education measures.

The strategy would entail (a) strengthening of the existing primary health care system with provision of antityphoid drugs; (b) necessary training of medical and paramedical personnel for case detection and treatment methodology of health education of the family/community, particularly those employed in food establishments; (c) development of simple field laboratory tests for confirmation of clinical diagnosis and detection of carriers; (d) immunization of the tarbet groups and (e) testing of water samples and education of food handlers.

16.3 Seventh plan proposal - Adequate budgetary provisions will have to be made for the following activities:-

16.3.1 Drugs - Drugs for treatment of typhoid cases will be provided to the districts and PHCs.

16.3.2 Immunization - Typhoid immunization will be extended to the target groups.

16.3.3 Training - Training of PHC medical and paramedical officers in clinical detection of typhoid cases, their laboratory confirmation and reporting will be undertaken.

16.3.4 Inter-sectoral collaboration - Inter-sectoral collaboration will be aimed for providing safe drinking water and improvement of environmental sanitation for monitoring, quality of water supply, establishment of laboratory facilities for testing water samples in each district will be required.

16.3.5 Areas of research -

a. Develop rapid diagnostic kit to detect resistant strains of chloremphenical.

b. Develop simple laboratory test for quick confirmation of diagnosis.

c. Evaluation of effectiveness of the available vaccines.

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17. Intestinal parasitic disease control

17.1 Current status - Common intestinal parasites in the country are Entamoeba histolytica, Giardia lamblia, Ascaris, lumbricoides, Ancylostoma, doudenale, Necator americenus and Trichuris trichiura. Prevalence of intestinal parasitic diseases in India is underestimated due to limitations of laboratory facilities. It is estimated that prevalence rate of intestinal parasitic diseases particularly in areas with inadequate environmental sanitation is 50% or more. Intestinal parasitic diseases should therefore, be considered as priority problems.

17.2 Objectives and strategies - The published data on the subject during the last 30 years indicates the magnitude of the problem of intestinal parasite and the relative frequency of different species of parasites are available only from 21 states/union territories. The magnitude of the problem in the other states/union territories would be delimited. The NICD would undertake stool sample surveys in the states from where no information is available.

No data exists on relative effectiveness of different methods of control of this infection in communities.

The control of intestinal parasitic infection would be dovetailed with the primary health care system. The laboratory techniques and treatment schedule would be standardized. The medical officer and paramedical staff would be educated in detection and treatment and also to ensure community participation.

17.3 Seventh plan proposal - Suitable budgetary provision will be required for the following activities:-

17.3.1 Drugs - Provision of adequate quantity of drugs to health institutions to treat persons with different species of parasites.

17.3.2 Training - Preparation of manual for PHC, medical officer and staff to help in diagnosis and treatment of different species of parasites.

17.3.3 Safe drinking water - Provision of safe water sources envisaged to be achieved during the 7th plan period would also help towards control of this group of infection.

17.3.4 Areas of research -

a. to develop methods for quick and easy laboratory diagnosis.

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b. to determine the relative effectiveness of different methods of control.

c. to develop methods of surveillance of these infections.

18. Measles control programme

18.1 Current situation - The attack rate of measles is 100% with clinical measles in about 75%. The case fatality rate is between 1 and 3 per cent. In other words, 15 million cases of measles with about 1.5 to 2.4 lakh deaths occur every year in the country. The disease leads to ill health of children by - - , precipitating malnutrition and secondary infection.

18.2 Objectives and strategies - A pilot study in 36 medical colleges in India indicate the necessity for introduction of measles vaccination in the national immunization programme. Measles vaccine is safe, effective and gives prolonged immunity with one injection, which may be considered as life long. It is suggested that measles vaccination be introduced in a phased manner by giving priority to those areas where the case fatality rate is high and large size outbreaks occur periodically. To achieve a high coverage rate, in addition to services through fixed centres, it will be necessary to organise annual outreach campaign. Vaccine will be given to the most susceptible group of children, 9 months to 2 years of age.

18.3 - Seventh plan proposal - At present, measles vaccine is not produced in the country. Measles vaccine has to be imported to initiate the programme. The CRI Kasauli is proposing a project for measles vaccine during the seventh plan with a production capacity for 20 lakhs doses by 1990. The Ministry of Chemicals and Fertilizers is examining the proposal for establishing a viral vaccine production unit, which will produce measles vaccine. The cost of measles vaccine is expected to be about Rs.1.50 per dose in a lo-dose vial. The area and population to be covered by auxillary mid-wife has to be decreased so that this additional workload of measles vaccination can be integrated with the general health services.

19. Rabies control programme

19.1 Current status

1. There is at present no comprehensive rabies control programme executed in our country. In India, Agriculture ministry has launched Canine Control Programme during the Sixth Plan period.

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2. Atleast 15,000 human deaths from rabies occur every year in India but even this recording is too low, since the recorded deaths are based on very limited reporting.

3. In India, atleast 5 lakhs persons bitten by presumably rabid animals undergo antirabies treatment annually.

4. About 55.6% of the persons bitten by proved rabid animals contract the disease after refusing the treatment. Atleast 39% of the animals suspected to be rapid contain the virus in the salivary glands and are capable of transmitting the diseases in nature.

5. The bitting animal involved in most instances in our country is the dog (95.4%). In wild life jackles, foxes, wolves, mangoose, bandicoots etc. are involved.

6. Atleast two types of inactivated antirabies vaccine for human use are produced in our country - the 5% BPL inactivated vaccine and 5% phenolised vaccine. Both are prepared from the brain of sheep. The total quantity of the vaccine produced is around 200 lakhs ml. of BPL vaccine and 175 lakhs ml. as phenolised vaccine. These vaccines carry a risk of post-vaccine neuro paralytic accidents at the rate of 1/5000 to 1/12000. Neural vaccines also have a shorter shelf life of 6 months.

7. At present a small quantity of tissue culture antirabies vaccine is imported in our country at a very high cost which is beyond the reach of common man. This vaccine, of course, is non-reactogenic, highly effective and given as 5 to 6 doses of 1 ml. each. The shelf life of this vaccine is long since this is freeze-dried.

8. Pilot project studies on the feasibility of producing this vaccine indigenously is being carried out at Pasteur Institute of India with WHO/UNDP aid. The results are encouraging. Project report for production of VERO cell tissue culture rabies vaccine at a reasonable cost within the reach of common man during the 7th plan at this institute has been drawn and submitted to the Min.of Health & F.W., Govt.of India.

9. At present the country does not have adequate supply of potent single dose tissue culture vaccine for the immunization of the pet dogs and other pet animals.

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19.2 Objectives and strategies

The objective will be to reduce the incidence of rabies in the country, to produce potent tissue culture antirabies vaccine for immunization of man and animals and expansion of rabies laboratory diagnostic facilities in the country for better surveillance of the disease.

The strategy followed will be elimination of stray dogs and cats, strengthening of one or two institutions, producing antirabies vaccine with facilities for freeze dried tissue culture antirabies vaccine, identification of laboratories for establishing rabies diagnostic facilities, health education and inter-sectoral collaboration with state governments and other ministries, namely ministry of agriculture, education and information and broadcasting.

19.3 Seventh plan proposal - Plan provision will be required for carrying out the following activities under the programme:-

19.3.1 Interministerial cooperation for setting up of field infrastructure.

Mechanism will be evolved to ensure cooperation and collaboration between Ministry of Health and Ministry of agriculture to identify areas where ministry of health's input will effectively supplement field infrastructure already existent in the ongoing cannine rabies control programme of the ministry of agriculture.

19.3.2 Vaccine production

The Pasteur Institute of Coonoor and another vaccine producing institute in the country will be identified for production and quality control of freezedried antirabies vaccine for man and animals required for the programme.

19.3.3 Expansion of laboratory diagnostic facilities

All medical colleges and ID hospitals in the country will be strengthened with this service.

19.3.4 Health education

Health education measures emphasising the need of prompt treatment of animal bite cases, regular immunization of pet dogs and beneficial effect of elimination of stray dogs will be intensified to enlist community support for the programme. For sustaining the continued interest of the community, mass communication media of Ministry of Information and Broadcasting will be involved.

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19.3.5 Areas of research

a. Operational research on canine rabies control by education/immunization of dogs under local conditions in different parts of the country.

b. The main reservoir species in wild life must be determined before the campaign for eradication of the disease in wild life is launched. Representative surveys are urgently needed. After determining the main reservoir species, the most effective way of halting the disease by reducing the species population etc. have to be formulated.

c. Surveillance efforts must be concentrated on the main species by estimation of population density at regular intervals which might forecast the potential danger and intensity of rabies outbreaks in wild life.

d. Efficacy of oral immunoprophylaxis of wild life population using oral rabies vaccine in baits.

e. The areas of research outlined require establishment of a permanent mechanism with administrative authority for ensuring inter-sectoral collaboration such as with the Ministry of Agriculture, Forest department and like.

20. Japanese encephalitis (JE) control

20.1 Current situation - Outbreak of JE have been reported from West Bengal, Uttar Pradesh, Bihar, Andhra Pradesh, Tamil Nadu and Karnataka. The disease has a high case fatality rate of about 50 per cent and the survirors are always permanently disabled.

20.2 Objectives and strategies - The objective will be to develop a better surveillance system for timely treatment and control measures in the event of an outbreak.

The strategy followed will be -

a. early detection and treatment of cases would continue. For this laboratory facilities would be created/augmented at the national, regional, state levels.

b. Production and use of JE vaccine.

c. Dte. NMEP would continue to support control measures against vectors.

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d. Malaria or communicable diseases bureaus in the State health directorates continue to undertake measures of prevention and control with the existing resources.

e. Antilarval measures are not practical and vaccine available is of limited effectiveness. However, high risk groups would be brought under vaccination.

20.3 Seventh plan proposal

20.3.1 Institution strengthening - Central research Institute, Kasauli has planned to produce the vaccine by 1986. Epidemiology division of NICD be strengthened to take up early detection and forecasting.

20.3.2 Areas of research -

a. Institutions with facilities would continue to investigate the outbreaks of JE and to develop reliable methods for forecasting of outbreaks.

b. Studies would be developed to forecaste the outbreaks. Vector surveillance and sero-surveillance form important components.

c. Relative effectiveness of different methods of control, namely immunization, personal prophylaxis, surveillance and anti-mosquito measures would be determined.

Medical apathy terrorises patients

Staff Reporter

New Delhi

IN THREE incidents of negligence and high-handedness reported from various parts of the city over the past few days, a woman died at the operation table of a quack, a patient jumped to death from the second floor of the Deen Dayal Upadhyay Hospital and the owners of a private nursing home beat up a patient's father for refusing to pay "exorbitant" medical bills.

In the first incident, a 35-year-old woman who was six months pregnant, died on the operation table of a quack at Mangolpuri in north-west Delhi on Monday while undergoing an operation to terminate her pregnancy.

Additional Commissioner of Police (northern range) B K Gupta said that the quack Vijaya Lakshmi has been arrested and charged under sections 304 A and 314 for causing the death of Jarawati.

Section 304 A pertains to death caused by a rash and negligent act and section 314 deals with death caused by an act done with intent to cause miscarriage."

Mr Gupta said that Vijaya Lakshmi, who claims to have passed class XII and to be a graduate in the Ayurvedic system of medicine, was neither qualified nor had the requisite facilities in her clinic to perform an abortion on a woman in the advanced stage of pregnancy. Even otherwise, an abortion in such an advanced stage is fatal, he added.

The ACP said that Jarawati, the wife of a factory worker living in Mangolpuri, was already a mother of four.

Realising that they could not afford to have the fifth child, the couple went to Saar Clinic run by Vijaya Lakshmi and asked her if it was possible for an abortion.

The quack allegdly told them that it was very much possible and admitted Jarawati at her clinic. The woman died of excessive bleeding during the operation.

In the second incident, a 32-year-old rickshaw-puller Ram Babu, undergoing treatment at Deen Dayal Upadhyay Hospital, jumped to death from the second floor of the hospital on June 17, allegedly due to the hospital staffs's apathy towards his worsening condition.

Chief Medical Officer of the DDU Hospital Dr C R Viswas confirmed the incident but denied that there was any negligence on the part of the hospital authorites. "The man was a little disoriented," he said. The police has not registered any case since no complaint has been lodged by any of the patient's relatives.

