A RANDOMIZED, CONTROLLED TRIAL OF VITAMIN A IN CHILDREN WITH SEVERE MEASLES

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Abstract *Background.* Measles kills about 2 million children annually, and there is no specific therapy for the disease. It has been suggested that vitamin A may be of benefit in the treatment of measles.

Methods. We conducted a randomized, double-blind trial involving 189 children who were hospitalized at a regional center in South Africa because of measles complicated by pneumonia, diarrhea, or croup. The children (median age, 10 months) were assigned to receive either vitamin A (total dose, 400,000 IU of retinyl palmitate, given orally; n = 92) or placebo (n = 97), beginning within five days of the onset of the rash. At base line, the characteristics of the two groups were similar.

Results. Although clinically apparent vitamin A deficiency is rare in this population, the children's serum retinol levels were markedly depressed (mean [±SEM], 0.405±0.021 μmol per liter [11.6±0.6 μg per deciliter]), and 92 percent of them had hyporetinemia (serum retinol level <0.7 μmol per liter [20 μg per deciliter]). Serum concentrations of retinol-binding protein (mean, 30.1±2.0 mg per liter) and albumin (mean, 33.4±0.5 g per liter) were also low. As compared with the placebo group, the children who received vitamin A recovered more rapidly from pneumonia (mean, 6.3 vs. 12.4 days, respectively; P<0.001) and diarrhea (mean, 5.6 vs. 8.5 days; P<0.001), had less croup (13 vs. 27 cases; P = 0.03), and spent fewer days in the hospital (mean, 10.6 vs. 14.8 days; P = 0.01). Of the 12 children who died, 10 were among those given placebo (P = 0.05). For the group treated with vitamin A, the risk of death or a major complication during the hospital stay was half that of the control group (relative risk, 0.51; 95 percent confidence interval, 0.35 to 0.74).

Conclusions. Treatment with vitamin A reduces morbidity and mortality in measles, and all children with severe measles should be given vitamin A supplements, whether or not they are thought to have a nutritional deficiency. (N Engl J Med 1990; 323:160-4.)

MEASLES remains a devastating disease, for which specific therapy is lacking. Hopes for its control and eventual eradication rest on immunization, but measles kills about 2 million children each year[1] and cripples an untold number through blindness[2] and lung disease.[3,4] The idea that vitamin A may have a protective effect in measles was first suggested more than 50 years ago[5] but was ignored until Barclay et al.,[6] in a randomized clinical trial, found twice as many deaths in the control group (12 of 92) as among children given high doses of vitamin A (6 of 88).[7] Although the overall results did not reach statistical significance, vitamin A was significantly protective in the group under two years of age.[6]

That vitamin A should be of benefit in measles is biologically plausible.[7] Measles depresses serum levels of vitamin A,[8-11] and hyporetinemia (a serum retinol level below 0.7 μmol per liter [20 μg per deciliter]) is associated with increased mortality from the disease, particularly in children under two years of age.[11] In almost every known infectious disease, vitamin A deficiency is known to result in greater frequency, severity, or mortality.[12] Increased susceptibility to infection was one of the first features of nutritional vitamin A deficiency to be recognized,[13] and even mild deficiency appears to be associated with an increased risk of pneumonia, diarrhea, and death in childhood.[14-17] According to Scrimshaw et al., "no nutritional deficiency in the animal kingdom is more consistently synergistic with infection than that of vitamin A."[12] They list nearly 50 studies (including 8 in humans) of diseases of bacterial, viral, or protozoan origin in which vitamin A deficiency resulted in increased frequency, severity, or mortality.[12] In fact, vitamin A is sometimes referred to as the "anti-infective" vitamin.[18]

We embarked on this study because measles is a pressing problem in our part of the world[19] and because the results of Barclay et al.[6] and the circumstantial evidence appeared promising. Subsequently, acting on the same evidence, the World Health Organization recommended routine vitamin A supplementation for all children with measles in regions where vitamin A deficiency was a recognized problem and suggested that elsewhere "in countries where the fatality rate of measles is 1% or higher it would be sensible to provide vitamin A supplements to all children diagnosed with measles."[20] One difficulty with this advice is that in the communities in which measles poses the greatest problem, the mortality rate is often unknown. Another is that the recommendation is based on the less than conclusive evidence from the only two studies to have addressed the question of vitamin A therapy in measles.[5,6] These are some of the reasons why vitamin A supplementation is still not given routinely to children who are seriously ill with measles in South Africa, and presumably elsewhere.

METHODS

Children with acute measles who required hospital admission for the treatment of associated complications were entered in a randomized, double-blind, placebo-controlled trial to assess the effect of oral vitamin A on morbidity and mortality. The study was limited by a priori considerations to a fixed termination date, with a maximal enrollment of 200 cases. It was conducted from March to July 1987 at the City Hospital for Infectious Diseases, a regional center serving a population of about 2 million in Cape Town and

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surrounding areas. The Medical Faculty's ethics and research committee approved the study protocol.

Patient Selection and Randomization

All children under 13 years of age who were referred to the hospital for admission with measles were eligible for entry into the trial. The criteria for exclusion were vitamin A therapy before admission, xerophthalmia on admission or thereafter, rash for more than four days, or lack of parental consent.

Patients in the trial were randomly assigned to receive either 400,000 IU (120 mg) of water-miscible vitamin A (retinyl palmitate; Arovit drops, Roche, Basel, Switzerland) or an identical-appearing placebo from syringes coded according to a random-number table. The senior ward nurse gave half the dose on admission and the remainder a day later, either by mouth or by nasogastric tube. The children were cared for by the regular ward staff. Concurrent therapy included oxygen, intravenous fluids, and antibiotics as appropriate, but no additional vitamin supplements. One of the study investigators assessed the patients each day. The treatment-assignment codes were broken only at the completion of the trial.

Initial Investigations

The children's weight and height were recorded, and a venous-blood sample was drawn on entry into the trial. The weights and heights were evaluated against the standards of the National Center for Health Statistics.[21] Hemoglobin levels, white-cell counts (by Coulter model S5, Coulter Electronics, Hialeah, Fla.), and differential counts were estimated, and serum was stored at −70°C. Serum levels of total protein and albumin were measured by automated analysis (Astra-8, Beckman Instruments, Brea, Calif.). Serum concentrations of vitamin A (as retinol) were measured by high-performance liquid chromatography (Dupont Instruments, Wilmington, Del.), with concentrations of vitamin E (as alpha-tocopherol) obtained incidentally.[22] A programmable integrator was used to quantify the chromatographic results (Spectra-Physics, San Jose, Calif.). Retinol-binding protein was measured by radial immunodiffusion with a commercial kit (LC-Partigen, Behringwerke, Marburg, Federal Republic of Germany). Chest radiographs and other investigations were performed when indicated.

Table 1. Base-Line Clinical Findings in 189 Children with Measles, According to Treatment Group.*

Characteristic	No. of Patients	Placebo (N = 97)	Vitamin A (N = 92)
Age (mo)		*15.06 (8, 10, 15)*	*15.89 (8, 10, 17)*
<6	7	3	4
6–12	117	64	53
13–23	37	18	19
≥24	28	12	16
Male/female		56/41	53/39
Mixed race/black		29/68	24/68
Weight for age†	189	*81.5 (74, 84, 92)*	*85.7 (77, 85, 96)*
<5th percentile	95	51	44
Height for age†	178	*96.0 (93, 97, 100)*	*97.1 (93, 96, 101)*
<5th percentile	52	25	27
Weight for height†	178	*89.0 (82, 88, 95)*	*90.3 (84, 91, 97)*
<5th percentile	70	41	29
Rash (days)‡		*1.91 (1, 2, 2)*	*1.72 (1, 1.5, 2)*
Diarrhea	152	75	77
No pneumonia	30	13	17
Pneumonia	146	74	72
No diarrhea	24	12	12
Pneumonia and diarrhea	122	62	60
Herpes stomatitis	4	1	3
Measles croup§	13	4	9

*Values in italics are means, followed in parentheses by 25th percentiles, medians, and 75th percentiles. All other values are numbers of patients.

†Expressed as a percentage of the 50th percentile of the standards of the National Center for Health Statistics.

‡P<0.05 for the comparison between groups.

§No patients with measles croup required airway intervention.

Assessment of Outcomes

Outcomes were assessed solely on the basis of clinical criteria. The outcome variables used were death and the severity of illness, as indicated by the duration of the hospital stay, the duration of pneumonia or diarrhea, the incidence of "postmeasles" croup or herpes stomatitis; and the need for a transfer to the Red Cross War Memorial Children's Hospital for intensive care. Pneumonia was defined as the presence of tachypnea (frequency of respiration >40 per minute) with retractions, crackles, or wheezes. Diarrhea was defined as the passage of four or more liquid stools a day. Measles croup was defined as croup presenting on or within a day of admission. Croup that developed subsequently was categorized as post-measles.

Statistical Analysis

The data were analyzed by computer with the Epi-Info program (version 3, USD, Stone Mountain, Ga.). Categorical data[23] (e.g., the number of patients per group) were evaluated by the chi-square test, with Yates' correction for continuity applied routinely,[24] or by Fisher's exact test when the expected number in a cell was five or less.[24] Confidence intervals for the relative risks were calculated according to the method of Greenland and Robins.[25] Continuous data[23] (e.g., vitamin level) were compared by the nonparametric Kruskal–Wallis test.[23,24] All P values reported are two-tailed, with values of less than 0.05 considered statistically significant.

Results

Exclusion of Patients

Of 224 patients under 13 years of age who were admitted to the hospital with measles during the study, 35 were excluded from the trial. In 12 of these cases the rash was present for five or more days, in 2 vitamin A had previously been given, in 18 consent could not be obtained because the child was unaccompanied by a parent on admission, and in 3 the parents refused consent. Hence, 189 patients were entered in the trial. There were no exclusions for xerophthalmia or withdrawals after entry.

Base-Line Characteristics

The placebo and treatment groups were generally comparable (Tables 1 and 2), except that the patients in the vitamin A group were admitted about 12 hours earlier in terms of the duration of the rash and had lower serum levels of total protein and albumin than those in the placebo group. Two thirds of the children were 12 months old or younger (median, 10 months; range, 2 months to 5 years), and most were boys (58 percent). Blacks predominated (72 percent), and the remainder were of mixed race. The five white patients admitted with measles were excluded; consent was refused in the cases of two, and three were more than 13 years old. The hospital is open to all. Immunization and socioeconomic factors are thought to account for differences in racial makeup between the study population and the general population 14 years of age or

under in Cape Town (57 percent mixed race, 25 percent black, 18 percent white).[27] Heights were not measured for 11 patients. Height for age was below the fifth percentile in 52 children (29 percent) — a prevalence similar to that in the local reference population.[28] Weight for age (below the fifth percentile in 50 percent), and weight for height (below the fifth percentile in 39 percent) were considered to reflect short-term weight losses from measles[29,30] rather than preexisting acute protein-energy malnutrition, since that occurs in 1 percent or less of the local reference population.[28] A combination of pneumonia and diarrhea was the usual indication for hospital admission (64 percent). Diarrhea (16 percent), pneumonia (13 percent), or measles croup (7 percent) appearing as isolated symptoms precipitated the other admissions.

Table 2. Base-Line Blood and Serum Values, According to Treatment Group.

Characteristic*	No. of Patients	Placebo	Vitamin A
		mean (25th, 50th, and 75th percentile)	
Hemoglobin (g/dl)	177	10.73 (10, 10.6, 11.5)	10.78 (10, 10.5, 11.7)
Hematocrit (%)	177	32.4 (30, 32.5, 35)	32.8 (30, 32, 35)
Leukocytes ($\times 10^{-9}$/liter)	177	8.63 (6.3, 7.7, 10.2)	8.99 (6.2, 8.15, 10.25)
Lymphocytes ($\times 10^{-9}$/liter)	177	3.39 (2, 3.1, 4.2)	3.42 (1.8, 2.9, 4.3)
Total protein (g/liter)†	155	58.54 (55, 57, 62)	53.94 (51, 54, 58)
Albumin (g/liter)†		34.5 (32, 34, 37)	32.4 (29, 33, 35)
RBP (mg/liter)	156	29.6 (14, 18, 30)	30.48 (14, 17, 37)
Vitamin A (retinol) (μg/dl)	156	12.19 (7.7, 10.7, 14.4)	10.95 (6.7, 9.5, 12.6)
Age <2 yr	131	12.84 (11.4, 15.1, 46.5)	11.1 (6.7, 9.5, 12.4)
Age ≥2 yr‡	25	8.38 (7.1, 8.1, 10.5)	10.29 (6.4, 10.5, 13.6)
Hyporetinemia	143	68§	75§
Vitamin E (mg/liter)	156	7.94 (5.5, 7.8, 9.4)	6.84 (4.7, 6.8, 8.8)

*Reference values for the characteristics shown are as follows[26]: hemoglobin, 11.5 to 15.5 g per deciliter; hematocrit, 35 to 45 percent; leukocytes, 6 to 17×10^9 cells per liter; total protein, 62 to 80 g per liter; albumin, 35 to 50 g per liter; retinol-binding protein, 22 to 45 mg per liter; vitamin A (as retinol), 30 to 80 μg per deciliter; vitamin E (as alpha-tocopherol), 5.0 to 20 mg per liter. No reference values are given for lymphocytes because of considerable variation with age. RBP denotes retinol-binding protein. To convert grams of hemoglobin per deciliter to millimoles per liter, multiply by 0.6206; to convert micrograms of vitamin A per deciliter to micromoles per liter, multiply by 0.03491; and to convert milligrams of vitamin E per liter to micromoles per liter, multiply by 23.22.

†$P<0.05$ for the comparison between groups.

‡In the placebo group, the retinol level was significantly lower in children ≥2 years old than in those <2 years old ($P = 0.026$).

§Indicates the number of cases of hyporetinemia (serum retinol concentration <0.7 μmol per liter [20 μg per deciliter]).

No blood samples were obtained from 15 patients, and only partial results were available for another 19 (Table 2). Serum levels were low for total protein (mean [±SE], 56.2±0.7 g per liter), albumin (mean, 33.4±0.46 g per liter), retinol-binding protein (mean, 30.1±2.02 mg per liter), and vitamin A as retinol (mean, 0.405±0.021 μmol per liter [11.6±0.6 μg per deciliter]). Low levels of total protein principally reflect depressed serum albumin concentrations ($r^2 = 72.6$ percent, $P<0.001$). Serum retinol levels were below the lower limit of the normal range (0.7 μmol per liter [20 μg per deciliter]) in 92 percent of the children (143 of 156), and 46 percent (72) had levels below 0.35 μmol per liter (10 μg per deciliter), placing them at risk for xerophthalmia,[31] although no cases of this were observed. Vitamin E levels were in the normal range.

Outcome

The children who received vitamin A had markedly diminished mortality and morbidity (Table 3), with no clinically apparent adverse effects. Of the 12 children who died (6.3 percent), 10 were in the placebo group ($P = 0.046$). The children who died were 5 to 29 months of age, and seven were boys. Death occurred 3 to 32 days after admission (median, 10.5). Pneumonia[3,32] caused 10 deaths, and the two remaining children died after 15 and 32 days, respectively, of fulminant sepsis following chronic diarrhea and measles-induced kwashiorkor. Croup was present as an incidental finding in 5 of the 10 children who died of pneumonia.

Cases of pneumonia lasted almost twice as long in the placebo group as in the vitamin A group ($P<0.001$), and 66 percent of the children with chronic pneumonia (>10 days) were in the placebo group ($P = 0.008$). Similarly, diarrhea continued for a third longer in the placebo group ($P<0.001$), and 72 percent of the children with chronic diarrhea were in that group ($P = 0.023$). Postmeasles croup was more common in the placebo group ($P = 0.033$), as was herpes stomatitis ($P = 0.08$). Finally, the hospital stay of the survivors was shorter by a third in the vitamin A–treated group ($P = 0.004$).

Overall, 77 children had adverse outcomes (Table 3), of whom 52 were in the placebo group ($P = 0.004$). As compared with the children in the placebo group, the children treated with vitamin A were at lower relative risk for death (relative risk, 0.21; 95 percent confidence interval, 0.05 to 0.94), prolonged pneumonia ≥10 days (relative risk, 0.44; 95 percent confidence interval, 0.24 to 0.80), prolonged diarrhea ≥10 days (relative risk, 0.40; 95 percent confidence interval, 0.19 to 0.86), postmeasles croup (relative risk, 0.51; 95 percent confidence interval, 0.28 to 0.92), airway intervention (relative risk, 0.35; 95 percent confidence interval, 0.10 to 1.26), herpes stomatitis (relative risk, 0.23; 95 percent confidence interval, 0.05 to 1.06), and the need for intensive care (relative risk, 0.38; 95 percent confidence interval, 0.13 to 1.16). The overall risk for an adverse outcome in children treated with vitamin A was half that in the control group (relative risk, 0.51; 95 percent confidence interval, 0.35 to 0.74). Of the 77 children who had adverse outcomes, only 2 were ≥2 years of age ($P = 0.002$), and the risk in a child ≥2 years old was substantially lower than in

Table 3. Mortality and Morbidity in 189 Children with Measles, According to Treatment Group.*

Characteristic	Placebo (N = 97)	Vitamin A (N = 92)	Relative Risk (95% CI)†	P Value
Death	10	2	0.21 (0.05–0.94)	0.046
Age at death (mo)				
<6	1	0		
6–12	7	1		
13–23	1	1		
≥24	1	0		
Pneumonia (days)				
Duration	*12.37 (5, 8, 17)*	*6.53 (3, 5, 8.5)*		<0.001
≥10	29	12	0.44 (0.24–0.80)	0.008
Diarrhea (days)				
Duration	*8.45 (5, 7, 10)*	*5.61 (3, 5, 7)*		<0.001
≥10	21	8	0.40 (0.19–0.86)	0.023
Postmeasles croup	27	13	0.51 (0.28–0.92)	0.033
With airway intervention	9	3	0.35 (0.10–1.26)	0.16
Herpes stomatitis	9	2	0.23 (0.05–1.06)	0.08
Intensive care	11	4	0.38 (0.13–1.16)	0.13
Adverse outcome‡	52	25	0.51 (0.35–0.74)	<0.001
Hospital stay (days)§	*15.24 (8, 11, 19)*	*10.52 (7, 9, 13)*		0.004

*In the columns representing the treatment groups, the values in italics are means, followed in parentheses by 25th percentiles, medians, and 75th percentiles. All other values are numbers of patients.

†Relative risk denotes the ratio of the incidence of an event in the vitamin A group to the incidence of the event in the placebo group. CI denotes confidence interval.

‡Defined as death, pneumonia ≥10 days in duration, diarrhea ≥10 days in duration, postmeasles croup, or transfer for intensive care.

§Refers to children who survived.

younger children (relative risk, 0.15; 95 percent confidence interval, 0.02 to 0.91). No child with a serum retinol concentration ≥0.7 μmol per liter (20 μg per deciliter) died, but the smallness of this group (n = 14) leaves the significance of the finding in doubt.

Discussion

The results of our randomized, controlled trial indicate a remarkable protective effect of vitamin A in severe measles, notwithstanding the provision of good general medical care and the presence of complicated advanced disease. Vitamin A reduced the death rate by more than half and the duration of pneumonia, diarrhea, and hospitalization by about one third. Vitamin A also appeared to reduce the incidence of herpes stomatitis and the need for intensive care. The consistency of benefit with respect to all measures of outcome is noteworthy, since mortality is not a sensitive criterion. Because of their reliance on mortality rates, previous studies of measles[5,6] lacked the statistical power to establish the benefit of vitamin A therapy.

The favorable response to vitamin A therapy may be understood in terms of the very high incidence (92 percent) of hyporetinemia in our patients (Table 2). Hyporetinemia implies a state of vitamin A deficiency at the tissue level, since there are virtually no peripheral-tissue stores of vitamin A except in the retina.[33-36] Serum retinol levels below 0.7 μmol per liter (20 μg per deciliter) appear to be inadequate for the body's biologic needs.[33] Oral vitamin A is absorbed well even in patients with diarrhea,[37] so the observed effects of treatment may reasonably be ascribed to correction of the tissue deficit of vitamin A. We do not know, however, whether the deficit was rectified by increases in the serum retinol concentration or by some other mechanism, since serum retinol levels were not measured after therapy.

Hyporetinemia appears almost invariable in children with severe measles,[8-11] as in this study, and the reduction in the serum retinol level is associated with increasingly severe disease.[11] Since many of these data come from populations in which nutritional vitamin A deficiency is a known problem,[8-10] it has been inferred that hyporetinemia in measles represents the exhaustion of hepatic stores.[6,7,20] There is a possible alternative mechanism, however. Hyporetinemia may occur in the presence of adequate hepatic stores of vitamin A when the stores are not mobilized fast enough to meet demand.[36] This has been found in fever, pneumonia, rheumatoid arthritis, hepatitis, acute tonsillitis, and rheumatic fever[36]; in protein-energy malnutrition[38]; and now also in measles.[8] Inadequate mobilization of hepatic stores may therefore underlie the hyporetinemia in children with severe measles from Kinshasa, Zaire,[11] and Cape Town, where nutritional vitamin A deficiency is uncommon. A study 25 years ago showed vitamin A deficiency to be rare in Cape Town, even in children with severe protein-energy malnutrition,[38] and it still appears to be rare. A search of the computer data-base listing of inpatients at our children's hospital, which predominantly serves the local underprivileged community, found only three instances of clinical vitamin A deficiency among 161,381 children admitted over a 13-year period, with no cases since 1985.

In view of the evidence that hyporetinemia may occur in the presence of adequate hepatic stores of vitamin A[36] and in populations not known to be deficient in vitamin A,[11] it would seem prudent to proceed on the assumption that previous nutritional adequacy may not ensure against the development of hyporetinemia in severe measles. For all children seriously ill with measles, vitamin A replacement should thus be provided at the dose given by Barclay et al.[6] (400,000 IU), which proved effective and safe in our study. A lower dose (100,000 to 200,000 IU) is recommended by the World Health Organization,[20] but its efficacy in measles has yet to be established.

It may be asked whether it is cost effective to advocate treatment with vitamin A for all children with

severe measles. Clearly, children under two years of age are at highest risk of an adverse outcome and derive the most benefit from vitamin A. When resources are scarce, such children should be given priority. In our study, however, half the children over two years of age were at risk of xerophthalmia because of serum retinol levels below 0.35 μmol per liter (10 μg per deciliter),[31] and hence they should have vitamin A prophylaxis. Thus, when resources permit, all children with severe measles should be given supplemental vitamin A.

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Vitamin A supplements and mortality related to measles: a randomised clinical trial

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Abstract

One hundred and eighty children admitted with measles were randomly allocated to receive routine treatment alone or with additional large doses of vitamin A (200 000 IU orally immediately and again the next day). Baseline characteristics of the two groups were virtually identical for age, severity of measles, and vitamin A and general nutritional states. In 91% of the children serum vitamin A concentrations were less than 0·56 µmol/l. Of the 88 subjects given vitamin A supplements, six (7%) died; of the 92 controls, 12 (13%) died ($p=0·13$). This difference in mortality was most obvious for children aged under 2 years (one death out of 46 children receiving supplements versus seven deaths out of 42 controls; $p<0·05$) and for cases complicated by croup or laryngotracheobronchitis. Mortality was several times higher in marasmic than in better nourished children, regardless of study allocation ($p<0·01$).

Introduction

Recent reports from Indonesia have shown that children with clinically mild vitamin A deficiency have a fourfold increase in mortality from all causes and a threefold increase in the incidence of respiratory and diarrhoeal diseases.[1] Vitamin A supplements reduced preschool age childhood mortality by over 30%.[1] After reviewing some 50 reports of the effect of vitamin A deficiency on bacterial, viral, protozoal, and helminthic infections in man and animals Scrimshaw *et al* concluded that "no nutritional deficiency is more consistently synergistic with infectious disease than that of vitamin A."[2] At the time that they wrote this they were unable to find data concerning the interaction between vitamin A and measles.

Vitamin A is essential for the maintenance of normal epithelial tissues throughout the body. In the absence of vitamin A mucosal epithelium undergoes squamous metaplasia, with a concomitant decrease in cell turnover.[3-5] Measles is a viral disease that infects and damages epithelial tissues throughout the body.[6-11] The disease can also decrease serum concentrations of vitamin A in well nourished children to less than those observed in non-infected malnourished children.[12] Measles probably increases utilisation of vitamin A, and children with marginal liver stores of the vitamin may thus develop acute vitamin A deficiency, resulting in eye damage and possibly increased mortality from respiratory and diarrhoeal causes. Indeed, measles is an important risk factor in the development of severe vitamin A deficiency and xerophthalmia in Asia.[13-14] It is also a particularly virulent disease among African children, accounting for most cases of childhood blindness and for considerable mortality.[10-11,15-17] Recent data suggest that vitamin A deficiency may be prevalent in areas of Africa, including Tanzania.[16-18]

This hospital based study sought to determine the effect of high dose vitamin A supplements taken during early infection with measles on subsequent mortality in African children.

Patients and methods

Mvumi Hospital is a rural general hospital in central Tanzania related to the church. Paediatric patients are drawn almost entirely from the local population, which comprises subsistence farmers living in a fairly arid environment. The staple diet is millet eaten with a green vegetable relish.

There is only one harvest a year, in April to May, and that is dependent on good rains. The rains in 1982 were very bad, leaving conditions of near famine for many, but the rains and harvest in 1983 were good. Malnutrition is a great problem in children. About a quarter of all children admitted are severely malnourished, and only 30% have a weight for age above 80% of the standard.[19] Anaemia is also common. The general paediatric background is more fully described elsewhere (A J G Barclay: unpublished).

We attempted to include in this study every child with measles presenting to the hospital from September 1982 to November 1983, a period that included an entire measles season. Measles was diagnosed on clinical grounds that included a history of prodromal disease and the presence of a typical rash. On admission all children were given a full clinical examination by the paediatrician. Shortly after admission they were seen by a member of the eye department. They were all weighed and measured by the nurses and had their haemoglobin concentration measured and a blood slide examined by staff in the hospital laboratory.

A venous blood sample was taken on admission for estimation of vitamin A state. Half of the subjects were then randomly allocated to receive vitamin A (200 000 IU in oil orally immediately and again the next day); the other children were given standard treatment. Randomisation was accomplished by sequential assignment of single digits from a random numbers table, odd digits dictating one group and even the other. Which children received vitamin A was known to the paediatrician but not recorded in the general notes: study allocation was therefore not known by any other staff dealing with care of the children. Other main therapeutic sources of vitamin A—for example, multivitamins—are not routinely given and therefore were not received by any children in the trial. The two groups were treated identically in the ward, fed the same diet, and given antibiotics or further investigations as indicated by their clinical condition.

Deaths caused by measles were taken to be deaths occurring within one month of onset of the rash. Most patients were still in the ward when they died; three returned of their own accord and were readmitted with dysentery or diarrhoea and died quickly and two ran away moribund and died at home.

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Baseline blood samples were allowed to clot and were then spun down. The serum was separated and stored in a deep freeze within four hours of taking the sample. The serum was later shipped to Baltimore, where concentration of vitamin A (as retinol) was measured by high performance liquid chromatography.[23] Because of losses in transport biochemical determinations are available for only 38 recipients of vitamin A and 47 controls.

As the study was designed to assess the beneficial impact of vitamin A supplements, and there was no biological, clinical, or epidemiological reason to suspect any deleterious effects from added vitamin A, results were assessed with a single tail normal deviate (z) and Fisher's exact test.

Results

Two hundred and twelve patients with measles were admitted during the trial. Thirty two were excluded from the trial, all but six before randomisation because of corneal ulcers (seven patients, who were automatically given vitamin A and are reported on separately[21]); death within 24 hours of admission (five); running away within 24 hours (one); receiving vitamin A before admission (nine); and admission while the study coordinator was absent (10). Of the 180 children in the trial, 11 did not have their height recorded and 15 did not have their haemoglobin concentration measured.

The distribution of baseline characteristics of recipient and control children was similar, including age (mean recipient 29·5 v mean control 30·7 months), weight for age (72% v 75% of standard), weight for height (83% v 86% of standard), haemoglobin concentration (85 v 89 g/l), interval between onset of rash and admission (3·5 v 3·4 days), and serum vitamin A concentration (0·30 v 0·32 μmol/l). Only 9% of patients had serum vitamin A concentrations greater than 0·53 μmol/l.

Of the 88 children given vitamin A, six (7%) died (table I). Of the 92 controls, 12 (13%) died. Despite the large clinical difference small numbers limit its significance ($p=0·13$). The difference was most obvious for children aged under 2 years ($p<0·05$).

TABLE I—*Mortality of children admitted with measles*

Age (months)	No of children admitted		No (%) who died	
	Given vitamin A	Controls	Given vitamin A	Controls
<9	14	9		2 (22)
9-11	12	10		2 (20)
12-23	20	23	1 (5)	3 (13)
24-35	11	16	1 (9)	2 (13)
36-47	11	13	1 (9)	1 (8)
48-59	8	6	1 (13)	
≥60	12	15		2 (13)
Total	88	92	6 (7)	12 (13)

Twenty five children (14%) were marasmic, and 104 (58%) were underweight as assessed by weight for age (table II). The mortality of marasmic children was several times higher than that of better nourished children, regardless of whether they had received vitamin A or not ($p<0·01$, two tailed test). In every nutritional category mortality was lower for vitamin A recipients.

Complications, usually already present at the time of admission, were equally common in the two groups, but mortality from such complications was higher in the control group (table III). Pneumonia was the commonest complication, affecting 85 children. Croup complicated measles in 13 of the control group, of whom four (31%) died; in contrast, of eight children with croup given vitamin A, none died. Very few children had dysentery; of those who did, half died.

TABLE II—*Weight for age and mortality*

Weight for age*	No of children in study		No (%) who died		
	Given vitamin A	Controls	Given vitamin A	Controls	Total
>80%	24	27	1 (4)	3 (11)	4 (8)
60-80%	47	57	4 (9)	6 (11)	7 (7)
<60%	17	8	4 (24)	3 (38)	7 (28)
Total	88	92	6 (7)	12 (13)	18 (10)

*Percentage of median National Center for Health Statistics standard.[19]

TABLE III—*Complications and associated mortality*

Complication	No (%) of children with complications		No (%) of children who died	
	Given vitamin A	Controls	Given vitamin A	Controls
Pneumonia	38 (43)	47 (51)	3 (8)	7 (15)
Otitis media	19 (22)	20 (22)	1 (5)	3 (15)
Croup or laryngotracheobronchitis	8 (9)	13 (14)		4 (31)
Dysentery	2 (2)	6 (7)	1 (50)	3 (50)
Haemorrhagic rash	28 (32)	34 (37)	1 (4)	4 (12)
Oral candidiasis	9 (10)	5 (5)	1 (11)	1 (20)

Discussion

Children randomised to receive vitamin A did not differ from the control group in baseline age, nutritional state, duration of illness, prevalence of complications, or haemoglobin or serum vitamin A concentrations. Mortality was twice as high in the control group as in the treated group, almost all of the difference being accounted for by children aged under 2 years ($p<0·05$).

Although the numbers were small, there was a remarkable consistency in the beneficial impact of vitamin A supplements on complicating illness and nutritional strata. This was especially obvious among children with croup or laryngotracheobronchitis. No child who received vitamin A died of laryngotracheobronchitis, whereas four in the control group died. Laryngotracheobronchitis is a particularly difficult condition to treat with limited resources. Because repair of epithelial surfaces in children with early vitaminA deficiency may be poor, with a tendency to develop into squamous metaplasia of the respiratory tract,[7] they may suffer increased susceptibility to laryngotracheobronchitis or its consequences.

Malnutrition is common in and around Mvumi, and the nutritional state of this study group is not atypical of general paediatric admissions. Children with low weight for age and weight for height, not shown, had the highest mortality in both study groups. Recent community studies have shown a varying relation between premorbid general nutritional state and death from measles, but most dealt with milder disease.[24-26] Schrimshaw *et al* noted a decrease in mortality from measles in children fed a vegetable extract rich in protein that may have contained considerable amounts of vitamin A.[27] In our study vitamin A recipients suffered lower mortality in every nutritional stratum.

The vitamin A concentrations among the children in our study were all very low, much lower than that reported by workers in Nigeria.[12] This is explained partly by the different analytical methods, populations, and diet. Tielsch and Sommer found that children with vitamin A concentrations of less than 0·53 μmol/l, a category that would include over 90% of our study group, were at very high risk of developing corneal ulcers.[14]

Vitamin A deficiency may be a large factor in determining the outcome of measles in Africa, just as it seems to affect morbidity and mortality in Asia.[3] When a child with marginal vitamin A stores gets measles available vitamin A is quickly depleted, presumably reducing the ability to resist secondary infections or their consequences, or both.[5 32] This would exacerbate the already reduced immunocompetence thought to be associated with measles infection.[33]

Further trials in different parts of Africa are urgently needed to define the role of vitamin A deficiency in measles morbidity and mortality and the importance of vitamin A supplements in their control.

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MATERIA NON MEDICA

On the beach

The lights of Ardentinny across the waters of Loch Long go out one by one as the bleak November evening moves imperceptibly into night. Now and again a gap in the blackness above allows moonlight to sparkle on the lapping waves, a welcome relief from the soaking northerly squalls that chill and dishearten. On the foreshore a dozen oyster catchers are busily feeding as the tide ebbs. No sign of the rafts of eiders or the shags or even the gulls so conspicuous by day. A Scottish sea loch has its charms even on a winter's night.

But this is no birdwatchers' outing. This is Coulport beach, right next to the naval base that will act as home to Britain's Trident submarines. We are five members of the local peace group who have chosen to spend a Friday night here. Our vigil is peaceful but not silent. We sing hymns, we chatter, and the laughter pervades even those dreaded small hours which the doctor on call knows and hates so keenly. We watch the comings and goings of the base and the swarms of Ministry of Defence police—and they in turn watch us, but in a much more sophisticated way. Though we speak to two policemen, we are unable to speak to the majority of the workers as they are bussed in and out, and our protest is made simply by our presence.

Dawn slowly creeps over the pines, and the birds return. The day shift replaces the night shift and it is time to extinguish the driftwood fire.

Have we changed anything? Nuclear weapons are an emotive issue. For those of us who see them as the greatest danger to public health of our time it is vital to protest, and I remember Edmund Burke's words: "Nobody made a greater mistake than he who did nothing because he could only do a little." At the very least, for a short while we were at peace with our consciences.—KENNETH F MCLEAN, Denny, Stirlingshire.

Music buffs

Orpington has culture. Never mind that it has little history. In fact Queen Elizabeth I stayed at the manor once, and there is the Buff Orpington chicken, but until the railway was electrified it was only a small place, mentioned in the Domesday Book but overshadowed by the neighbour which it now dwarfs, St Mary Cray. Today it is a pleasant middle class dormitory suburb, perhaps slightly less refined than Petts Wood, with a fast train to London taking a mere 20 minutes, but only three miles from the real country—at least until the green belt is raped by the mushrooming plans for houses and out of town leisure precincts with which the developers hope to fill the green fields between us and the M25.

Opposite our house is St Olave's School, relocated from the shadow of Southwark Cathedral. The hall, with its brick columns, gallery, and, clerestoried roof, has excellent accoustics and for some time now it has been the setting for a yearly recital programme featuring world famous musicians. You buy a ticket for the whole series, and it is always sold out. There is always a wonderful flower arrangement on the stage (our next door neighbour does them). To get the seat of your choice you must appear early—up to an hour early—and recently we were seated in the gallery for the first time to hear the Takacs String Quartet play Haydn and Bartok and then, with Michael Collins, Brahms's *Clarinet Quintet in B Minor*, with a little Mozart for an encore. It was a superb performance, but you come to expect this at St Olave's. We are lucky. Not many people can boast fine concerts less than a minute from their house.

It is interesting to observe a large audience from above. You can spot the people you know, run a detailed survey of the incidence of pattern baldness, watch the smaller children growing weary, and, above all, sense the absorption and enjoyment of a crowd in a way which is impossible when you are within it. The audience was spellbound by the Brahms and the Haydn. Not a cough barked, not a programme rustled. But Bartok's *String Quartet No 4* is not easy listening, and during that the throng seethed, wriggled, and fidgeted. There was manifest discomfort.

Oh yes, Orpington has culture. But perhaps it is not quite ready for Bartok.—ANDREW BAMJI, Orpington.

Some hosts ask their guests to take off their shoes when entering a carpeted house. Does this increase the spread of tinea pedis. What discreet prophylactic measures are recommended?

Whereas this is clearly the subject for a fascinating study, there is little information on the risks of transferring desquamated but infected skin scales to others via a carpet. Clearly many of the skin scales are exfoliated on to socks and into footwear and provided that socks are worn these should provide some sort of a barrier. One study from Belgium suggested that carpets were a potential source of desquamated hair from cats with ringworm infection.[1] The actual proof, however, that shed hairs could cause infection in members of the household is difficult to establish. Presumably, the best prophylaxis is that if guests are asked to take their shoes off they should be persuaded to leave their socks on.—R J HAY, consultant dermatologist, London.

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REDUCED MORTALITY AMONG CHILDREN IN SOUTHERN INDIA RECEIVING A SMALL WEEKLY DOSE OF VITAMIN A

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Abstract *Background.* Clinical vitamin A deficiency affects millions of children worldwide, and subclinical deficiency is even more common. Supplemental vitamin A has been reported to reduce mortality among these children, but the results have been questioned.

Methods. We conducted a randomized, controlled, masked clinical trial for one year in southern India involving 15,419 preschool-age children who received either 8.7 μmol (8333 IU) of vitamin A and 46 μmol (20 mg) of vitamin E (the treated group) or vitamin E alone (the control group). Vitamin supplements were delivered weekly by community health volunteers who also recorded mortality and morbidity. Weekly contact was made with at least 88 percent of the children in both study groups. The base-line characteristics of the children were similar and documented a high prevalence of vitamin A deficiency and undernutrition.

Results. One hundred twenty-five deaths occurred, of which 117 were not accidental. The risk of death in the group treated with vitamin A was less than half that in the control group (relative risk, 0.46; 95 percent confidence interval, 0.30 to 0.71). The risk was most reduced among children under 3 years of age (6 to 11 months — relative risk, 0.28; 95 percent confidence interval, 0.09 to 0.85; 12 to 35 months — relative risk, 0.46; 95 percent confidence interval, 0.26 to 0.81) and among those who were chronically undernourished, as manifested by stunting (relative risk, 0.11; 95 percent confidence interval, 0.03 to 0.36). The symptom-specific risk of mortality was significantly associated with diarrhea, convulsions, and other infection-related symptoms.

Conclusions. The regular provision of a supplement of vitamin A to children, at a level potentially obtainable from foods, in an area where vitamin A deficiency and undernutrition are documented public health problems contributed substantially to children's survival; mortality was reduced on average by 54 percent. (N Engl J Med 1990; 323:929-35.)

TWENTY to 40 million children worldwide are estimated to have at least mild vitamin A deficiency, and nearly half are said to reside in India.[1] Controlled field trials in an area of endemic vitamin A deficiency in Indonesia revealed a reduction of 34 percent in mortality among infants and young children given high-dose vitamin A supplements,[2] and a reduction of up to an estimated 75 percent[3] after periodic mass treatment with large-dose (209 μmol [200,000 IU]) vitamin A. Reductions in mortality of 11 to 45 percent were reported after the normal marketing of vitamin A–fortified monosodium glutamate.[4] The results of these studies and an earlier observational trial in Indonesia[5] have been questioned because of aspects of the study designs[6] and because the mortality data provided no cause-specific information and were obtained retrospectively, assuming compliance.[4]

Clarifying the role of vitamin A deficiency in child health and survival and defining successful, sustainable control measures have broad public health, public policy, and programmatic importance. For this reason, we conducted a randomized, placebo-controlled, masked clinical trial among 15,419 preschool-age children using a small, weekly dose of vitamin A (8.7 μmol [8333 IU]) given directly to the children by community health volunteers. We monitored morbidity and mortality weekly for one year. The dose of vitamin A was meant to simulate the amount that could be obtained from food, if food consumption was near the level recommended by international groups (approximately 1 to 1.4 μmol [300 to 400 μg] of vitamin A daily[7,8]).

METHODS

The study was carried out in three drought-prone, economically and environmentally deprived *panchayat* unions (local-government areas) in the Trichy district of Tamil Nadu in southern India. The people of the area had been underserved by child-care programs, including the national program of administering a large-dose (209

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μmol) supplement of vitamin A every six months. A survey of all children under 60 months of age in the study area revealed that only 1 percent had participated in this program.

The study was reviewed and approved by the human-subjects internal review boards of the Indian Council of Medical Research and the Aravind Eye Hospital. Informed consent was obtained from the leaders of the *panchayat* unions and then from the individual families at the time of the base-line survey.

Survey Personnel and Procedures

All the communities within the areas selected for study were mapped by locally recruited enumerators. A house-by-house demographic and socioeconomic survey was carried out by specially trained local workers, who also obtained from each mother a five-year history of mortality among her preschool-age children. Households with children under 60 months of age were identified and assigned a census number.

Two medical-examination teams were formed, consisting of a medical officer, nurses, and child-care and social workers. The child-care and social workers were trained to undertake ocular examinations, anthropometric measurements, and a morbidity history. The ocular examination was checked by the medical officer who conducted the medical examination and verified the morbidity history. The ocular examination was repeated by the same trained fieldworkers after six months of intervention, and all the indexes measured at base line were reassessed by the medical teams at the end of the study.

A finger-prick blood sample and a dietary history detailing the frequency of intake of locally available foods containing vitamin A[9] were obtained from a randomly selected 2 percent of the children by specially trained community workers.

At the base-line medical examination, all the children with symptoms of xerophthalmia, including night blindness, were treated with a large-dose combination of vitamin A (209 μmol) and vitamin E (46 μmol), and they continued to be followed as part of the study. The data were analyzed both including and excluding them. Children with symptoms of xerophthalmia at the six-month and final ocular examinations were treated in a similar manner. All the children were given the large-dose supplement during their final medical examination at the end of the study.

The children's height (or length for those under 24 months) was measured to the nearest centimeter with a calibrated board. Weight was determined to the nearest 0.1 kg with a hanging Salter scale.

The ocular examination was performed with the classification criteria of the World Health Organization.[10] A history of night blindness was obtained by interviewing the mother about the incidence in her children of *malai ken*, a term used in Tamil Nadu to describe the commonly recognized symptom of "evening eyes," the inability to see well in dim light. The same term was subsequently used by the community health volunteers to monitor the occurrence of night blindness on a weekly basis.

Fieldworkers were aware that they were involved in a study to determine the effect on morbidity of giving vitamins, but they were not told that the study was specifically one of vitamin A or that mortality was an outcome variable.

Randomization

Because of the varied population density in the *panchayat* unions, we used a cluster-sampling design. From the 15,419 children identified and examined at base line, 206 clusters were formed on the basis of the minimal and maximal workloads that could be expected from the community health volunteers. The majority of clusters consisted of 50 to 100 children 6 to 60 months of age. The clusters were arranged according to population size; after a random start, they were assigned alternately to the treated or control groups. The adequacy of randomization in achieving matching according to base-line data was checked for the following characteristics: age and sex distribution, one-month history of diarrhea and respiratory disease, anthropometric indexes of nutritional status, xerophthalmia status, five-year retrospective history of mortality of children under five, household economic and hygienic status, and serum retinol levels. Matching was satisfactory at base line for all the variables examined.

Implementation and Management

Community health volunteers were trained to dispense the supplement, collect morbidity data, and record mortality according to a standard procedure. The volunteers visited each home assigned to them every week for 52 weeks. During the visits they recorded illnesses according to symptoms and duration and checked for any deaths. They dispensed the appropriate liquid supplement directly into the mouth of the study child from a calibrated, color-coded amber bottle. Community health volunteers knew that they were responsible for dispensing from one color-coded bottle, but they were unaware of what it contained other than vitamins.

Trained supervisors were each assigned to oversee seven or eight community health volunteers. The supervisors were responsible for weekly meetings with the volunteers to verify the completeness of the morbidity-data forms for the previous week and to review their proper use. The supervisors also collected the dispensers each week and distributed refilled bottles. In addition, they checked the accuracy of the data gathered from a random 5 percent of the households weekly.

A block officer met every week with the supervisors to review the forms and procedures, discuss problems, and provide refilled bottles for delivery to the community health volunteers. The supervisors were informed weekly of the performance — in terms of rates of contact and accuracy in data recording — of the community health volunteers for whom they were responsible. Evidence of problems was sought and the difficulties were remedied within a two-week period. Unannounced spot checks on households were conducted by block officers and headquarters staff.

Data were verified and then recorded on diskettes with use of portable computers in the field offices. The diskettes were sent weekly to the headquarters office, where they were again checked for completeness and accuracy. The procedures for personnel and data management allowed close surveillance and a two-week feedback to the field staff regarding their performance, thus giving them time to correct any possible errors.

Supplements

Liquid supplements (kindly provided by Hoffmann–LaRoche, Basel, Switzerland) were provided in color-coded aluminum cans containing approximately 1 liter each. The appearance and taste of the solutions were identical. The solution containing vitamin A was prepared to contain approximately the following: 8.7 μmol (8333 IU or 2500 μg) of vitamin A palmitate and 46 μmol (20 mg) of vitamin E per milliliter dissolved in peanut oil. The placebo solution contained approximately 46 μmol (20 mg) of vitamin E per milliliter dissolved in peanut oil.

The stability of the solutions was checked by Hoffmann–LaRoche initially and after 1, 3, 6, and 12 months of storage, at room temperature, 35°C, and 45°C, in both the dispenser bottles and the aluminum flasks. In the flasks there was no loss of vitamin A and about a 10 percent loss of vitamin E, and in the bottles there was a loss of less than 5 percent of vitamin A after one year or less at room temperature and at 35°C. Stability was also checked by randomly withdrawing dispensers from the study areas halfway through and at the end of the study. The field-laboratory analyses, done approximately 18 to 24 months after the supply had been received in India and used under the conditions of storage prevailing in the field, revealed a vitamin A loss of approximately 25 percent.

Data Monitoring

Six months after the weekly distribution began, a data-monitoring committee reviewed the data, summarized according to dose color code only. No one associated with the study was aware of the color code, which was held by Hoffmann–LaRoche until the study ended. Although differences were evident in the mortality trends of the study groups after six months, they could not be associated

unambiguously with the incidence, severity, or duration of morbidity. The committee concluded that the study should continue.

Statistical Analysis

Randomization according to cluster rather than according to child introduced a moderate increase (about 30 percent) in the variance of the estimators of the relative risk of death in the treated group as compared with the control group. Relative risks, significance, and confidence intervals were therefore calculated according to the cluster design.[11] The risk of death among the controls was used as the reference value for relative risk of death; a relative risk of 0.5 means that the risk in the treated group was half that among the controls, or conversely, that the risk among the controls was twice that in the treated group. All ages were adjusted to reflect age at the start of the intervention, which began on the same date for all the children.

Nutritional status was assessed with use of the CASP anthropometric software package (version 3.0) provided by the U.S. Centers for Disease Control. Values more than 2 SD below the reference value were considered abnormal.

Results

Mortality data and associated morbidity are reported here. An analysis of morbidity in the 15,419 children is currently under way.

Contact with the Children

During each of the 52 weeks of the study, at least 88 percent of the children were contacted. There was no difference in rates of contact between the treated and control groups. The reasons for lack of contact (of which some children had more than one) included moving from the study area (10 percent), temporary absence (13 percent), refusal to participate (28 percent), sickness (29 percent), and other reasons (30 percent). Table 1 summarizes the study contact and compliance in terms of the number of weeks the dose was missed. Nearly 42 percent of the children received all the doses. For those in the treated group, this was equivalent to more than 453 μmol (433,000 IU) of vitamin A, or approximately the amount available in the commonly used large-dose supplement (209 μmol every six months). More than 90 percent of the children received at least 322 μmol (307,000 IU), which is equivalent to more than 70 percent of what they would have received in a large-dose supplement.

Table 1. Doses Missed and Minimal Amount of Vitamin A Received during 52 Weeks of Intervention.

No. of Doses Missed	Percent of Children (N = 15,419)	Minimal Amount Received*
		μmol (IU)
0	41.8	453 (433,000)
1–5	38.7	410 (390,000)
6–10	6.9	366 (349,000)
11–15	3.2	322 (307,000)
16–20	2.0	279 (266,000)
21–26	1.7	227 (216,000)
27–31	0.7	183 (174,000)
>31	5.0	

*The minimal amount received was calculated with the following equation: 453 μmol − (maximal number of doses missed × 8.7 μmol) = minimal amount received.

Base-Line Characteristics

Sex, age, xerophthalmia status, serum retinol level, and nutritional status at base line are shown in Table 2. There were no substantial differences in these indexes between the control and treated groups. Although the study was meant to include only children from 6 to 60 months of age, birth records were unavailable, and our recall records include a small number of younger (1.8 percent) and older (5.4 percent) children.

The base-line prevalence of xerophthalmia was 11 percent. The risk of xerophthalmia did not differ according to sex, except for a slight predominance among boys after three years of age. Thirty-seven percent of the serum retinol values from the randomly sampled subgroup (n = 280) were ≤0.70 μmol per liter, and 21 percent were ≤0.35 μmol per liter. The prevalence of vitamin A deficiency in each of the clinical and biochemical categories thus exceeded the World Health Organization's criteria for a public health problem.[10] Seven cases of active corneal involvement (category X2, X3A, or X3B) were seen

Table 2. Base-Line Characteristics of the Study Population.

Characteristic	Percentage of Children
Sex	
Male	52
Female	48
Age (mo)*	
≤5	1.8
6–11	7.1
12–23	20.0
24–35	21.2
36–47	22.1
48–60	22.4
61–71	5.4
Xerophthalmia status†	
XN	3.7
X1B	7.2
X2, X3A, X3B	0.05
X5	0.07
Serum retinol (μmol/liter)	
≤0.35	21.4
0.351–0.70	16.1
0.701–1.05	16.4
>1.05	46.1
Nutritional status‡	
Stunted	31
Wasted	23
Stunted and wasted	18
Normal	25
Unknown	3

*Age at the start of intervention.

†XN indicates night blindness, X1B Bitôt's spot, X2 corneal xerosis, X3A corneal ulceration or keratomalacia of less than one third of the corneal surface, X3B corneal ulceration or keratomalacia of one third or more of the corneal surface, and X5 corneal scar.

‡As determined with the CASP anthropometric software package. Stunted indicates height for age < the mean minus 2 SD and weight for height ≥ the mean minus 2 SD; wasted indicates height for age ≥ the mean minus 2 SD and weight for height < the mean minus 2 SD; stunted and wasted indicates height for age < the mean minus 2 SD and weight for height < the mean minus 2 SD; and normal indicates height for age ≥ the mean minus 2 SD and weight for height ≥ the mean minus 2 SD.

(four in the control group and three in the treated group). Night blindness accounted for about one third and Bitôt's spots for about two thirds of the milder cases of xerophthalmia.

Seventy-two percent of the children were classified by anthropometry as undernourished (defined as more than 2 SD below the reference mean). Approximately one third of the children were stunted, 18 percent stunted and wasted, and 23 percent wasted (Table 2). Stunting thus affected a somewhat larger proportion of the children than wasting, indicating that prolonged malnutrition was more common than acute undernutrition among the study children.

The five-year history of mortality among children under five years of age taken at base line was not significantly different between families of control and families of treated children (data not shown).

Mortality Outcome

There were 125 deaths in the study population during the 52 weeks of surveillance, for an overall mortality rate of 8.1 per 1000. Eight of these deaths, however, involved accidents unrelated to symptoms that could have been associated with the intake of vitamin A: animal bite (two deaths), drowning (three), poisoning (one), and falling (two). Five of the accidental deaths were in the treated group and three in the control group.

Figure 1 shows the cumulative deaths according to study group. Regardless of treatment, girls were at somewhat higher risk of death than boys, but not significantly so (relative risk, 1.5 in the control group and 1.2 in the treated group). Vitamin A significantly reduced the risk of death for both sexes, the effect being somewhat larger for girls (relative risk, 0.41 for girls [$P<0.01$] and 0.52 for boys [$P<0.05$]).

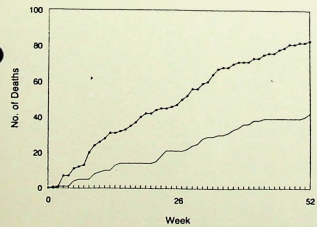

Figure 1. Cumulative Deaths Monitored Weekly, According to Study Group.

The solid line represents the group treated with vitamin A, and the line broken by squares the control group. Children who died in accidents (five in the treated group and three in the control group) are included.

Table 3 shows the mortality according to age and study group for the 117 nonaccidental deaths. The risk of death in the group receiving vitamin A was 46 percent of that in the control group. The relative risk was reduced most for infants (relative risk, 0.28; 95 percent confidence interval, 0.09 to 0.85) and those 12 to 35 months of age (relative risk, 0.46; 95 percent confidence interval, 0.26 to 0.81); it was less than 1.0 in all age groups. Excluding the children who had received the high-dose supplement at any time or who received it only at base line did not substantially change the age-specific relative risks shown in Table 3. In addition, these relative risks were not significantly changed by excluding those who did not receive the study supplements for more than seven consecutive weeks ($n = 1863$) or those who did not receive the supplements for more than four weeks on four occasions ($n = 11$). These exclusions were designed to minimize any possible confounding due to a differential participation effect or missing the supplements for a prolonged period.

Among the nonaccidental deaths, 18 occurred among children with xerophthalmia at base line. All 18 occurred in children over 12 months of age (12 children in the control group and 6 in the treated group). The death rate among children with xerophthalmia was 10.6 per 1000, as compared with 7.2 per 1000 among the children without xerophthalmia.

Table 4 shows the symptom- and disease-specific relative risk of death in the treated and control groups. According to the "verbal autopsy," there were too few deaths specifically associated with the symptoms of respiratory disease and malnutrition to provide a reliable relative risk. Excluding these two categories of symptoms, the relative risk was consistently lower for the treated group — and significantly so, except for deaths associated with measles. More than 40 percent of the deaths were associated with diarrhea, 16 percent with measles, and the remainder with symptoms suggesting other infections.

Table 5 shows the mortality according to treatment group and base-line nutritional status. Data on nutritional status were missing for 469 children (3 percent), among whom 7 died (6 in the control group and 1 in the treated group). Among the children not treated with vitamin A (the control group), the death rate of those who were both stunted and wasted was 1.5 to 2 times higher than the death rate of those who were either stunted or wasted, and it was 2.7 times higher than the rate of normal children. Thus, the risk of death was increased by acute undernutrition superimposed on chronic malnutrition. But the effect of treatment with vitamin A was pronounced (relative risk, 0.11; $P = 0.01$; 95 percent confidence interval, 0.03 to 0.36) among stunted children, whereas it was not significant among wasted, stunted and wasted, or normal children.

A hierarchical log-linear model was used to assess the multivariate relation among death, treatment, age,

sex, and nutritional status. The significant association between treatment and death persisted when adjusted simultaneously for age, sex, and nutritional status.

Discussion

The results of this community-based, masked controlled field trial clearly indicate that in an area where clinical vitamin A deficiency and chronic undernutrition are common, ensuring a constant consumption of vitamin A at least equivalent to the recommended dietary allowance enhanced children's survival. In Indonesia, somewhat similar effects among preschool-age children (a 45 percent reduction in mortality) were reported with vitamin A–fortified monosodium glutamate when it was a consistent part of the food supply.[4]

For the one-year follow-up period the overall mortality rate among children 6 to 60 months of age was 8.1 per 1000 in our study, comparable to the 7.8 per 1000 for the 12- to 71-month age group reported by the Aceh, Indonesia, study.[2] It was higher, however, than the 5 per 1000 reported from an area near Hyderabad, India, where a placebo-controlled, blinded trial with a high-dose supplement has also been performed.[12] These rates are considerably below the 20 per 1000 reported as the national average for India.[12] We monitored infant mortality in the study area for a one-year period in 1988 and 1989 and obtained a rate of 64 per 1000, a figure somewhat lower than the 83 per 1000 reported for Tamil Nadu in 1982[13] and the 98 per 1000 for India generally.[14] The mortality rate among infants less than 6 months old was 42 per 1000 live births, and among those 6 to 11 months old it was 22 per 1000. We were unable to find any reliable information on mortality rates among one-to-five-year-olds in Tamil Nadu. The lower mortality figures we report undoubtedly reflect in part the well-recognized effect of the frequent contact of households with trained fieldworkers.[12,15] Nonetheless, because the contact was comparable in our two study groups, the efficacy of vitamin A supplementation at the level of the recommended dietary allowance in reducing mortality by 54 percent remains evident; mortality rates were 10.5 per 1000 in the control group as compared with 4.8 per 1000 in the treated group.

We found an insignificant sex-related difference in the risk of death without regard to treatment. Treatment with vitamin A reduced the risk of mortality in both sexes, but the reduction was somewhat greater among girls. This finding contrasts with that reported from Indonesia, in which a significant treatment effect of large-dose supplementation was found only in boys, among whom the prevalence of xerophthalmia was also higher.[2] In our study, the prevalence of xerophthalmia at base line was not significantly different between the sexes until after three years of age, whereas the effect on mortality of treatment with vitamin A was pronounced among the younger groups.

The efficacy of our low-dose supplementation was considerably higher than the 34 percent reduction in mortality reported after high-dose supplementation in Indonesia as determined by intention-to-treat analy-

Table 3. Mortality, According to Age and Study Group.

Age and Study Group	No. of Children	No. of Deaths	Cumulative Mortality Rate	Relative Risk*
0–11 Mo				
Control	678	14	0.021	0.28 (0.09, 0.85)†
Treated	689	4	0.006	
12–35 Mo				
Control	3185	52	0.016	0.46 (0.26, 0.81)‡
Treated	3179	24	0.008	
≥36 Mo				
Control	3792	14	0.004	0.63 (0.26, 1.50)
Treated	3896	9	0.002	
Total				
Control	7655	80	0.010	0.46 (0.29, 0.71)‡
Treated	7764	37	0.005	
Age-adjusted total				0.46 (0.30, 0.71)‡

*Relative risk for the treated group, as compared with the control group. Values in parentheses are 95 percent confidence limits.
†P = 0.05. ‡P = 0.01.

Table 4. Symptom- and Disease-Specific Mortality, According to Treatment Group.

Symptoms or Disease	Control Group	Treated Group	Relative Risk*
	no. of children		
Measles	12	7	0.58 (0.17, 1.92)
Diarrhea	33	16	0.48 (0.24, 0.96)†
Respiratory	3	2	—
Malnutrition	1	3	—
Convulsions	12	3	0.25 (0.07, 0.85)†
Other	19	6	0.31 (0.12, 0.78)†
Total deaths	80	37	

*Relative risk for the treated group, as compared with the control group. Values in parentheses are 95 percent confidence limits.
†P = 0.05

Table 5. Mortality, According to Nutritional Status.*

Nutritional Status and Study Group	No. of Children	No. of Deaths	Cumulative Mortality Rate	Relative Risk†
Unknown				
Control	201	6	0.030	0.13 (0.01, 1.14)
Treated	268	1	0.004	
Stunted				
Control	2385	27	0.011	0.11 (0.03, 0.36)‡
Treated	2418	3	0.001	
Wasted				
Control	1806	14	0.008	0.72 (0.30, 1.72)
Treated	1798	10	0.006	
Stunted and wasted				
Control	1373	22	0.016	0.65 (0.30, 1.41)
Treated	1340	14	0.010	
Normal				
Control	1890	11	0.006	0.80 (0.32, 2.00)
Treated	1940	9	0.005	

*The categories of nutritional status are defined in Table 2.
†Relative risk for the treated group, as compared with the control group. Values in parentheses are 95 percent confidence limits.
‡P = 0.01.

sis,[2] but lower than the estimated 75 percent reduction reported with an analysis based on actual receipt of the capsules.[3] The estimate based on receipt of the capsules was derived from a total of only 18 deaths over a four-month follow-up period. As the authors noted, its validity awaits verification by a study that ensures consistent, periodic verification of compliance in taking the large-dose supplement, which has not been a feature of most large-scale programs to date.[16]

Vitamin A was most efficacious in children under three years of age, most prominently in infants. This finding contrasts with reports from Indonesia. In the Aceh study the effect of treatment was most marked among those 60 to 71 months old,[2] and in the study involving vitamin A–fortified monosodium glutamate, mortality was reduced by 11 percent among infants and 45 percent among preschoolers.[4] In the monosodium glutamate study the infants probably received a considerable portion of their food as breast milk, and the effect of the program would therefore be expected to be less. The reasons for the discrepancy between our results and those of the Aceh study are less clear but may be related to the relative level of underlying malnutrition in the two study populations. Our base-line prevalence of xerophthalmia was 11 percent, as compared with about 1 to 2 percent in Indonesia, and only 25 percent of the Indian children had normal anthropometric features, whereas at least 40 to 69 percent of the Indonesian children were classified within 10 percent of the median standards of the U.S. National Center for Health Statistics.

In accordance with many reports from developing countries where vitamin A deficiency is endemic, diarrhea was associated with the highest number of deaths, followed by measles and symptoms associated with other infections — convulsions, jaundice, and encephalitis, for example. The protective effect of vitamin A was significant for all these conditions except measles. This finding contrasts with hospital-based case–control reports from Africa, in which the protective effect of very large doses of vitamin A was exceptionally high in measles.[17,18] Previous studies suggest that measles is a less severe disease in India than in Africa, and that factors other than vitamin A — the severity of concurrent malnutrition, for example — may be a more critical determinant of measles-associated morbidity and mortality.[19,20] It may also be that a large dose of vitamin A is required to prevent a fatal outcome in severe measles complicated by vitamin A deficiency.