Ram Babu had reported to the hospital with symptoms of malaria and pneumonia on June 16 and was admitted to the casualty department. He was later shifted to ward 8 on the second floor.

Finding that no one was attending on him, he reportedly started shouting for attention on the following day, but was instead scolded by the nurses.

Frustrated by the apathy, Ram Babu then jumped from the floor. He sustained multiple fractures and was referred to Safdarjung Hospital, where he died on June 18.

In the third incident, a 28-year-old man was beaten up and critically injured on Sunday by the doctor and two of his brothers who were running a private nursing home at Sarai Rohilla in north Delhi.

The man was thrashed reportedly after a dispute over an "exorbitant" medical bill for his three-year-old daughter's treatment.

The police said that Manoj Kumar, a Sarai Rohilla resident, had taken his daughter to the Dewan Nursing Home after she fell down while playing and sustained a cut on her chin.

The doctors put three stiches on the chin and handed a bill of Rs 2,200 to Mr Manoj Kumar.

When Mr Kumar objected to the bill, saying it was exorbitant, the nursing home staffers insisted that they would let him take away the child only after the bill was cleared. This led to an altercation following which Dr B S Dewan and his brothers allegedly attacked Mr Kumar and hit him on the head with iron rods.

Mr Kumar sustained head injuries and was rushed to Bara Hindu Rao Hospital, where he is stated to be in a critical condition. The Sarai Rohilla police have registered a case against the three brothers and are investigating.

Man jumps to death frustrated over hospital insensitivity

Quack performs abortion on 6-month pregnant woman

Doctor thrashes patient's father for not paying bill

AIDS victim's death sets alarm bells ringing in Meerut village

People suspect quack used contaminated syringe

S Raju
Meerut

A PANIC button has been pressed at a village in Meerut following the news that a young villager died of AIDS acquired after the local quack administered a shot using a contaminated syringe.

Many of the villagers who went to the quack for treatment now recall having been given injections. They fear contaminated syringes might have been used on them too.

The village is situated on Baghpat-Chandinagar road and is hardly 40 kilometers from Delhi. Chandinagar is an important base of the Indian Air Force.

After Jogendra's death on May 25 this year, the almost sleepy village has woken up to the danger of AIDS. There was no knowledge of the virus until then.

The village is home to more than 20,000 people, majority of whom belong to the Jaat community. The village comes under the Baghpat constituency which is represented by former Cabinet Minister Ajit Singh in Parliament.

Jogendra, whose painful death was witnessed by the villagers, was the second son of Chaudhary Jaipal Singh.

Since his death the villagers have only this to talk of. Lal Singh, a farmer in the village, said that Jogendra died a painful death. Jogendra was almost bed-ridden fro seven months and did no work.

Once known as an active boy he slowly became dull and sick. Nothing seemed to work and nobody could do anything to cure him. Sardar Singh and Master Sukhpal also had the similar things to say. They also quizzed this reporter about the cure of the disease and the source of the infection, as if trying to confirm the truth in the village gossip.

When the reporter told them that contaminated syringes could transfer the infection from one carrier to another, their faces paled. Lal Singh, Sardar Singh, Sukhpal and Sanjeev said that many villagers had been given injections by the quacks with used syringes.

They said that Jogendra was suspected of carrying the AIDS virus since last six years.

It was only confirmed in February this year when he was admitted to All India Institute Of Medical Sciences (AIIMS) following a deterioration in his health from November 1996.

The villagers said he was treated for various diseases by the local quacks who are known to use same syringes on many patients. Jogendra, they suspect, was infected during when given a shot with a contaminated needle.

The village pradhan, Mr Dhanpal, accused the quacks of using syringes without sterilisation. "The villagers are in a panic and everybody is afraid of being an AIDS carrier," he said.

However, Jogendra's father completely ruled out that his son was treated by any local doctor. But a village doctor, Rajendra, refuted the claim and said that in 1994 he treated Jogendra when he suffered from some skin allergy and gave him two shots of penidule with the disposable syringes. The doctor said: "How can we claim that local doctors were aware of infected syringes three to four years ago when they are still in the practice of applying same syringe on different patients without proper sterilisation.

The name of a certain quack practising in the village is also doing rounds.

He is known to be in the habit of using syringes and other apparatus many times over.

When quizzed, the quack said he was properly sterilising the syringes. He also said he had never treated the deceased. Later, he recanted and admitted to treating Jogendra once at his father's request.

It is alarming that most of the quacks practising in the village have assumed the titles of doctor.

Mr Dhanpal charged the Health Department for the situation and said that due to the negligence of the health officials the MBBS doctor of the primary health centre visits the village once or twice a month.On the other hand, the Jogendra's father claimed that his son became infected after being given a blood transfusion at the Narendra Mohan Hospital followed an accident in 1994.

Then in November 1996 his health started failing. Then the family consulted a doctor in Ghaziabad where Jogendra's elder brother is a transporter. But Jogendra's condition did not improve. Someone suggested that he should be taken to Apollo Hospital in Delhi.

Then they contacted Mr Ajit Singh in Delhi, who fixed an appointment with Dr Ajay Niramjan of Apollo Hospital. Dr Ajay thoroughly investigated the case and suggested the patient be removed to AIIMS.

Jogendra was at AIIMS for 11 days before the doctors disclosed his state. They also told his family that he would not survive for long.

He died on May 25 leaving behind two daughters and a widow. Jogendra's father said the widow's blood has been sent for ELISA test and the report was awaited.

He said that he is thinking of getting the rest of the family examined too.

The villagers too are looking for help to test their blood.

Meanwhile, Chief Medical Officer (CMO) Dr Rajendra Prasad has ordered a survey of the village. Dy CMO Dr J Prasad has been given the task of monitoring the operation. The nodal officer of the AIDS control program in the district, Dr S K Srivastava, is to assist him.

TB spreading on wings of ignorance

Rahul Gupta
New Delhi

TUBERCULOSIS IS a great leveller. It torments not only people living in a maze of gullies in the Walled City but also those living in air-conditioned comfort in south Delhi.

A general physician in Ballimaran area of the Walled City Dr Talat Aziz says, "I get at least five or six new cases of TB every month. There is a very high incidence of TB and even higher is the number undiagnosed cases." He adds that these cases act as a reservoir for spreading the disease.

Another private practitioner in Sitaram Bazar, Dr Chitra Astavans, says that almost 35 per cent of the patients coming to her suffer from TB.

The crowded lanes of Old Delhi harbour an astonishing number of people, crafts and industries. Lanes are so narrow that shoulders brush and hands collide if two people pass by.

Tucked away in these lanes are various industries. Carpenters hammering away at stubborn nails, printing presses reeking of paper and ink, sewing machines whirring, artisans making mirror frames and many other mechanical works.

Factories operate in single rooms that also serve as accommodation for families. With such overcrowding, one can imagine how much air-sharing is taking place. And TB is an airborne disease.

While trudging in the gullies one comes across various medical practitioners. One "doctor" who has been practicing in Ballimaran has not received a single TB patient in the last three years. He believes that TB is on the decline. The gullies of old Delhi shelter quite a few such "doctors".

Dr Aziz stresses that in the Walled City, the culprits are poor hygiene and paan chewing. "All the walls carry red marks of pan and zarda. A person suffering from TB can easily spread the disease by his incorrigible habit of spitting pan all over."

The TB bacteria has extended its reach even to the posh localities. Secretary general of the Delhi Medical Association (DMA) Dr G S Grewal, who practices in New Friends Colony, says that hygiene is coming down even in posh areas. "One can find a big garbage dump right in the middle of a posh locality. And poor hygiene is aggravated by slums on the fringes."

Finding a solution to TB is a tall order. Fifty per cent of the people in India are infected by the microbacterium TB. Doctors say that these people run a high risk of succumbing to the dreaded disease.

According to senior consultant in the Department of Respiratory Medicine at Apollo Hospital Dr Rajesh Chawla, "The body's defence mechanisms in these 50 per cent cases are able to overcome most of the bacteria. Still, a few remain in the body in dormant form. During their lifetime, whenever the resistance of these people declines, the dormant bacteria multiply and cause tuberculosis. Stress and tension, smoking, alcoholism and even diabetes overpower body resistance and the TB bacteria take over."

Dr Grewal says, "Because of pollution and the rise in suspended particulate matter (SPM), the air has become heavier. As heavy air moves slowly, the movement of bacteria slows down and more TB bacteria are inhaled."

He also observes that "we have relapses occurring after ten years. People who took incomplete treatment a decade back are now reporting with tuberculosis." He adds that earlier bacteria were not as strong but now bacteria strike fast and relapses occur faster.

Dr Chawla says that he comes across nearly 50 TB patients in a week. "Almost all of them are from the affluent sections. Not all are new cases, a lot of them are referral patients."

The biggest hurdle for doctors is that people still don't regard TB as a curable illness. It is considered a stigma even in educated families.

Dr Aziz says, "Initially we find it difficult to convince people that they are suffering from TB, and later on to convince them to continue the treatment till its full course."

Medicine is so effective that symptoms of TB disappear within no time, which wrongly encourages a patient to give up the medicine.

Doctors say that education has to be imparted on a war footing not only to the masses but also to the upper classes.

The Government will have to provide free medicine, whatever the cost.

This also means that even MDR medicines, though prohibitively expensive, will have to be provided.

No country is safe from threat of infectious diseases: WHO

NEW DELHI: There is no country in the world which is safe from the threat of infectious diseases and the need of the hour is sustained effort to control these diseases effectively and prevent epidemics, warns World Health Organisation (WHO).

On the occasion of "World Health Day" to be observed on Monday, Dr Uton Muchtar Rafei, regional director of WHO's south-east asia region (SEAR), told a news conference here on April 4 that member countries of SEAR should develop effective warning mechanisms by improving their disease ssurveillance systems and be ready to respond to control disease outbreaks.

"Today there is a growing concern at national and international levels about the problem of emerging and re-emerging infectious diseases and new diseases such as new strain of cholera and HIV infections which are the leading cause of death and morbidity in these regions," Dr Rafei said.

"As the countries move towards the 21st century, the need for comprehensive and appropriate strategies for controlling infectious diseases has become more urgent than even before," he added.

For this year's World Health Day, who has chosen the theme "emerging infectious diseases global alert — global response."

Dr Rafei said rapid growth of population, unplanned urbanisation, disturbance of environmental balance and the increased speed and frequency of travel within and between countries are some of the important factors contributing to the emergence of these infectious diseases.

"The situation has worsened due to the growing phenomenon of resistance of micro-organisms to antimicrobial agents and of vectors of pesticides," he added.

Dr Rafei said the success achieved in smallpox eradication and the considerable progress made in polio and guineaworm eradication should not create a sense of complacency since new and emerging diseases in the region pose daunting challenges.

"Diseases such as malaria and tuberculosis, once thought to have been controlled, threaten the lives of millions of people in the region. Plague and kala-azar which were on the verge of eradication have resurfaced. New diseases, such as a new strain of cholera and HIV infection are spreading rapidly in some countries in the region," he said.

Replying to a question on mad cow disease, scientifically called movine spongiform encephalopathy (MSE), Dr Rafei said, "This possibly links with a form of brain disease in humans. A new variant of creutzfeldt-jakob disease (CJD) has not been reported in south-east Asia."

However, he said, "India and Thailand have reported sporadic cases of CJD but due to non-occurrence of its transmissible agent the disease has not occurred."

Ruling out the entry of yellow fever in India, he said, it never came to India as it was a disease of western Africa. Though, as it has been moving towards eastern Africa, yellow fever may move towards the south-east asia region (SEAR), he apprehend.

On another question, he said, hanta virus infection causing haemorrhagic fever with renal syndrome (kidney disease) has been reported only from Myanmar and Sri Lanka. Antibody studies by the National Virology Institute suggests, "no threat to Indians", he added.

Dr N K Shah, WHO-representative to India, said the re-occurrence of diseases like malaria, dengue, cholera and plague in INdia were due to a number of reasons including environmental degradation, pollution, weakness in public health infrastructure, economic factors, education level and drug resistance on causal strains. (PTI)

Taiwanese blame China for epidemic

TAIPEI (Taiwan), April 20.

If truth is the first casualty of war, trust must be the second, especially between old enemies like mainland China and Taiwan. To prove it, plenty of Taiwanese apparently suspect that the epidemic of hoof-and-mouth disease now ravaging their pork industry could have been an act of economic sabotage by China.

"A lot of people here have been saying they believe the mainland sent this disease over here deliberately," said Ms. Shen Yi, a radio talk show host.

Was it just a coincidence, she asked, that the outbreak began at about the time the Dalai Lama visited? Beijing views the exiled spiritual leader as a separatist promoting Tibetan independence from China, just as it accuses Taiwan's President, Mr. Lee Teng-hui, of promoting Taiwan's independence.

When two adversaries have spent so much time in the last 50 years eyeball to eyeball from armed ramparts on either side of the Taiwan Strait, it is no surprise that the arrival of disaster on Taiwan's shores has incited some dark thoughts.

Tens of thousands of Taiwanese pig farmers are looking for someone to blame for the billions of dollars' worth of devastation caused by the outbreak, which is leading to the greatest animal slaughter on the planet since "mad cow" disease struck Britain.

So far, more than 1.5 million of Taiwan's 14 million pigs have been destroyed, and more than 1 million more are scheduled for execution. Some experts are guessing that half or more of Taiwan's pig population will be wiped out by the plague, which could take a year or two to arrest fully. The disease is very contagious and deadly to livestock but harmless to humans.

The industry, which generates $3.5 billion a year in business, much of it for supplying Japan's voracious appetite for pork, has ground to a halt, endangering the jobs of 100,000 workers raising hogs and 600,000 in related industries.

Last year, the Japanese market bought the meat from 6 million pigs in Taiwan, representing 95 per cent of the island's pork exports. But Tokyo froze all shipments last month, and Singapore and South Korea followed suit.

"It is just devastating," said Mr. Wesley Yu, a local assemblyman in southern Taiwan's largest city, Kaohsiung. "And the Government has handled things poorly. But no one will lose their job. In Taiwan culture, no one likes to admit that they made a mistake."

Opposition legislators accuse the Government of being unprepared and incompetent in fighting the viral onslaught. A month into the crisis, Taiwan's agricultural bureaus have failed to get adequate supplies of vaccines to farmers, even though vaccines are abundant in international markets.

Some Opposition politicians say the Government's handling of the crisis will be a factor in crucial local elections later this year. In those elections, candidates who forsake claims to the mainland could seize a majority of municipal and county offices.

Mr. Lee, worried that the blame might settle on the shoulders of his governing Nationalist Party, went before the television cameras last week to munch on a feast of pig knuckles and declare, "Eating pork is healthy and safe." But his constituents weren't buying. Pork prices have declined more than 60 percent since the epidemic broke out.

In an unsubtle attempt to point the finger, Mr. Lee said Taiwan would have to do a much better job stopping the smuggling of pigs from China, as if that were the only place that the contamination could have come from. Malaysia and the Philippines have also had hoof-and-mouth outbreaks of late.

Many Taiwanese, as well as some prominent experts, apparently believe that the most likely source of the hoof-and-mouth plague was across the 100-mile Taiwan Strait. Mainland pigs are banned from Taiwan because China refuses to comply with international reporting standards on the incidence of hoof-and-mouth disease, and rumors of epidemics in Fujian and Zhejiang provinces have reached here.

The mainland has been silent, except in its offer to sell vaccines at a good profit to its beleaguered neighbour. But the quality of mainland vaccines is suspect.

It is certainly true that Taiwanese and Chinese smugglers have been caught plying the strait in the dead of night with loads of piglets destined for the Taiwan market, where they can bring double the price they fetch on the mainland. One of those boats could well have landed a Trojan pig. — New York Times

THE TIMES OF INDIA, MUMBAI

Victims of negligence demand justice

By Rakesh Bhatnagar

NEW DELHI: In a historic agreement, the US tobacco industry has undertaken to cough up a whopping $ 368 billion as compensation for treating people with smoking-related diseases.

The industry would also concede that tobacco is addictive, a fact which it was always shy of accepting.

In a belated realisation that smoking can cause cancer and other health problems, various state governments in India have resolved to declare certain public places as "no smoking zones"; many have imposed certain restrictions on the free sale of cigarettes and children below 14 have been barred from either vending or smoking cigarettes.

The Delhi government has declared public places including railway stations, public transport, cinema halls and restaurants to name a few, out of bounds of smokers. There

LEGAL VIEW

seems to be an urge for implementing the law but the administrations lacks political will to do so, except a few instances when 'no-smoking' slogans were painted and some persons were caught "red-handed' and fined. Elsewhere in the country, no one has so far been caught "red-handed" while smoking and made to pay a fine for something which has been an age-old habit.

Any legal challenge of the ban on smoking in the Capital may not succeed as the courts have declared on many occasions that the government is responsible for the upkeep of citizen's health.

On prohibition, the court's view has been that it cannot interfere with the legislation because it is meant to better the people's standard of living.

Article 47 of the Constitution emphatically states that it is the duty of the State to raise the level of nutrition and the standard of living and to improve public health.

It elaborates: "The State shall regard the raising of the level of nutrition and the standard of living of its people and the improvement of public health as among its primary duties and, in particular, the State shall endeavour to bring about prohibition of consumption, except for medicinal purposes of intoxicating drinks or drugs which are injurious to health."

But the ban on sale of liquor can also be construed as going against the citizens right to profession, which also means right to livelihood.

Consumption of liquor or smoking may pose a serious threat to one's life, but our laws lack teeth when it comes to actually implementing them.

Therefore neither the breweries nor the cigarette industry in India can ever face a situation which the US tobacco companies have found themselves in.

Even in the US, damages had been granted in only two tobacco-related cases. The first was the Cipollone case, which was reviewed by the US Supreme Court. In that case, a federal jury in 1988 awarded $ 400,000 to the husband of Rose Cipollone, who smoked for 42 years and died of lung cancer at the age of 58.

In the other case, the jury awarded $ 750,000 to a man who smoked for 44 years before developing lung cancer. It found that the cigarette brand he smoked was a defective product and the manufacturer was "negligent" by not informing the public about health risks of smoking.

These were the personal injury cases in which adequate compensation was granted by US courts. But in India such cases get bogged down by procedural law and loopholes which enable the 'culprits' to escape punishment. Thus the first casualty is justice.

Fire tragedies, road accidents involving government vehicles, negligence by government doctors or even others, besides civic authorities' negligence which result in accidents are some of the cases which, despite their gravity, invariably drag on for years before the delinquent is punished or acquitted for lack of evidence.

Some laws are so obsolete that certain accidents could not have been foreseen when the legislations were enacted.

However, with progressive US case laws as examples, people here are coming to have greater expectations from the judiciary in administering justice in cases of negligence.

Nurse charged over death of two old patients

London: A British nurse has been charged with the attempted murder of two elderly patients and incitement to murder another, police said Friday.

Ms Kathleen Ann Atkinson, 47, of Wallsend, Tyne and Wear, in the northeast of England, was dismissed from her job as a nursing sister in the intensive care unit at Newcastle's Royal Victoria Infirmary in March 1996 over allegations that life-supporting drugs to critically-ill patients were withheld.

On Tuesday, after a year-long police inquiry, she was arrested and questioned over a number of deaths at the hospital, and Friday she was charged with the attempted murders of Mary Burdon, 69, in February 1991 and Miriam Egen, 60, in February 1992, and incitement to murder of Thomas James Luke, 77, in December 1995.

A police spokeswoman said a file of evidence on other matters was being prepared for submission to the state prosecutor's office. *(AFP)*

5 die of food poisoning

AMRITSAR, June 16 (HTC) Tragedy struck at the shrine of Ram Tirath located 11 km from Amritsar when five persons died and many others fell sick due to food poisoning last night.

The S.P. headquarter Darshan Singh told *The Hindustan Times* that *langar dal* which victims had was poisonous. The sample of the *dal* has been sent for the chemical examination. However, no case has been registered so far, he said.

Russia sitting on AIDS bomb

Rise in intravenous drug use and loose sexual habits lead Russians to a medical catastrophe, reports **Fred Weir**

RUSSIA is facing an epidemic of sexually-transmitted diseases, particularly the deadly acquired immuno-deficiency syndrome (AIDS). The crumbling medical services and public education system are totally unprepared for this experts warn.

"We are observing an exponential increase in people infected with the AIDS virus," says Mikhail Narkevich, head of the Russian Health Ministry's AIDS unit. "In the first five months of this year, the number doubled. We expect it to double again over the summer."

The USSR's first case of infection with HIV, the virus thought to cause AIDS, was registered in 1987. Six years ago, when the Soviet Union collapsed, the country had fewer than ten HIV carriers.

Russia currently has 4,200 officially registered cases of HIV infection and 290 people with the full-blown AIDS condition.

These numbers are small by comparison with many other countries, but experts say that's only because Russia had a late start on the epidemic.

"The Soviet Union was a closed society, and that to some extent insulted us from the epidemic that was sweeping the world," says Mr Narkevich.

"But now intravenous drug use is sharply on the rise, and loose sexual habits are more widespread. These things are driving a catastrophic upsurge in AIDS and other diseases," he says.

Due to the breakdown of the Russian health system and the social stigma that still goes with reporting a sexually-transmitted disease, experts believe the numbers of registered HIV cases reflect as little as a tenth of the actual numbers of infected people.

"If the present rate of increase continues, we can expect 800,000 to a million HIV-infected Russians by the end of this decade," says Mr Narkevich. "That in itself is a huge medical catastrophe, for which we are utterly unprepared."

The incidence of syphilis has increased by a staggering 40 times since 1989. Syphilis infection now stands at 177 per 100,000 people — a rate that is more than 50 times higher than most European countries. Gonorrhea, trichomoniasis and chlamydia infections have shown similar patterns of explosive growth.

"We have noticed a direct link between syphilis and HIV infection," says Mr Narkevich.

Public education about the health risks of unprotected sex is virtually non-existent. Russia's first attempt to introduce sex education classes for teenagers began only last year, with a modest pilot project in a handful of schools.

Until 1995 about 80 per cent of all new HIV cases in Russia were traced to sexual transmission. Experts point to the dramatic rise in prostitution since the end of the communist welfare system, with its guaranteed opportunities and job security for women."

They also warn that the post-Soviet social environment has fuelled an upsurge in popular cynicism, with accompanying patterns of sexual promiscuity and devil-may-care attitude to the consequences.

The obvious causes that have led to this drastic rise in sexually-transmitted diseases is the fact that sex and pornography are widely advertised by the mass media," argues a recent article in Russia's main medical journal, 'Meditsinsky Kourier'. "One of the consequences of the propaganda of sexual emancipation is the increasing number of pregnancies among teen-agers. As many as 95 per cent of the pregnant women of the age from 18 to 20 have no permanent jobs, 70 per cent are not married, and 50 per cent have sex with chance partners."

Over the past two years, however, intravenous drug abuse has exploded in Russia and, with shared syringes, AIDS transmission has gone through the roof.

At the end of 1995 there were only 3 cases of HIV-positive drug addicts, says Mr Narkevich. A year later there were almost 800. Health officials say that 70 per cent of new cases are now found among drug addicts.

Russia's estimated 600,000 intravenous drug abusers are the pipeline bringing the AIDS epidemic in full force to Russia. At the same time deteriorating public health institutions are less able than ever to cope.

19 die in Malaysia virus menace

Kuala Lumpur: The death toll from a new virus strain in Malaysia's Borneo state of Sarawak has climbed to 19, the local newspapers reported on Saturday.

Sarawak state director of medical and health services department Mohammed Taha Arif was quoted by the papers as saying that two more infants succumbed to the Coxsackie B virus on Thursday. He said 29 children were in an isolation ward at the general hospital in Sibu, a coastal town in Sarawak state officials have said. Symptoms include fever, nervous fits, paralysis and finally heart failure. *(Reuter)*

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1. INTRODUCTION

1.1 Role of Outbreak Investigations

The primary purpose of an outbreak investigation is to control the outbreak, limit its spread to other areas and assess how prevention strategies could be further strengthened to reduce or eliminate the risk of such outbreaks in the future. Control measures are most effective when selective interventions are applied early to provide maximum impact with minimum diversion of scarce resources required for achieving and sustaining high immunization coverage levels.