Prolonged undernutrition, as evidenced by stunting, characterized nearly one third of the children in our study at base line, and a continuous supply of vitamin A reduced the risk of dying to one-ninth that of the controls. The protective effect of vitamin A was unremarkable in children with wasting, an indicator of acute malnutrition, and in those with normal anthropometric features. Stunting reflects — in addition to an inadequate food supply — many characteristics of social deprivation that are frequently found in poor households. Our data suggest that these persistent ecological and physiologic insults undermine the ability of a child who is deficient in vitamin A to ward off a fatal outcome when confronted by an infection. The programmatic implication of this is that maximal reductions in mortality can be expected from vitamin A prophylaxis targeted to children who are chronically undernourished and to those with superimposed acute malnutrition.

Children with xerophthalmia are reported to be at 4 to 12 times the risk of death of neighboring children with normal eyes, and the risk increases with the increasing severity of symptoms.[5] The mortality rate among children with xerophthalmia in our study was about 50 percent higher than among children without the condition (7.2 vs. 10.6 per 1000). When we adjusted for those who received a large dose of vitamin A because of xerophthalmia, the treatment effect of the continued small dose persisted — that is, half as many died among those who continued to receive the weekly supplement as among those who did not.

Sommer et al.[2] noted that daily consumption of the recommended dietary allowance was the ideal approach to vitamin A prophylaxis, but considered it to be impractical from a programmatic point of view and chose distribution of the large-dose capsule every six months instead. Sommer et al. subsequently commented that the single most important limitation to achieving the maximal effect with large-dose capsules was inadequate contact and verification of compliance[3]; the large-dose approach requires careful monitoring of distribution channels to avoid possible overdosing. In contrast, our approach involving frequent low doses showed that when the supplement is provided at a safe dosage level in an easily dispensed form, community workers can be effective in attaining high rates of contact and verification if there is also an appropriate managerial and supervisory system. Importantly, the efficacy of supplementation at the level of the recommended dietary allowance suggests that a similar effect could be achieved by an equivalent supply of vitamin A from foodstuffs, an approach that would potentially address other nutritional deficiencies as well.

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LOCATION ON CHROMOSOME 15 OF THE GENE DEFECT CAUSING MARFAN SYNDROME

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Abstract *Background.* Marfan syndrome, "the founding member" of the heritable disorders of connective tissue, is a common autosomal dominant disorder with highly variable clinical manifestations in the skeletal, ocular, and cardiovascular systems. The fundamental defect leading to this disease has escaped definition despite decades of research efforts by several groups of investigators.

Methods and Results. Using linkage analyses with polymorphic markers of the human genome, we mapped the genetic defect to chromosome 15 in five families with Marfan syndrome. With three polymorphic markers we obtained definitive proof of linkage in these families (lod score = 3.92, $\theta = 0.0 \pm 0.11$). The most probable location of the gene for the disease is currently D15S45 (lod score = 3.32, $\theta = 0.0 \pm 0.12$).

Conclusions. The chromosomal localization of the mutation in Marfan syndrome is a first step toward the isolation and characterization of the defective gene and serves as a diagnostic test in families in which cosegregation of these markers with the disease has been confirmed. (N Engl J Med 1990; 323:935-9.)

MARFAN syndrome is one of the most common inherited connective-tissue disorders, with an estimated prevalence of 40 to 60 cases per million population.[1] It is inherited in an autosomal dominant fashion, although it is sporadic in 15 percent of cases.[1] The most prominent clinical manifestations of the disorder occur in the skeletal, ocular, and cardiovascular systems.[1] Diagnosis has been problematic because of the extreme variability of clinical expression. The current diagnostic criteria were established at the Seventh International Congress on Human Genetics in 1986 and defined at the First International Symposium on Marfan Syndrome in 1988.[2,3] These criteria include "more specific manifestations," which are ectopia lentis, aortic-root dilatation, aortic dissection, and dural ectasia; and "other manifestations" in the musculoskeletal, cardiovascular, ocular, integumentary, pulmonary, and central nervous systems. The penetrance of the disease is considered complete, but variable expression of its clinical manifestations is the rule even within a single family.[4]

Despite intensive research carried out in various laboratories, nothing is known about the genetic defect leading to Marfan syndrome. Several abnormalities of connective-tissue proteins have been observed in patients,[5-11] but their role as the primary defect in the disease is unclear. In fact, linkage analyses have allowed many of the genes coding for these proteins to be excluded as the defective gene in the syndrome. The excluded genes include genes coding for Type I, Type II, and Type III collagens and fibronectin, as well as genes coding for one polypeptide chain of Type V and Type VI collagens.[12-15]

Over the past four years we have been collecting information on Finnish families with Marfan syndrome. We studied eight three-generation families, each with a minimum of three living members who were affected. In these families, linkage analysis of

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Effect of massive dose vitamin A on morbidity and mortality in Indian children

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K. V. RAMESHWAR SARMA VINODINI REDDY

The effect of vitamin A supplementation on preschool child morbidity and mortality was assessed in a prospective double-blind placebo-controlled study around Hyderabad, India. Every six months 200 000 IU vitamin A was given to 7691 children (treatment group) whereas 8084 children received a placebo (control group). Morbidity and mortality data were collected every three months. Risk of respiratory infection was higher in children with mild xerophthalmia than in children with normal eyes. Vitamin A supplementation had no effect on morbidity status. Mortality rates were similar in the two groups: it was highest in children who did not receive either vitamin A or placebo. The findings suggest that vitamin A supplementation alone may not reduce child mortality.

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Introduction

Vitamin A deficiency is widespread in India and in several other developing countries. About 5–10% of children have conjunctival xerosis and Bitot spots. Severe deficiency of vitamin A with corneal involvement is more serious. There are about 500 000 new cases of xerophthalmia, half of which lead to blindness, each year in India, Bangladesh, the Philippines, and Indonesia combined.[1] Only 30% of these children survive.[2] Thus, the morbidity and mortality due to vitamin A deficiency is very high, even if only that associated directly with severe xerophthalmia is considered.

Studies from Indonesia suggest that even mild vitamin A deficiency is associated with increased morbidity/mortality in children.[3,4] Furthermore, vitamin A supplementation was shown to reduce the mortality rate by about 30%.[5] These observations have generated much interest world wide about the role of vitamin A in child survival. Analysis of available data in India indicated that respiratory disease developed twice as often in children with mild xerophthalmia as in children with normal eyes.[6] However, this study was retrospective and the sample size was not adequate to assess mortality.

We have done a prospective study in a rural community to assess the effect of vitamin A supplementation on morbidity and mortality in preschool children.

Children and methods

The study was done between January, 1987, and January, 1989, in five primary health centres, which served 84 villages (total population of about 165 000) in one of the backward districts of

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TABLE I—DISTRIBUTION OF CHILDREN BY AGE AND SEX

Age (yr)	Treatment	Control	Total
< 1	868/855	913/922	1781/1777
1–2	867/871	880/901	1747/1772
> 2 < 3	889/882	934/902	1823/1784
> 3 < 4	890/884	972/910	1862/1794
> 4 < 5	369/316	374/376	743/692
Total	3883/3808	4073/4011	7956/7819

Values are for M/F.

Andhra Pradesh in India. The villages were allocated randomly into two groups—treatment and control.

All preschool children (1–5 years old) in the treatment areas received vitamin A (200 000 IU) according to the national programme of blindness prevention; children in control areas received a placebo, which consisted of arachis oil—the same oil base used in the vitamin A concentrate. There had been no distribution of vitamin A in this area before the study was started. We intended to give at least two doses of vitamin A or placebo to all children. At the time of administration, some children were not available at their homes because they had gone out of the village or had gone to field with their parents. Hence, some children received two doses, and some received only one dose. Those children who could not be contacted on both occasions received no dose. The trial was double blind: the investigators and medical officers did not know which were the treatment and which were the control areas. They were not aware whether the dose they were distributing was vitamin A or placebo. Decoding was done only after data had been collected.

Households with preschool children were identified. Mothers were contacted by trained field workers at their homes once every three months after vitamin A or placebo had been given, and information about morbidity, with particular reference to diarrhoea, respiratory infection, and measles, was obtained for the previous one month in the local language. Diarrhoea was defined as the passing of three or more loose motions a day. Respiratory disease was defined as the presence of clinically significant cough with or without expectoration. The same investigators collected mortality data during the three-monthly home visits by questioning parents about each child. The villages were revisited in the same order.

A clinical examination for signs of vitamin A deficiency was done by trained medical officers at the time of the baseline survey and therafter every six months until completion of the study. The first dose was distributed soon after the first clinical examination. Children were examined in adequate light with a loupe. Standard diagnostic criteria for xerophthalmia were used. Mothers were questioned about nightblindness with appropriate terms in the local language. Children with corneal involvement were given immediate treatment and dropped from the study; those with mild xerophthalmia were managed in the same way as non-xerophthalmic (normal) children. Anthropometric measurements, such as weight and weight-for-height, were done every six months on each alternate child. Weight was measured with a beam balance and weight-for-height was measured by a leanness board.[7]

In about 5% of households, supervisory staff randomly checked morbidity and mortality data and receipt of vitamin A or placebo about 2–3 weeks after the investigators. Children who had night blindness (XN), conjunctival xerosis (X1A), or Bitot spots (X1B) were classified as mild xerophthalmia and those without eye signs as normal. All the data were analysed by computer. Incidence of diarrhoea and of respiratory diseases was calculated separately for each three-month interval.

TABLE III—CHILD MORTALITY ACCORDING TO DOSES OF VITAMIN A OR PLACEBO

No of doses	Group (1–5 yr)	
	Vitamin A	Placebo
0	397 (17·6)	638 (17·2)
1	2274 (9·7)	1857 (10·8)
2	4405 (2·3)	4511 (2·2)

Values are of no of cases (no of deaths/1000)

The overall incidence rates according to ocular status were calculated by addition of incidences for the five intervals and are presented per 100 child intervals. Morbidity rates for diarrhoea and respiratory infections were calculated by: (Cases of given morbidity during all the observation periods ÷ total number of child intervals) × 100. Relative risk of morbidity in children with xerophthalmia was calculated by: incidence of morbidity in children with xerophthalmia ÷ incidence of morbidity in children without xerophthalmia. Confidence intervals for relative risk were also calculated. We calculated morbidity rates separately, taking into consideration the vitamin A status during the interim between the initial clinical examination and the examination six months later. There were thus four groups: mild xerophthalmia both at baseline and six-months later; mild xerophthalmia at baseline, normal six months later; normal at baseline, mild xerophthalmia six months later; and normal both at baseline and six months later. The morbidity and mortality rates were calculated for each of these groups.

We also analysed data, allowing for the anthropometric status of the children. They were divided into 2 groups with 80% weight-for-height as the cut-off level. The effect of vitamin A supplementation was assessed by calculation of morbidity and mortality rates according to the number of doses of vitamin A or placebo received by the children—ie, rates were calculated for no dose, one dose, and two dose groups.

Results

15 775 children between the ages of 1 and 5 years were studied (7691 treatment, 8084 control) (table I). The two groups were similar at baseline with respect to income status, distribution of weight for age, and crude birth and death rates. The distribution of children according to age and sex was similar in the two groups. About 6% of the children had night blindness and Bitot spots at baseline; after vitamin A administration, the prevalence was 1·3% in the treatment areas and 2·9% in the control areas. About 58% of the treatment group had received two doses of vitamin A and 34% had received at least one dose—ie, about 92% of the children had received one or more doses of vitamin A. In the control area 57% of children had received two doses and 32% had received one dose of placebo.

Risk of respiratory infection was significantly higher in children who had mild xerophthalmia, either at the initial clinical examination or six months later. However, the incidence was higher in the group whose eyes were normal at baseline but in whom xerophthalmia developed during the six months period (table II). There was no relation between risk of diarrhoea and ocular status. When weight-for-height was considered, there was no difference in morbidity of

TABLE II—INCIDENCE OF INFECTIONS ACCORDING TO VITAMIN A STATUS

Clinical vitamin A status		Diarrhoea		Respiratory infection	
Baseline	After 6 months	Incidence (%)	Relative risk	Incidence (%)	Relative risk
Mild xerophthalmia	Mild xerophthalmia	8·6	1·19	16·6	1·29*
Mild xerophthalmia	Normal	8·2	1·13	17·5	1·35*
Normal	Mild xerophthalmia	9·5	1·31	22·5	1·74†
Normal	Normal	7·3	1·0	12·9	1·0

*$p < 0.05$; †$p < 0.01$.

TABLE IV—ODDS-RATIOS OF DEATH WITH INDEPENDENT VARIABLE

Independent variable	No of doses		
	2	1	0
Vitamin A	1·12	1·20	0·92
Sex	1·22	0·80	1·76
Schedule tribe	1·46	3·41*	4·05*
Agriculture labourer	2·61	1·98	0·83
Other labourer	1·10	0·97	2·26
Father illiterate	1·74	0·96	2·71
Age (mo)	0·95†	0·93‡	0·93‡

*p < 0·01; †p < 0·05; ‡p < 0·001 for association with mortality.

children with or without xerophthalmia. There was no beneficial effect of vitamin A supplementation on morbidity status compared with placebo.

Mortality was higher in children with xerophthalmia than in those with normal eyes (number of cases, 403 *vs* 5318; death rate/1000, 4·96 *vs* 2·26) but relative risk (2·27) was not statistically significant. After the intervention programme was started there were no differences in mortality rates between treatment and control groups (table III). Mortality was higher in children who had not received any dose of either vitamin A or placebo. There was a significant reduction in mortality in the group which had received two doses of vitamin A or placebo compared with those who had received one dose or no dose. Results of logistic regression analysis, including variables such as age, sex, father's educational status, caste, and number of doses, indicated that there was a higher mortality in younger children and in those who belonged to scheduled tribes (table IV).

Discussion

The role of vitamin A in maintaining the integrity of the epithelium in the respiratory and gastrointestinal tracts is well recognised. In laboratory animals, vitamin A deficiency leads to alterations in the mucosal lining of these sites, so they are more vulnerable to bacterial invasion.[8] Similar changes can account for a higher incidence of infections in human vitamin A deficiency which leads to higher mortality. However, the available evidence is not unequivocal. In the Indonesian study[3] xerophthalmia was associated with increased risk of both diarrhoea and respiratory infection, whereas in our study the incidence of respiratory infection, but not of diarrhoea, was higher in vitamin A deficient children. In both studies, morbidity data were collected every three months and recall of events of such a long interval may not be very accurate. However, even in an earlier study carried out on Hyderabad slum children, in which morbidity data were collected weekly, mild xerophthalmia was associated with increased risk of respiratory infection, but not diarrhoea.[6] The influence of other environmental factors on diarrhoea may perhaps be greater than that of vitamin A deficiency.

The relation between vitamin A deficiency and mortality is even more complex because of other confounding factors, and is difficult to interpret. Several workers have shown that the risk of death is very high in children with severe corneal xerophthalmia.[9] However, most of these children also have severe protein energy malnutrition and infections, which can independently contribute to the high mortality. It is therefore difficult to say how much of this mortality is due to vitamin A deficiency itself.

The prevalence of severe vitamin A deficiency with corneal involvement is low, whereas mild deficiency, as evidenced by night blindness, conjunctival xerosis, and Bitot spots, is much more common. In our study, we found no significant association between mild xerophthalmia and mortality in children. There was no difference in the mortality rates of children who received vitamin A or placebo. Our results differ from those reported by Sommer et al,[5] who showed that mortality in Indonesia was reduced by as much as 34% after vitamin A supplementation. However, the design of the Indonesian study was criticised because it was not double-blind, sufficient care was not taken to eliminate contact effect between investigators and community, and ascertainment of deaths was not by active surveillance.[10]

We attempted to take care of these criticisms to a large extent. However, one of the limitations of our study was the low child mortality that we recorded in the study areas compared with the reported national average. Although, it can be argued that this might have invalidated the results, the mortality rates observed in our study are not very different from those of the Indonesian study.

It is noteworthy that mortality in the non-recipient children (no dose group) was higher in the experimental and placebo groups than in those who had received the supplement. Likewise, in Indonesia, Tarwotjo et al[11] reported a substantially higher mortality among non-recipients than among controls of the same age and sex. These observations may be due to differences in the health care received by the two groups; frequent contacts by the project staff, both in treatment and in control villages, may have motivated the community to seek health care and use the services better. Although, the field investigators were instructed to avoid active intervention, seriously ill children were referred to the nearest health centre for treatment. As Gopalan[12] pointed out, it would not have been possible to have accomplished their jobs successfully if the investigators had not earned the cooperation of the families by giving some advice on health care.

Sommer et al[3] had suggested that reduction in child mortality may be due to reduction in morbidity, such as diarrhoea and respiratory infections. Administration of vitamin A had no impact on morbidity in our study, despite an association of mild xerophthalmia with increased incidence of respiratory infection; this could be due to the influence of other environmental factors. Alternatively, the high incidence of respiratory infection in mild xerophthalmia was an association only and was not causally related. The relation between vitamin A deficiency and mortality can vary in different regions depending on morbidity pattern, socioeconomic characteristics, diet, and health care practices. Thus, vitamin A supplementation alone cannot be expected to improve child survival in all ecological and cultural settings; this does not deny the importance of vitamin A supplementation to improve nutrition status. Prevention of blindness is a good enough reason to strengthen the continuing vitamin A programme combined with other health care services, it can have a better impact on child health.

We thank Dr G. V. S. Nagabhushana Rao, Medical and Health Services, Government of Andhra Pradesh, for cooperation and help in conducting the study. The valuable suggestions and guidance received from Dr K. Ramachandran, All India Institute of Medical Sciences, New Delhi, about data analysis is gratefully acknowledged.

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Infective dermatitis of Jamaican children: a marker for HTLV-I infection

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In Jamaican children infective dermatitis is a chronic eczema associated with refractory nonvirulent *Staphylococcus aureus* or beta-haemolytic streptococcus infection of the skin and nasal vestibule. 14 children between the ages of 2 and 17 years with typical infective dermatitis, attending the dermatology clinic at the University Hospital of the West Indies in Jamaica, were tested for antibody to human T-lymphotropic virus type 1 (HTLV-1). All were seropositive, whereas 11 children of similar age with atopic eczema were all negative. In 2 of 2 cases of infective dermatitis, the biological mother was HTLV-1 seropositive. None of the 14 patients showed signs of adult T-cell leukaemia/lymphoma, though experience with previous cases of infective dermatitis indicates the possibility of such progression.

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Introduction

In 1966 Sweet[1] described a unique dermatitis in Jamaican children which he called infective dermatitis.[1] The following year Walshe[2] documented the clinical features and bacteriology of this disease in 25 Jamaican children, noting an association with *Staphylococcus aureus* and beta-haemolytic streptococcus infection and a poor response to treatment.

Typically the condition begins acutely without preceding infantile eczema. The dermatitis can be controlled with long-term antibiotics but relapses promptly when these are discontinued. The resistance to treatment, the frequent exacerbations, and the infections with bacteria that are usually non-virulent raised the possibility that infective dermatitis is a disorder of immunosuppression. We have looked for an association with human T-lymphotropic virus type 1 (HTLV-1) infection.

Patients and methods

Among 147 consecutive patients between the ages of 2 and 17 years, referred to the dermatology outpatients clinic at the University Hospital of the West Indies between March, 1989, and March, 1990, 14 met the clinical definition of infective dermatitis—namely, (*a*) severe exudative eczema with crusting, involving the scalp, eyelid margins, perinasal skin, retroauricular areas, axillae, and groins; (*b*) generalised fine papular rash; (*c*) chronic nasal discharge in the absence of other causes of rhinitis; (*d*) positive cultures for *S aureus* or beta-haemolytic streptococci from nasal discharge and/or skin lesions. No patient had a history of blood transfusion. 11 patients with atopic eczema from this same clinic served as controls: their dermatitis was mainly flexural, they did not have chronic nasal discharge, and *S aureus* and beta-haemolytic streptococci were recovered from the skin only in the presence of secondary infection.

In each patient the full blood count was done including total lymphocyte count and percentage eosinophils, and smears were examined for the presence of atypical polylobated lymphocytes. Serum was tested for HTLV-I antibodies by enzyme linked immunosorbent assay (Dupont) with confirmation by recombinant p21e enhanced western blot (Biotech/Dupont), core and envelope antibodies being required for a positive result. Swabs from nasal discharges and skin were cultured by routine methods for bacterial pathogens. Skin biopsy was performed in 4 patients who were refractory to treatment and lymph node biopsy in 2 patients who had persistent generalised lymphadenopathy.

Results

5 boys and 9 girls had infective dermatitis (current ages 3–16 years, mean 8, median 8·5); 3 boys and 8 girls had atopic dermatitis (current ages 2–12 years, mean 7, median 7). All the children had low socioeconomic backgrounds.

All 14 infective dermatitis patients were positive for HTLV-I antibodies (confirmed by western blot), as were both the biological mothers whom we tested; by contrast, none of the 11 children with atopic dermatitis was antibody positive. The table shows the results of nasal swabs and skin swabs from the infective dermatitis patients. In 2 of the 11 children with atopic dermatitis *S aureus* and beta-haemolytic streptococci were grown from obviously infected lesions.

Of the children with infective dermatitis 11 had normal white blood cell and differential counts and 3 had a raised neutrophil count compatible with bacterial infection. 12 had a normal haemoglobin level and 2 were mildly anaemic (with

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IMPACT OF VITAMIN A SUPPLEMENTATION ON CHILDHOOD MORTALITY
A Randomised Controlled Community Trial

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Summary 450 villages in northern Sumatra were randomly assigned to either participate in a vitamin A supplementation scheme (n = 229) or serve for 1 year as a control (n = 221). 25 939 preschool children were examined at baseline and again 11 to 13 months later. Capsules containing 200 000 IU vitamin A were distributed to preschool children aged over 1 year by local volunteers 1 to 3 months after baseline enumeration and again 6 months later. Among children aged 12–71 months at baseline, mortality in control villages (75/10 231, 7·3 per 1000) was 39% greater than in those where supplements were given (53/10 919, 4·9 per 1000) ($p<0·05$). The impact of vitamin A supplementation seemed to be greater in boys than in girls. These results support earlier observations linking mild vitamin A deficiency to increased mortality and suggest that supplements given to vitamin A deficient populations may decrease mortality by as much as 34%.

Introduction

A LONGITUDINAL observational study in rural central Java indicated that children with ocular signs of mild vitamin A deficiency were more likely than neighbourhood controls to die, that mortality was directly related to severity of vitamin A deficiency, and that poor survival was probably attributable, at least partly, to high rates of respiratory disease and diarrhoea.[1-3] We report here the results of a randomised, controlled, community trial of vitamin A prophylaxis in northern Sumatra.

Subjects and Methods

The study was carried out in Aceh Province, which is at the northern tip of Sumatra and where xerophthalmia is prevalent.[4,5] The population is ethnically distinct from that of Java, where the earlier observational study had been conducted.[1-3]

For political and administrative reasons a cluster sampling scheme was employed. The sampling frame consisted of 2048 villages in Aceh Utara and Pidie, two contiguous rural kabupatens (districts) chosen because they had no current or planned development projects or vitamin A supplementation schemes. From a random start, 450 villages were systematically selected for the study; these were then randomised for capsule distribution after the baseline examination (programme villages, n = 229) or after the follow-up examination (control villages, n = 221). 18 villages from among those still in the sampling frame were substituted for adjacent villages found to have started vitamin A supplementation before the baseline survey.

All members of the two study teams, each consisting of an ophthalmologist (team leader), a nurse, an anthropometrist, a dietary interviewer, five enumerators, and a driver, all fluent in the local dialect received a month's classroom, hospital, and field training. The enumerators, responsible for collecting demographic data, were unaware that mortality was a research question. Standardisation exercises were done before and regularly throughout the study. First, each village was visited to identify households containing children aged 0–5 years and to mark their dwellings. Within 2 days the village was visited by the full team. Enumerators visited every house containing preschool children, collected socioeconomic, demographic, and medical data, and rounded up children at a central point for their clinical examination. Dates of birth were ascertained by reference to local events charted on the Muslim calendar and then translated to their roman equivalent by the use of a specially prepared conversion table. Eyes were examined with a focused light and 2X loupes and diagnoses were made according to standard diagnostic criteria.[5,6] Parents were carefully questioned about the presence of nightblindness.[5,7] They were also asked about a history of diarrhoea (4 or more loose, watery stools per day), of fever or cough lasting at least 24 h in the previous 7 days, and of "ever having" measles.

Recumbent length (if less than 24 months old) or standing height (if 24 months or older) to the nearest 0·1 cm, and weight (using a calibrated Salter scale) to the nearest 0·1 kg, were measured on a 10% subsample of all study children.

All children with active xerophthalmia at baseline examination received at least one large dose of vitamin A and were referred to the local health unit. They were excluded from the analyses of subsequent morbidity and mortality. All children received vitamin A at the follow-up examination 9–13 months later.

Teams first visited villages between September, 1982, and August, 1983, and follow-up visits were made by the same team in the same sequence 9–13 months later. The variation in follow-up time resulted from attempts to minimise the potential confounding influence of the Muslim fasting month and post-fasting holidays.

Standard capsules (supplied by UNICEF) were given to every child aged 1–5 years in programme villages, by a local volunteer trained to do so. The capsule nipple was snipped off and the contents (200 000 IU vitamin A and 40 IU vitamin E) were expressed into the child's mouth. This volunteer kept a list of children treated and issued the household with a distribution card. The first dose was given 1–3 months after the baseline examination and the second 6–8 months later. A distribution monitor visited each village 2–4 weeks after the scheduled distribution and interviewed 10% of eligible households. If coverage was less than 80% the local distributor was encouraged to reach children previously missed.

All data were collected on precoded forms, entered onto diskettes, and shipped to the data management facility at the International Center for Epidemiologic and Preventive Ophthalmology, Johns Hopkins University, where the information was processed with the SIR data management package run on an IBM 4341 computer. Statistical analyses were made with SIR, SAS, and GLIM software. Statistical tests for significance and development of confidence intervals were adjusted for clustering associated with randomisation by village rather than by individual, and for the small number of events expected and observed in any one village by applying poisson regression with extra-poisson variation to account for natural variability in mortality among villages.[8,9] Two-tailed tests were used.

The study was designed to examine overall differences between non-infant preschool-age children in programme versus control villages, on the assumption that mortality would be reduced by at least 20% and allowing for an alpha error of 0·05 and a beta error of

Sugar and Obesity

At a conference on the link between sugar and obesity, organised in London on May 7 by the Sugar Bureau, Prof John Durnin (Institute of Physiology, University of Glasgow) reviewed research on the subject, found much of it inconclusive, and came to the view that sugar intake did not play an important part in the development of obesity. He stated: "It is unfortunate that absolute proof one way or another is unattainable because it leaves the field open to the nutritional missionary who is prepared to ignore the considerable weight of scientific evidence pointing clearly to no link between sugar and obesity".

University of Edinburgh

Prof R. E. Kendell, professor of psychiatry, has been elected dean of the faculty of medicine with effect from Oct 1.

A one-day course on **Managing a Clinical Team** will be held at the British Postgraduate Medical Federation, London WC1, on Tuesday, May 20: Mrs E. Macklin, Education Department, British Postgraduate Medical Federation, 33 Millman Street, London WC1N 3EJ (01-831 6222).

A one-day meeting entitled **The Assurance of Quality in Medical Imaging** is to be held at the Middlesex Hospital Medical School, London W1, on Wednesday, May 21. Mrs S. Gaffey, Assistant Secretary, British Institute of Radiology, 36 Portland Place, London W1N 3DG (01-580 4085).

A one-day workshop on **Child Care Law for Medical Practitioners** will take place at the Charing Cross and Westminster Medical School, London W6, on Wednesday, May 21: Sue Hilton, British Association for Adoption and Fostering, 11 Southwark Street, London SE1 1RQ.

A one-day meeting on **Multiple Sclerosis Research** will take place at the Town Hall, Stourbridge, on Thursday, May 22: Michele Jones, Exter Consultancy 4 Bouverie Street, London EC4Y 8AB (01-353 5272).

A one-day conference on **Dementia—Action on Training** is to be held at the Royal College of Physicians, 9 Queen Street, Edinburgh, on Thursday, May 22. Jan Killeen, Co-ordinator, Scottish Action on Dementia, 33 Castle Street, Edinburgh EH2 3DN (031-225 5000).

A one-day conference on **Care in the Community—Voluntary and Statutory Services** is to be held at the County Hall, Norwich, on Thursday, May 22: Conference Department, Royal Society of Health, RSH House, 38a St George's Drive, London SW1V 4BH (01-630 0121).

A one-day meeting entitled **Topics in Cardiac Transplantation** will take place at the Royal Society of Medicine, London W1, on Thursday, May 22: Dr B. T. Marsh, Library and Scientific Research Section, Royal Society of Medicine, 1 Wimpole Street, London W1 (01-408 2119).

A one-day meeting on **Aspects of Forensic Science** is to take place at the Pharmaceutical Society of Great Britain, London SE1, on Friday, May 23: Analytical Division, Royal Society of Chemistry, Burlington House, London W1V 0BN (01-437 8656).

A one-day workshop entitled **An Encounter with Educational Ideas** will be held at St Bartholomew's Hospital Medical College, London EC1, on Friday, May 23: Maureen Gyle, Association for the Study of Medical Education, 2 Rosesangle, Dundee, Scotland DD1 4LR (0382 26801).

A one-day meeting entitled **Facing the Void—Death, Loss and Redundancy** is to take place at the British Postgraduate Medical Federation, London WC1, on Wednesday, May 28: Mrs E. Macklin, Education Department, British Postgraduate Medical Federation, 33 Millman Street, London WC1N 3EJ (01-831 6222).

A one-day workshop on **Research into Restoration of Health—Models, Method, Markers and Measurements** will be held at the Charing Cross and Westminster Medical School, London W6, on Wednesday, May 28: Pam Edwards, Cardiac Department, Charing Cross Hospital, Fulham Palace Road, Hammersmith, London W6 8RF (01-748 2040 Ext 2191).

A 2-day symposium entitled **Pharmaceutical Industry Interfaces** is to be held at the Royal College of Physicians, London NW1, on May 28–29: Mrs J. Wase-Bailey, Association of Medical Advisers in the Pharmaceutical Industry, 20 Queensberry Place, London SW7 2DZ (01-589 9076).

A one-day meeting on **Advances in Physiological Measurement as Applied to Audiology** is to take place at the Postgraduate Centre, York District Hospital, York, on Thursday, May 29: Graham Frost, Department of Audiological Physics, Royal National Throat, Nose and Ear Hospital, Grey's Inn Road, London WC1X 8DA.

A 2-day meeting entitled **NHS Health Economics Group** will be held at the James Gracie Centre, Birmingham, on May 29–30. John Todd, District Medical Officer, Sheffield Health Authority, Westbrook House, Sharrow Vale Road, Sheffield S11 8EU.

A one-day meeting on **Gastrointestinal Medicine** is to take place at The Royal College of Physicians, London, on Friday, May 30: Barbara Cavilla, Institute of Biology, 20 Queensberry Place, London SW7 2DZ (01-581 8333).

Diary of the Week

MAY 18 TO 24

Monday, 19th

ROYAL COLLEGE OF RADIOLOGISTS, 2 Carlton House Terrace, London SW1Y 5AF
4.30 pm Prof M. A. Ferguson-Smith: The Molecular Pathology of Sex Determination.