This field guide is designed to help the immunization programme managers at district and PHC levels in making decisions regarding field investigations, specific interventions and follow-up measures. The general approaches and recommendations of the field guide may need to be adapted to specific situations, geographical locations, immunization coverage levels and resources available. The maximum benefit from these guidelines can be derived if:

- the field guide is studied thoroughly and clarifications, if any, are sought before circumstances compel its use.

- an inventory is made of the facilities available before an outbreak actually occurs, such as manpower and vehicular resources; names of experts who could be requested to assist; referral treatment centres and laboratory facilities and source of transport media (in situations where laboratory facilities are available for confirmation of the diagnosis).

- a list of indications for outbreak investigations is established. Some indications are suggested in this field guide and may be common to all areas. In places with high immunization coverage levels, programme managers may wish to include additional items, including the criterion that even a single case may be considered an outbreak.

1.2 Diseases Covered by This Field Guide

This field guide covers the vaccine preventable diseases included under the Expanded Programme on Immunization (EPI), viz., diphtheria, pertussis, tetanus, poliomyelitis, measles and childhood tuberculosis. An attempt has been made to prepare a common methodology and format for the investigation of these diseases to simplify its use.

Tetanus differs from other diseases because it is not transmitted person to person. The level of neonatal tetanus cases tends to remain relatively constant in areas with a low quality of obstetric care and without adequate immunization. An investigation should be conducted, however, if there are increases in the number of cases which cannot be attributed to improved surveillance.

A section on serious adverse events following vaccination is included so that prompt investigation of these events can also be undertaken. A report of even a single case of severe adverse event following vaccination is an indication for investigation.

1.3 Use of Data Collected During Outbreak Investigation

Data collected during outbreak investigations can serve many important functions, including better understanding of the epidemiological features of the disease; estimation of vaccine efficacy in field use; surveillance system weaknesses and identification of high-risk areas and age-groups. Outbreak investigation data, such as other forms of surveillance data, are information for action. The results of outbreak investigations should lead to action in improving and sustaining immunization services.

2. EPI TARGET DISEASES

2.1 Epidemiological Features

It is necessary to know the epidemiological features of the diseases to effectively investigate and control outbreaks. For easy reference, the major items have been summarized in tabular form (Annex 1).

2.2 Criteria for Diagnosis

The criteria used for diagnosis (case definitions) is important. A suggested set of standard case definitions is shown in Annex 2. The case definitions include only major signs and symptoms of typical cases.

First reports of outbreaks may often come from the general public or peripheral health workers. It is expected that the recognition of the diseases by these health workers or members of the community will be based primarily on history, which, in some of the vaccine preventable diseases, can be typical. The diagnosis should be confirmed by a medical officer based on history and clinical investigations. Laboratory confirmation of the diagnosis would be needed only under special circumstances and suggested tests have also been included in the table of case definitions.

2.3 Verification of the Diagnosis

The first principle of outbreak investigation is to confirm the diagnosis of as many reported cases as possible. Much time and effort may be wasted due to misdiagnosis.

(1) Clinical diagnosis

The reported cases should be investigated by a medical officer to confirm the diagnosis. The majority of the cases should fall within the case definitions given in Annex 2. In situations of doubt about whether an illness meets the case definition, a second opinion may be sought.

(2) Laboratory confirmation

Laboratory confirmation of clinically-diagnosed cases is usually not essential. Laboratory tests for diphtheria, and tuberculosis meningitis may, however, be helpful if such facilities exist.

Although laboratory tests are not required for confirmation of the diagnosis of paralytic poliomyelitis, such tests are necessary for classification of the type of polio virus.

Laboratory tests may be useful for the detection of carriers and infected asymptomatic persons and, in the post-epidemic period, may help assess the extent of silent infection resulting in immunity. Although such studies may provide useful epidemiological data, they are not directly relevant to outbreak control.

The details regarding the types of tests, sample collection and transportation procedures are shown in Annex 3.

3. PROCESS OF OUTBREAK INVESTIGATION

3.1 Identification of the Existence of a Possible Outbreak

Outbreaks of vaccine preventable diseases usually occur in areas with low immunization coverage. When large outbreaks are reported from areas with high immunization coverage, it is important to reliably verify these reported coverage levels through such methods as careful review of records of immunization performance over the previous few years and vaccination coverage evaluation surveys. Outbreaks in highly immunized communities are usually localized to certain population sub-groups or places which did not receive adequate immunization coverage.

An outbreak or epidemic is defined as the occurrence in a community of cases of an illness clearly in excess of expected numbers. Increases in the total number of cases do not, however, necessarily indicate increase in the incidence of diseases. Variation in the number of reporting sites, completeness of reporting, geographical size of the catchment area and size of the population are factors that must be taken into consideration while analysing reports.

Outbreaks can sometimes be forecast in areas with reliable surveillance systems. Many infectious diseases have cyclic patterns and outbreaks are observed after regular intervals of one, two or more years depending on the disease and immunization coverage levels in the community. Cyclic peaks of measles and poliomyelitis, for example, have been observed every second or third year in many states of India. Graphs on the incidence rates of measles and poliomyelitis (Figures 1 and 2) illustrate this point. If similar graphs are plotted for each district, preventive measures can be taken in advance and the treatment centres can be alerted to provide an early warning should an outbreak occur. Intervals between epidemic peaks may increase and the magnitude of the peaks fall as immunization coverage levels increase.

FIGURE 1. Incidence of measles, India , 1975-1987

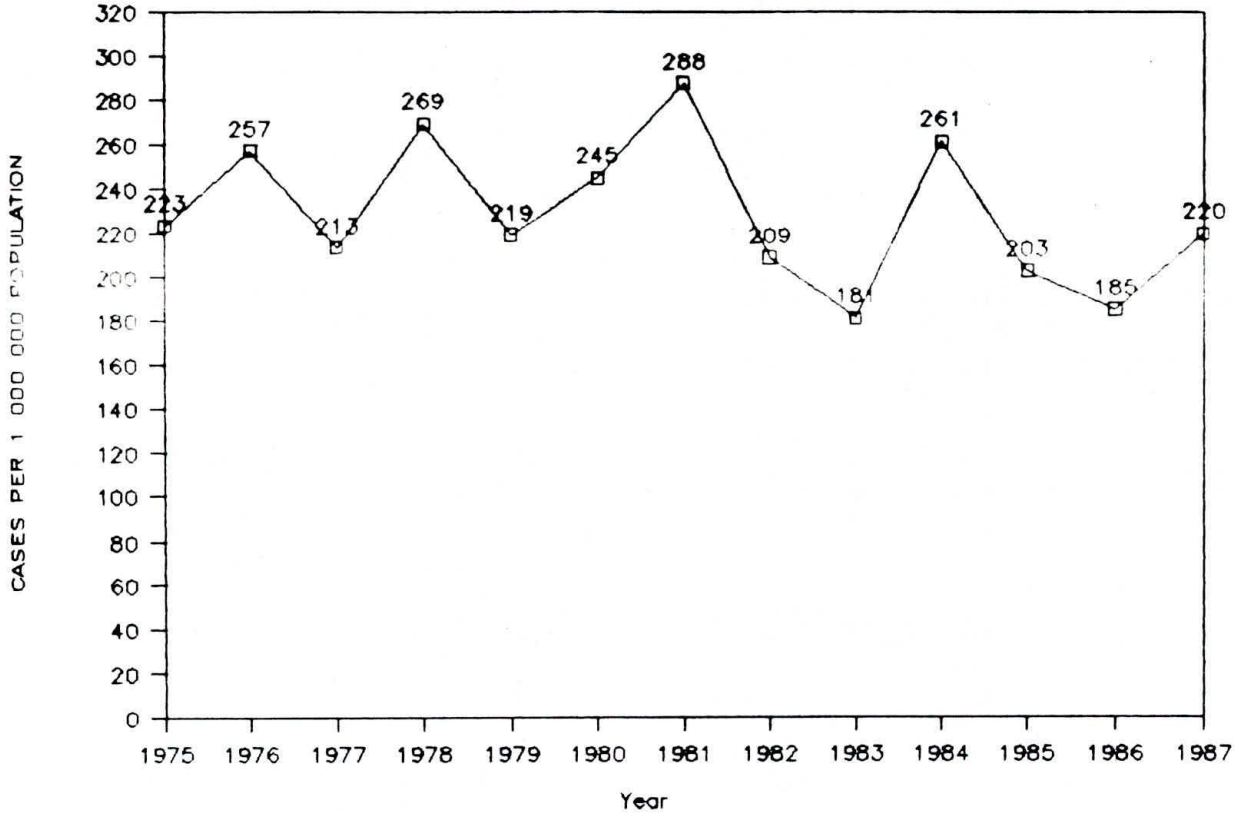
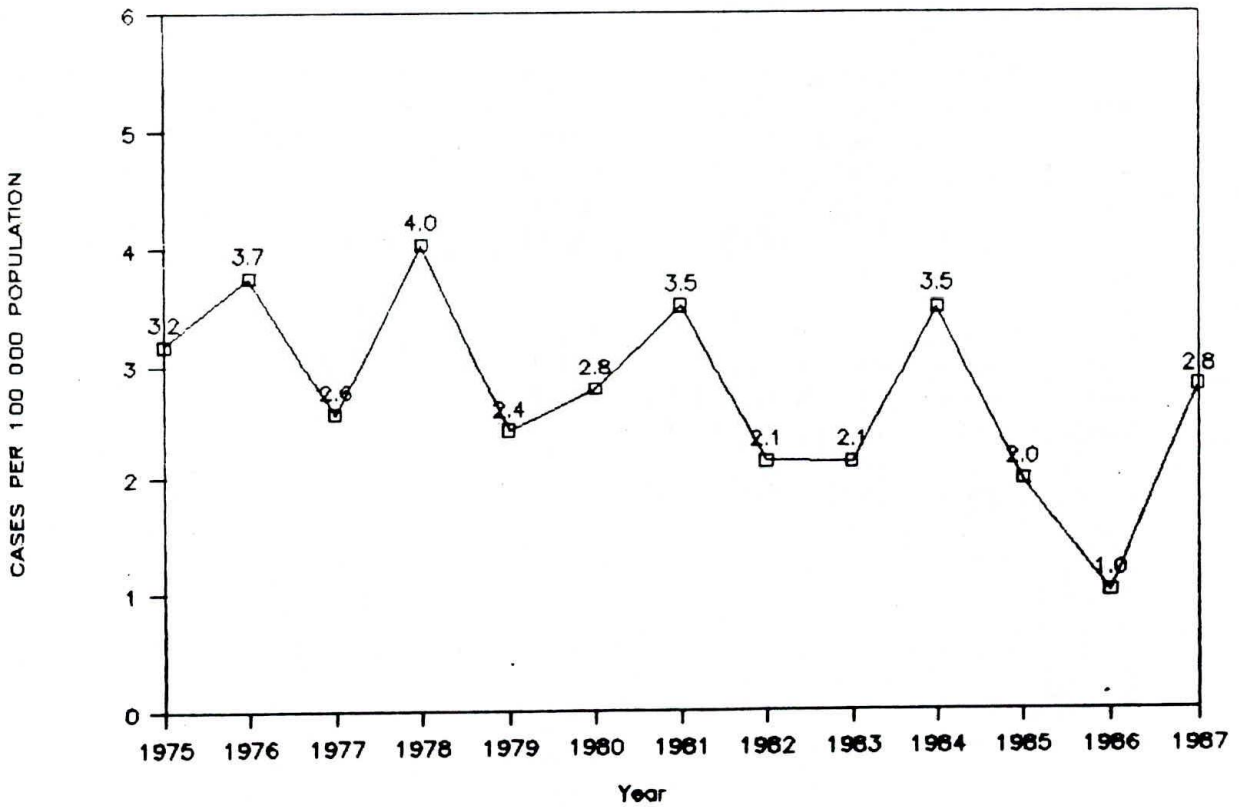


FIGURE 2. Incidence rate of polio in a State, 1975-1987



Sentinel centres, institutions that promptly and reliably report all cases of disease under surveillance, may be particularly useful for forecasting and early warning of outbreaks.