INSTITUTE OF DERMATOLOGY, St John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London WC2H 7BJ
4.45 pm Dr C. H. Cameron: Virus Diseases of the Skin.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London WC1N 3BG
5.30 pm Dr Arnold Starr (California): Auditory Memory Deficits in Man and their Evaluation with Event Related Potential.

ST GEORGE'S HOSPITAL MEDICAL SCHOOL, 3rd Floor, Lanesborough Wing, Cranmer Terrace, London SW17 0RE
12.30 pm Film—Laser Surgery For Cervical Intraepithelial Neoplasia.

Tuesday, 20th

INSTITUTE OF DERMATOLOGY
4.45 pm Dr R. S. Tedder: Virological Methods.

ICRF CANCER EPIDEMIOLOGY AND CLINICAL TRIALS UNIT, Ida Gieve Seminar Room, Observer's House, Green College, Oxford
5 pm Prof M. A. Epstein: EB Virus Vaccines—Current Progress and Future Strategies.

Wednesday, 21st

INSTITUTE OF ORTHOPAEDICS, Middlesex Hospital, Mortimer Street, London W1
6 pm Mr R. W. Porter: Neurogenic Claudication.
7 pm Mr E. O'G. Kirwan: Assessment of the Problem Back.

ROYAL FREE HOSPITAL, Pond Street, London NW3 2QG
5 pm Dr Robert Henderson (New Haven): Microelectrode Studies of Isolated Hepatocytes.

NORTHWICK PARK HOSPITAL AND CLINICAL RESEARCH CENTRE, Watford Road, Harrow, Middlesex HA1 3UJ
1 pm Mrs T. Rutter: Development of a District Drugs Guide and Possible Relevance to General Practice.

CHACE POSTGRADUATE MEDICAL CENTRE, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex
1 pm Mr G. Mountain: The Accident and Emergency Department—10 Years On.

DURHAM POSTGRADUATE MEDICAL CENTRE, Dryburn Hospital, Durham
1.15 pm Dr R. Boxton: Electrical Treatment of Arrhythmias.

Thursday, 22nd

MANCHESTER MEDICAL SOCIETY, John Rylands University Library, Oxford Road, Manchester M13 9PP
5.30 pm Prof M. Clarke: Epidemiology in a New Medical School.

Friday, 23rd

CARDIOTHORACIC INSTITUTE, Fulham Road, London SW3 6HP
8 am Dr Peter Cole: Bacterial Subinfage

Correction

Rationale for and Results from a Randomised Double-blind Trial of Tetrachlorodecaoxygen Anion Complex in Wound Healing.—We apologise to Dr J. Hinz and his colleagues for errors in their April 12 paper (p 825). Fig 1 and fig 3 were transposed. In table II the number of missing controls should have been 134. The formula in the first line on p 828 should have read $y = ax^b e^{-c}$. Table III should have been:

Wound diagnosis	Control*	TCDO	p
Venous ulcers	−0·1414	−0·4147†	<0·001
Postoperative problem wounds	−0·1414	−0·3757†	<0·001
Arterial ulcers	−0·1414	−0·2422	<0·001
Other wounds	−0·1414	−0·2422	<0·001

*q unaffected by diagnosis (see text).
†Also significantly better ($p < 0{\cdot}01$) than values for TCDO (arterial ulcers) and TCDO (other wounds).

0·2 (1-tailed). Stratified subgroup analyses are, strictly speaking, inappropriate, and, because of the small numbers, not very reliable.

Although Indonesian government regulations proscribe administration of vitamin A prophylactically to infants, a considerable proportion of them received capsules nonetheless, so the impact on infant mortality was also examined.

All study procedures were approved by a steering committee consisting of representatives of the Indonesian Center for Nutrition Research, the Directorate of Community Health Services, the provincial health authorities, Johns Hopkins University, and Helen Keller International.

Results

29 236 preschool-aged children were enumerated at baseline. Follow-up information was available on 89·0% of the programme children and 88·4% of the controls. The age and sex distribution of children lacking follow-up was identical in the two groups.

Baseline Characteristics

Of the 25 939 children with baseline and follow-up information, details of the initial ocular examination are available for 91·9% of programme children and 90·5% of controls. Active xerophthalmia was more prevalent in controls than in the programme group (2·25 versus 1·88%), but the difference was not significant and was accounted for almost entirely by the males (table I). Xerophthalmia was more prevalent among males than females, especially among controls. Xerophthalmia prevalence was negligible during the first 2 years of life (less than 0·5%).

TABLE I—BASELINE PREVALENCE OF ACTIVE XEROPHTHALMIA

—	No of patients with:		
	Night blindness* (XN)	Bitot's spots* (X1B)	Active xerophthalmia* (XN, X1B, X3)
Total†			
Programme (n = 12 781)	136 (1·11%)	143 (1·16%)	231 (1·88%)
Control (n = 11 378)	150 (1·32%)	164 (1·44%)	256 (2·25%)
Males			
Programme (n = 6043)	69 (1·14%)	72 (1·19%)	120 (1·99%)
Control (n = 5383)	88 (1·63%)	102 (1·89%)	150 (2·69%)
Females			
Programme (n = 6881)	66 (1·12%)	69 (1·17%)	108 (1·84%)
Control (n = 5494)	61 (1·11%)	59 (1·07%)	103 (1·87%)

*Prevalence rates for XN and X1B are not mutually exclusive. For "active xerophthalmia" an individual was counted only once. There were only 6 patients with corneal ulceration (X3), 3 in each group. Conjunctival and corneal xerosis were excluded as being potentially less reliable."

†Includes 357 programme and 301 control children whose sex was unknown.

TABLE II—AGE AND SEX DISTRIBUTION ON NON-XEROPHTHALMIC CHILDREN

—	Programme	Control
*Total**	12 991 (*100·0%*)	12 209 (*100·0%*)
Sex†		
Male	6365 (*50·0%*)	5975 (*50·0%*)
Female	6243 (*50·0%*)	5888 (*50·0%*)
Total	12 608 (*100·0%*)	11 863 (*100·0%*)
Baseline age (months)		
<12	2074 (*16·0%*)	1979 (*16·2%*)
12–23	1979 (*15·2%*)	1941 (*15·9%*)
24–35	2086 (*16·1%*)	2072 (*17·0%*)
36–47	2374 (*17·5%*)	2016 (*16·5%*)
48–59	1887 (*14·5%*)	1724 (*14·2%*)
60–71	2686 (*20·7%*)	2465 (*20·2%*)
Total	12 986 (*100·0%*)	12 197 (*100·0%*)

*Includes infants, as well as children on whom age and/or sex are unavailable.

†Sex not known for some children.

The age and sex distributions of the non-xerophthalmic children in the two groups were similar (table II). The disproportionate number of children purported to be in the 6th year of life probably includes children really in their 5th and 7th years, as has been noted previously.[5] Programme and control children were also similar for most other baseline demographic and socioeconomic variables, including occupation of the head of the household, maternal education, source of drinking water, distance to the nearest elementary school, and distance to the nearest health centre.

The two groups were also similar in most health variables such as recent history of fever or cough or of ever having had measles; relative risks of these variables for the two groups differed by less than 5% (table III) except for diarrhoea, a recent history being 23% commoner among control than programme children ($p = <0·05$), with the greatest excess in girls. Recent diarrhoea was commonest during the 2nd year of life, when the frequency was 9·8% in programme villages and 10·7% in control villages. Thereafter it steadily declined. The most objective baseline health variable was nutritional status. Anthropometric indices were similar for the two groups, both total and sex-specific (table IV).[10]

In 99% of children in the two study groups, the interval between baseline and follow-up examination was at least 11 months, and for 59%, at least 12 months. This interval did not vary among age-sex-specific categories by more than ±2%.

Vitamin A Distribution Level

Of our three methods of monitoring for capsule administration only interrogation of the child's guardian(s) proved feasible. Report forms provided by the local distributors were largely illegible, and most cards issued to households were faded, torn, or lost.

Over 93% of preschool children (12–71 months at baseline) living in programme villages received at least one large dose of vitamin A between baseline and follow-up examinations;

TABLE III—BASELINE MORBIDITY VARIABLES

—	Programme		Control		Relative risk compared with that for control
	Total no	% positive	Total no	% positive	
Cough*	12 781	31·2	11 555	32·7	1·05
Fever*	12 781	45·7	11 555	46·7	1·02
Measles†	11 753	22·3	10 659	21·7	0·97
Diarrhoea*	12 781	7·1	11 555	8·7	1·23

*Present in past seven days. Dat., missing on 210 programme children and 654 controls.

†Any time in past. Smaller denominator because of change in question shortly after survey began.

TABLE IV—BASELINE ANTHROPOMETRY

—	Programme (n = 1382)	Control (n = 1271)
*Height for age (% of median)**		
<85†	8·2%	8·9%
85–89	23·9%	27·6%
90–94	43·0%	37·8%
≥95	24·9%	25·7%
*Weight for height (% of median)**		
<80	3·0%	3·7%
80–89	38·3%	35·6%
≥90	58·6%	60·7%

*Median NCHS standards.[11] Represents 10% subsample of children.

†Less than 1·5% of children in either group were below 80% of median.

TABLE V—NUMBER* REPORTED TO HAVE RECEIVED VITAMIN A CAPSULES DURING FOLLOW-UP

Age (months) at baseline	Programme villages		Control villages	
	At least 1 capsule	2 capsules	At least 1 capsule	2 capsules
12–23	1899 (93·1)	1854 (77·7)	1707 (0·7)	1895 (0·2)
24–35	2007 (93·3)	1946 (78·1)	1792 (1·2)	2010 (0·1)
36–47	2192 (94·0)	2130 (78·7)	1771 (1·3)	1956 (0·2)
48–59	1806 (93·5)	1765 (78·4)	1509 (0·7)	1683 (0·1)
60–71	2593 (92·4)	2528 (77·5)	2121 (1·2)	2400 (0·2)
Total	10 497 (93·2)	10 223 (78·1)	8900 (1·1)	9944 (0·2)
<12	1968 (82·4)	1879 (61·8)	1728 (1·1)	1914 (0·1)
Respondent uncertain about capsules	259	259	130	130
Information unavailable	260	623	1438	208

*Number of those for whom information was complete (age not known for 7 other programme children and 13 other controls).
Numbers in parentheses are percentages.

78% received two doses (table V). In every age-group coverage of boys and girls differed by less than 1%.

In theory, only two-thirds of the infants were eligible for one capsule and less than one-quarter for two. Surprisingly, 82% received at least one capsule and almost 62% both. This discrepancy may reflect disregard of normal government guidelines or of small differences in age.

Only 1% of control subjects received any capsule, presumably obtained at the health centres by children presenting with xerophthalmia.

Impact on Xerophthalmia and Mortality

The prevalence of active xerophthalmia in programme villages declined from 1·9% at baseline to 0·3% at follow-up and that in the control villages declined from 2·3% to 1·2%. These changes meant that the risk of xerophthalmia in control villages relative to that in programme villages rose from 1·2 at baseline to 4·0 at follow-up ($p<0·05$). Sex-specific prevalence rates followed a similar pattern.

During the follow-up period 75 preschool study children from control villages and 53 from programme villages died, giving mortality rates of 7·4 and 4·9 per 1000, respectively ($p<0·05$, two-tailed) (table VI). The relative risk of dying in control versus programme villages was therefore 1·51 (95% confidence limits 1·03, 2·28), equivalent to a reduction in mortality in programme villages of 34%. Infants in control villages had a mortality rate 21% greater than those in programme villages.

To compare age/sex/study group-specific mortality, children were classed as preschool children and infants (table VI). Both infant and preschool control boys died 70% more frequently than did those in the programme villages. The relative risk of death for boys in control versus programme villages was 1·69 (95% confidence limits 1·14, 2·51). Excess mortality was less pronounced among control girls, in whom it was limited to preschool children.

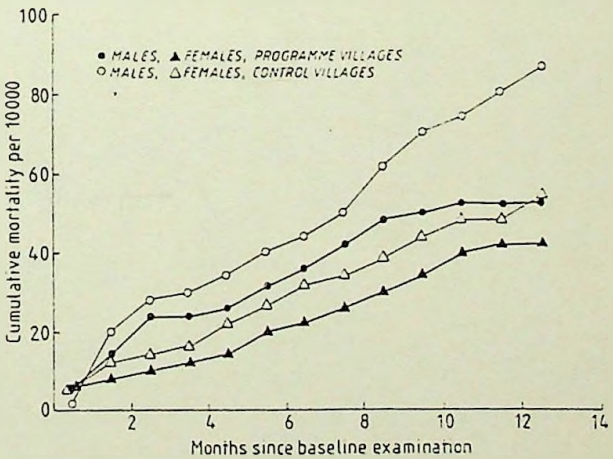
To examine further the effect of large doses of vitamin A on mortality, cumulative sex-specific mortality rates for preschool children were calculated every month after baseline examination (see accompanying figure). Boys and girls show similar patterns: mortality in control villages was initially the same as (females) or lower (males) than that in programme villages; with time, mortality in control villages gradually

TABLE VI—AGE AND SEX-SPECIFIC MORTALITY DURING FOLLOW-UP

Baseline age (months)	Programme villages		Control villages		
	Proportion dying	Rate per 1000	Proportion dying	Rate per 1000	RR
Both sexes					
12–23	19/1979	9·6	22/1941	11·3	1·17
24–35	14/2086	6·7	25/2072	12·1	1·81
36–47	11/2274	4·8	8/2016	4·0	0·83
48–59	5/1887	2·6	7/1724	4·1	1·58
60–71	4/2686	1·5	13/2465	5·3	3·53
Total preschool*	53/10 917	4·9	75/10 230	7·4	1·51 (1·03, 2·28)‡
Infants (<12)	48/2074	23·1	55/1979	27·8	1·21 (0·73, 1·97)‡
Total* (0–71)	101/12 991	7·8	130/12 209	10·6	1·36 (1·01, 1·85)‡
Males†					
0–11	18/1014	17·8	29/970	29·9	1·68
12–71	28/5348	5·2	44/4998	8·8	1·69
Total (0–71)	46/6362	7·2	73/5968	12·2	1·69 (1·14, 2·51)‡
Females†					
0–11	28/994	28·2	25/942	26·5	0·94
12–71	23/5245	4·4	27/4933	5·5	1·25
Total (0–71)	51/6239	8·2	52/5875	8·9	1·09 (0·71, 1·71)‡

*Includes children with age unknown
†Excludes children for whom age and/or sex are unknown.
‡95% confidence limits.

exceeded mortality in programme villages, a trend which was more pronounced in boys; by the end of the follow-up period, 2–4 months after the second dose of vitamin A, cumulative mortality had reached a plateau in programme villages, but it continued to climb in control villages. The pattern among infant boys mimicked that of preschool boys. Cumulative mortality among infant girls in control villages was virtually indistinguishable from that in programme villages.



Cumulative sex-specific mortality at monthly intervals after baseline examination for preschool children (aged 12–71 months at baseline examination).

First dose given during months 1–3; second a mean of 6 months later.
Males—denominator for first 12 months in programme villages, 5351 (no further deaths); in control villages, 5005 initially, 3046 during the last month.
Females—denominator for first 12 months in programme villages, 5249 (no further deaths); in control villages, 4946 initially and 2978 during the last month.

Discussion

Mortality rates have been reported to be higher in malnourished children in hospital with xerophthalmia than in those with normal eyes.[11,12] However, another study has shown that in children admitted to hospital for xerophthalmia, severe malnutrition was the most important factor associated with mortality.[3] Interpretation of these studies is hindered by the biases inherent in family motivation and hospital admission criteria, and the impact intensive therapy has on mortality.

In a longitudinal study of 4000 preschool-aged Javanese children we found that children with mild xerophthalmia (night blindness, Bitot's spots, or the two conditions together—a ranking shown to be closely correlated with serum vitamin A levels[3,7]) died at four times the rate for their non-xerophthalmic peers; the excess mortality was related to the severity of the xerophthalmia, and this "dose-related" risk was independent of the child's general nutritional status.[1,2] The shape of the dose-response curve suggested that subclinical vitamin A deficiency (ie, in the absence of detectable xerophthalmia) was also associated with increased mortality. Follow-up of surviving children revealed that respiratory and diarrhoeal diseases were 2–4 times more likely to have developed in those who had been xerophthalmic than in their non-xerophthalmic peers.[1] Again, vitamin A status seemed to be more important than anthropometric status in predicting morbidity.

The present study was thus undertaken, partly to determine whether supplements of vitamin A given to preschool children (12–71 months of age) would reduce their mortality by at least 15%. Ideally all "treatment" children would have received at least the recommended daily allowance. But this would have required a special, impracticable delivery system. Instead we opted for the regular Indonesian government scheme of twice-a-year administration of UNICEF-supplied capsules by trained local volunteers, although we realised that it did not cover infants. The Government of Indonesia would not condone the use of placebos but field-workers collecting demographic data were unaware that mortality was a research issue.

Strict randomisation of the 450 study villages seemed to have worked reasonably well. The populations were similar in most baseline characteristics investigated except for xerophthalmia and history of recent diarrhoea, which were slightly more prevalent among the controls. The differences between programme and control populations in mortality were out of proportion to their baseline differences; the baseline difference in diarrhoeal history was greatest for females, whereas excess mortality was greatest for males; and the most objective, quantifiable baseline indices of health status, weight-for-height and height-for-age, were virtually identical in the two groups on both an age and sex specific basis.

There was no evidence during the course of the study of differences in economic or medical initiatives in the study area, though clearly the vitamin A status throughout the province was improving as shown by a substantial reduction in prevalence of xerophthalmia between the 1978 nationwide survey and the baseline examination in the present study. The reduction in prevalence of xerophthalmia in control villages during our study may have been part of the general spontaneous improvement, which is the reason for having controls.[3,6] The mortality rates in this study were also lower than previously recorded for Java,[13] where rates seem to be falling, and more closely resemble those of neighbouring "medium" infant mortality rate countries (eg, Philippines, Malaysia, Thailand), where the median mortality in preschool-aged children is 3 per 1000.[14]

Results were strongly positive, even in this "intent-to-treat" analysis. Xerophthalmia prevalence among preschool children living in programme villages declined by 85%, a result similar to those obtained in other carefully conducted pilot trials,[3,15-17] and it confirms the high distribution rate of capsules reported. Preschool control children died 1·5 times more frequently than did programme children (95% confidence limits 1·03, 2·28), equivalent to a 34% reduction in non-infant mortality among residents of programme villages. To control for baseline differences in prevalence of xerophthalmia and history of recent diarrhoea between programme and control villages, the proportion of children with xerophthalmia or recent history of diarrhoea at baseline was included as a covariate (predictor variable) in the analysis. Mortality results (relative risks and their confidence limits) were nearly identical when either xerophthalmia alone or when both xerophthalmia and diarrhoea were included in the analysis.

Although the study was not designed to investigate subgroups, and the numbers concerned preclude definite conclusions, they provide additional evidence consistent with the beneficial impact of vitamin A supplementation: mortality among controls was greater at almost every age, including the first year of life; the difference in cumulative mortality increased with time, even though male and female controls had initial mortality rates that were the same as or lower than those in programme villages; the impact was greatest among boys, in whom vitamin A deficiency is generally far more prevalent,[3,17-20] and among boys, the time-related mortality pattern corresponded with the expected temporal impact of capsule distribution. This internal consistency and agreement with previous studies is more important than the size of the p value or width of the confidence limits, which are direct consequences of the enormous sample size required.

These results are especially encouraging for the following reasons: capsule distribution was less than universal and probably missed those who needed it most;[21] single large-dose supplementation maintains raised serum vitamin A levels for only 1–3 months;[22] distribution did not start until 1–3 months after enumeration; xerophthalmic controls took vitamin A at health centres and those in whom the greatest impact might have been expected (children xerophthalmic at baseline) were treated and dropped from the analysis.

How vitamin A reduces mortality remains uncertain. Vitamin A deficiency is associated with changes in surface epithelium and these may disrupt normal barrier function, support bacterial growth (as seen on the conjunctiva[23] and presumably the bladder[24]), and obstruct smaller branches of the tracheobronchial tree. Abnormalities in systemic immune competence associated with vitamin A deficiency may also be as important in contributing to mortality; in animals at least, vitamin A deficiency interferes with humoral and especially cell-mediated immunity.[25-27] Limited data suggest similar effects in man.[28] High doses of vitamin A given to otherwise normal animals have been reported to produce a non-specific, adjuvant-like increase in resistance to infection.[29] The response to the high doses given in our study was unlikely to be due to non-specific changes. The children came from a vitamin A deficient population[3,7] and the impact was

sustained. The rise in blood retinyl ester levels after one large dose of vitamin A given to deficient patients do not last for more than 8–12 weeks;[22,30] and holo-retinol-binding-protein levels rise, but not above normal levels.[30,31]

The presence of the study teams was unlikely to have influenced the results of our study because the only difference between programme and control villages in their interaction with study personnel consisted of at most two contacts in 12 months with the local vitamin A distributor in treatment areas. This distributor was neither trained nor instructed to undertake any other intervention.

Vitamin A status probably modulates the incidence and severity of disease caused by a variety of pathogenic organisms. The impact that vitamin A supplementation will have on mortality will therefore depend upon a constellation of factors, including the prevalence and severity of vitamin A deficiency; the frequency of exposure to pathogenic organisms, size of the inoculum, and their virulence; and the presence and degree of other adverse influences with which the young child must contend (eg, malnutrition, parasitic load). The results of the study reported here and those done in Java[1-3] confirm the importance that vitamin A deficiency in childhood has on mortality in Indonesia and show the impact that supplementation can have on child survival.

This study was carried out under cooperative agreement DSAN-CA-0267 with the Office of Nutrition, United States Agency for International Development, with additional financial assistance from Hoffman-La Roche, F. T. Vicks, Ford Foundation, UNICEF, and the Asian Foundation for the Prevention of Blindness.

The Aceh Study Group includes the following professional staff, apart from those listed as authors: Dr Akbar Pandji, Dr Koesdiono, Dr Daniel Kraushar, and Dr Hugh R. Taylor, Barbara Hawkins, Imam Satibi, and William Fumenbaum. Dr Scott Zeger developed the statistical methodology.

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References continued at foot of next column

PRE-OPERATIVE IDENTIFICATION OF PATIENTS AT HIGH RISK OF DEEP VENOUS THROMBOSIS AFTER ELECTIVE MAJOR ABDOMINAL SURGERY

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J. ANDREW DAVIES

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Summary Eighteen items of clinical and laboratory information were measured on the day before operation in 85 patients who underwent elective major abdominal surgery. Postoperatively, deep venous thrombosis (DVT) was detected by ^{125}I-fibrinogen scan in 23 patients. Stepwise logistic discriminant analysis was used to identify factors which predicted DVT. Seven such factors were identified, which were then used to construct a predictive index. In descending order of predictive power, they were: age, euglobulin lysis time (ELT), previous abdominal surgery, varicose veins, antithrombin III concentration, cigarette smoking, and platelet count. Pre-operatively, the predictive index correctly identified 91% of the patients in whom DVT developed, and wrongly allocated to the high-risk group 19% of those in whom it did not. A shortened version of the predictive index based only on age and ELT ($I = -11{\cdot}5 + 0{\cdot}133$ age $+ 0{\cdot}006$ ELT) was 91% sensitive and 63% specific in the prediction of DVT. In a prospective study of 43 patients, this shortened predictive index correctly identified pre-operatively 93% of patients in whom DVT developed, and wrongly allocated to the high-risk group only 17% of those in whom it did not.

Introduction

DEEP venous thrombosis (DVT) develops in approximately 30% of general surgical patients after elective major abdominal surgery.[1,2] Prophylactic measures, such as the administration of low-dose heparin or dextran, significantly reduce the frequency of postoperative deep venous thrombosis and pulmonary embolism.[3-5] However,

A. SOMMER AND OTHERS REFERENCES—*continued*

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REDUCED MORTALITY AMONG CHILDREN IN SOUTHERN INDIA RECEIVING A SMALL WEEKLY DOSE OF VITAMIN A

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Abstract *Background.* Clinical vitamin A deficiency affects millions of children worldwide, and subclinical deficiency is even more common. Supplemental vitamin A has been reported to reduce mortality among these children, but the results have been questioned.

Methods. We conducted a randomized, controlled, masked clinical trial for one year in southern India involving 15,419 preschool-age children who received either 8.7 μmol (8333 IU) of vitamin A and 46 μmol (20 mg) of vitamin E (the treated group) or vitamin E alone (the control group). Vitamin supplements were delivered weekly by community health volunteers who also recorded mortality and morbidity. Weekly contact was made with at least 88 percent of the children in both study groups. The base-line characteristics of the children were similar and documented a high prevalence of vitamin A deficiency and undernutrition.

Results. One hundred twenty-five deaths occurred, of which 117 were not accidental. The risk of death in the group treated with vitamin A was less than half that in the control group (relative risk, 0.46; 95 percent confidence interval, 0.30 to 0.71). The risk was most reduced among children under 3 years of age (6 to 11 months — relative risk, 0.28; 95 percent confidence interval, 0.09 to 0.85; 12 to 35 months — relative risk, 0.46; 95 percent confidence interval, 0.26 to 0.81) and among those who were chronically undernourished, as manifested by stunting (relative risk, 0.11; 95 percent confidence interval, 0.03 to 0.36). The symptom-specific risk of mortality was significantly associated with diarrhea, convulsions, and other infection-related symptoms.

Conclusions. The regular provision of a supplement of vitamin A to children, at a level potentially obtainable from foods, in an area where vitamin A deficiency and undernutrition are documented public health problems contributed substantially to children's survival; mortality was reduced on average by 54 percent. (N Engl J Med 1990; 323:929-35.)

TWENTY to 40 million children worldwide are estimated to have at least mild vitamin A deficiency, and nearly half are said to reside in India.[1] Controlled field trials in an area of endemic vitamin A deficiency in Indonesia revealed a reduction of 34 percent in mortality among infants and young children given high-dose vitamin A supplements,[2] and a reduction of up to an estimated 75 percent[3] after periodic mass treatment with large-dose (209 μmol [200,000 IU]) vitamin A. Reductions in mortality of 11 to 45 percent were reported after the normal marketing of vitamin A–fortified monosodium glutamate.[4] The results of these studies and an earlier observational trial in Indonesia[5] have been questioned because of aspects of the study designs[6] and because the mortality data provided no cause-specific information and were obtained retrospectively, assuming compliance.[4]

Clarifying the role of vitamin A deficiency in child health and survival and defining successful, sustainable control measures have broad public health, public policy, and programmatic importance. For this reason, we conducted a randomized, placebo-controlled, masked clinical trial among 15,419 preschool-age children using a small, weekly dose of vitamin A (8.7 μmol [8333 IU]) given directly to the children by community health volunteers. We monitored morbidity and mortality weekly for one year. The dose of vitamin A was meant to simulate the amount that could be obtained from food, if food consumption was near the level recommended by international groups (approximately 1 to 1.4 μmol [300 to 400 μg] of vitamin A daily[7,8]).

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Methods

The study was carried out in three drought-prone, economically and environmentally deprived *panchayat* unions (local-government areas) in the Trichy district of Tamil Nadu in southern India. The people of the area had been underserved by child-care programs, including the national program of administering a large-dose (209

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μmol) supplement of vitamin A every six months. A survey of all children under 60 months of age in the study area revealed that only 1 percent had participated in this program.

The study was reviewed and approved by the human-subjects internal review boards of the Indian Council of Medical Research and the Aravind Eye Hospital. Informed consent was obtained from the leaders of the *panchayat* unions and then from the individual families at the time of the base-line survey.

Survey Personnel and Procedures

All the communities within the areas selected for study were mapped by locally recruited enumerators. A house-by-house demographic and socioeconomic survey was carried out by specially trained local workers, who also obtained from each mother a five-year history of mortality among her preschool-age children. Households with children under 60 months of age were identified and assigned a census number.

Two medical-examination teams were formed, consisting of a medical officer, nurses, and child-care and social workers. The child-care and social workers were trained to undertake ocular examinations, anthropometric measurements, and a morbidity history. The ocular examination was checked by the medical officer who conducted the medical examination and verified the morbidity history. The ocular examination was repeated by the same trained fieldworkers after six months of intervention, and all the indexes measured at base line were reassessed by the medical teams at the end of the study.

A finger-prick blood sample and a dietary history detailing the frequency of intake of locally available foods containing vitamin A[9] were obtained from a randomly selected 2 percent of the children by specially trained community workers.

At the base-line medical examination, all the children with symptoms of xerophthalmia, including night blindness, were treated with a large-dose combination of vitamin A (209 μmol) and vitamin E (46 μmol), and they continued to be followed as part of the study. The data were analyzed both including and excluding them. Children with symptoms of xerophthalmia at the six-month and final ocular examinations were treated in a similar manner. All the children were given the large-dose supplement during their final medical examination at the end of the study.

The children's height (or length for those under 24 months) was measured to the nearest centimeter with a calibrated board. Weight was determined to the nearest 0.1 kg with a hanging Salter scale.

The ocular examination was performed with the classification criteria of the World Health Organization.[10] A history of night blindness was obtained by interviewing the mother about the incidence in her children of *malai ken*, a term used in Tamil Nadu to describe the commonly recognized symptom of "evening eyes," the inability to see well in dim light. The same term was subsequently used by the community health volunteers to monitor the occurrence of night blindness on a weekly basis.

Fieldworkers were aware that they were involved in a study to determine the effect on morbidity of giving vitamins, but they were not told that the study was specifically one of vitamin A or that mortality was an outcome variable.

Randomization

Because of the varied population density in the *panchayat* unions, we used a cluster-sampling design. From the 15,419 children identified and examined at base line, 206 clusters were formed on the basis of the minimal and maximal workloads that could be expected from the community health volunteers. The majority of clusters consisted of 50 to 100 children 6 to 60 months of age. The clusters were arranged according to population size; after a random start, they were assigned alternately to the treated or control groups. The adequacy of randomization in achieving matching according to base-line data was checked for the following characteristics: age and sex distribution, one-month history of diarrhea and respiratory disease, anthropometric indexes of nutritional status, xerophthalmia status, five-year retrospective history of mortality of children under five, household economic and hygienic status, and serum retinol levels. Matching was satisfactory at base line for all the variables examined.

Implementation and Management

Community health volunteers were trained to dispense the supplement, collect morbidity data, and record mortality according to a standard procedure. The volunteers visited each home assigned to them every week for 52 weeks. During the visits they recorded illnesses according to symptoms and duration and checked for any deaths. They dispensed the appropriate liquid supplement directly into the mouth of the study child from a calibrated, color-coded amber bottle. Community health volunteers knew that they were responsible for dispensing from one color-coded bottle, but they were unaware of what it contained other than vitamins.

Trained supervisors were each assigned to oversee seven or eight community health volunteers. The supervisors were responsible for weekly meetings with the volunteers to verify the completeness of the morbidity-data forms for the previous week and to review their proper use. The supervisors also collected the dispensers each week and distributed refilled bottles. In addition, they checked the accuracy of the data gathered from a random 5 percent of the households weekly.

A block officer met every week with the supervisors to review the forms and procedures, discuss problems, and provide refilled bottles for delivery to the community health volunteers. The supervisors were informed weekly of the performance — in terms of rates of contact and accuracy in data recording — of the community health volunteers for whom they were responsible. Evidence of problems was sought and the difficulties were remedied within a two-week period. Unannounced spot checks on households were conducted by block officers and headquarters staff.