All health workers must be aware of the major signs and symptoms of the vaccine preventable diseases. They should be encouraged to report these cases to the medical officer of the concerned PHC. Any unusual increase must be notified immediately. Such information should also be reported immediately by the medical officer to the concerned district officer. Reports of outbreaks can also be received from members of the community.

Incidence of diseases should be an agenda item in the monthly meetings at PHC and district levels so that any unusual reports can be identified and discussed. Even relatively small increases in the incidence of diseases seen in individual PHCs may indicate serious problems in the district as a whole if such increases are noted in several of the PHCs. Moreover, neighbouring PHCs can be alerted to the possibility of potential outbreaks in their catchment areas and they can take preventive measures.

It is obvious that sensitivity, reliability and timeliness of the source of reports and alertness of the local staff are very important. In areas with poor surveillance systems, outbreaks are sometimes identified only towards the end when preventive measures are least effective.

3.2 Criteria for the Number of Cases That Constitute an Outbreak

The number of cases which are needed to be called an outbreak varies according to several factors. It depends on past historical patterns of the disease, virulence of the disease (toxigenic strains of C.diphtheriae, for example) and immunization status in the community. In places with established epidemic cycles, it may be worthwhile to initiate necessary preventive measures and alert treatment centres in the area in anticipation of an outbreak.

States and districts should establish criteria on the number of cases that constitute an epidemic based on their local situations. These criteria could include:

- a 25 per cent increase in the number of cases reported as compared to the corresponding period (month or quarter) of the previous year. This may not, however, be sufficiently sensitive in the year that follows an outbreak;

- a 25 per cent increase in the number of cases reported as compared to the average number of cases over the last four non-epidemic years for the corresponding period;

- five or more cases or a single death reported by a health worker from his area in a month or 2 or more cases in a week;

- a single case in an area which has had no case during the previous 12-month period, and

- a single case in an area with reported immunization coverage levels of 80 per cent or higher.

The reporting centres and medical officers in the OPDs should be encouraged to report any unusual increase in the number of cases without waiting for the submission of their routine monthly report. Similarly, while the current number of cases should be compared with the previous month or quarter, if the number exceeds the criteria for an outbreak, it is not necessary to wait for the completion of the monthly or quarterly period to declare an outbreak. This is important in avoiding any delay in starting control measures.

3.3 Criteria for Investigating an Outbreak

After an outbreak has been confirmed, a decision must be made as to the amount of resources (manpower, time, monies etc.) that should be committed to investigating it, or even if it should be formally investigated at all.

If it is known, for example, that immunization coverage levels in the community are low, then outbreaks should be expected to occur. If resources are limited, it may be counter-productive to the routine immunization service that is trying to improve coverage if all activities are stopped to focus only on the outbreak.

The decision whether or not to investigate and the depth of investigation must be made at the level where the outbreak occurs. The decision should be based on factors that include immunization coverage in the community (whether or not an epidemic could be expected to occur); severity of the disease; effectiveness of control interventions; duration of the epidemic to the time it has been recognized, importance of investigating vaccine efficacy and better understanding of the epidemiology of the disease, etc.

It is the responsibility of the local medical officer to arrange for the treatment and follow-up of cases and contacts. It should be noted that during an outbreak a higher percentage of more severe forms may also occur.

4. FIELD INVESTIGATIONS AND ANALYSIS OF REPORTS

4.1 Case-Finding Through Active Surveillance

After establishing the existence of an outbreak and verifying the diagnosis, it becomes important to accurately define and count the cases. During the period of the outbreak, all the cases of the disease under consideration occurring in that area should be identified and listed.

Active surveillance is necessary to obtain more accurate and complete information. Active surveillance refers to actively seeking out cases. This may include visits or telephone calls to all the medical facilities or private practitioners that might expect to admit or attend cases of the disease. Depending on the disease and the resources available to investigate the outbreak, it may even be desirable to conduct house-to-house visits (especially in the homes of contacts of cases) to find cases. In some circumstances, community assistance may be enlisted for house-to-house visits.

Active surveillance also provides a means for standardizing and increasing the amount of information about each case. In this way it may be possible to develop a more complete line-listing, including data on immunization status, residence, age, symptomatology, etc. This supplementary information is especially helpful in outbreak investigations to assess vaccine efficacy, determine complication rates, and further understand the epidemiology of the disease.

Active surveillance, once initiated, should be maintained until the outbreak is over. Developing a regular schedule of daily or weekly (depending on the urgency of the situation) visits or telephone calls to concerned institutions or individuals will help maintain the flow of surveillance information to those analysing the outbreak and directing control activities.

4.2 Line-Listing, Defining and Counting of Cases

It is important that information from surveillance be recorded in a standardized manner. Persons who are ill and meet the case definition for the outbreak disease should be entered onto what is called a "line-listing". This is a list of all cases with the relevant data on each case which provides the basis for counting of cases. It is the data-base on which the descriptive epidemiology of the outbreak can be made and it can serve as the basis for other, more sophisticated, analytical epidemiological studies, such as risk-factor analysis, vaccine efficacy, etc.

The line list suggested for field use is shown in Annex 4. Summary tables have been included (Tables 1-5) to facilitate analysis of data. Forms for investigating individual cases of poliomyelitis and neonatal tetanus are given in Annexes 5 and 6.

TABLE 1. Weekly distribution of cases and deaths

Week ending	Number of cases	Number of deaths
Total		

TABLE 2. Determining high-risk age-groups

Age-group	Male		Female		Total		Population in the age-group	Attack rate per 1 000
	No.	%	No.	%	No.	%		
0-11 months								
12-23 months								
24-59 months								
5 -9 years								
10-14 years								
15+ years								
Total								

TABLE 3. Immunization status of the cases, by age

Age-group	Immunization coverage												Total	
	0 dose		1 dose		2 doses		3 doses		> 3 doses		NK			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0-11 months														
12-23 months														
23-59 months														
5+ years														
Total														

TABLE 4. Complications within six weeks of measles

Complaint	Number of cases				
	Mild	Moderate	Severe	Died	Total
Diarrhoea					
URI					
Pneumonia					
Conjunctivitis					
CNS complications					
Others (Specify)					

TABLE 5. Reported vaccination coverage

Year	Population	Estimated infants	Vaccination performance					Percent coverage[a]
			0 dose	1 doses	2 doses	3 doses	3+/B	

[a]Percentage coverage = $\frac{\text{1,2 or 3 doses (as appropriate)}}{\text{Estimated number of infants}} \times 100$

4.3 Descriptive Epidemiology

In investigating an outbreak, it is necessary to develop a detailed description in terms of time, place and person, as follows:

(1) Cases by time

The onset of illness of the cases should be graphed by days, weeks or months, as appropriate (example in Figure 3). This type of graph is commonly referred to as an epidemic curve. The epidemic curve can be helpful in identifying the index (first) case or cases, generation of disease (peaks of disease separately by troughs during incubation period), and may even suggest patterns or modes of transmission.

It is also useful to present previous year's information or possibly an average of several previous years for comparison on a line graph. Such graphs help to demonstrate the magnitude of the outbreak compared to the previous reported incidence, how rapidly the disease is spreading and if control efforts are succeeding.

(2) Cases by place

A map of the area or even a rough sketch can be drawn showing where each reported case resides to indicate geographical distribution of cases (example in Figure 4). In some situations, serial spot maps, by week or by month (or by disease generation) may provide insight into the pattern of the spread of the disease over time.

Cases tend to cluster and it may also be useful to mark affected schools or other institutions on the map in addition to residential locations. Such mappings may assist in identifying the sources of infection.

(3) Cases by person

Cases should be described in terms of age, sex, vaccination history and other relevant data. It is usually sufficient to group cases by age-groups like 0-11 months, 12-23 months, 24-59 months, 5-9 years, 10-14 years and 15 years and above. Sex differentiation may also be helpful.

Immunization status is an important descriptive as well as analytical parameter. The immunization status of each case must be carefully investigated to ascertain the number of doses of the vaccine received by the patient. Immunization cards or immunization registers should be checked to verify the immunization status. Verbal history should be used only if such records cannot be obtained. Ideally, the place of immunization should also be examined for quality of the cold chain.

4.4 Determination of Immunization Coverage in the Community

The immunization status in the community can be assessed through immunization performance records available at the PHC. Percentage immunization coverage is estimated by dividing the total number of doses (measles and BCG) or third doses (OPV and DPT) of the vaccine administered to a specific age-group by the total population of that age-group in the village. The data may be summarized as in Table 5.

FIGURE 3. Polio epidemic in a district, July 1986

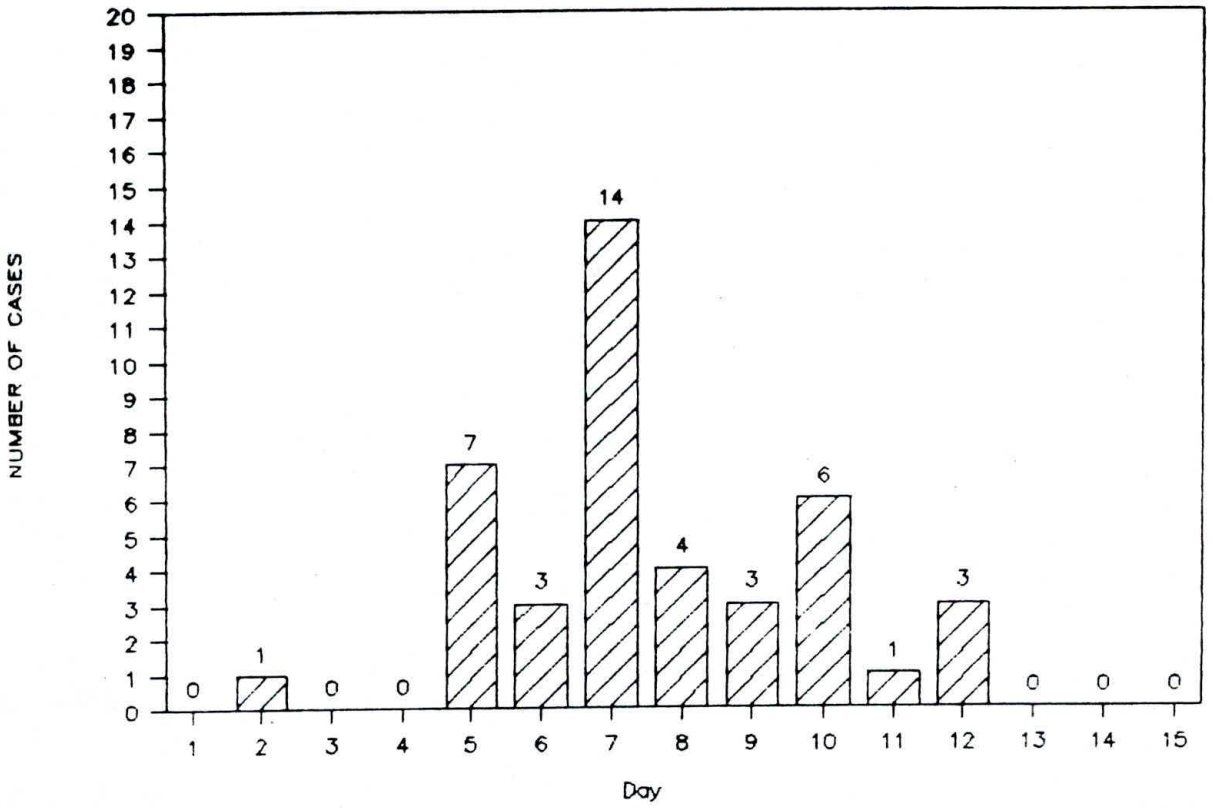
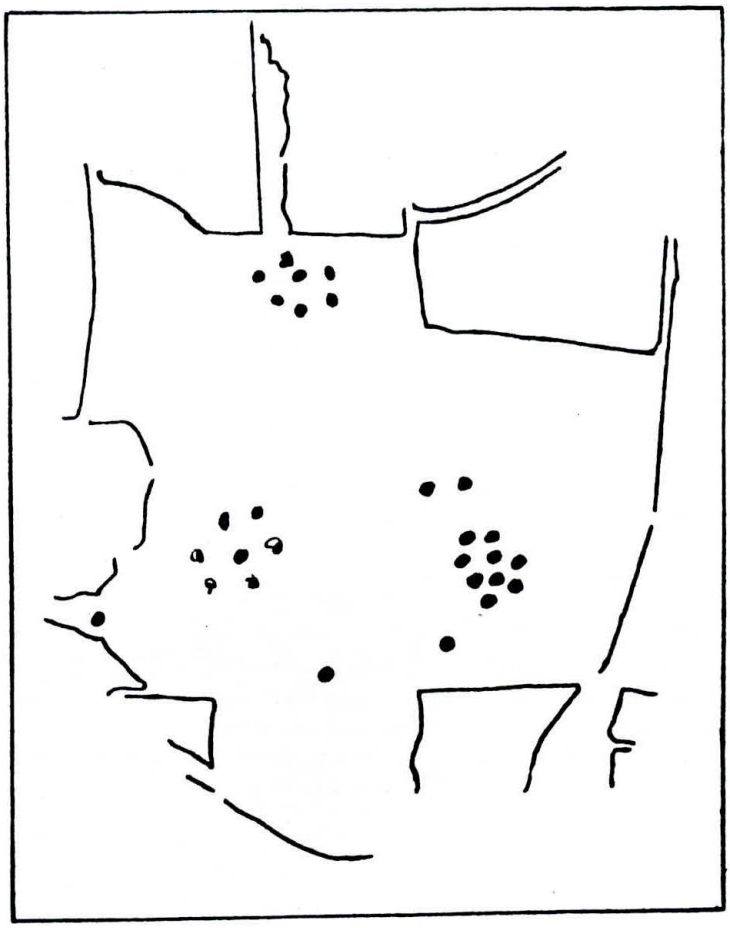