Data were verified and then recorded on diskettes with use of portable computers in the field offices. The diskettes were sent weekly to the headquarters office, where they were again checked for completeness and accuracy. The procedures for personnel and data management allowed close surveillance and a two-week feedback to the field staff regarding their performance, thus giving them time to correct any possible errors.

Supplements

Liquid supplements (kindly provided by Hoffmann–LaRoche, Basel, Switzerland) were provided in color-coded aluminum cans containing approximately 1 liter each. The appearance and taste of the solutions were identical. The solution containing vitamin A was prepared to contain approximately the following: 8.7 μmol (8333 IU or 2500 μg) of vitamin A palmitate and 46 μmol (20 mg) of vitamin E per milliliter dissolved in peanut oil. The placebo solution contained approximately 46 μmol (20 mg) of vitamin E per milliliter dissolved in peanut oil.

The stability of the solutions was checked by Hoffmann–LaRoche initially and after 1, 3, 6, and 12 months of storage, at room temperature, 35°C, and 45°C, in both the dispenser bottles and the aluminum flasks. In the flasks there was no loss of vitamin A and about a 10 percent loss of vitamin E, and in the bottles there was a loss of less than 5 percent of vitamin A after one year or less at room temperature and at 35°C. Stability was also checked by randomly withdrawing dispensers from the study areas halfway through and at the end of the study. The field-laboratory analyses, done approximately 18 to 24 months after the supply had been received in India and used under the conditions of storage prevailing in the field, revealed a vitamin A loss of approximately 25 percent.

Data Monitoring

Six months after the weekly distribution began, a data-monitoring committee reviewed the data, summarized according to dose color code only. No one associated with the study was aware of the color code, which was held by Hoffmann–LaRoche until the study ended. Although differences were evident in the mortality trends of the study groups after six months, they could not be associated

unambiguously with the incidence, severity, or duration of morbidity. The committee concluded that the study should continue.

Statistical Analysis

Randomization according to cluster rather than according to child introduced a moderate increase (about 30 percent) in the variance of the estimators of the relative risk of death in the treated group as compared with the control group. Relative risks, significance, and confidence intervals were therefore calculated according to the cluster design.[11] The risk of death among the controls was used as the reference value for relative risk of death: a relative risk of 0.5 means that the risk in the treated group was half that among the controls, or conversely, that the risk among the controls was twice that in the treated group. All ages were adjusted to reflect age at the start of the intervention, which began on the same date for all the children.

Nutritional status was assessed with use of the CASP anthropometric software package (version 3.0) provided by the U.S. Centers for Disease Control. Values more than 2 SD below the reference value were considered abnormal.

Results

Mortality data and associated morbidity are reported here. An analysis of morbidity in the 15,419 children is currently under way.

Contact with the Children

During each of the 52 weeks of the study, at least 88 percent of the children were contacted. There was no difference in rates of contact between the treated and control groups. The reasons for lack of contact (of which some children had more than one) included moving from the study area (10 percent), temporary absence (13 percent), refusal to participate (28 percent), sickness (29 percent), and other reasons (30 percent). Table 1 summarizes the study contact and compliance in terms of the number of weeks the dose was missed. Nearly 42 percent of the children received all the doses. For those in the treated group, this was equivalent to more than 453 μmol (433,000 IU) of vitamin A, or approximately the amount available in the commonly used large-dose supplement (209 μmol every six months). More than 90 percent of the children received at least 322 μmol (307,000 IU), which is equivalent to more than 70 percent of what they would have received in a large-dose supplement.

Table 1. Doses Missed and Minimal Amount of Vitamin A Received during 52 Weeks of Intervention.

No. of Doses Missed	Percent of Children (N = 15,419)	Minimal Amount Received*
		μmol (IU)
0	41.8	453 (433,000)
1–5	38.7	410 (390,000)
6–10	6.9	366 (349,000)
11–15	3.2	322 (307,000)
16–20	2.0	279 (266,000)
21–26	1.7	227 (216,000)
27–31	0.7	183 (174,000)
>31	5.0	

*The minimal amount received was calculated with the following equation: 453 μmol − (maximal number of doses missed × 8.7 μmol) = minimal amount received.

Base-Line Characteristics

Sex, age, xerophthalmia status, serum retinol level, and nutritional status at base line are shown in Table 2. There were no substantial differences in these indexes between the control and treated groups. Although the study was meant to include only children from 6 to 60 months of age, birth records were unavailable, and our recall records include a small number of younger (1.8 percent) and older (5.4 percent) children.

The base-line prevalence of xerophthalmia was 11 percent. The risk of xerophthalmia did not differ according to sex, except for a slight predominance among boys after three years of age. Thirty-seven percent of the serum retinol values from the randomly sampled subgroup (n = 280) were ≤0.70 μmol per liter, and 21 percent were ≤0.35 μmol per liter. The prevalence of vitamin A deficiency in each of the clinical and biochemical categories thus exceeded the World Health Organization's criteria for a public health problem.[10] Seven cases of active corneal involvement (category X2, X3A, or X3B) were seen

Table 2. Base-Line Characteristics of the Study Population.

Characteristic	Percentage of Children
Sex	
Male	52
Female	48
Age (mo)*	
≤5	1.8
6–11	7.1
12–23	20.0
24–35	21.2
36–47	22.1
48–60	22.4
61–71	5.4
Xerophthalmia status†	
XN	3.7
X1B	7.2
X2, X3A, X3B	0.05
XS	0.07
Serum retinol (μmol/liter)	
≤0.35	21.4
0.351–0.70	16.1
0.701–1.05	16.4
>1.05	46.1
Nutritional status‡	
Stunted	31
Wasted	23
Stunted and wasted	18
Normal	25
Unknown	3

*Age at the start of intervention.

†XN indicates night blindness, X1B Bitôt's spot, X2 corneal xerosis, X3A corneal ulceration or keratomalacia of less than one third of the corneal surface, X3B corneal ulceration or keratomalacia of one third or more of the corneal surface, and XS corneal scar.

‡As determined with the CASP anthropometric software package. Stunted indicates height for age < the mean minus 2 SD and weight for height ≥ the mean minus 2 SD; wasted indicates height for age ≥ the mean minus 2 SD and weight for height < the mean minus 2 SD; stunted and wasted indicates height for age < the mean minus 2 SD and weight for height < the mean minus 2 SD; and normal indicates height for age ≥ the mean minus 2 SD and weight for height ≥ the mean minus 2 SD.

(four in the control group and three in the treated group). Night blindness accounted for about one third and Bitôt's spots for about two thirds of the milder cases of xerophthalmia.

Seventy-two percent of the children were classified by anthropometry as undernourished (defined as more than 2 SD below the reference mean). Approximately one third of the children were stunted, 18 percent stunted and wasted, and 23 percent wasted (Table 2). Stunting thus affected a somewhat larger proportion of the children than wasting, indicating that prolonged malnutrition was more common than acute undernutrition among the study children.

The five-year history of mortality among children under five years of age taken at base line was not significantly different between families of control and families of treated children (data not shown).

Mortality Outcome

There were 125 deaths in the study population during the 52 weeks of surveillance, for an overall mortality rate of 8.1 per 1000. Eight of these deaths, however, involved accidents unrelated to symptoms that could have been associated with the intake of vitamin A: animal bite (two deaths), drowning (three), poisoning (one), and falling (two). Five of the accidental deaths were in the treated group and three in the control group.

Figure 1 shows the cumulative deaths according to study group. Regardless of treatment, girls were at somewhat higher risk of death than boys, but not significantly so (relative risk, 1.5 in the control group and 1.2 in the treated group). Vitamin A significantly reduced the risk of death for both sexes, the effect being somewhat larger for girls (relative risk, 0.41 for girls [$P<0.01$] and 0.52 for boys [$P<0.05$]).

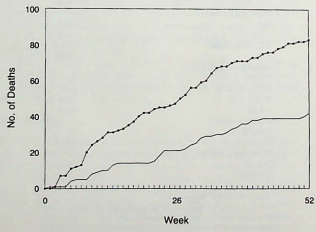

Figure 1. Cumulative Deaths Monitored Weekly, According to Study Group.

The solid line represents the group treated with vitamin A, and the line broken by squares the control group. Children who died in accidents (five in the treated group and three in the control group) are included.

Table 3 shows the mortality according to age and study group for the 117 nonaccidental deaths. The risk of death in the group receiving vitamin A was 46 percent of that in the control group. The relative risk was reduced most for infants (relative risk, 0.28; 95 percent confidence interval, 0.09 to 0.85) and those 12 to 35 months of age (relative risk, 0.46; 95 percent confidence interval, 0.26 to 0.81); it was less than 1.0 in all age groups. Excluding the children who had received the high-dose supplement at any time or who received it only at base line did not substantially change the age-specific relative risks shown in Table 3. In addition, these relative risks were not significantly changed by excluding those who did not receive the study supplements for more than seven consecutive weeks ($n = 1863$) or those who did not receive the supplements for more than four weeks on four occasions ($n = 11$). These exclusions were designed to minimize any possible confounding due to a differential participation effect or missing the supplements for a prolonged period.

Among the nonaccidental deaths, 18 occurred among children with xerophthalmia at base line. All 18 occurred in children over 12 months of age (12 children in the control group and 6 in the treated group). The death rate among children with xerophthalmia was 10.6 per 1000, as compared with 7.2 per 1000 among the children without xerophthalmia.

Table 4 shows the symptom- and disease-specific relative risk of death in the treated and control groups. According to the "verbal autopsy," there were too few deaths specifically associated with the symptoms of respiratory disease and malnutrition to provide a reliable relative risk. Excluding these two categories of symptoms, the relative risk was consistently lower for the treated group — and significantly so, except for deaths associated with measles. More than 40 percent of the deaths were associated with diarrhea, 16 percent with measles, and the remainder with symptoms suggesting other infections.

Table 5 shows the mortality according to treatment group and base-line nutritional status. Data on nutritional status were missing for 469 children (3 percent), among whom 7 died (6 in the control group and 1 in the treated group). Among the children not treated with vitamin A (the control group), the death rate of those who were both stunted and wasted was 1.5 to 2 times higher than the death rate of those who were either stunted or wasted, and it was 2.7 times higher than the rate of normal children. Thus, the risk of death was increased by acute undernutrition superimposed on chronic malnutrition. But the effect of treatment with vitamin A was pronounced (relative risk, 0.11; $P = 0.01$; 95 percent confidence interval, 0.03 to 0.36) among stunted children, whereas it was not significant among wasted, stunted and wasted, or normal children.

A hierarchical log-linear model was used to assess the multivariate relation among death, treatment, age,

sex, and nutritional status. The significant association between treatment and death persisted when adjusted simultaneously for age, sex, and nutritional status.

Discussion

The results of this community-based, masked controlled field trial clearly indicate that in an area where clinical vitamin A deficiency and chronic undernutrition are common, ensuring a constant consumption of vitamin A at least equivalent to the recommended dietary allowance enhanced children's survival. In Indonesia, somewhat similar effects among preschool-age children (a 45 percent reduction in mortality) were reported with vitamin A–fortified monosodium glutamate when it was a consistent part of the food supply.[1]

For the one-year follow-up period the overall mortality rate among children 6 to 60 months of age was 8.1 per 1000 in our study, comparable to the 7.8 per 1000 for the 12- to 71-month age group reported by the Aceh, Indonesia, study.[2] It was higher, however, than the 5 per 1000 reported from an area near Hyderabad, India, where a placebo-controlled, blinded trial with a high-dose supplement has also been performed.[12] These rates are considerably below the 20 per 1000 reported as the national average for India.[12] We monitored infant mortality in the study area for a one-year period in 1988 and 1989 and obtained a rate of 64 per 1000, a figure somewhat lower than the 83 per 1000 reported for Tamil Nadu in 1982[13] and the 98 per 1000 for India generally.[14] The mortality rate among infants less than 6 months old was 42 per 1000 live births, and among those 6 to 11 months old it was 22 per 1000. We were unable to find any reliable information on mortality rates among one-to-five-year-olds in Tamil Nadu. The lower mortality figures we report undoubtedly reflect in part the well-recognized effect of the frequent contact of households with trained fieldworkers.[12,15] Nonetheless, because the contact was comparable in our two study groups, the efficacy of vitamin A supplementation at the level of the recommended dietary allowance in reducing mortality by 54 percent remains evident; mortality rates were 10.5 per 1000 in the control group as compared with 4.8 per 1000 in the treated group.

Table 3. Mortality, According to Age and Study Group.

Age and Study Group	No. of Children	No. of Deaths	Cumulative Mortality Rate	Relative Risk*
0–11 Mo				
Control	678	14	0.021	0.28 (0.09, 0.85)†
Treated	689	4	0.006	
12–35 Mo				
Control	3185	52	0.016	0.46 (0.26, 0.81)‡
Treated	3179	24	0.008	
≥36 Mo				
Control	3792	14	0.004	0.63 (0.26, 1.50)
Treated	3896	9	0.002	
Total				
Control	7655	80	0.010	0.46 (0.29, 0.71)‡
Treated	7764	37	0.005	
Age-adjusted total				0.46 (0.30, 0.71)‡

*Relative risk for the treated group, as compared with the control group. Values in parentheses are 95 percent confidence limits.
†P = 0.05. ‡P = 0.01.

We found an insignificant sex-related difference in the risk of death without regard to treatment. Treatment with vitamin A reduced the risk of mortality in both sexes, but the reduction was somewhat greater among girls. This finding contrasts with that reported from Indonesia, in which a significant treatment effect of large-dose supplementation was found only in boys, among whom the prevalence of xerophthalmia was also higher.[2] In our study, the prevalence of xerophthalmia at base line was not significantly different between the sexes until after three years of age, whereas the effect on mortality of treatment with vitamin A was pronounced among the younger groups.

The efficacy of our low-dose supplementation was considerably higher than the 34 percent reduction in mortality reported after high-dose supplementation in Indonesia as determined by intention-to-treat analy-

Table 4. Symptom- and Disease-Specific Mortality, According to Treatment Group.

Symptoms or Disease	Control Group	Treated Group	Relative Risk*
	no. of children		
Measles	12	7	0.58 (0.17, 1.92)
Diarrhea	33	16	0.48 (0.24, 0.96)†
Respiratory	3	2	—
Malnutrition	1	3	—
Convulsions	12	3	0.25 (0.07, 0.85)†
Other	19	6	0.31 (0.12, 0.78)†
Total deaths	80	37	

*Relative risk for the treated group, as compared with the control group. Values in parentheses are 95 percent confidence limits.
†P = 0.05.

Table 5. Mortality, According to Nutritional Status.*

Nutritional Status and Study Group	No. of Children	No. of Deaths	Cumulative Mortality Rate	Relative Risk†
Unknown				
Control	201	6	0.030	0.13 (0.01, 1.14)
Treated	268	1	0.004	
Stunted				
Control	2385	27	0.011	0.11 (0.03, 0.36)‡
Treated	2418	3	0.001	
Wasted				
Control	1806	14	0.008	0.72 (0.30, 1.72)
Treated	1798	10	0.006	
Stunted and wasted				
Control	1373	22	0.016	0.65 (0.30, 1.41)
Treated	1340	14	0.010	
Normal				
Control	1890	11	0.006	0.80 (0.32, 2.00)
Treated	1940	9	0.005	

*The categories of nutritional status are defined in Table 2.
†Relative risk for the treated group, as compared with the control group. Values in parentheses are 95 percent confidence limits.
‡P = 0.01.

sis,[2] but lower than the estimated 75 percent reduction reported with an analysis based on actual receipt of the capsules.[3] The estimate based on receipt of the capsules was derived from a total of only 18 deaths over a four-month follow-up period. As the authors noted, its validity awaits verification by a study that ensures consistent, periodic verification of compliance in taking the large-dose supplement, which has not been a feature of most large-scale programs to date.[16]

Vitamin A was most efficacious in children under three years of age, most prominently in infants. This finding contrasts with reports from Indonesia. In the Aceh study the effect of treatment was most marked among those 60 to 71 months old,[2] and in the study involving vitamin A–fortified monosodium glutamate, mortality was reduced by 11 percent among infants and 45 percent among preschoolers.[4] In the monosodium glutamate study the infants probably received a considerable portion of their food as breast milk, and the effect of the program would therefore be expected to be less. The reasons for the discrepancy between our results and those of the Aceh study are less clear but may be related to the relative level of underlying malnutrition in the two study populations. Our base-line prevalence of xerophthalmia was 11 percent, as compared with about 1 to 2 percent in Indonesia, and only 25 percent of the Indian children had normal anthropometric features, whereas at least 40 to 69 percent of the Indonesian children were classified within 10 percent of the median standards of the U.S. National Center for Health Statistics.

In accordance with many reports from developing countries where vitamin A deficiency is endemic, diarrhea was associated with the highest number of deaths, followed by measles and symptoms associated with other infections — convulsions, jaundice, and encephalitis, for example. The protective effect of vitamin A was significant for all these conditions except measles. This finding contrasts with hospital-based case–control reports from Africa, in which the protective effect of very large doses of vitamin A was exceptionally high in measles.[17,18] Previous studies suggest that measles is a less severe disease in India than in Africa, and that factors other than vitamin A — the severity of concurrent malnutrition, for example — may be a more critical determinant of measles-associated morbidity and mortality.[19,20] It may also be that a large dose of vitamin A is required to prevent a fatal outcome in severe measles complicated by vitamin A deficiency.

Prolonged undernutrition, as evidenced by stunting, characterized nearly one third of the children in our study at base line, and a continuous supply of vitamin A reduced the risk of dying to one-ninth that of the controls. The protective effect of vitamin A was unremarkable in children with wasting, an indicator of acute malnutrition, and in those with normal anthropometric features. Stunting reflects — in addition to an inadequate food supply — many characteristics of social deprivation that are frequently found in poor households. Our data suggest that these persistent ecological and physiologic insults undermine the ability of a child who is deficient in vitamin A to ward off a fatal outcome when confronted by an infection. The programmatic implication of this is that maximal reductions in mortality can be expected from vitamin A prophylaxis targeted to children who are chronically undernourished and to those with superimposed acute malnutrition.

Children with xerophthalmia are reported to be at 4 to 12 times the risk of death of neighboring children with normal eyes, and the risk increases with the increasing severity of symptoms.[5] The mortality rate among children with xerophthalmia in our study was about 50 percent higher than among children without the condition (7.2 vs. 10.6 per 1000). When we adjusted for those who received a large dose of vitamin A because of xerophthalmia, the treatment effect of the continued small dose persisted — that is, half as many died among those who continued to receive the weekly supplement as among those who did not.

Sommer et al.[2] noted that daily consumption of the recommended dietary allowance was the ideal approach to vitamin A prophylaxis, but considered it to be impractical from a programmatic point of view and chose distribution of the large-dose capsule every six months instead. Sommer et al. subsequently commented that the single most important limitation to achieving the maximal effect with large-dose capsules was inadequate contact and verification of compliance[3]; the large-dose approach requires careful monitoring of distribution channels to avoid possible overdosing. In contrast, our approach involving frequent low doses showed that when the supplement is provided at a safe dosage level in an easily dispensed form, community workers can be effective in attaining high rates of contact and verification if there is also an appropriate managerial and supervisory system. Importantly, the efficacy of supplementation at the level of the recommended dietary allowance suggests that a similar effect could be achieved by an equivalent supply of vitamin A from foodstuffs, an approach that would potentially address other nutritional deficiencies as well.

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COCO NEWS:August 15,1995

Life, Death, Food and Medicine

Agriculture and indigenous systems of health care in our country are more than 2000 years old. The advent of western science & technology in various spheres of human activity have mystified the common sense approach and discredited indigenous wisdom world over.

An interesting reading and thought provoking question raised by Ken Taylor founder member of the Minnesota Food Association.....

"My comparison of the conventional systems of agriculture and medicine goes something like this: Both systems are based on the assumption (perhaps subconsciously) that death is the enemy and can be defeated. Through human cleverness (technology) we will be able to identify the problem and fix it, and because we think we can, we should. The language of the two systems is different. In medicine, it's called a cure". In U.S. agriculture, it's called "feeding the world". This assumption represents the fundamental flaw in both systems, because it violates a basic law of nature - death is part of life. Denial of this reality only delays action and increases consequences.

In medicine, this belief that death is the enemy to be defeated at all costs tends to put physicians' focus on the disease entity, not the human being who is the patient. In this scenario, the patient becomes the medium or the pathway to the problem to be solved." In agriculture, the enemy is death from starvation, and exploding population growth is the "disease" to be cured. Food production becomes the treatment to defeat that disease. As this treatment is relentlessly pursued, the planet, or patient, is put at risk because the diagnosis of population growth requires all the wondrous production enhancing tools that our industries and universities can make available. Whatever gets in the way of production is zapped with some poison or tools.

The sustainable agriculture movement and the alternative health care movement have a lot in common and much to learn from each other.... Wouldn't it be wonderful for [an] unlikely coalition to form, of urban and rural exiles of the agriculture and medical priesthoods? It is time for a community -oriented coalition of people who have identified their common ground as concern for their food and their health, with a commitment to reclaim responsibility for the complete cycle of their lives and for the life of the earth. Will this require a miracle?))

It is encouraging that queries on organic farming, its nuances and availability of organically produced food are trickling in everyday at the coco office.

Welcome new members to the coalition of producers and consumers.

Insecticide pollution in potable water resources in rural areas

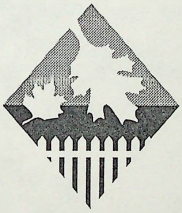
The consumption of pesticides used to increase the agricultural production, to minimise the food loss during storage is increasing in India for the last two decades. BHC and DDT constitute about 50% of the total consumption of pesticides in India. Certain pesticides are persistent and result in the contamination of water resources due to spray drift, direct application run off resulting from rainfall and irrigation. A comprehensive review illustrated how the surviving insecticide residues have polluted soil, water, food and air, thereby causing the death of several species of birds aquatic species and other organism.

A survey has been conducted to investigate the magnitude of contamination of water resources with pesticide residues in rural areas of Mysore District. The studies revealed that all the water samples invariably contained BHC and some of the samples showed DDT and methyl parathion residues.

A decontamination technique has been described to remove pesticide residues from water. To protect public health a pesticide residue decontamination technique in potable water is described. A two kg batch of wood charcoal powder passing through mesh 60 packed upto a height of 8-10 cm can decontaminate about 14 insecticide residues in the range of 20 mg present in 400 litres of water.

Excerpted from

(G. SURYANARAYANA RAJU, K. VISWESWARIAH, J. M. M. GAUNDO AMANULLA KHAN and S. K. MAJUMDER Infestation Control and Pesticides Discipline, Central Food Technological Research Institute, Mysore - 570013, India)



TURMERIC *Curcuma domestica*

Turmeric is a perennial plant with a short stem and tufted leaves. It originated in India and Southeast -Asia where it grows in deciduous monsoon forest, and has now reached worldwide distribution. It thrives up to 2000 metres in places with a rainfall of 1000 -2000 m. It grows well on loams and alluvial soils. It can be grown as a mixed cultivation with vegetables.

It has insecticidal and repellant properties.

Target Insects

Army worms
Caterpillars
Cowpea beetle
Grain borer
Lesser grain borer
Mites
Rice flour beetle
Rice weevil

Methods of Use

There is relatively little information from practical experience on the use of insecticidal plants and most of it refers to storage protection:

* PERIES in Sri Lanka describes the following method

-Turmeric root is shredded and cow urine added. The mixture is diluted with water in proportions between 1 : 2 and 1 : 6 and used against insects and in particular against caterpillars. The exact quantities are not given.

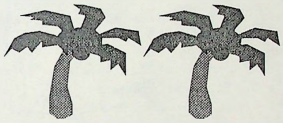
-Threads can be dipped in grated turmeric and stretched over the fields which have then a repellent effect.

* In trials a turmeric preparation caused a 90 - 100 % death rate of the army worm (Spodoptera litura) in 2 days. Dried rhizomes were grated and extracted with acetone and the solution was diluted with 5 parts of water.

Nature cure:

Turmeric has anti -cancer activity. Research at the NIN Hyderabad confirmed the anti mutagenic effects of turmeric in humans, reporting that it may act as a preventive against several dietary carcinogens.

Turmeric boiled in milk along with a dash of black pepper powder may be taken two or three times a day for sore throat, cough, cold.
Pharyngitis and other acute respiratory infections.
A hot poultice made of turmeric powder applied three to four times a day alleviate the pain of abscesses.
For fissures on sole of the feet, mix some castor oil with turmeric powder and apply.



Nutritious crops threatened with extinction

Finger millet (Eleusine coracana)

Ragi is know by different names such as ragica, mandua, madira, nagli, regalu and kepni in different parts of India. Ragi is grown in Karnataka, Tamil Nadu, Andhra, Orissa, Maharasthra, Bihar, Uttar Pradesh and Gujarat.

Many varieties of Ragi existed in these different parts of the country where they were traditionally grown. Some of the varieties that have been favorites with farmers for example from one district in Deccan region described in the Gazetteer.

Hullupore Ragi	*Green open*
Gidda bili Ragi	*Green compact*
Karigidda Ragi	*Violet compact*
Jenu goodu Ragi	*Green open*
Madayana Ragi	*Violet open*
Hasaru Kambi	*Green open*
Dodda Ragi	*Green open*
Jade shanka Ragi	*Green compact*
Rudrajede	*Violet compact*
Muttige Ragi	*Green open*
Karimurukalu	*Green open*
Balepatta	*Green open*
Biliragi	*Green open*

These strains had their very unique characteristic. For instance, Madayanagiri which is along duration variety with open earheads were best suited to the area. The varietal names given by the farmers speak for the characteristics of these varieties. Ragi as a crop is one of the hardiest, suited to the dry land tracts, and can withstand severe drought conditions, reviving again with remarkable vigour. The crop is remarkably free from pest and diseases. The Ragi grain can be stored for long periods, even upto 50 years without damage.

Varieties in Ragi differ in colour of the grains and in their sizes. A deep brown colour is the predominant colour of most varieties, but shades of this colour ranging from orange red at one end and very deep brown, almost black at the other, are met with. Differences in quality of the grain are also recognised. These are probably due to variations in the composition of the grain. Apart from all the above meritorious characteristics, Ragi is a highly nutritious millet.

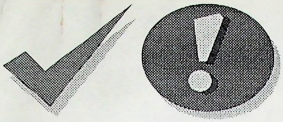
Nutrients per 100 gms of Ragi

Protein	*7.3 gms*
Phosphorous	*283 mg*
Energy	*328 Kcal*
Iron	*3.9mg*
Calcium	*344mg*
Carotene	*42 mg*

Ragi has been an important part of the every day food intake. Ragi is powdered and is used in different ways. In the vernacular, they are known as 'mudde'. 'roti','kanji', and 'seri' for children. Ragi preparations are enriched nutritionally with locally available greens and pulses to make a complete food. The flattened roti resembles maize tortilla. Mudde from the flour is prepared by steaming the dough and making it into balls. The flour is also suspended in cold water containing a little butter milk and is left overnight for mild fermentation. The slurry is then cooked to prepare porridge.

Malting of Ragi has been a traditional process in certain parts of India. It is mostly used for feeding young children. Among the tropical cereals, finger millets possess very high malting characteristics. In order to malt, the millet is cleaned and steeped in water for at least 16 hours. Then it is allowed to germinate for two days. This is de vegetated and the green malt is separated by grinding. The sieved portion is dried and malt flour is obtained. This is added to the malted flour of mung (Phaseolus aureus) and has an excellent nutritive value as food for children and invalids.

Popping the finger millet is another way of cooking the grain. Since the grain cannot be debranned, popping is an excellent way of retaining the fibre content and preparing ready-to-eat foods. The grain can be processed in a temperature of 250° C, with low moisture content. This flour is consumed along with jaggery and milk and its traditionally called 'hurihittu'.



Profiles of Coco Members

From this newsletter, we intend bringing out brief profiles of **COCO** members. This time, we feature *Anjela Sudharshan* and *Bhavani Krishnakumar.*

Anju (Anjela) Sudharshan

Spent the first 10 years since 1977 as a junior/middle level executive handling consumer electronic goods for aspects of inventory control, purchase, retailing, general merchandising and office administration. For the last six years involved in the rural development work through NGO's on various aspects of development like gender, sustainable agriculture, environment and awareness building.

Interested in working for conservation of environment , rural poor, cooking and travelling.

Bhavani Krishnakumar

Bhavani Krishnakumar is a *bharata natyam* dancer, having undergone training in this art for more than 30 years. She has performed on stage several times, with the notable ones being in National Centre for Performing Arts and Godrej Theatre in Bombay, Krishna Ghana Sabha and Vani Mahal in Madras. Her last performance was in December 1993 at National Centre for Performing Arts at Bombay.

Love for physical fitness has led her to aerobics. She is now an instructor for aerobics in a local gym.

Interested in travelling, languages, cooking and enjoying good food.

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Recipes

You are encouraged to contribute new and interesting recipes that you come across.

Here's one by Laxmi

Soya upma

Ingredients:

One cup soya (soaked overnight);
Chillies (Green and red), two each;
Scraped Coconut: two to three tbs;
Jeera: 1/2 tsp;
Mustard seeds: 1/2 tsp;
Turmeric powder: 1/4 tsp;
Aesofetida: a pinch;
Salt to taste;
Coriander and curry leaves;
Oil: two tbs;

Method:

Pressure cook the soaked soya and grind it to paste along with aesofetida, chillies and salt. Heat the oil in a saucepan and when hot, add mustard, jeera and turmeric. When the mustard sputters, add the ground soya with coconut, coriander and curry leaves. Cook it on medium flame for three to four minutes. Serves four.

Design and Layout: Krishnakumar

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ISSUES FOR DEBATE

Health and Nutrition: People, Policies and Politics

Ritu Priya

An intensive debate occurred on issues relating to poverty, nutrition and health in the seventies and early eighties declining soon thereafter (Dandekar,[1] Sukhatme,[2] Gopalan,[3]). Prof. Sukhatme and the Edmundsons presented one side of the debate in a more developed and sophisticated form in their book, *Diet, Disease* and *Development*.[4]

Today, when 'poverty' is being sought to be erased from national planning and health policy, this book is an important document for public debate regarding evolving public health and development perspectives suited to the specific context of India and other developing countries. The authors' articulation of their perspective allows it to be interpreted as anti-poor and to be used by anti-poor social forces. It is important to reopen the debate and deal with recent as well as earlier issues.

The Context of Contemporary Public Health Perspectives

The latest document largely setting the current trend in health planning is the World Bank's *World Development Report: Investing in Health*.[5] It looks at health planning entirely from the point of view

of finance and the role of financial structures in changing or ascertaining certain kinds of human behaviour. Presenting a plan for a techno-centric, modern, expert-based, marketized health service system with extreme commodification of health, it appears as the most practical in the given socio-political and economic context because it is entirely in tune with the centralized organisational structures, the current economic structural changes and the elite, urban oriented development model. The book authored by Sukhatme and the two Edmundsons tends, in large part, to provide 'scientific' support to this approach and is, therefore, important to read and analyse. But that is not all one should read into it. Contradictions within its perspective offer ideas for other creative possibilities as well.

At the other end of the ideological spectrum from the World Bank, we have the perspective articulated by the Bhore Committee (GOI, 1946)[6] and followed up by others attempting to adapt it in the light of practical experience and changing conditions. One major drawback of the Bhore Committee was that it assumed sufficiency of resources and permitted itself the luxury of looking at every aspect of health services without emphasizing the need to prioritize (Qadeer and Priya 1992).[7] The suggestions for a complete public sector medical care system such as Britain's National Health Service too would require unrealistic economic resource inputs from the state. This book, on the other hand, gives primary consideration to the problem of resources in the implementation of public health programmes and insists on low resource input options. In fact, it may be faulted for its over-balancing on the other side; cutting on absolute basics on the plea of resource constraints. Later work (ICSSR-ICMR 1982,[8] Antia 1993[9]) argues for a public health policy based on encouragement to people's action, use of indigenous systems of knowledge, panchayati raj as an instrument of wielding people's control over development efforts and services and an efficient, well-funded public sector. While success stories of this approach are available largely through NGO efforts in small pockets, this perspective seems to be somehow unable to come to grips with the existing socio-political situation. It does not indicate the process by which societal conditions, very adverse to implementation of the model presented, are to be turned in a more conducive direction.

Between these two extreme models lie others which propose a mix of the two. For instance, there is the suggestion of identifying a package of services through an epidemiological approach including the concept of community felt need, people's health related perception and behaviour, the decentralisation of services and due attention to the high degree of disparities in the socio-economic structure of developing societies (Banerji 1993).[10] This perspective acknowledges the primacy of the political process in development planning. It recognizes that implementation of a holistic approach is dependent on processes which manage to break the socio-political constraints on it. Meanwhile, it sees the developing of appropriate principles and methods of health planning and then making them widely understood and accepted as the primary tasks before public health scholars. The planning of the National Tuberculosis Programme (NTP) is offered as an example of appropriate planning.[11] That the NTP has not succeeded in practice shows how isolated appropriate efforts cannot work unless the overall health service system is conducive to it.

This book presents another 'in-between' perspective. Its limitation is that it attempts to address the issues of 'culture' without addressing the issues of social structure. Combining the two would be a potent mixture for change towards a more healthy society. Focussing exclusively on any one is a travesty of the human reality. An exclusive reliance on the former is likely to support the status quo in an extremely unhealthy society.

The Book

This book brings together the ideas developed by Professor Sukhatme over thirty-seven years (twenty-seven as Director of Statistics, FAO, Rome and then, since 1981, as President, Maharashtra Association for the Advancement of Science, Pune) as also by his disciples Wade C. Edmundson (also a statistician) and Stella A. Edmundson (a nutritionist). Their understanding of several public health problems is put together to present a perspective on how both health and development can be effectively promoted in developing countries. In the process it makes one reflect upon the economics of health and the relationship between science, policy, politics and social trends.

The authors' general perspective emphasizes health as a dynamic process, a resultant of the interplay between mind and body, and of

the internal milieu with the external environment. In their view, an understanding of the ecology of health must inform all health planning with due consideration of the interaction between different components of the external environment - the physical, the biological, the economic and the cultural - which sets the boundaries within which the internal environment adjusts to maintain stability and normal function. Therefore, health and economic development must be examined together in all their complexity.

The principles underlying their policy guidelines emphasise the importance of human resource development (basically education and health) as the primary focus of developmental activity by governments of developing countries. Economic growth alone is not enough to improve health. "Human resource development is the key causal priority motivating economic growth" (p. 8).

Secondly, improving health in the developing world is a matter of setting priorities, particularly given the low health budgets. The authors advocate the use of the cost-benefit approach for determining intervention priorities.

Thirdly "give what the people want" (p. 29) is offered as the starting point for any health improvement programme: easy-to-do cures for their ailments; health workers treating them with courtesy, patience and regard; giving people advice but allowing them the right not to carry it out.

Analysing the health situation in developing countries, with the specific cases of India and Indonesia, the authors spell out the well accepted scenario that malnutrition and infectious diseases are the major sources of ill-health in developing countries, that children under five are the most affected age group, and, that there is more ill-health in rural rather than in urban areas.

The authors accept that dietary inadequacies and infectious disease are strongly synergistic, one compounding the problems created by the other, but see *disease as a more important component of health than diet*. Three scientific arguments are presented in support of this contention. The direct scientific basis for this statement comes from a statistical analysis of the factors leading to increase in life expectancy in Japan from 1949 to 1963. This contention is further supported by their old statistical argument (part of the well-known public debate between Professors Sukhatme and V.M. Dandekar in the early 1980s) that people adapt to low energy intakes with little functional loss and therefore the quality of food intake is not a major problem. Here the authors also invoke the synergism between disease and nutritional status to hypothesise that the low manifestation of quantitative food deficiency is due to the disease load and its siphoning off of the adequate dietary intake. This line of argument is pushed further by a discussion of protein vitamin-A and iron deficiency, and goiter; that the primary responsibility for the existing forms of malnutrition lies in the quality of diets. Thus, as a corrective, what is needed are either changes in eating habits, or specific nutrient additives.

The book also contains a detailed discussion on the microbiological and pharmacological aspects of the major infectious diseases - diarrhoea and dysentery, pneumonia, malaria, helminthic 'infections'. There is, however, little consideration of their ecological correlates.

Following this analysis, the authors make some concrete recommendations for health policy and programmes:

1. *Direct action against disease needs to be given priority over action against malnutrition.*
2. Common diseases should be tackled largely through self-care by lay persons with basic medical services handled by primary health workers. Education of villagers in relevant modern scientific knowledge, use of indigenous medical practitioners and folk knowledge is recommended.
3. The importance of curative care is underlined even as a part of public health programmes aiming at prevention. This is what people want most. In the authors' view, after it is provided, people will start seeing the purpose of preventive measures.
4. Public health measures such as provision of safe water and latrines, environmental sanitation, etc. though desirable, "are costly and difficult, specially in the villages. *Simple behavioural change in the individual without extensive government intervention*" (p.150) is emphasized as the feasible method of prevention of disease. At the same time, the authors see the government programme for immunisation of children against the

six vaccine preventable diseases as an important intervention. Involving people in the Universal Immunisation Programme and using knowledge of local customs and beliefs to make it acceptable is stated to be crucial for its successful implementation.

5. The authors categorically reject supplementary feeding programmes as an answer to the problem of malnutrition in children. Quality of diets should be improved through educating people in using locally available foods, fortification in marketed products and specific supplements to be given by the medical system. These measures plus the control of diseases which compound the effect of dietary deficiencies, are the preferred means of improving nutritional status.
6. Besides behavioural changes being brought about through health education by primary health care workers, *a more appropriate primary school syllabus is recommended as the starting point for improving rural people's culture and lifestyle to decrease morbidity and increase economic productivity.*

In addition to the three "Rs" the appropriate curriculum is meant to equip the child with an understanding of his/her surroundings via focusing on relevant health, agricultural and social issues using a mix of traditional and modern knowledge sources and technologies.

The Perspective: Its Significance and Limitations

The principles set out in this book for public health theory, policy making and practice are important contributions to the current debate in public health. However, it does appear that the authors miss out some elements crucial to the wholesome application of those very principles when they analyse the health situation and when they draw out guidelines for public health policy. These are discussed below, since ignoring them would undermine the power of the conceptual principles offered by the authors.

Principle 1

One of the primary principles enunciated in the book is *being holistic and ecological with sensitivity to complexity and diversity.* The authors themselves go well beyond the cliched use of phrases like 'inter-sectoral coordination', 'inter-disciplinarity' and 'environment friendliness.' In their words: "There is a tendency for economic and technologic theory to be too simplistic... The real world where human beings interact with their environment is a complex place with room only for a holistic social and technological approach (p. vii)."

The authors remind us of the power of the individual human being, an element often missing in the epidemiologically generated, large numbers-based public health approaches. The introduction of this conceptual element can well make public health more effective in understanding human reality and in dealing with it.

Similarly, they highlight the situational specificity of health and disease in different human populations. They emphasize the role of the physical, biological, economic, and cultural environment in causing health and disease. This understanding is widely shared today. On the other hand, the conceptual significance of adaptation by human groups to their ecological setting is still to be fully appreciated, though it has been discussed by other scholars (Dubos 1968,[12] Banerji 1988[13]).

This perspective also provides a counter to the 'universal', 'neutral' view of medicine and public health. The belief that 'West is best' is questioned by this ecological view of health.

The authors' work demonstrates how problems of different locations may not only need different solutions, but that they also need to be defined differently. As some earlier studies in the early seventies had highlighted, protein deficiency in India needed to be interpreted differently from how it had to be seen in children in the African context, given the differences in dietary patterns (Sukhatme, 1972).[14] The malnutrition in African children primarily demonstrated protein deficiency, because of the reliance on carbohydrate-rich cassava-based weaning diets with almost no proteins. In India, the cereal and pulses-based diets carry the correct proportion of carbohydrates and proteins, and thus, malnutrition is a reflection of the inadequacy of quantity.

Fallacy 1

In dealing with such inter-country, inter-regional differences, the authors neglect internal disparities (other than gender) within the population of a geographical region. They constantly refer to poverty, but largely only to show how it is not a barrier to better health, except in very extreme situations. They suggest that lack of

education is the prime reason for the poor being unable to raise their standard of living. The specificity of the economic and social environment of the poor and thereby the difference in the meaning of physical and cultural adaptation as compared to the better off in the some society is totally ignored.

Principle 2

Another important principle presented in the book is the necessity of giving importance and respect to the perceptions of rural peoples of the developing countries. Their need for curative care as the primary service of any health system, their desire to be treated with respect and dignity, the recognition that they are not just helpless beings in the hands of power-wielders but have their own means of dealing with problems are important insights for the planning and implementation of a public health service.

Fallacy 2

Yet, when it comes to the underfed and chronically malnourished, the authors say that only "a very small proportion of these are actually 'starving to death'. They are suffering from 'psychic hunger' and
70 malnutrition, but not from physiologic 'starvation' " (p. 74). This means that most of those who feel that they are not being able to fill their stomachs adequately and want more food must not be 'given what they want' because they are not "physiologically starving" nor are they economically more productive when they eat more!

Principle 3

The authors take great care to emphasize human resource development (HRD). They argue against the macro-economistic model of development which suggests that economic growth and industrial development automatically bring social development. They also speak of a spiritually higher form of human beings who "can mould their minds as well as their bodies" in a healthy manner, whose "egoism is tempered with the knowledge that self interest is often well served by group interest", "need, not greed" forming the basis of community action, etc.

Fallacy 3

However, the rationale they offer for HRD is an entirely economic one: that HRD will stimulate economic development. This is a constant refrain throughout the book. The link between better health and development is seen primarily in terms of increase in economic productivity. HRD for human well-being finds no mention at all. The perspective on adaptation to low intakes and their dismissal of 'hunger' as an issue (only starving to death or loss of economic work output being of real consequence) is consistent with this approach to HRD.

The societal goal is thus to be an increase in national economic productivity, even HRD being geared towards that goal. The hungry must learn to adapt better to their hunger and primarily develop culturally and spiritually not economically! Not once is there a mention of how the better off of the world are to develop culturally and spiritually; how their lifestyles must change to improve their own health and that of the poor. This expectation of dichotomised social values in the present world (with an upsurge of egalitarian democratic aspirations at all levels of society) is *a major flaw in the practical feasibility of the process the authors suggest* for better health and development. *There has to be a consistency between socially articulated values and the values one wants to see inculcated in individuals.*

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Principle 4

Shaping of values, attitudes and behaviour is an important aspect of social policy. In this regard, the authors progress beyond mere 'health education' to the overall educational system. Formal educational channels are proposed as the basis for changing people's knowledge levels and behaviour so as to promote self-care and community action and inculcate an ecological perspective.

Fallacy 4

One may grant that education which helps people deal more effectively with their environment is an important intervention for the deprived groups to improve their material conditions and health. But it is not enough. For it to happen at all requires that the educators and the better-off sections allow the deprived groups the space to gain self-confidence and support them in the expression of their full potential. What process the authors envisage to build such a social environment is not clear. *The entire tenor of the argument detracts from any humanistic trend if not provide the basis for its opposite, i.e., anti-poor tendencies.*

Fallacy 5

Similarly, the advocacy of prioritizing of interventions by the cost-benefit approach also demonstrates the contradictions in the authors' application of the stated principles. This method evaluates individual interventions for their economic cost and for the benefits they provide in terms of the cure of specific health problems. *This limits one to specific interventions without examining their interlinkages.* It does not take social costs or benefits into account.

The access of all citizens to all basic needs warrants little prioritizing but that is what the authors do. *How can one prioritize between 'satisfying people's hunger' and 'cure of illness' specially if one is to "give people what they want"?* We must, of course, examine various optional ways of meeting each of these basic needs and find out the optimal one within the given economic, social, cultural and organisational constraints. There we can use the cost-benefit analysis *as one of the many tools* which will help identify the optimal method of intervention.

In fact, their very methodology in field studies and data analyses is

indicative of their perspective towards development. Take, for instance, the indices used by them. The use of mortality and life expectancy rather than incidence and prevalence of disease or the gaining of physical stature as the measures of health status is one example. The use of economic activity alone for measuring work output as against economic activity plus domestic and social activities is another. We will discuss these at greater length in the next section. Here it is sufficient to appreciate that consideration of the quality of life is missing from the indices which form the bases of the authors' scientific arguments.

Fallacy 6

The interventions highlighted as solutions to each of the health problems discussed in the book do not deal with any problem in a manner that links it to other health problems or to its basic social and environmental causes. Another aspect which finds no place in the author's perspective is the role of developmental interventions in shaping of societal concepts and values around health.

Consider the Universal Immunisation Programme. Compared to immunisation as the prime measure for decreasing mortidity and mortality from the six vaccine preventable diseases, other general measures would minimise a whole range of diseases - these six as well several more common ones which are responsible for a greater quantum of childhood morbidity and mortality. For instance, safe water supply and excreta disposal would not only deal with poliomyelitis but also control the larger problems of diarrhoea and dysentery, typhoid etc. Similarly, improving the nutritional status of children will minimise the complications and mortality secondary to measles as well as to the more common diarrhoea, dysentery, pneumonia, tuberculosis and other respiratory diseases. The general measures would improve other aspects of human lives as well and increase well-being in general. In addition, they would provide concrete shape to an ecological perspective. Immunisation promotes the view that freedom from disease can be bought or acquired through an injection while the general measures convey messages of a hygienic lifestyle, environmental sanitation, etc. as important for health.

The authors put the latter at low priority because they see them as costly and difficult to implement. However, if locally appropriate technologies are used, if the community is convinced of their usefulness and actively involved, such measures may not be too difficult to implement. Professor Sukhatme's own project in eight villages near Pune seems to testify to this (p. 254-55). As for the cost, it too will not be high as these appropriate technologies are generally cheaper and more so if all thebenefits of these measures are counted. Nor is mass immunisation as cheap and easy to implement as is often made out to be. Maintenance of an effective cold chain, administration of vaccines in the right manner and adequate coverage are difficult things to ensure under our conditions. The National Evaluation of the UIP (NIHFW, 1989)[15] clearly shows the failure in implementation even within the 'intensive programme' districts which got special resources and devoted extra attention to UIP.

The technocentric, commodified nature of interventions selected as priorities by the authors will convey messages contrary to what is expected from the 'appropriate curriculum' for primary education. It is likely that the concrete expression of health interventions will have greater impact than any formal education. In addition, when the overall developmental process is moving towards a more

homogenising, consumerist culture, the creative use of local genius and knowledge is likely to be weakened further by the proposed interventions.

Science and Policy

The relationship between science, policy and socio-political perspective seems to explain the nature of discrepancies between the conceptual principles stated by the authors and their work. The methodology and analysis used in their scientific studies produce results which support certain kinds of policy objectives and go counter to other perspectives. Let me take up specific examples to examine these links.

Protein Deficiency: Then and Now

Prof. Sukhatme had earlier made significant interventions in health policy debates. In the early seventies, international agencies were harping on protein deficiency and its serious implications for developing countries in terms of physical and mental retardation of large proportions of their populations. Influenced by the newly marketed technologies for producing high protein foods, they advocated special fortification of foods, promotion of high protein foods, etc. At that time, Prof. Sukhatme highlighted data from India which showed that the common diets of cereals and pulses provided adequate proteins if eaten in quantities sufficient to fulfil calorie requirements. The deficiency was primarily of calories due to underfeeding. He demonstrated statistically how this led to utilisation of proteins for conversion into calories rather than body building and therefore a secondary deficiency of protein (Sukhatme, 1972).[1] Alongwith the work of scientists such as Gopalan and his colleagues at the National Institute of Nutrition, this helped to effectively stem the 'protein gap' hysteria.

In this book, the authors take a slightly different position on protein deficiency, arguing that, "All things being equal, qualitative protein deficiency is more likely to occur than quantitative energy deficiency. However, quantitative energy deficiency may cause qualitative protein deficiency" (p. 37). While this statement presents the physiological picture, it does not take the cultural and social reality into account. In fact, read together with their contention that "In the future more emphasis needs to be placed on the quality of the diet and less on the quantity of food intake" (p. 75), it leads to a complete reversal of Prof. Sukhatme's earlier contribution to the understanding of nutritional problems and to nutrition policy of the seventies! From earlier demonstrating how quantitative energy deficiency does in reality lead to protein deficiency in a majority of the malnourished (Sukhatme 1972),[13] they now state that this *may* happen (as in the quote above). Can this change in position be accounted for, at least in part, by the change in policy issues they choose to address at the two points of time? Earlier the question was whether to give primacy to protein deficiency or to calorie deficiency. Today the question being posed is of giving primacy to disease control or to increasing nutritional intakes of the undernourished.

Variability and Energy Requirements

Sukhatme's second major contribution has been in highlighting the variability in calorie requirements between individuals with similar weights engaging in similar amounts of physical work as also within the same individual from day to day. His data analysis shows that while intakes of large numbers average out in similar ways, an individual's energy balance may not be negative even if intakes are below the mean or the Recommended Dietary Allowance (RDA) for calories (Sukhatme, 1981).[2] This was a significant point to be made at a time when RDAs had come to be used by medical persons, nutritionists and dietitians as sacred numbers in assessing and deciding each individual's diet. This is patently a misinterpretation and misuse of statistical averages whose purpose is to facilitate comparison across groups of a large number of individuals. Sukhatme's argument would have served the cause of nutrition science and its praxis greatly had this point been taken up adequately. However, it seems to have got lost as the use of RDAs largely continues as before.

Sukhatme then went on to propose that instead of the mean, two standard deviations below the mean of intakes in the group be taken as the cut-off point while labelling diets as adequate or inadequate in terms of proteins or calories. This needs to be examined further.

If the physiological nutrient requirements of individuals with a certain body weight, age and activity level in a population follow a

normal Gaussian curve, the natural RDA of 50% of the individuals in a population will fall below the mean ('m'), of 16.5% below mean minus standard deviation ('m-s') and of 0.25% below 'm-2s'. Thus, individuals even below m-2s may be getting their full physiological requirement because persons of any population may actually need only those few calories. However, dietary intakes are dependent not just on physiological need but also on the cultural pattern and psychological state of the individual, on the one hand, and the access to food items both in terms of the types of foodstuffs and their quantity, on the other. Individual physiological nutrient requirements are difficult to establish as a result of these three, what statistically are conventionally called, 'confounding variables' and because of natural variability. Epidemiological measures such as RDAs are available but only for purposes of assessing and planning for large populations. Modern nutrition science should take the logic of Sukhatme's argument seriously. The ICMR Expert Group on RDAs did dwell on the question of variability while resetting RDAs (ICMR 1992).[15] However, the scientific argument needs to be taken further. Nutrition science needs to incorporate within its body of knowledge the nature of variations in nutrient needs and in dietary patterns meant to meet those needs.

The understanding of variability offers possibilities of advancing the horizons of science by relating it to the complexity of diversity in physiological, ecological and social contexts. However, Sukhatme's own recommendation of using 'm-2s' for setting dietary requirements *only lowers the RDA to another arbitrary numerical point; it does not make the conceptual shift his own perspective demands.*

The reason given for this shift of cut-off point from 'm' to 'm-2s' was that use of the former puts too many people in the,under-nourished category even when many of them are not adversely affected by their low intake. For some, this may be their natural requirement (as expected of persons at the margins of any random distribution curve) while others adapt to the low intakes as an 'auto-regulatory process' and without any functional loss. Attempting to raise their calorie intakes would be a waste of public effort and resources. *The basis of his policy proposal was cutting down the waste of resources.*

Those disagreeing with his proposition of 'adaptation to low intakes as a healthy process' based their argument on two issues. One was that low intakes lowered economic work output thus also perpetuating poverty (Dandekar 1982, Gopalan 1983). Secondly, that individuals who have 'adapted' to a poverty situation are the end result of a process which involves deterioration of physiological functions and high levels of morbidity in early life. Many succumbed to this morbidity and are martyred on the way to 'adaptation', while others who survive become physically stunted. Acceptance of stunting as 'healthy adaptation' is only legitimation of a process involving high costs to the community and the individual (Gopalan 1986).[16]

For the past couple of decades, Sukhatme and the Edmundsons have been studying the two relationships challenging the normal adaptation hypothesis -the relationship between calorie intake and work output and the relationship between nutrition and morbidity-mortality levels.

In terms of work output they find that economic work output is not significantly different between those with different calorie intakes. The work by the Edmundsons among the villagers of Indonesia and India has shown that *people adapt to low energy intakes by (i) a slowing of growth and resultant reduction in body mass leading to less food energy utilisation for a given amount of physical work, (ii) greater metabolic efficiency in energy use, more by decrease in basal metabolic rate but also by some decrease in energy used for work, and, (iii) decrease in time and energy spent on leisure activity (resting, social and religious activity).* Thus persons with low energy intakes can perform more economically productive work per unit of food energy consumed.

This may well be considered good adaptation from the economic policy makers point of view. However, economic work output is hardly a direct measure of physiological work capacity, because it is modified significantly by other economic and social factors such as possibilities within the occupation to increase output, the incentives and motivations for harder work inputs, etc. A study by the National Institute of Nutrition eliminated these factors and showed that those with higher weights and heights at age five, and in adulthood at the time of measuring work output, had significantly greater work output

as compared to their counterparts with lower weights and heights, if habitual physical work done by them was the same. Habituation to greater physical work improved performance giving an illusion of healthy adaptation. However, a physiological parameter of adaptation for physical work, the increase in heart rate with increasing work, showed the latter group to be poorly adapted, i.e., the same intensive work put greater stress on the body of the village boys with lower weights and heights than with higher body measurements (Satyanarayana et al, 1979).[17] The lower work output of those with lesser physical growth and the evidence of greater stress on them indicates a lower level of physiological adaptation in the malnourished.

These findings differ significantly from those of Sukhatme and the Edmundsons. Satyanarayana et al have extricated the natural processes from their social overlay by taking the latter into account methodologically. Sukhatme and the Edmundsons examine the phenomenon from the point of view of a socially set goal, that of maximum physical activity for economic output by human beings who avail of the least possible resources. We must clearly distinguish between the description of phenomena from these two points of view when using such information for policy formation, specially since there may not be universal agreement on the definition of social goals.

Disease vs. Diet

The second argument against the acceptance of healthy 'adaptation' to chronic undernutrition is sought to be countered by the authors of this book by making the point that infectious diseases are more important in determining health status than malnutrition. They attempt to do this through a statistical correlation of data on diets and on five major diseases causing death with life expectancy at birth (LEO). The data pertains to Japan from 1949 to 1963. They find that diet and disease indices together explain 99.6% of the change in LEO. Using some "complex statistical analyses" they find that on separating out the effects of the two, "the fall in disease mortality (of the five major causes) accounted for fully 60% or more of the increase in life expectancy, whereas the improvement in nutritional sufficiency accounted for only 40% or less of the improvement in health (measured as LEO)" (p. 16). They conclude that "disease was more important than diet"!

As a scientific conclusion, this statement is on very shaky ground. It is well known that in situations of chronic undernutrition, deaths directly due to malnutrition are few. It is rather that the severity of diseases and mortality due to them is high in the malnourished. Thus malnutrition increases the mortality due to disease. The statistical correlation of diet and disease does not take this synergism into account. Also, taking total mortality rates for the five most common causes of death as the index of disease status is bound to show higher statistical correlation with LEO than if actual morbidity rates are used. With these biases inherent in the statistical analysis, if nutritional sufficiency was still found to account for 40% of the improvement in health, can that be said to be a crucial difference compared to 60% by fall in disease mortality? Can this be legitimately further extended to guide policy?

The exact weightage of diet and nutrition in determining health status is neither scientifically established yet, nor is it likely to be the same in any two situations - so intertwined and complex is the relationship. That is why, giving a 'scientific' basis for priority to disease control over malnutrition control, facilitates the evasion of difficult policy decisions addressing a broader canvas, including agricultural policy and the social distribution of resources. This is yet another instance of policy issues impinging on the making of science as knowledge.

The understanding of the phenomenon of healthy human adaptation to the environment is meaningful only when its limits are also stated. While the various elements forming the environment, the physical, economic, cultural and biological, interact with each other, the extreme form of one can overwhelm the impact of others and produce an environment beyond the limits of normal adaptability.

Due to the specificity of environmental settings of different human groups, the degree of impact of each factor varies. If we divide societies very crudely into three broad economic groups, *concepts like 'wasteful feeding' and 'psychic hunger' apply primarily to the well-off of the 'developed countries and to the elite of the developing' countries* in whom disease related to over-nutrition is much more common than in the rest of the population. *The picture of well-adjusted diets but nutritional deficiencies due to the stress of infectious disease loads presented in this book, could well apply to the middle class of 'developing' countries.* In their case it could be

pertinent to debate whether additional dietary intakes to provide a safety margin is the solution or priority be given to the control of infectious diseases. Probably a combination of the two will better reflect the 'cultural adaptation' in practice.

For the poor, the external environmental conditions are largely beyond the limits within which adaptation can occur without detracting from expression of human potential. Their process of adaptation for survival is at high human cost. Other than the high childhood morbidity and mortality and the lowered physiological work capacity discussed earlier, *the decrease in non-economic work including resting and social activity found by Edmundson's own studies means a decline in human well-being.* The decrease in leisure and social time would also be a major barrier to the individual and community action recommended by the authors as the starting point.

Education for better living is also likely to achieve little benefits because, as other scholars have estimated and Sukhatme's early work on protein deficiency shows, the poor traditionally have "the best diets within their economic resources". In addition, it has been amply demonstrated that women of poor households are not able to attend adequately to child care and on maintaining hygiene because of being over-worked and lack of many physical resources (e.g. Zurbrigg, 1984). Therefore, unless the structural constraints to healthy adaptation of the poor are simultaneously highlighted and addressed, the health and development for the poor is unlikely to be achieved.

While the health service system may have little direct role in overcoming the structural constraints, it is for holistic public health to point out these linkages. Denying or obscuring them will only be counter-productive to the purpose of science as a 'truthful description of reality' or for the policy aims of health and development for all. Only when public health focusses on such issues, are the overall planners and policy makers likely to take a holistic view of development and health. *The decision to address or not address these issues is a political one - the third corner of the triangle, 'science' and 'policy' forming the other two. It is a decision each one of us concerned with health issues will have to take.*

In Conclusion

Thus, in spite of all its contradictions, the importance of the book lies in the principles it carries into public health planning and the issues a critical reading of it reveal.

The contradictions in the application of their stated conceptual principles do not detract from the significance of the ideas themselves. In fact, the book allows one to examine how the enunciated principles, which are humanistically incontrovertible and very worthy of emphasis in the present health and development scenario, can get moulded into inhuman, anti-poor arguments. The authors' conclusions from their empirical studies make us realize the importance of public health analysis distinguishing between a scientific understanding of natural processes and a scientific study of the relationship between the natural processes and social factors (e.g., on the issue of diet and work output). Both are of value, more so if their boundaries are respected and their linkages recognised. The fallacies in the book highlight the need for consideration of prescriptions for problems of poverty and health in terms of societal processes of change, not restricting them to a programmatic orientation alone. They also highlight the need for a universally accepted clear definition of terms often used today, such as 'holistic' public health.

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WEDNESDAY,
JUNE 4, 1997

'Fish is ideal food for thought'

Kochi, June 3: Fish is the best food for human brain, nerves and eyes, according to nutritional experts.

A group of 500 nutrition experts and scientists met at Barcelona and recommended regular intake of fish by pregnant and nursing mothers and young children as fish contains great of docosahexaenoic acid (DHA)—a long chain of omega-3 poly saturate—which accounts for 25 per cent of the fat content of the brain, reports the latest newsletter of the Marine Products Export Development Authority here.

It was also pointed out at the meet that breast milk also contains small amounts of the acid which is needed by a foetus.

If the mother's diet does not include enough fish, then she may not be able to supply the DHA that the foetus needs, say scientists.

In animals a shortage of DHA makes them less intelligent, less capable of learning and generally more disturbed in behaviour while in humans a low DHA supply could result in poorer eye sight and slower development in babies and perhaps hyperactivity and dyslexia in childhood the scientists who participated in the meet pointed out.

The meet also pointed out that among human adults, a poor DHA supply was likely to cause depression, aggressive behaviour, perhaps even schizophrenia.

It was recommended that fish should be taken at least twice a week by all and two to three times a week by pregnant and nursing mothers.

It was also suggested that for children it was important to encourage fish eating from an early age.

The meet had urged the industry to develop more fish products aimed specifically at the young children, the newsletter adds. PTI

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VITAMIN A DEFICIENCY

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Vitamin A deficiency in pre-school children is yet one more nutritional disorder of public health importance in many developing countries. It contributes to a significant proportion of preventable blindness, a self-explanatory tragic situation. Some ophthalmologists in India believe that the problem of blindness due to cataract is seen in a greater proportion and hence demands greater attention than vitamin A deficiency. However, in my opinion, such problems should not be viewed with a statistician's mind. Cataract is a disorder of adulthood whereas hypovitaminosis A has its peak between 1 and 10 years of age. Thus young children become blind before they can see anything of the world and become a soci-economic burden. It is hence that vitamin A deficiency should be looked upon as a public health problem.

Vitama A deficiency, like other nutritional disorders of childhood, is seen mainly in the poorer classes and is mostly due to inadequate intake of foods rich in vitamin A. As in the case of PCM (Protein Calorie Malnutrition), the foundations for vitamin A deficiency may be said to be laid down during foetal life itself. The intake of vitamin A by pregnant mothers of the poorer classes is very low and their serum vitamin A levels are also low[1, 2]. They may therefore be expected to transfer smaller amounts of the vitamin to the foetus.

The breast milk of such mothers also has low concentrations of vitamin A. The levels being not more than 200/μg per 24 hours[3]. The infant thus is not only born with low stores of vitamin A but receives low quantities of it during the immediate post-natal life. In spite of this, however, ocular signs of vitamin A deficiency are rarely seen in the first 6 months of life. One may hence believe that this amount of vitamin A is probably adequate during infancy. I say this because as yet there are no techniques by which vitamin A requirements can be reliably assessed.