FIGURE 4. Example of spot map



The age-groups vaccinated should be carefully assessed as inclusion of older children may give a false sense of higher coverage. The immunization activities, including periodicity of the immunization sessions, quantities of vaccines received and cold chain system, should be reviewed.

Information on immunization coverage may also be available through past vaccination coverage evaluation surveys. If no such coverage evaluation surveys have been performed recently, if estimates of immunization coverage by reports of doses administered are unavailable or suspect, or if a large number of vaccinations are given by the private sector and are not reported, then it may be useful to conduct a coverage evaluation survey as a part of the outbreak investigation which may also be used to facilitate estimation of vaccine efficacy.

4.5 Determining Who is at Risk of Disease

The descriptive epidemiology will help to define the population groups at high risk of disease in terms of age-groups, geographical location, activity (school, mela, etc.), and immunization status.

It is more appropriate to determine attack rates rather than absolute numbers because rates take into account variation in the population size of different age-groups. Such rates are generally computed by dividing the number of cases by the population size for the same age-group.

Example: There are 45 cases of poliomyelitis among 11 000 children less than 5 years of age in the affected town.

$$\text{Attack rate} = \frac{45}{11000} = 0.004 \text{ or } 4 \text{ cases per } 1\,000 \text{ population less than 5 years of age}$$

4.6 Follow-up Visits

It is important that arrangements are made for follow-up visits so that late cases are not missed. Some of the diseases, especially measles, can lead to secondary infections in children. Prompt treatment of these secondary infections in such children can save many lives. Post-measles complications, most commonly diarrhoea and pneumonia, can occur at any time up to six weeks after the onset of the illness. However, since these diseases can also occur in children without measles, records of the diseases in children following measles and without measles should be maintained separately.

5. CONTROL MEASURES

A sensitive surveillance system, prompt investigation and pre-defined control strategies are helpful in the successful control of the spread of the outbreak, limiting the total number of cases and providing proper medical attention to those already affected. Such measures are most effective when started as soon as possible.

For most of the vaccine preventable diseases, immunization of the susceptibles is the first priority. While close contacts of cases should not be excluded from immunization, they are likely to have already experienced their highest risk of acquiring the infection. For neonatal tetanus, although immunization of pregnant women will control the disease, it is important that delivery practices in the area are reviewed and necessary corrective steps taken to reduce the risk of tetanus immediately. For tuberculosis, chemotherapy is a major feature of control measures.

An appropriate cut-off age for vaccination is determined from the public health and epidemiological perspective based upon case analysis and immunization coverage data. Immunization should be directed to achieve the maximum impact in the most susceptible age-group. There are several ways to determine this cut-off age. One possible method is to direct all immunization activities to the age-group that contains 85 per cent of all cases, and to allow immunization, on demand, to older age-groups that contain between 85 to 95 per cent of the cumulative total cases. Immunizations provided to the age-groups containing the remaining 5 per cent of total cases are not of epidemiological importance for containing the outbreak, and may actually divert scarce resources and manpower away from the high-risk groups.

At the initial stages of an outbreak, before precise data are known about the age distribution of cases, the cut-off age may be determined from data from the non-epidemic years or from a previous epidemic of the disease.

A dose of vaccine should be provided to all children who have not completed a full immunization series even if less than four weeks have elapsed since the last dose of a multiple dose vaccine. If the dose given during the outbreak was at an interval of less than four weeks for the multiple dose vaccines, then it should not be counted as one of the primary series of three doses. Such children should be advised to return to complete the course.

Records should be kept of immunization administered during an outbreak. Ideally, these records can be the same immunization registers used for the routine programme. If this is not possible, relevant data may be entered in the registers subsequently. Ideally, the immunization data should also be recorded on the immunization card of the child.

The affected areas and villages/wards in the immediate neighbourhood should be covered. Contacts should be traced if they have moved outside the affected area and such village(s)/ward(s) should also be covered.

All control measures should help to strengthen the existing immunization delivery system. Outbreak "campaigns" of immunization, moving from one area of low coverage to another and leaving no sustainable routine immunization delivery system in place is disruptive and will simply lead to other outbreaks in the future when sufficient number of susceptibles accumulate.

Elective surgical procedures and injections, including immunization, should be discontinued during an outbreak of poliomyelitis to avoid the possibility of surgical or injection-associated paralysis. It is important

that such postponement is done only during the period of an epidemic. Immunizations should continue in areas of endemic poliomyelitis, even during the seasonal peak, so that the routine services designed to reduce other vaccine preventable disease incidence will not be compromised. It should be recognized that the risk of injection-induced poliomyelitis is insignificant if children are immunized at the earliest recommended age-group while still under the protection of maternally-acquired antibodies. The risk is further reduced as coverage levels in the community increase.

Appropriate treatment of patients and contacts should be started. Such treatment may be life-saving and should not be delayed pending laboratory confirmation of the diagnosis. This will also serve to reduce transmission while the outbreak is investigated. The treatment procedures are available in standard medical texts and should be undertaken ideally in consultation with a peadiatrician.

While there is no specific treatment for poliomyelitis and measles, proper medical attention can, however, reduce complications and early treatment of secondary infections can be life-saving. All patients with fever should be advised to take adequate amounts of fluids to avoid dehydration. A normal diet should be encouraged.

Isolation of patients is difficult and rarely effective. However, potentially susceptible visitors should be discouraged from entering the household of a patient during the period of communicability.

6. WRITE-UP AND REPORT RESULTS

The following is a suggested format for writing up the results of an outbreak investigation:

6.1 General Information

State : _____

District : _____

Town/PHC : _____

Ward/Village : _____

Population : _____

6.2 Background Information

Person reporting the outbreak : _____

Date of report : _____

Date investigations started : _____

Person(s) investigating the outbreak : _____

6.3 Details of Investigation

Describe how the cases were found (may include: (a) house-to-house searches in the affected area; (b) visiting blocks adjacent to the affected households; (c) conducting record reviews at local hospitals; (d) requesting health workers to report similar cases in their areas, etc.):

_____
_____
_____

6.4 Descriptive Epidemiology

- Cases by time, place and person (attach summary tables and relevant graphs and maps).
- Age-specific attack rates, mortality rates and complication rates.
- Immunization status of cases and immunization coverage levels in the community.
- High-risk age-groups and geographical areas.

6.5 Description of Control Measures Taken

Depending on the disease, all or some of the following may be applicable:

No. of households visited: _____
No. of children examined: _____
No. of cases treated: _____
No. of contacts of cases treated (if applicable): _____
No. of children hospitalized: _____
No. of children vaccinated during the outbreak (see Table 6 below): _____

TABLE 6. Vaccination of children, by age

Age-group	No. of children vaccinated (by prior status)					Population in age-group
	0 dose	1 dose	2 doses	3 doses	NK	
0-11 months						
12-23 months						
24-59 months						
5+ years						

6.6 Description of Measures for Follow-up Visits:

_____
_____
_____

6.7 Brief Description of Problems Encountered (During Outbreak Investigations and Control):

_____
_____
_____

6.8 Factors Which, in Your Opinion, Contributed to the Outbreak (may include: low immunization coverage; cyclic recurrence; local festival; common nursery/school; etc.):

_____
_____
_____

6.9 Estimates of Vaccine Efficacy:

_____
_____
_____

6.10 Conclusions and Recommendations

- For future outbreak investigations and control:

_____
_____
_____

- For improvement in immunization services to minimize recurrence of outbreaks:

_____
_____
_____

_____ Date

_____ (Namd and Designation)

6.11 Reporting Procedure

Information on the existence of an outbreak should be reported immediately to the next higher level (by courier or by telephone and telegram, if available). Such action is necessary to keep the authorities informed so that they are able to provide timely assistance and alert others, if necessary.

Information on the outbreak should also be provided to the other nearby health units to alert them of possible increase in numbers of cases in their areas.

Copies of the investigation report should be sent immediately and directly to the concerned district, state and central officers.

Feedback should be provided to the community leaders in the area regarding the outcome of the outbreak investigation and preventive action planned for the future.

6.12 Dealing With the Public and the Media

Reports of outbreaks often appear in the newspapers and can create panic. It is, therefore, advisable that accurate information is provided in a timely manner to the news media regarding the numbers of persons affected and the control measures undertaken. The press and other news media can be of great assistance in informing the public of the services available and where they can receive them. The government procedures for dealing with the press should be followed and necessary information provided through a nominated government spokesperson.

7. PLAN PREVENTIVE MEASURES

Long-term measures are necessary to ensure that outbreaks do not recur in the future. The epidemiological data collected during investigations should be utilized for streamlining operations, directing programme activities and determining future strategies for improving immunization coverage in high-risk age-groups and geographical areas.

Regular field monitoring is essential to ensure high quality of services. The worst situation is to develop a false sense of security and be caught unawares. Some of the parameters that should be checked regularly include the following:

- Uniformity of high coverage levels. Pockets of unvaccinated children and pregnant women should be identified since outbreaks are likely to occur in such areas.

- Adequacy of cold chain. Breaks in cold chain can result in reduced potency of vaccine and low vaccine efficacy. Estimates of vaccine efficacy, use of cold chain monitors and testing potency of field samples of OPV may be useful in monitoring the quality of the cold chain.

- Adequacy of sterilization procedures. Improper sterilization techniques can result in "outbreaks" of adverse reactions (e.g. abscesses) and, if injection equipment is not allowed sufficient time to cool, may also be a source of reduced vaccine potency.

- Proper recording and reporting of immunizations. If doses of vaccine given on demand to children over 12 months of age are recorded and reported as given to children under 12 months of age, an inaccurately high estimate of vaccination coverage levels in infants may lead to a false sense of security.

- Routine use of vaccination coverage evaluation surveys. Such surveys will provide a better estimate of true immunization coverage and will also indicate the source of vaccines and reasons for failure to fully immunize which may help direct programme operations to improve coverage.

- Completeness of the disease surveillance system. Most routine surveillance systems need strengthening and the use of sentinel surveillance during the period of strenghthening of the routine system may be useful in ascertaining disease trends.

Data obtained from monitoring these indicators should be actively used in the planning process to improve immunization coverage.

8. INVESTIGATION OF ADVERSE EVENTS

8.1 Adverse Events Following Vaccination

The adverse events that follow vaccination may be common or rare reactions to the vaccines administered. Such reactions are known and are difficult to avoid. In rare instances, convulsions or collapse after DPT vaccination may occur. Under such circumstances, subsequent needed doses of DPT are replaced with a dose of DT. It is important to understand, however, that the risk of these adverse reactions is small compared to the morbidity and mortality due to the vaccine preventable diseases.