Beyond 6 months of age the vitamin A intake drastically falls because

(1) the breast milk output diminishes

(2) the infant does not receive any extra milk (either animal or formula made)

(3) the weaning foods being largely based on cereals contain virtually no retinol and only small amounts of B-carotene,

As you are all aware retinol is found in high concentrations only in animal foods. Plant foods contain only carotenes, of which B-carotene is nutritionally the most important. The absorption of B-carotene is not as good as that of retinol and its biological availablity is also poor. Hence 1/μg B-carotene is equivalent to only 0.25/μg retinol. Diet surveys have showed that pre-school children in South India receive only 300-500 I.U. vitamin A daily, mostly as B-carotene, through their diets[4, 5]. In pre-school children the incidence of ocular signs of vitamin A deficiency is quite high. In children of school-going age,

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the incidence is higher but the lesions are mainly Bitot's spots and conjunctival xerosis. Below 5 years, corneal xerosis and keratomalacia are more frequent and hence the condition is of more serious concern in this age period. The reason for this age pattern is not known; this may include factors like the serverity of the deficiency, requirements for growth, influence of infections and presence of PCM etc. The incidence of vitamin A deficiency in children with kwashiorkor and marasmus is higher than in children with milder degrees of PCM.

Ocular manifestations of vitamin A deficiency

The first functional evidence of vitamin A deficiency is night blindness. Being subjective, it is difficult to establish its presence in children, but in most cases the mother do notice that the children do not see well at dusk The conjunctival lesions include xerosis and Bitot's spot. In adults and adolescents, Bitot's spots do not always respond to vitamin A therapy and hence their association with vitamin A deficiency has been questioned But in pre-school children they do disappear with therapy and are generally indicative of vitamin A deficiency. The conjunctival lesions do not interfere with vision but may be considered as red signals, indicating the presence of vitamin A deficiency of sufficiently high degree.

Blindness due to vitamin A deficiency is due to cornal involvement corneal xerosis (the drv, hazy cornea) leading to keratomalacia (necrosis of cornea), the irreversible stage.

Therapy

1. Conjunctival xerosis and Bitot's spots may be treated with oral preparations of vitamin A. Therapy for at least 4 weeks will ensure fair storage of the vitamin in the body.

2. Corneal xerosis can progress rapidly to keratomalacia and must be treated immediately. Since it is necessary to raise the serum vitamin A levels rapidly, it is not advisable to start the treatment with oral preparations. Recent studies show that the rise in serum vitamin A levels is delayed when oily preparations are injected[6]. Hence it is advocated that children with corneal xerosis and children with kwashiorkot and vitamin A deficiency be given an intramuscular injection of water-miscible preparation of vitamin A, immediately on diagnosis and again, 48-72 hours later. This may be followed up with oral therapy; oral therapy should be with oily preparations. Repeated parenteral administration is not recommended for fear of inducing acute hypervitaminosis A.

Prevention

1. The ideal way to control and prevent vitamin A deficiency would be to provide the children with foods rich in preformed vitamin A like eggs, liver, milk and milk products, butter, ghee, etc. However, this being the ideal method, it may not be expected to take shape in the near future.

2. In the present economic circumstances, the next method would be to ensure adequate intakes of B-carotene (1200-1600/μg daily for children, 3000/μg for adults and 4500/μg for pregnant and lactating women). This entails intake of good amounts of green leaves (beetroot leaves, carrot leaves, arwi-ka-sag, methi, hara dhaniya, sarson, rajagira, palak, muli-ka-sag etc.) and fruits (jack fruit, mango, orange, papita, tomatoes, etc.) This need vigorous nutrition education to the community. In certain communities, this may call for change in food habits and correction of wrong notions like believing that fruits cases cough and colds or greens cause diarrhoea, etc.

In view of the serious nature of the deficiency, it is necessary that some public health measures be taken for prevention rather than rely on the above two idealistic approaches. McLaren[7] suggested that since the human liver has a large capacity to store vitamin A, massive prophplactic doses of vitamin A may be given to control vitamin A deficiency, Following on this suggestion, the National Institute of Nutrition at Hyderabad had carried out field trials and concluded that oral administration of 200,000 I. U. of vitamin A (as palmitate) every six months during the first 5 years of life, will considerably reduce the incidence of ocular signs of vitamin A deficiency[8]. It was found during this study that 75-90% of the children are protected from developing any sign of vitamin A deficiency and also, no new case of keratomalacia occurred during this period. Following the recommendation of Institute[7]. States in India had accepted in principle to implement this programme. These States are Andhra Pradesh, Bihar, Karnataka, Kerala, Orissa, Tamil Nadu and West Bengal (these cover the southern and eastern regions where vitamin A deficiency is rampant). The early stages of the trials at Karnataka were followed up by this Institute and the results confirmed the earlier observations.[9].

The programme has now been taken up in Indonesia and Philippines, also. I may, however, mention here that not everyone is willing to accept the efficacy of this programme. Dr. Pereira from Vellore (Tamil Nadu) has some reservations ragarding this programme[10, 11]. However, a group from West Bengal[12] have conducted a similar study and observed total elimination of night blindness and no new cases of Bitot's spot. In those who already had the latter, the lesion disappeared in only some children.. It must be remembered here that in older children and adults, Bitot's spot may not disappear despite vigorous vitamin A therapy. More importantly it must also be remembered that this programme is mainly intended to prevent the development of serious eye lesions which could lead to permanent blindness; this regime may not totally eliminate vitamin A deficiency.

The aqueous preparation of massive-dose vitamin A is made available by the Family Planning Units of the Union Ministry of Health and of the States where the programme is running. It is also supplied by the Anglo-French Drug Company (Pardon me ! I have no vested interest; I am only giving you information).

Those of you who are concerned with vitamin A deficiency may also be interestd to know that there is an organisation called the Xerophthalmia Club (supported by the Royal Commonwealth Society for the Blind, U.K.). They bring out bulletins which give infornation on various programmes the world over, aimed at prevention of vitamin A deficiency blindness. The Voluntary Health Association of India has brought out some pamphlets on this subject, in English as well as regional languages, which will be helpful to the paramedical workers. Those interested may write to the following addresses :

Xerophthalmia Club
Nuffield Lab. of Ophthalmology
Oxford, U.K.

Voluntary Health Association of India
C-14, Community Centre
Safdarjung Development Area
New Delhi - 110016

The World Health Chronicle (30: 117, 1976) has an article which touches on some of the points discussed here.

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NOT

THE STORY OF VITAMIN A

With 30-42,000 children blinded each year in India from Vitamin A deficiency, it is essential for us to know the story of Vitamin A.

This is a brief background on Vitamin A. Several issues arise from this story and we would appreciate your feedback. You may begin to wonder why nutritional blindness should be an entity at all, when it is easily preventable.

Ignorance of the nutritive value of many edible green leaves, like drumstick leaves is the main causative factor. The common man does not have to strive to buy the expensive yellow fruits, instead he can use leafy vegetables.

Our Government has made a provision for the prevention of nutritional blindness in the form of a program "Vitamin A prophylaxis program". You need to know about this service, because Vitamin A should be available in every Primary Health Centre, and it is there for the benefit of your children.

Do think about what action you can take in spreading the simple message about Vitamin A and how it can lead to better eye sight.

HISTORY :

Night blindness was apparently first described in Egypt around 1500 BC and topical treatment with roasted or fried liver was widely recommended ! Hippocrates later suggested eating beef liver as a cure for the disorder. Experimental observations led to the discovery of Vitamin A Xerophthalmia (dryness and thickening of the conjunctiva) was recognised in World I as a result a decrease in the content of butter fat in the diet.

Steenbock (1919) observed that Vitamin A content of vegetables varies with the degree of pigmentation, and led to the discovery of the chemical nature of the vitamin.

CHEMISTRY :

Euler and associate, and Moose (1929) demonstrated that the plant pigment carotene (Provitamin A) is a potent source of Vitamin A.

B Carotene is the active carotenoid found in plants. Retinol (Vitamin A_1) a primary alcohol is present in esterified from in the tissues of animals and salt water fishes, in the liver.

3 Hydro retinol (Vitamin A_2) is found in fresh water fish and occurs mixed with retionl.

Retinoic acid (Vitamin A acid) in which the alcohol has been oxidised shares some of the actions, of retinol. It is important in promoting growth and controlling differentiation and maintainence of epithalial tissue in Vitamin A deficient animals, but is ineffective in restoring visual, auditory or reproductive function in certain species where retinol is active.

2...

Physiology

Vitamin A is a nutrient which is necessary for good health.

1. It has an essential role in the function of the retinal (inner) layer of the eye.
2. In growth and differentiation of epithelial tissue.
3. Growth of bone and embryonic development.
3. Stabilising effect on various membranes.
5. Progression of premalignant characteristics is slowed or reversed in experimental animals.

In Vitamin A deficient animals nuclear RNA synthesis is diminished.

Adaption to dark is a function of both rods and cones. Primary adaptation is by the cones and completed in few minutes. Secondary adaptation is a function of rods and not completed for 30, minutes. When human beings are fed diets deficient in Vitamin A, their ability for dark adaptation is reduced. Rod vision is affected more than cone vision.

Vitamin A plays an important role in the induction and control of epithelial differentiation in mucus secreting or keratinizing tissues. In the absence of retinol, mucus cells disappear and atrophy of epithelium occurs, and is replaced by stratified keratinizing epithelium. The suppression of normal secretion leads to irritation and infection.

Vitamin A deficiency and protein malnutrition are the two most serious nutritional deficiency diseases in the world today. Vitamin A deficiency can be fatal in young children with marasmus or kwashiorkor.

Mild Vitamin A deficiency manifests in skin lesions like hyperkeratosis and infections, but the most recognisable is night blindness even though its onset occurs when Vitamin A depletion is severe.

Vitamin A is fat soluble. Absorption is reduced when diets are low in protein.

After absorption most Vitamin A stored in liver. Symptom of Vitamin A deficiency /occurs/ when concentration falls below 10-20 ug/dl.

When there is protein deficiency plasma levels of Vitamin A falls, replenishment with calories and protein is then required. During infections Vitamin A level falls, partially because of increased urinary excretion.

Pregnancy increases demand of Vitamin A. Concentration of Vitamin A in fatal blood is less than maternal blood. Colostrum and milk offers the new born an adequate supply of Vitamin A.

1 USP Unit of Vitamin A = 0.3 ug retinol
0.6 ug of β carotene

3...

Manifestation of Vitamin A deficiency

Eye :- Xerophthalmia (dryness of eye)
Bitots spots
Keratomalacia (destruction of the eye)

Respiratory tract :- Increased respiratory infection
Skin :- Dry skin, papular eruptions on extremities.
Genito Urinary :- Urinary calculi (from Epithelial debris forming foci)
Impaired spermatogenesis
Abortion
Malformed offspring

GI Tract :- Diarrhoea, due to alteration in intestinal epithalium and metaplasia of pancreatic duct epithalia.

Sweat glands : Atrophy

Bone : Faulty modeling of bone

Miscellaneous : Taste, smell and hearing decreased.

Recommended daily intake of Vitamin A

Infants : 300 units
Children (1-10 years) - 250-400 units
11 years and above : 575-750 units
Women during pregnancy and lactation - 1200 units

Vitamin A content in 100 gms.

Mango	1120 I.U.
Papaya	640 I.U.
Banana	200 I.U.
Guava	160 I.U.
Jackfruit	160 I.U.
Cabbage	1800 I.U.
Leaves of drumstick	12,000 I.U.
Spinach	13,000 I.U.
Carrots	20,000 I.U.
Sweet Potatoes	6000 I.U.
Butter	3500 I.U.
Egg	1500 I.U.
Cod Liver Oil	200,000 I.U.
Milk	Breast - 1898 I.U./litre ; Cow's - 1025 I.U./litre
Meat	100 I.U.
Liver	6000 to 60,000 I.U.

Vitamin A Deficiency and Nutritional Blindness

Vitamin A deficiency is the single most frequent cause of blindness among pre-school children in developing countries.

Young children are at the greatest risk because Vitamin A requirements are proportionately greater than other groups and because they suffer most from infections.

Blinding corneal destruction is most frequent between the ages of 6 months to 6 years. (WHO No.29/1985. "In point of fact")

As long as the infant is on mother's milk there is little danger of xerophthalmia. But diluted substitute milk, or weaning foods which lacks Vitamin A can bring on the disease.

A sick child loses appetite and in addition the illness may interfere with the body's ability to absorb and use Vitamin A in the food, and then the Vitamin A stored in the liver is drained.

The foundation for Vitamin A deficiency may be laid down during foetal life itself. If the intake of Vitamin A by a pregnant woman is low, then transfer of Vitamin A to the foetus is low. Breast milk of such mothers will also be low.

Plant foods contain B carotene, but its absorption is not as good as retinol, which is found in high concentration in animal foods.

Surveys in South India conducted by Dr. Swaminathan have shown that pre school children receive only 9 units of Vitamin A daily, and so incidence of ocular signs are high. In the school going age, the incidence is higher, but mainly include Bitot's spots and conjunctional xerosis. Below 5 years, corneal xerosis and keratomalacia are more frequent.

The first symptom of xerophthalmis is often night blindness. A mother finds her child no longer moves about easily in the house.

Xerophthalmia means dry eye.
Another early sign is the appearance of white foamy spots on the white part of the eye, called Bitot's spots.

The dryness then gives way to softening of the corneal tissue with resultant ulceration, destruction of the eye and blindness.

Treatment of xerophthalmia WHO 1982	Vitamin A
Immediately	200,000 I.U. by month
Day 2	"
Day 14	"

Under 12 months : ½ the dosage

Diarrhoea and Vitamin A :

Nutritional blindness occurs in areas where diarrhoea is common among children, and this is not a chance happening.

Children who lack Vitamin A in their diet are at risk not only of blindness, but also of getting diarrhoea and other infections. Repeated attacks of diarrhoea may bring about the final eye damage which destroys sight.

The combined effects of poverty and ignorance add to the problem.

During an episode of diarrhoea, food intake is limited, and absorption decreased. Diarrhoea occurs more often and more seriously in malnourished children who have poor stores of Vitamin A in the liver.

A study in Bangladesh showed that at least half the children who had serious xerophthalmia had suffered from diarrhoea the previous month.

In an Indonesian study, the children with xerophthalmia were 5 times as likely to have had diarrhoea in the last week as children without signs of Vitamin A deficiency.

However prospective study undertaken by NIN Hyderabad, showed that malnutrition does not increase the frequency of diarrhoea or duration, but affects the severity of the episode itself.
(Indian Journal of Paediatrics Vol.52, Sept.-Oct. '85, 418, 463-67)

70% of water miscible Vitamin A is absorbed in a child with diarrhoea.

A dose of Vitamin A is advisable before ORS is started.

6...

Measles and Vitamin A

The incidence of corneal lesions in measles is 3%.
Serum levels of Vitamin A show a drop during the measles episode, returning to premeasles level within 8 weeks after the acute episode without Vitamin A supplementation.

Superficial punctate keratopathy was identified in 15% of children. None of these children showed mild signs of xerophthalmia. Measles per se may cause corneal damage, followed by secondary bacterial infection.

Vitamin A deficiency could weaken the structural integrity of the cornea itself. (UNICEF Vitamin A consultancy Susan T. Eastman April 1986)

A large dose of Vitamin A may not help during the acute attack, but is likely to reduce the risk of post measles corneal involvement, in children with low Vitamin A stores.

Protein Calorie Malnutrition (PCM) and Vitamin A

The incidence of Vitamin A deficiency in children with kwashiorkor and marasmus is higher than in children with milder forms of PCM.
Corneal lesions have been rarely seen in children suffering from minor grades of PCM.

In Severe protein deficiency, Vitamin A in the diet does not reach the liver and Vitamin A in the liver is not available for use. Thus a functional deficiency of Vitamin A may occur in kwashiorkor, independent of its dietary intake.

Arroyave suggests that if the rate of growth were accelerated by the supplementation with proteins alone, the clinical manifestations of Vitamin A deficiency may suddenly become more serious.
(Am J. Clin. Nuti 22:1119, 1969)

Vitamin A status can be improved by giving a food source of Vitamin A or B Carotene without changing existing habitual diets of children belonging to poor income groups.

Acute Respiratory Infection

Even mild degrees of Vitamin A shortage can damage the body's protective epithelial surfaces which line intestinal, respiratory, urinary tracts and the eyes.

Alfred Sommer et al described in a study of Indonesian children, that those with mild xerophthalmia developed respiratory disease at twice the rate of children with normal eyes. The risk of respiratory disease was more closely associated with Vitamin A status than with general nutritional status.

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SOME EPIDEMIOLOGICAL STUDIES

1. Prevalence of ocular signs of Vitamin A deficiency in preschool children (3 rural and 3 urban areas of India).

(ICMR Technical Report Series No.26 studies on preschool children).

Age Years	Sample Size	% prevalence		
		Conj. xerosis	Bitot spots	Corneal lesions
1 - 2	4687	1.6	1.1	0.1
2 - 3	4257	3.9	2,5	0.15
3 - 4	4029	5.6	3.5	0.1
4 - 5	5379	5.9	4.5	0.1

Pooled data of ten states over time actually suggests that the prevalence of Bitot spots in rural India has increased almost 3 fold between 1974 and 1982.

(S.G. Srikantia, The Problem of Vitamin A deficiency in Indian Children, UNICEF, 1985).

Prevalence rate shows seasonal variations, being higher in summer, hence the timing of the administration of massive doses, of Vitamin A, is important.

2. The report for the Royal Commonwealth Society for the Blind, stated in 1978 that there would be 220000 children in 1-5 year age group, with corneal lesions at any point of time.

It has been suggested that prevalence rated of 0.5% Bitot's spots or 0.01% active corneal lesions may be used as cut off levels and by either criteria, Vitamin A deficiency is of Public Health Importance.

3. School Children : Studies were done in Baroda, involving 2000 school children 9-12% of children were found to be Vitamin A deficient.

4. Measles : A study in Andhra Pradesh looked into the relationship between measles and blindness. 3% of a large sample of children with measles had corneal manifestations.

(Tenth IVACG meeting, Hyderabad, 1985 - Bhaskaran P., Vinodini Reddy and Roy Milton).

5. Diarrhoeal Disease : More than 27000 children in 450 villages in North Sumatra were studies by Alfred Sommers et al.

Results showed that children with mild xerophthalmia are at 2-3 times greater risk of infection and 4-12 times greater risk of dying compared to children with normal Vitamin A status.

9...

UNICEF reports a range of 30-42000 children blinded each year in India from Vitamin A deficiency.

Pattern of Vitamin A intake

From a study of NNMB, intake of Vitamin A is widely different between individual families, states, and within a state from one year to another.

Table :Vitamin A intake : ug/consumption unit in ten states : Rural (NNMB)

State	Year			
	1975	1978	1981	1984
Kerala	107	97	350	236
Tamil Nadu	135	258	211	190
Karnataka	185	213	209	276
Andhra Pradesh	232	135	296	220
Maharashtra	296	194	NA	271
Gujarat	300	240	264	304
Madhya Pradesh	344	192	NA	NA
West Bengal	533	387	495	1078
Uttar Pradesh	191	337	207	NA
Orissa	NA	NA	472	350

NA : Not Available

Vitamin A Intake : ug/consumption unit in Ten Urban Areas 1975-78 (NNMB)

	Mean	Range
Slums Dwellers	248	119 - 434
Industrial workers	352	116 - 482
Low Income Groups	332	232 - 382

Food Sources :- Green leafy vegetables and milk.

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NATIONAL PROGRAMME :

The Govt. of India in 1970 launched a National Vitamin A prophylaxis Programme for the prevention of blindness in children in the endemic states. The cost works out to 50 paise per child per year.

India was one of the first countries to involve itself in systematic applied research in Vitamin A deficiency investigating the effectiveness and feasibility of using a megadose Vitamin A distribution.

Vitamin A deficiency blindness prevention is within the Govt.'s 20 point programme.

Till a few years ago the existing maternal and child Health and Family Welfare organisations were responsible for running the programme. Since the Integrity Child Development Services (ICDC) was introduced in 1976, this agency too is concerned.

In rural areas the programme is implemented through the PHC and its subcentres, under the supervision of the Medical Officer of the Primary Health Care (PHC).

The paramedical staff are responsible for identifying the target children and ensuring that the dose is delivered, supplies of Vitamin A come from the Directorate of Health Services, New Delhi.

In the ICDS programme, the Aganwadi worker is responsible for identifying target children and ensuring that the massive dose is distributed.

The Village Health Guide assists the ANM in the program.
An evaluation of the programme done in 1978 involved 13 states.
In only 21 of 59 rural areas studied was the programme effective.
(40% coverage).

11...

Community awareness of the programme was poor.

Functionaries themselves were not aware of all aspects of the programme.

Vitamin A supplies were irregular and insufficient.

Health education was poor.
(Vijayraghavan K and Prahlad Rao N, Nut. Rep. International 25,431, 1982).

Target Coverage : There was a fall from 76% in 81/82 to 65% in 82/83. The number of doses do not indicate whether the same children have received both doses.

Applied Nutrition Programme :

This programme helps rural communities grow more food and consume them.
Objectives are :

(a) to impart nutrition education

(b) to improve the nutrition intake and dietary habits of nursing and expectant mothers and children through promoting local production of protective foods.

(c) to set up community kitchens and school gardens.
(d) to set up poultry, fishing units and centres for animal husbandry.

It would have been possible to encourage people to grow foods containing Vitamin A, but the lack of land, water and education, contributed to poor impact of this programme.

12...

Massive Dose Prophylaxis :

It has been suggested that 200,000 I.U. given once every 6 months effectively protects, both against Bitot spots and corneal lesions, in rural areas and urban slums.

The massive dose approach when properly implemented leads to a substantial reduction in the prevalence of Bitot's spots.

Studies in NIN Hyderabad have shown that the prevalence of corneal lesions showed a reduction of almost 80% in areas where the massive dose was effectively delivered.

However on the basis of falling serum Vitamin A levels well before 6 months after dosing, it has been suggested that it is desirable to administer the dose once every 4 months instead of 6 months.

Breast feeding to protect sight

The unborn child gets Vitamin A from its mother through the placenta. If the mother has an inadequate diet, the new born has an insufficient store of Vitamin A.

Young children need a small but regular supply of Vitamin A in the diet.

The highest concentrations occur in colostrum (secretion of breast in the first few days after delivery). If the child is not given colostrum a valuable source of Vitamin A is lost.

The amount of Vitamin A in the breast milk gradually decreases but is higher than in cow's milk.

Breast feeding protects against xerophthalmia.

When the mother's diet is Vitamin A deficient mothers can be given a mega dose 200,000 I.U. by month after delivery so the breast milk will contain enough Vitamin A for at least 3-4 months.

Too much Vitamin A can do harm, doses more than 10,000 I.U. should not be given to a pregnant woman.

Children who are not breast fed have 6-8 times greater chance of developing xerophthalmia, than those receiving breast milk.

(Treating the whole child :

Diarrhoea Dialogue, Issue 21, June '85)

13...

Pharmaceutical Preparations of Vitamin A :

The megadose products of Vitamin A are as follows :-

(1) Aquasol A caps. (USV)

Water soluble, Vitamin A 50,000 I.U./Cap.

30 costs 11.02

Also Injection 50,000 I.U./ml.

3 Amps. 4.86

(2) Arovit (Roche)

Vit. A 50,000 I.U. Tab.

8 costs 1.96

Also injection Vitamin A 100,000 I.U., 300,000 I.U./ml.

3 X 1 ml costs 4.00

Arovit drops Vitamin A 150,000 I.U. per ml. 7.5 ml.

costs 5.05 Rs.

(3) Carofral (Duphar)

Vitamin A 50,000 I.U. Tab.

30 costs 6.72 Rs.

Also injection Vitamin A 50,000 I.U./ml.

4. Conc. Vitamin A solution (Seamless) each gram contains 50,000 I.U.

5. Vitamin A Injection (BPL). Each ml. contains 10,000I.U.

/Injection

Only preparations of/Vitamin A are of no use, as they are released very slowly.

The rational programme for prevention of Vitamin A deficiency utilises the Vitamin A syrups manufactured in India. The main source is from Indian Drugs and Pharmaceuticals producing bottles containing 100 ml. concentration Vitamin A solution. Each ml. contains 100,000 I.U. Vitamin A. A spoon of 2 ml. size is included with the bottle.

The State Trading Corporation monitors supply and demand. Demand is estimated by the Dept. of Family Welfare.

Vitamin A is mainly produced by Roche, who also supply Indian Drugs and Pharmaceuticals. They have also assisted Kerala State Drugs.

However several Pharmaceuticals prepare multiple vitamin preparations, containing Vitamin A.

The production figures of Vitamin A for the period 84-87 are :-

1984-85	60.58 MMU	Target : 105 MMu
1985-86	61.03 MMu	Target : 120 MMu
1986-87	69.34 MMu	

The import of Vitamin A

1983-84	20.346 MMu
1984-85	12.585 "

The production of Vitamin A falls far short of targets !

Food Fortification by Vitamin A :

Milk is fortified with Vitamin A to contain a final level of 3,500 I.U. per litre. All of this is consumed in the cities, and does not even reach the slum population who need it most. However the recent information is that fortification of milk is being discontinued.

Miltone : A preparation made of 50% milk and 50% groundnut protein is being fortified with Vitamin A, in 5 large cities. It is used in Govt. sponsored feeding programmes, but would be restricted to the peripheries of the cities where miltone is produced.

Vanaspati is fortified with Vitamin A to contain 25 I.U. per gm. Storage and cooking losses may be 50 to 70%. Besides intake of Vanaspati by preschool children is very low.

Modern bread is fortified with Vitamin A.

Common salt fortified with Vitamin A has low stability. Fortification with iodine and iron is being considered. Countries in Central America are using sugar fortified with Vitamin A to prevent blindness.

Hyper Vitaminosis A

Overzealous Vitamin A therapy, eg. increased intake during acne, pregnancy, lactation, can cause the following :-

- Irritability
- Headache
- Vomiting
- Decreased appetite
- Dry skin
- Skin Peeling
- Reddening of skin
- Enlarged liver, spleen
- Increased intra cranial pressure
- Tender hard swelling on extremities, occiput

Once the Vitamin is withdrawn, most signs and symptoms disappear within a week.

Pregnant women should not take excess Vitamin A as congenital abnormalities can occur.

eg. Multivitaplex forte (Pfizer) is a multiple Vitamin therapy, one cap a day is advised. This cap. contains 10,000 I.U. of Vitamin A and taken daily could lead to overdosage.

15...

Issues that arise :

1) While we wish to prevent nutritional blindness by improved nutrition, teaching people to grow and use green leafy vegetables, and fruits (yellow), the scarcity of land, water, the exploitation of the tribals, deforestation, increasing prices of basic commodities, use of fruits in preparing costly and junk soft drinks, increased exports all make us wonder where to begin !

2) In a health awareness programme, recognising early signs of the disease is essential. Are PHC and ICDS workers being taught the earliest signs of Vitamin A deficiency - like stumbling in the dark due to night blindness, identifying Bitot's spots ? Do these workers use every opportunity in teaching people about nutrition, or do they mechanically dole out Vitamin A ?

3) In the strategy for Vitamin A distribution :
   - age groups in months need to be specified instead of saying 1-6 years.
   - fixed times for Vitamin A distribution needs to be done after identifying the target beneficiaries.
   - those who do not come to the clinic need to be given Vitamin A at the home.
   - the same child should get Vitamin A twice in the year.
   - ICDS programme workers should not confine to 2-5 years age group.
   - lactating mothers and pregnant women need to be included as beneficiaries.
   - sick children with measles, diarrhoea, PCM need to be beneficiaries.
   - the special 2 ml. spoon has to be used, not the ordinary tea spoon.
   - registers to be maintained so that supply, utilisation and related problems can be identified.

4) Vitamin A production, as seen from the figures is far below the targets. There is increasing import of Vitamin A. Vitamin A is not mentioned in Category I list of essential drugs for National Health Programs.

   We need a policy for increased production of essential medicines like Vitamin A, and curbing hazardous and irrational drugs.

Prepared by Dr. Susy Aya Ram, MD
People's Education for Health Action

:b: 22.4.88

QUESTIONNAIRE - Vitamin A prophylaxis programme

1. Do you have a programme for distribution of Vitamin A in your area ?

2. Where is the Vitamin A obtained from ?

3. Who distributes Vitamin A solution ?

4. Who are the beneficiaries in this programme ?

5. Where is the Vitamin A given, home/health centre ? and how often ?

6. Is a special 2 ml. spoon used for this purpose, or is a tea spoon used ?

7. What are the problems in this program, is Vitamin A supply erratic, lack of awareness among people, irregular visit by health worker etc.?

8. Is a register maintained for this programme, can you give us a specimen copy ?

9. Are simple messages of consuming leafy vegetables and yellow fruits to obtain Vitamin A, propagated ?

10. What are your suggestions for improving this programme ?

11. Do you have children with keratomalacia (KM) in your area ?

We would like you to participate in the Vitamin A prophylaxis programme. In this context, can you fill in the above questionnaire and mail it to us ?

VOLUNTARY HEALTH ASSOCIATION OF INDIA
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663071
668072

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Our Government has made a provision for the prevention of nutritional blindness in the form of a program "Vitamin A prophylaxis program". You need to know about this service, because Vitamin A should be available in every Primary Health Centre, and it is there for the benefit of your children.

Do think about what action you can take in spreading the simple message about Vitamin A and how it can lead to better eye sight.

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CHEMISTRY :

Euler and associate, and Moose (1929) demonstrated that the plant pigment carotene (Provitamin A) is a potent source of Vitamin A.

β Carotene is the active carotenoid found in plants. Retinol (Vitamin A_1) a primary alcohol is present in esterified from in the tissues of animals and salt water fishes, in the liver.

3 Hydro retinol (Vitamin A_2) is found in fresh water fish and occurs mixed with retionl.

Retinoic acid (Vitamin A acid) in which the alcohol has been oxidised shares some of the actions, of retinol. It is important in promoting growth and controlling differentiation and maintainence of epithalial tissue in Vitamin A deficient animals, but is ineffective in restoring visual, auditory or reproductive function in certain species where retinol is active.

2...

Physiology

Vitamin A is a nutrient which is necessary for good health.

1. It has an essential role in the function of the retinal (inner) layer of the eye.
2. In growth and differentiation of epithelial tissue.
3. Growth of bone and embryonic development.
3. Stabilising effect on various membranes.
5. Progression of premalignant characterestics is slowed or reversed in experimental animals.

In Vitamin A deficient animals nuclear RNA synthesis is diminished.

Adaption to dark is a function of both rods and cones. Primary adaptation is by the cones and completed in few minutes. Secondary adaptation is a function of rods and not completed for 30, minutes. When human beings are fed diets deficient in Vitamin A, their ability for dark adaptation is reduced. Rod vision is affected more than cone vision.

Vitamin A plays an important role in the induction and control of epithelial differentiation in mucus secreting or keratinizing tissues. In the absence of retinol, mucus cells disappear and atrophy of epithelium occurs, and is replaced by stratified keratinizing epithelium. The suppression of normal secretion leads to irritation and infection.