Severe complications and even death may result if the guidelines for the handling and administration of vaccines are not followed. The most common complication is the formation of abscesses following the use of inadequately sterilized syringes and needles. Abscesses require prompt attention from health workers since, in some instances, such abscesses can lead to death in the absence of adequate medical care. Abscesses are also an 'indicator' of poor programme implementation and follow-up measures are necessary to ensure that these do not continue to occur. Such events are totally avoidable.

Sudden onset of severe diarrhoea, vomiting and fever within a few hours of measles vaccine administration has been reported. The case-fatality rate in these incidents was high with death occurring within 24 to 48 hours after the onset of symptoms. Although the precise cause of the symptoms and deaths

has not been identified, the most likely reason appears to be contamination and then reuse of the vial of measles vaccine.

Vaccines are usually administered to children at an age when infections are common. Some of the adverse events reported may have only a temporal relationship to vaccination, the primary cause of the adverse event being unrelated to vaccine administration. Investigations are necessary to establish the causal relationship. It is important that children of the same age-group in the area who did not receive vaccines are also examined.

The state health authorities may be advised to have a standing committee of an epidemiologist, a peadiatrician and a microbiologist on call to ensure prompt and thorough investigation of severe adverse events.

8.2 Measures to Minimize Risks

The following measures will help to minimize risks of adverse events following vaccination:

- Procedures for sterilization of syringes and needles should be scrupulously followed and monitored.
- A single, sterile syringe and a single, sterile needle should be used for each injection.
- Measles vaccine should be discarded at the end of the session. Opened vials of measles vaccine should not be used the next day under any circumstances.
- Diluent for measles vaccine should be kept separate from other potentially harmful injectable drugs.
- Training programmes for all categories of personnel should receive the highest priority to ensure high quality of services.
- Field monitoring of the services should be regular and any deficiences should be noted and corrected in a timely manner.

8.3 Field Investigations and Analysis of Reports

The basic principles of field investigations of outbreaks can be adopted for the investigation of adverse events. The first principle is to examine as many cases as possible to confirm diagnosis. All children immunized during the particular session should be followed up and relevant details entered in the line list (Annex 7). It is important that non-immunized children of the same age-group in the locality are also examined to rule out temporal relationship.

An analysis of the data should be made, by time, place and person in the same manner as described in section 4. The details of children vaccinated may be summarized as shown in Table 7.

TABLE 7. Number of children vaccinated, with reactions and number of deaths

Date of vaccination	Vaccine	Number vaccinated	No. with reactions	Date(s) of reaction	No. died	Date(s) of death

Operational aspects of the programme need to be carefully reviewed with special reference to procedures followed for the collection, storage and issue of vaccines; methods adopted for the sterilization of syringes and needles (including the total quantities of syringes and needles available for a session) and frequency and quality of routine field monitoring of services.

Where the adverse events are unexpected and not easily explainable, it is important that the signs and symptoms of each case are carefully noted. The promptness and completeness of investigations is of prime importance.

Vaccine samples should be sent for testing to the national control laboratory. The samples should be well packed in ice and sent by a courier. The forwarding note should clearly state the circumstances under which the sample(s) is sent. It is important that the used vial with the remaining vaccine is sent for testing along with unused vials of the same batch.

A report on severe adverse events should be sent immediately to the concerned state and central officers so that a decision regarding possible holding or recall of the concerned batch of vaccine can be taken pending laboratory investigations.

8.4 Write-up and Report Results

A report should be prepared detailing the investigations conducted. This report should start with general information regarding the place where

the event occured. The name of the state, district and PHC/ward should be clearly stated. The following points should be covered in such a report:

(1) Cases

- How and when were the first symptoms observed and who reported the event?
- Who conducted the investigations and when were they started?
- How were the investigations conducted?
- Number of children vaccinated and the type of reactions observed. The line list and summary tables should be attached to the report.
- Whether any children of the same age-group in the area, who were not vaccinated, had similar symptoms.

(2) Clinical aspects

- Detailed clinical picture.
- Treatment provided to the children.
- Outcome of illness.
- Diagnosis by clinicians and observations, if any, made by them.

(3) Operational aspects

- How are immunization services generally provided in the area? Procedure followed on the day of the event.
- When and from where the vaccines were received? How were the vaccines stored and transported?
- How many syringes and needles are available and procedures followed for the sterilization of the equipment?
- Who administered the vaccines and the training they received?
- Have similar reactions been observed in the past and were not reported?

(4) Laboratory investigations

- Samples sent for testing and the names of the laboratories. The testing of the vaccine can take 2-4 months depending on the vaccine and the tests.

(5) Suggestions and recommendations

- What was the likely cause of the adverse event?
- Measures recommended to minimize the risks in future.

_____ _____

Date (Name and Designation)

8.5 Reporting Procedure and Dealing With the Public and the Media

These are the same as for reporting and dealing with an outbreak of the disease. However, there is often a greater emotional sensivity when adverse events occur following vaccination since it is perceived that the health worker has performed an act that has injured or killed an otherwise healthy child. It is important that the community's concerns are dealt with in a professional but sympathetic manner.

9. ACKNOWLEDGEMENT

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Annex 1

EPIDEMIOLOGICAL FEATURES OF VACCINE PREVENTABLE DISEASES

Disease	Causative agent	Mode of transmission	Reservoir	Incubation period	Communicability	Major complications	Specific treatment	Immunity
Poliomyelitis	Polio viruses types I,II and III	Faecally contaminated material Pharyngeal secretions	Man	7-14 days (range 3-25 days)	First week before & after onset of symptoms (range 3-6 weeks)	Residual paralysis of limbs Paralysis of respiratory muscles can lead to death	None	Type specific lifelong
Measles	Measles virus	Air-borne Direct contact with nasal or throat secretions	Man	8-13 days	Slightly before prodromal period to 4 days after rash	Diarrhoea Pneumonia Otitis media Conjunctivitis Encephalitis Malnutrition	None	Life-long
Diphtheria	Corynebacterium diphtheriae	Air-borne Direct contact	Man	2-5 days	2 weeks or less	Respiratory obstruction Myocarditis Nerve palsies	20,000 -100,000 units of antitoxin Antibiotics	Clinical disease may not provide life-long immunity
Pertussis	Bordetella pertussis	Air-borne Direct contact	Man	7-10 days (not exceeding 21 days)	Early cattarrhal stage to 3 weeks after onset of symptoms	Brain damage Secondary infections Malnutrition	Antibiotics	Prolonged
Tetanus	Clostridium tetani	Broken skin	Spores found in soil	3-21 days	Not transmitted directly	Death	Sedatives Muscle relaxants Antibiotics Tetanus immune globulin	Clinical disease does not give immunity
Tuberculosis	Mycobacterium tuberculosis M.africanum M.bovis	Air-borne Raw milk	Man Cattle	4-12 weeks (may persist life-time as latent infection)	Variable (as long as tubercle bacilli being discharged) -	Progressive pulmonary disease Meningitis Hematogenous(miliary)	Antimicrobals: Izoniazid and one or more of: Rifampicin, streptomycin ethambutol or pyrazinamide	Variable

Annex 2

CASE DEFINITION OF VACCINE PREVENTABLE DISEASES

Classification	Suspect	Physician confirmed	Laboratory confirmed
Personnel	Lay Public/ MPWs	Medical Officers	Medical Officers
Methods	History	History + Clinical Investigations	Laboratory Identification
Neonatal tetanus	Normal suck or cry for first 2 days Onset between 3-28 days Inability to suck Stiffness or convulsions	Trismus Generalised muscle rigidity Convulsions	None
Tetanus	Injury or ear infection Difficulty in opening mouth Stiffness or convulsions	Trismus Generalised muscle rigidity Convulsions	None
Poliomyelitis	Fever Abrupt onset of weakness or paralysis of the leg(s) or arm(s) No progression of paralysis after first three days Paralysis not present at birth or associated with serious injury or mental retardation	Flaccid paralysis No sensory loss Muscle tenderness Absent or depressed deep tendon reflexes Asymmetrical findings Wasting of affected muscles(late findings) Residual paralysis 60 days after onset of illness should be added as a criteria in areas of low incidence	Positive virus culture for polio virus Positive serology (4-fold or greater rise in serum polio antibody titre)
Measles	Generalized blotchy rash lasting 3 or more days Fever Cough, runny nose or red eyes Exposure to a suspect case of measles in the previous 2 weeks or an epidemic of measles in the area	Generalized maculopapular rash Fever 38°C. (101°F) or more Cough, coryza, conjunctivitis or Koplik's spots	Positive serology (4 fold or greater rise in serum antibody titre)

Whooping cough (pertussis)	Cough persisting 2 weeks or more Fits of coughing which may be followed by vomiting Typical 'whoop' in older infants and children Exposure to a suspect case in previous 2 weeks or epidemic of whooping cough in the area	Prolonged coughing followed by apnoea, cyanosis or vomiting Typical 'whoop'in older infants and children Subconjunctival haemorrhages	White blood cell count with 15000 lymphocytes/cu mm or more (supportive of diagnosis but non-specific) Positive culture or immunofluorescence of nasopharyngeal secretions for Bordetella pertussis bacteria.
Diphtheria	Sore throat (with or without difficulty in swallowing) Mild fever Greyish-white membrane in throat (with or without difficulty in breathing) Exposure to a suspect case of diphtheria in the previous 1 weeks or epidemic of diphtheria in the area	Greyish-white membrane in throat (with or without difficulty in breathing) Acute pharyngitis, naso-pharyngitis or laryngitis Airway obstruction Myocarditis or neuritis (paralysis) one to six weeks after onset of symptoms	Common alternative diagnosis excluded by appropriate tests: negative throat culture for group A streptococci, negative blood test for mononucleosis Positive culture of Corynebacterium diphtheriae (demonstration of toxin production recommended but not required) Microscopic examination of a direct smear of a clinical specimen is not sufficiently accurate to substitute for a culture

Tuberculosis (childhood)	Listless Loss of weight Prolonged low grade fever Tuberculosis in family or close neighbour	BRAIN - Dazed condition, stiffness of neck, convulsions, severe headache, fever GLANDS - lymphadenopathy in neck and axilla which may suppurate LUNGS - Fever, cough, weakness, poor appetite BONES - Fever, pain, swelling and crippling of joints And any one of the following: Positive reaction on tuberculin testing (>10 mm induration) Favourable response to anti-TB therapy	Microscopy or culture of tubercle bacilli, identified as mycobacterium tuberculosis, from secretions or tissues CSF findings consistent with TB Suggestive radiological appearances on films of chest, bones or joints Suggestive histological findings in biopsy material

Note: Children may come for ... measles/pertussis secondary infections
A history of possible antecedent measles or pertussis in the last six weeks should be taken for all children with pneumonia or diarrhoea (for measles)

Record immunization status of all cases

Investigate all suspect cases of neonatal tetanus and poliomyelitis within two days to confirm diagnosis

Annex 3

LABORATORY INVESTIGATIONS OF VACCINE PREVENTABLE DISEASES

Disease	Specimen	Period	Transportation medium	Refrigeration	Test
Poliomyelitis	1. Stool 2-5 g	As early as possible in the acute phase (72 hours to 6 weeks)	Not necessary if transportation time less than 48 hours	4-8 ' C	Virus isolation and type identification
	2. Pharyngeal swabs	As early as possible in the acute phase (36 hours to 10 days)	Buffered broth with 1% protein and antibiotics	Freeze	Virus isolation and type identification
	3. Blood 5-10 ml or 3-4 ml serum	Two samples - - at onset (acute) - one month later (convalescent)	None (Serum should be separated to prevent heamolysis)	4-8 ' C	CFT Neutralization
Measles	1. Blood 5-10 ml or 3-4 ml serum	Two samples - - at onset (acute) - one month later (convalescent)	None (Serum should be separated to prevent heamolysis)	4-8 ' C	HI
	2. Blood on filter paper	Two samples - - at onset (acute) - one month later (convalescent)	None	None (can be kept at room t'	HI
Diphtheria	Throat swab	As early as possible (before treatment with antibiotics)	Loeffler serum medium combined with tellurite Amies or Carey Blair or silica gel	4-8 ' C	Isolation Toxin production
Pertussis	Throat swab Nasal swab	As early as possible (before treatment with antibiotics)	Bordet-Gengou Charcoal agar	4-8 ' C	Culture
Tuberculosis a	CSF Sputum	As early as possible			Microsopy Culture

a - Skin test - an intradermal tuberculin test with 2 TU PPD shows an induration of 10 mm or more, 48-72 hours after injection. Children with HIV, miliary tuberculosis or severe malnutrition may not respond

a - Radiological findings

Annex 4

LIST OF CASES

Sl. No.	Name	Address	Age	Sex	Immunization status[a]	Date of onset	Date of Examination	Diagnosis	Remarks

a - Give number of doses of vaccine received; the last dose should be at least one month prior to onset of illness

Annex 5

INVESTIGATION OF NEONATAL DEATHS

To be completed by the Medical Officer on all infants who died within the 1st month of life (a separate form for each neonatal death).

I. GENERAL INFORMATION

1. State/U.T._____
2. District_____
3. Town (Mohalla)/PHC/Village ___
4. Physician's Name_____
5. Date_____
6. Cluster No._____

II. BACKGROUND INFORMATION ON NEONATAL DEATH

1. Name of child_____
2. Sex of child_____
3. Father's name_____
4. Head of household_____
5. Date of birth of child_____
6. Address of child_____
7. Name of person interviewed_____
8. Relationship of person interviewed to child_____
9. Date of death of child_____

III. SYMPTOMS PRECEDING INFANT'S DEATH (Please circle appropriate answer)

1. Was the infant able to suck milk after birth?	Yes	No
2. Did the infant stop sucking milk when illness began?	Yes	No
3. Did the infant have a fever?	Yes	No
4. Did the infant have convulsions?	Yes	No
5. Was the infant noted to be stiff?	Yes	No

IV. INFANT'S CARE SINCE BIRTH (Please circle appropriate answer)

1. Who delivered the child?
   - Doctor/LHV/ANM
   - Dai (trained)
   - Dai (untrained)
   - Non-dai family members
   - Other (please specify)_____
2. Where the child delivered?
   - Hospital/Health centre
   - Home
   - In the fields
   - Other (please specify)_____
3. When the child became ill, who treated the child?
   - Government health centre
   - Resitered Physician (Allopathic/Ayurvedic/Homeopathic)
   - Un-registered Physician
   - No treatment was received

V. MOTHER'S IMMUNIZATION HISTORY

1. Does the mother know about vaccination with TT? Yes No (Circle)
2. Number of doses received during this pregnancy_____

VI. OTHER INFORMATION ON MOTHER

1. Is the mother alive? Yes No (Circle)
2. If dead, date of death_____
3. Symptoms preceding death_____

VII. MEDICAL OFFICER'S DIAGNOSIS

1. Cause of neonatal death_____
2. Cause of mother's death_____

_____
Signature of Medical Officer

Annex 6

CLINICAL OBSERVATIONS OF LAME CHILDREN

To be completed by the Medical Officer on all lame children (a separate form for each lame child).

I GENERAL INFORMATION

1. State/U.T._____
2. District_____
3. Town (Mohalla)/PHC (Village)_____
4. Physician's Name_____
5. Date_____
6. Cluster No._____

II BACKGROUND INFORMATION ON LAME CHILD

1. Name of child_____
2. Sex_____
3. Father's Name_____
4. Head of Household_____
5. Date of birth of child_____
6. Address of Child_____
7. Person interviewed_____
8. Relationship of person interviewed to child_____

III HISTORY OF ILLNESS RESULTING IN LAMENESS OF THE CHILD

1. Date of onset of lameness_____
2. Address of child at onset of lameness (Outside the district or not)_____
3. Number of doses of polio vaccine received by child preceeding onset of lameness_____
4. Medical care during illness resulting in lameness—(circle correct answer)
   (a) Registered physician (Allopathic/Ayurvedic/Homoeopathic)
   (b) Health Centre.
   (c) Un-registered physician
   (d) Other (please specify)_____
   (e) No treatment received
5. Did the child have fever at the time of onset of lameness ? Yes No
6. Was the onset of the lameness acute ? Yes No
7. Did the lameness progress (increase) after onset ? Yes No

IV PHYSICAL EXAMINATION OF CHILD (Circle correct answer)

1. Paralysis of lower limb present Yes No
2. Affected Limb Right Left Both
3. Type of Paralysis present Flaccid Spastic No Paralysis
4. Sensation in affected limbs Normal Impaired
5. Muscle atrophy (wasting) in affected limb Yes No
6. Gait normal impaired requires assistance unable to evaluate

V EVALUATION OF LAMENESS (circle appropriate answer)

1. Lameness not present
2. Lameness present
   (a) does not require mechanical aid to walk
   (b) requires mechanical aid to walk
   (c) unable to walk

VI PHYSICIAN'S DIAGNOSIS ON CAUSE OF LAMENESS (circle appropriate answer)

1. Poliomyelitis
2. Trauma (please specify)_____
3. Congenital deformity (please specify)_____
4. Other (please specify)_____

Medical Officer's Signature_____

Annex 7

LIST OF CASES WITH ADVERSE REACTIONS

Sl. No.	Name	Address	Age	Sex	Vaccine administered[a]	Time of onset	Time of examination	Major signs and symptoms	Diagnosis	Remarks

[a]Give name of vaccine and the dose (1, 2, 3 or booster, as relevant).

Annex 8

CALCULATION OF VACCINE EFFICACY

Estimation of vaccine efficacy is an important measure of the quality of the immunization programme and indicates that potent vaccines are being properly administered. Vaccine efficacy is measured by the following formula which estimates the percentage reduction in the incidence rates (attack rates, AR) of disease among vaccinated persons compared to unvaccinated persons:

$$VE = \frac{(PPV)(PCU) - (PPU)(PCV)}{(PPV)(PCU)}$$

where:

VE = vaccine efficacy
PCU = proportion of cases unvaccinated
PPU = proportion of population unvaccinated
PCV = proportion of cases vaccinated with the number of doses being examined for vaccine efficacy
PPV = proportion of population vaccinated with the number of doses being examined for vaccine efficacy

It is possible to calculate vaccine efficacy using this formula as shown in the following example: Suppose that an outbreak of poliomyelitis has occurred in a district. The immunization coverage in the district in children 12 to 23 months of age as determined from a vaccination coverage survey is known to be 60 per cent for OPV3 and 25 per cent of children are unimmunized (15 per cent of children had received only one or two doses). Of children 12 to 23 months of age who are residents of the district and who are suffering from poliomyelitis, it is found that 15 per cent had received three doses of OPV vaccine and 75 per cent were unimmunized (10 per cent of children had received only one or two doses). Using the above formula, vaccine efficacy would be estimated to be:

$$VE = \frac{(.60)(.75)-(.25)(.15)}{(.60)(.75)} = \frac{.450 - .0375}{.450} = \frac{.4125}{.450} = .92 \text{ or } 92\%$$

In the situation where only one dose of vaccine is required (e.g., BCG and measles), or where only efficacy of the third dose of a multiple dose vaccine (e.g., OPV3 and DPT3) is desired and the drop-out rate from the first to third dose is relatively small, then the formula can be further simplified as follows:

$$VE = \frac{PPV - PCV}{PPV - (PPV)(PCV)}$$

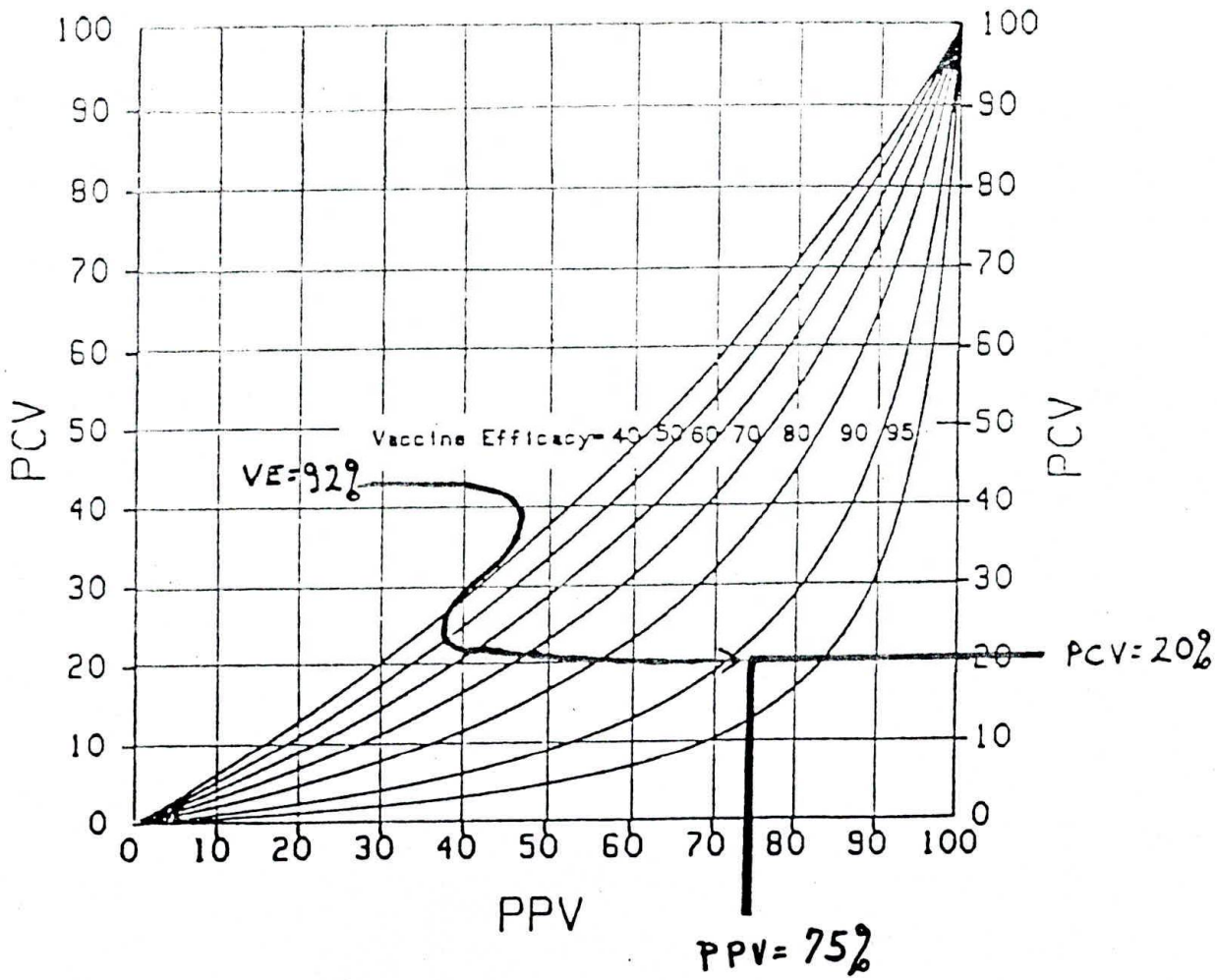
It is possible to simply calculate vaccine efficacy using this formula as shown in the following example: Suppose that an outbreak of measles has occurred in a district. The immunization coverage in the district is known to be 75 per cent for measles vaccine in children 12 to 23 months of age as

determined from a vaccination coverage survey. Of children 12 to 23 months of age who are residents of the district and who are suffering from measles, it is found that 20 per cent had received a dose of measles vaccine. Using the above formula, vaccine efficacy would be estimated to be:

$$VE = \frac{.75 - .20}{.75 - (.75)(.20)} = \frac{.55}{.75 - .15} = \frac{.55}{.60} = .92 \text{ or } 92\%$$

If this simplified formula is graphed for different values of the three variables, it is possible to develop a set of curves to easily estimate vaccine efficacy in the actual field setting. By knowing values for PPV and PCV, vaccine efficacy can be estimated by looking at where the lines intersect on the graph. An example using the same outbreak data given above is illustrated in the figure below.

Percentage of cases vaccinated (PCV) per
percentage of population vaccinated (PPV),
for 7 values of vaccine efficacy (VE)



Source: Weekly Epidemiological Record, No.18, pp 133-136