Vitamin A deficiency and protein malnutrition are the two most serious nutritional deficiency diseases in the world today. Vitamin A deficiency can be fatal in young children with marasmus or kwashiorkor.

Mild Vitamin A deficiency manifests in skin lesions like hyperkeratosis and infections, but the most recognisable is night blindness even though its onset occurs when Vitamin A depletion is severe.

Vitamin A is fat soluble. Absorption is reduced when diets are low in protein.

After absorption most Vitamin A stored in liver. Symptom of Vitamin A deficiency occurs when concentration falls below 10-20 ug/dl.

When there is protein deficiency plasma levels of Vitamin A falls, replenishment with calories and protein is then required. During infections Vitamin A level falls, partially because of increased urinary excretion.

Pregnancy increases demand of Vitamin A. Concentration of Vitamin A in fatal blood is less than maternal blood. Colostrum and milk offers the new born an adequate supply of Vitamin A.

1 USP Unit of Vitamin A = 0.3 ug retinol
0.6 ug of β carotene

3...

Manifestation of Vitamin A deficiency

Eye :- Xerophthalmia (dryness of eye)
Bitots spots
Keratomalacia (destruction of the eye)

Respiratory tract :- Increased respiratory infection
Skin :- Dry skin, papular eruptions on extremities.
Genito Urinary :- Urinary calculi (from Epithelial debris forming foci)
Impaired spermatogenesis
Abortion
Malformed offspring

GI Tract :- Diarrhoea, due to alteration in intestinal epithalium and metaplasia of pancreatic duct epithalia.

Sweat glands : Atrophy

Bone : Faulty modeling of bone

Miscellaneous : Taste, smell and hearing decreased.

Recommended daily intake of Vitamin A

Infants : 300 units
Children (1-10 years) - 250-400 units
11 years and above : 575-750 units
Women during pregnancy and lactation - 1200 units

Vitamin A content in 100 gms.

Mango	1120 I.U.
Papaya	640 I.U.
Banana	200 I.U.
Guava	160 I.U.
Jackfruit	160 I.U.
Cabbage	1800 I.U.
Leaves of drumstick	12,000 I.U.
Spinach	13,000 I.U.
Carrots	20,000 I.U.
Sweet Potatoes	6000 I.U.
Butter	3500 I.U.
Egg	1500 I.U.
Cod Liver Oil	200,000 I.U.
Milk	Breast - 1898 I.U./litre ; Cow's - 1025 I.U./litre
Meat	100 I.U.
Liver	6000 to 60,000 I.U.

Vitamin A Deficiency and Nutritional Blindness

Vitamin A deficiency is the single most frequent cause of blindness among pre-school children in developing countries.

Young children are at the greatest risk because Vitamin A requirements are proportionately greater than other groups and because they suffer most from infections.

Blinding corneal destruction is most frequent between the ages of 6 months to 6 years. (WHO No.29/1985. "In point of fact")

As long as the infant is on mother's milk there is little danger of xerophthalmia. But diluted substitute milk, or weaning foods which lacks Vitamin A can bring on the disease.

A sick child loses appetite and in addition the illness may interfere with the body's ability to absorb and use Vitamin A in the food, and then the Vitamin A stored in the liver is drained.

The foundation for Vitamin A deficiency may be laid down during foetal life itself. If the intake of Vitamin A by a pregnant woman is low, then transfer of Vitamin A to the foetus is low. Breast milk of such mothers will also be low.

Plant foods contain B carotene, but its absorption is not as good as retinol, which is found in high concentration in animal foods.

Surveys in South India conducted by Dr. Swaminathan have shown that pre school children receive only 9 units of Vitamin A daily, and so incidence of ocular signs are high. In the school going age, the incidence is higher, but mainly include Bitot's spots and conjunctional xerosis. Below 5 years, corneal xerosis and keratomalacia are more frequent.

The first symptom of xerophthalmia is often night blindness. A mother finds her child no longer moves about easily in the house.

Xerophthalmia means dry eye.
Another early sign is the appearance of white foamy spots on the white part of the eye, called Bitot's spots.

The dryness then gives way to softening of the corneal tissue with resultant ulceration, destruction of the eye and blindness.

Treatment of xerophthalmia WHO 1982	Vitamin A
Immediately	200,000 I.U. by month
Day 2	"
Day 14	"

Under 12 months : ½ the dosage

Diarrhoea and Vitamin A :

Nutritional blindness occurs in areas where diarrhoea is common among children, and this is not a chance happening.

Children who lack Vitamin A in their diet are at risk not only of blindness, but also of getting diarrhoea and other infections. Repeated attacks of diarrhoea may bring about the final eye damage which destroys sight.

The combined effects of poverty and ignorance add to the problem.

During an episode of diarrhoea, food intake is limited, and absorption decreased. Diarrhoea occurs more often and more seriously in malnourished children who have poor stores of Vitamin A in the liver.

A study in Bangladesh showed that at least half the children who had serious xerophthalmia had suffered from diarrhoea the previous month.

In an Indonesian study, the children with xerophthalmia were 5 times as likely to have had diarrhoea in the last week as children without signs of Vitamin A deficiency.

However prospective study undertaken by NIN Hyderabad, showed that malnutrition does not increase the frequency of diarrhoea or duration, but affects the severity of the episode itself.
(Indian Journal of Paediatrics Vol.52, Sept.-Oct. '85, 418, 463-67)

70% of water miscible Vitamin A is absorbed in a child with diarrhoea.

A dose of Vitamin A is advisable before ORS is started

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Measles and Vitamin A

The incidence of corneal lesions in measles is 3%.
Serum levels of Vitamin A show a drop during the measles episode, returning to premeasles level within 8 weeks after the acute episode without Vitamin A supplementation.

Superficial punctate keratopathy was identified in 15% of children. None of these children showed mild signs of xerophthalmia. Measles per se may cause corneal damage, followed by secondary bacterial infection.

Vitamin A deficiency could weaken the structural integrity of the cornea itself. (UNICEF Vitamin A consultancy Susan T. Eastman April 1986)

A large dose of Vitamin A may not help during the acute attack, but is likely to reduce the risk of post measles corneal involvement, in children with low Vitamin A stores.

Protein Calorie Malnutrition (PCM) and Vitamin A

The incidence of Vitamin A deficiency in children with kwashiorkor and marasmus is higher than in children with milder forms of PCM.
Corneal lesions have been rarely seen in children suffering from minor grades of PCM.

In Severe protein deficiency, Vitamin A in the diet does not reach the liver and Vitamin A in the liver is not available for use. Thus a functional deficiency of Vitamin A may occur in kwashiorkor, independent of its dietary intake.

Arroyave suggests that if the rate of growth were accelerated by the supplementation with proteins alone, the clinical manifestations of Vitamin A deficiency may suddenly become more serious.
(Am J. Clin. Nuti 22:1119, 1969)

Vitamin A status can be improved by giving a food source of Vitamin A or B Carotene without changing existing habitual diets of children belonging to poor income groups.

Acute Respiratory Infection

Even mild degrees of Vitamin A shortage can damage the body's protective epithelial surfaces which line intestinal, respiratory, urinary tracts and the eyes.

Alfred Sommer et al described in a study of Indonesian children, that those with mild xerophthalmia developed respiratory disease at twice the rate of children with normal eyes. The risk of respiratory disease was more closely associated with Vitamin A status than with general nutritional status.

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SOME EPIDEMIOLOGICAL STUDIES

1. Prevalence of ocular signs of Vitamin A deficiency in preschool children (3 rural and 3 urban areas of India).

(ICMR Technical Report Series No.26 studies on preschool children).

Age Years	Sample Size	% prevalence		
		Conj. xerosis	Bitot spots	Corneal lesions
1 - 2	4687	1.6	1.1	0.1
2 - 3	4257	3.9	2,5	0.15
3 - 4	4029	5.6	3.5	0.1
4 - 5	5379	5.9	4.5	0.1

Pooled data of ten states over time actually suggests that the prevalence of Bitot spots in rural India has increased almost 3 fold between 1974 and 1982.
(S.G. Srikantia, The Problem of Vitamin A deficiency in Indian Children, UNICEF, 1985).

Prevalence rate shows seasonal variations being higher in summer, hence the timing of the administration of massive doses, of Vitamin A, is important.

2. The report for the Royal Commonwealth Society for the Blind, stated in 1978 that there would be 220000 children in 1-5 year age group, with corneal lesions at any point of time.
It has been suggested that prevalence rated of 0.5% Bitot's spots or 0.01% active corneal lesions may be used as cut off levels and by either criteria, Vitamin A deficiency is of Public Health Importance.

3. School Children : Studies were done in Baroda, involving 2000 school children 9-12% of children were found to be Vitamin A deficient.

4. Measles : A study in Andhra Pradesh looked into the relationship between measles and blindness. 3% of a large sample of children with measles had corneal manifestations.
(Tenth IVACG meeting, Hyderabad, 1985 - Bhaskaran P., Vinodini Reddy and Roy Milton).

5. Diarrhoeal Disease : More than 27000 children in 450 villages in North Sumatra were studies by Alfred Sommers et al.

Results showed that children with mild xerophthalmia are at 2-3 times greater risk of infection and 4-12 times greater risk of dying compared to children with normal Vitamin A status.

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UNICEF reports a range of 30-42000 children blinded each year in India from Vitamin A deficiency.

Pattern of Vitamin A intake

From a study of NNMB, intake of Vitamin A is widely different between individual families, states, and within a state from one year to another.

Table :Vitamin A intake : ug/consumption unit in ten states : Rural (NNMB)

State	Year			
	1975	1978	1981	1984
Kerala	107	97	350	236
Tamil Nadu	135	158	211	190
Karnataka	185	113	209	276
Andhra Pradesh	232	135	296	220
Maharashtra	296	214	NA	271
Gujarat	300	210	264	304
Madhya Pradesh	344	192	NA	NA
West Bengal	533	387	495	1078
Uttar Pradesh	191	337	207	NA
Orissa	NA	NA	472	350

NA : Not Available

Vitamin A Intake : ug/consumption unit in Ten Urban Areas 1975-78 (NNMB)

	Mean	Range
Slums Dwellers	248	119 - 434
Industrial workers	352	116 - 482
Low Income Groups	332	232 - 382

Food Sources :- Green leafy vegetables and milk.

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NATIONAL PROGRAMME :

The Govt. of India in 1970 launched a National Vitamin A prophylaxis Programme for the prevention of blindness in children in the endemic states. The cost works out to 50 paise per child per year.

India was one of the first countries to involve itself in systematic applied research in Vitamin A deficiency investigating the effectiveness and feasibility of using a megadose Vitamin A distribution.

Vitamin A deficiency blindness prevention is within the Govt.'s 20 point programme.

Till a few years ago the existing maternal and child Health and Family Welfare organisations were responsible for running the programme. Since the Integrity Child Development Services (ICDS) was introduced in 1976, this agency too is concerned.

In rural areas the programme is implemented through the PHC and its subcentres, under the supervision of the Medical Officer of the Primary Health Care (PHC).

The paramedical staff are responsible for identifying the target children and ensuring that the dose is delivered, supplies of Vitamin A come from the Directorate of Health Services, New Delhi.

In the ICDS programme, the Aganwadi worker is responsible for identifying target children and ensuring that the massive dose is distributed.
The Village Health Guide assists the ANM in the program.
An evaluation of the programme done in 1978 involved 13 states.
In only 21 of 59 rural areas studied was the programme effective.
(40% coverage).

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Community awareness of the programme was poor.

Functionaries themselves were not aware of all aspects of the programme.

Vitamin A supplies were irregular and insufficient.

Health education was poor.
(Vijayraghavan K and Prahlad Rao N, Nut. Rep. International 25,431, 1982).

Target Coverage : There was a fall from 76% in 81/82 to 65% in 82/83. The number of doses do not indicate whether the same children have received both doses.

Applied Nutrition Programme :

This programme helps rural communities grow more food and consume them.
Objectives are :

(a) to impart nutrition education

(b) to improve the nutrition intake and dietary habits of nursing and expectant mothers and children through promoting local production of protective foods.

(c) to set up community kitchens and school gardens.
(d) to set up poultry, fishing units and centres for animal husbandry.

It would have been possible to encourage people to grow foods containing Vitamin A, but the lack of land, water and education, contributed to poor impact of this programme.

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Massive Dose Prophylaxis :

It has been suggested that 200,000 I.U. given once every 6 months effectively protects, both against Bitot spots and corneal lesions, in rural areas and urban slums.

The massive dose approach when properly implemented leads to a substantial reduction in the prevalence of Bitot's spots.

Studies in NIN Hyderabad have shown that the prevalence of corneal lesions showed a reduction of almost 80% in areas where the massive dose was effectively delivered.

However on the basis of falling serum Vitamin A levels well before 6 months after dosing, it has been suggested that it is desirable to administer the dose once every 4 months instead of 6 months.

Breast feeding to protect sight

The unborn child gets Vitamin A from its mother through the placenta. If the mother has an inadequate diet, the new born has an insufficient store of Vitamin A.

Young children need a small but regular supply of Vitamin A in the diet.

The highest concentrations occur in colostrum (secretion of breast in the first few days after delivery). If the child is not given colostrum a valuable source of Vitamin A is lost.

The amount of Vitamin A in the breast milk gradually decreases but is higher than in cow's milk.

Breast feeding protects against xerophthalmia.

When the mother's diet is Vitamin A deficient mothers can be given a mega dose 200,000 I.U. by month after delivery so the breast milk will contain enough Vitamin A for at least 3-4 months.

Too much Vitamin A can do harm, doses more than 10,000 I.U. should not be given to a pregnant woman.

Children who are not breast fed have 6-8 times greater chance of developing xerophthalmia, than those receiving breast milk.

(Treating the whole child :

Diarrhoea Dialogue, Issue 21, June '85)

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Pharmaceutical Preparations of Vitamin A :

The megadose products of Vitamin A are as follows :-

(1) Aquasol A caps. (USV)

Water soluble, Vitamin A 50,000 I.U./Cap.

30 costs 11.02

Also Injection 50,000 I.U./ml.

3 Amps. 4.86

(2) Arovit (Roche)

Vit. A 50,000 I.U. Tab.

3 costs 1.96

Also injection Vitamin A 100,000 I.U., 300,000 I.U./ml.

3 X 1 ml costs 4.00

Arovit drops Vitamin A 150,000 I.U. per ml. 7.5 ml.

costs 5.05 Rs.

(3) Carofral (Duphar)

Vitamin A 50,000 I.U. Tab.

30 costs 6.72 Rs.

Also injection Vitamin A 50,000 I.U./ml.

4. Conc. Vitamin A solution (Seamless) each gram contains 50,000 I.U.

5. Vitamin A Injection (BPL). Each ml. contains 10,000I.U.

/Injection

Oily preparations of Vitamin A are of no use, as they are released very slowly.

The national programme for prevention of Vitamin A deficiency utilises the Vitamin A syrups manufactured in India. The main source is from Indian Drugs and Pharmaceuticals producing bottles containing 100 ml. concentration Vitamin A solution. Each ml. contains 100,000 I.U. Vitamin A. A spoon of 2 ml. size is included with the bottle.

The State Trading Corporation monitors supply and demand. Demand is estimated by the Dept. of Family Welfare.

Vitamin A is mainly produced by Roche, who also supply Indian Drugs and Pharmaceuticals. They have also assisted Kerala State Drugs.

However several Pharmaceuticals prepare multiple vitamin preparations, containing Vitamin A.

The production figures of Vitamin A for the period 84-87 are :-

1984-85	60.58 MMU	Target : 105 MMu
1985-86	51.03 MMu	Target : 120 MMu
1986-87	69.34 MMu	

The import of Vitamin A

1983-84	20.345 MMu
1984-85	12.585 "

The production of Vitamin A falls far short of targets !

Food Fortification by Vitamin A :

Milk is fortified with Vitamin A to contain a final level of 3,500 I.U. per litre. All of this is consumed in the cities, and does not even reach the slum population who need it most. However the recent information is that fortification of milk is being discontinued.

Miltone : A preparation made of 50% milk and 50% groundnut protein is being fortified with Vitamin A, in 5 large cities. It is used in Govt. sponsored feeding programmes, but would be restricted to the peripheries of the cities where miltone is produced.

Vanaspati is fortified with Vitamin A to contain 25 I.U. per gm. Storage and cooking losses may be 50 to 70%. Besides intake of Vanaspati by preschool children is very low.

Modern bread is fortified with Vitamin A.

Common salt fortified with Vitamin A has low stability. Fortification with iodine and iron is being considered. Countries in Central America are using sugar fortified with Vitamin A to prevent blindness.

Hyper Vitaminosis A

Overzealous Vitamin A therapy, eg. increased intake during acne, pregnancy, lactation, can cause the following :-

- Irritability
- Headache
- Vomiting
- Decreased appetite
- Dry skin
- Skin Peeling
- Reddening of skin
- Enlarged liver, spleen
- Increased intra cranial pressure
- Tender hard swelling on extremities, occiput

Once the Vitamin is withdrawn, most signs and symptoms disappear within a week.

Pregnant women should not take excess Vitamin A as congenital abnormalities can occur.

eg. Multivitaplex forte (Pfizer) is a multiple Vitamin therapy, one cap a day is advised. This cap. contains 10,000 I.U. of Vitamin A and taken daily could lead to overdosage.

Study by VHAI of Jhelu Village :

Dr. Arora and Miss D. David conducted a study to assess the magnitude of Vitamin A deficiency in Jhelu Village of Rajasthan.

Jhelu is 20 km. away from the PHC in Mathania, and the nearest subcentre is at Gagadi, 5 km. away. There is no ICDS Project in the area.

Of a study of 150 children, 2/3 were below 6 years and 1/3 were in the school going age, above 6 years Distribution of 150 children showing signs of Vitamin A deficiency.

Age	No.	Normal %	Affected
Under 2 years	32	87.5	12.5
2-6 years	68	55.8	44.2
6-14 years	50	58	42

Sex distribution of 55 Vitamin A deficient children

	M	F
Below 2 years	2	2
2-6 years	16	14
6-14 years	14	7
	32	23

/made

Plans are being/for action and follow up.

Issues that arise :

1) While we wish to prevent nutritional blindness by improved nutrition, teaching people to grow and use green leafy vegetables, and fruits (yellow), the scarcity of land, water, the exploitation of the tribals, deforestation, increasing prices of basic commodities, use of fruits in preparing costly and junk soft drinks, increased exports all make us wonder where to begin !

2) In a health awareness programme, recognising early signs of the disease is essential. Are PHC and ICDS workers being taught the earliest signs of Vitamin A deficiency - like stumbling in the dark due to night blindness, identifying Bitot's spots ? Do these workers use every opportunity in teaching people about nutrition, or do they mechanically dole out Vitamin A ?

3) In the strategy for Vitamin A distribution :
   - age groups in months need to be specified instead of saying 1-6 years.
   - fixed times for Vitamin A distribution needs to be done after identifying the target beneficiaries.
   - those who do not come to the clinic need to be given Vitamin A at the home.
   - the same child should get Vitamin A twice in the year.
   - ICDS programme workers should not confine to 2-5 years age group.
   - lactating mothers and pregnant women need to be included as beneficiaries.
   - sick children with measles, diarrhoea, PCM need to be beneficiaries.
   - the special 2 ml. spoon has to be used, not the ordinary tea spoon.
   - registers to be maintained so that supply, utilisation and related problems can be identified.

4) Vitamin A production, as seen from the figures is far below the targets. There is increasing import of Vitamin A. Vitamin A is not mentioned in Category I list of essential drugs for National Health Programs.

   We need a policy for increased production of essential medicines like Vitamin A, and curbing hazardous and irrational drugs.

Prepared by Dr. Susy Aya Ram, MD
People's Education for Health Action

:b: 22.4.88

QUESTIONNAIRE - Vitamin A prophylaxis programme

1. Do you have a programme for distribution of Vitamin A in your area ?

2. Where is the Vitamin A obtained from ?

3. Who distributes Vitamin A solution ?

4. Who are the beneficiaries in this programme ?

5. Where is the Vitamin A given, home/health centre ? and how often ?

6. Is a special 2 ml. spoon used for this purpose, or is a tea spoon used ?

7. What are the problems in this program, is Vitamin A supply erratic, lack of awareness among people, irregular visit by health worker etc.?

8. Is a register maintained for this programme, can you give us a specimen copy ?

9. Are simple messages of consuming leafy vegetables and yellow fruits to obtain Vitamin A, propagated ?

10. What are your suggestions for improving this programme ?

11. Do you have children with keratomalacia (KM) in your area ?

We would like you to participate in the Vitamin A prophylaxis programme. In this context, can you fill in the above questionnaire and mail it to us ?

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International Council of Scientific Unions

Committee on the Teaching of Science

NUTRITION, AND THE QUALITY OF LIFE

Professor C. den Hartog and Dr C.E. West
for the International Union of Nutritional Science

NUTRITION AND THE QUALITY OF LIFE

In order to understand the relationship between "nutrition" and the "quality of life", it is desirable that the two terms be defined as well as possible. Many definitions have been given for "nutrition". We would like to use that proposed by the Dutch Nutrition Council which states: "Nutrition is the process of choosing and utilising food, its assimilation by the human body and the resulting effect on health". It is much more difficult to define "quality of life". One of the reasons for this is that the expectations from life differ enormously between individuals. What a Kalahari bushman or a Fulani herdsman expects of life is completely different to that expected by the upper middle class, let alone the very rich in the USA, China or the Netherlands. Nevertheless, there are a few elementary needs which are the same for everyone: safety, a sense of security, a sense of belonging, housing and freedom from worry about having food each day. One is reminded of the prayer: "Give us this day our daily bread"; the first requirement of life.

Good nutrition is therefore a *sine qua non* condition for the quality of life. The condition of the mind and body is to a large extent determined by nutrition. Incidental consequences of incorrect nutrition, such as food poisoning, occasionally eating too little or too much, or the occasional eating of food of poor quality, do not affect the quality of life. It is the diet over a long period which is one of the determinants of the quality of life.

The quality of life begins at birth

The way in which a child enters the world has a considerable influence on his future life. For example there is a great deal of difference perceptible between the birth of many children in the Third World and those in affluent countries.

It has become apparent in the last few years that inadequate maternal nutrition often produces, generation upon generation, children with incomplete brain development and the chance of a lower IQ for the rest of their lives compared with children with adequate maternal nutrition.

In the Western World, the two most important factors during pregnancy which can impair a child's development are excessive smoking and the excessive use of alcohol by the mother. One could argue that heavy smoking has nothing to do with nutrition. However, this is not so. Smoking indirectly and adversely influences the supply of oxygen and nutrients via the placenta to the unborn child. Compared with children born to women who do not smoke, when the mother smokes the risk of

having a premature baby doubles and the average birthweight is 150 to 400g lower, while the cranial circumference is smaller. Carbon monoxide and nicotine are both toxic to the placenta and the children of mothers who have smoked during pregnancy have lower iron reserves in the bone marrow. The placenta is also smaller than usual. This last trait is also found when excessive alcohol is used by a pregnant mother and is coupled with intellectual retardation and some physical abnormalities in the newborn baby. It is clear that these children will not grow up to become "normal" adults and will remain on the negative side of the quality norm, only being able to hold their own with the support of others.

Influence of nutrition during childhood

The influence of nutrition during childhood can be positive as well as negative and can therefore improve or diminish the quality of life. In any case, as far as nutrition is concerned, what happens during childhood helps to determine subsequent physical and mental health. Here too, the problems differ from culture to culture and are likewise dependent upon the availability of food. In many cultures, the concept that food has a spiritual value is conveyed to children from a very early age and these values remain throughout life. The spiritual value of food is externally manifested in the form of sacrifices to gods, fasts, taboos and magical happenings. In monotheistic religions, prayer is usually an essential element for communication with God and is often associated with food. Muslims, for example, use eating as a means of worshipping God through prayer, fasting and other religious customs. Thus the relationship between food and the worship of God takes an important place in the quality of life.

Food is expensive in developing countries; the money required to provide food for a family often represents a very high proportion of the total income of the family. Thus the amount of food available is often not sufficient for survival, optimum growth, and physical development. High child mortality and retarded growth of young children are, we feel, signs of a reduced quality of life.

Slightly retarded growth and remaining smaller do not in themselves necessarily diminish the quality of life. They are only signs that less than optimal development has taken place. However, when there is high child mortality, one can presume that not only do the strong survive but also that many have sustained permanent damage from the serious malnutrition and infections suffered.

The role of breastmilk in providing a well-balanced diet and protection against infection, especially in less developed countries, cannot be overemphasized. It is particularly unfortunate that many mothers in these countries do not continue breastfeeding for a sufficient period

of time. Breastmilk can usually provide all the food required by an infant up to age of 6 months. The reasons for giving up breastfeeding early are many and varied but one factor responsible has been the marketing strategy of companies selling breastmilk substitutes. In affluent societies, the use of breastmilk substitutes has less influence on the subsequent development of children than is the case in the Third World. Welfare can be temporarily damaged by infections or over-feeding but permanent adverse effects have not been confirmed with the exception of possible allergies to proteins of cow's milk.

The period in which a child is an infant and toddler (up to 3 years) is one in which the child is particularly vulnerable: the chance of a good quality of life in the future can be jeopardized during this time. Proof for this is provided by children who survive severe malnutrition due to deficiencies of vitamin A, vitamin D, or iodine.

Severe vitamin A deficiency leads not only to night blindness which is reversible but also to xerophthalmia ("dry eyes") and keratomalacia. The deficiency of vitamin A produces a lesion in the cornea of the eye ultimately resulting in its perforation and therefore irreversible loss of vision. Between 50,000 and 100,000 people mostly children under the age of 3 years become blind in this way each year throughout the world.

Vitamin D deficiency is a frequently occurring phenomenon which can be prevented not only by ingestion of pre-formed vitamin D but also by exposure to sunlight which converts a precursor in the skin to the vitamin. Deficiency of vitamin D produces rickets with permanent harmful effects to the skeleton. In Western countries with good child care facilities, rickets has been reduced to a minimum. However, rickets does occur in a number of countries where one would not expect it because of the abundance of sunshine. This is the case among very young children of some black African tribes who are kept in dark tents for a long time and among women of Bedouin tribes who spend most of their lives in dark tents. The Bedouin women often also suffer from osteomalacia which produces a great deal of pain in the pelvis. This is often in addition to rickets which gives rise to a deformed pelvis making the process of child birth difficult.

Goitre is one of the most widely occurring dietary diseases and results from iodine deficiency caused by the flushing away of iodine from the earth's surface. This can lead to retardation in children ranging from real cretinism to growth retardation, decreased metabolism and decreased physical and mental capacity.

It should be said that intervention programmes aimed at reducing the incidence and severity of malnutrition due to dificiencies of vitamin A, vitamin D and iodine and also to protein and energy deficiency have

been very effective. The developed world has a responsibility to continue helping developing countries overcome these serious problems of malnutrition.

Impaired quality of life in adults related to nutrition

This often occurs in adults as the result of undernutrition or over-eating (a form of malnutrition) during youth. Nevertheless, adulthood has its own syndromes which detract from optimal health and working capacity. In developing countries, the main problem for adults is lack of energy rather than lack of protein. Lack of energy in adults causes bodily exertion to be reduced to a minimum in order to keep a balance between energy intake and energy expenditure. Under such conditions, it is impossible for physical activity to reach a desirable level thus giving an apparent air of laziness.

In affluent countries, the problems are more complicated and often result from over-eating or failing to eat a well-balanced diet. Many diseases with a nutritional basis occur including cardiac and vascular diseases, gall bladder disease, cirrhosis of the liver, and carcinoma of the colon. Not only does an individual suffer from such a disease but the society suffers because of reduced working capacity and increased absentee rates in the workforce and because of premature death. Correction of the nutritional problems in affluent countries presents a task of similar magnitude to correction of the nutritional problems in developing countries. Detrimental nutritional factors can exist for years before disease symptoms become apparent. As much research is yet to be carried out to determine the role of food constituents in nutritional diseases such as those mentioned above, it is not possible to implement completely effective prevention programmes. Prevention is made more difficult not only because the disease exists before symptoms become apparent but also because the willingness of individuals to change their eating habits is only minimal.

Finally in this section on adults, mention should be made of dental caries and also of the use of alcohol. It could be asked "How much does dental caries influence the quality of life?". Is it normal that a high percentage of adults should be left with none of their own teeth? Just because it occurs frequently, this situation should not be regarded as the norm. Dental caries is a disease which must be fought right from the beginning in youth but, because such technically perfect dentures are available, it is barely considered a defect. In the same way, the excessive use of alcohol by many young adults in so-called advanced countries is becoming to be regarded as the norm. However, many such people are ruining their health through cirrhosis of the liver which often leads to premature death.

The Aged

The aim of nutrition, in so far as this influences the quality of life, is to reach old age in good health without disablement from nutrition-associated diseases or aberrations such as cardiac or vascular diseases, advanced osteoporosis, high blood pressure or apoplexy. As people get older, it is difficult to change their eating habits. Thus it is desirable to establish good eating habits at an early age and to modify the diet to maintain a good, balanced, age-related diet with increasing age.

Positive influences

An overview of diets and nutrition mainly having a negative influence on the quality of life has been presented above. It is just as useful to consider how a diet can exert a positive influence and contribute to optimal physical and mental health. This is a diet which throughout life is adapted to the specific requirements at each different age period. It is not possible to describe such a diet in the limited space available. However, it should include all nutrients in sufficient qualities and the right proportions to enable the body to meet all reasonable demands made of it both internally and externally with as little stress as possible to its natural defence and adaption mechanisms. The diet can be made up from an amazing array of foods depending on the availability and acceptability of the foods within the culture concerned. Such aspects as hygiene and the absence of toxins should be taken into account.

Good diet should begin at an early age. In fact, as mentioned earlier, it should begin before the baby is born with good nutrition for the mother. In developing countries, the mother is usually faced with nutritional deficiencies while in developed countries, it is more important for mothers to abstain from smoking and not to consume excessive amounts of alcohol. Breastfeeding of babies should be encouraged throughout the world as it provides the child with the best chance of being healthy.

AM To — TN

Then → Resource f/le

evised Note of May 3. 2001

king into account feedback received; please see also comments of MFC members in the Annual Meet Organising Committee at the end of this note)

An Outline for the MFC 2002 Annual Meet on Food and Nutritional Security

n Food Security

ood security appears to be about getting rid of hunger and ensuring "two square meals" per day for erybody. What kind of food? Who produces the food? How much control do people, especially the orest of the poor, have over the production, distribution and consumption of the kinds of food?

losely related is the question of whether the kind of food available and being consumed ensures long-term *rritional* security -- the latter term understood as being able to access sufficient number of calories for l persons in one's family for sustained periods of time, access that would hopefully lead to better health id quality of life. How many calories are really necessary for various occupation groups and what has been e progress in this regard since the last decade? Can poor people purchase the required calories at the wage vels actually on offer on farms and fields? In Gujarat for instance the minimum wage for farm labour is ound Rs 80/- per day but nobody really gets it all the time.

utritional Issues

f medical scientific interest is: Why are specific nutritional anemia being caused? What is the etiology and idemiology of the same? On the other hand why are some kinds of deficiency (Vit A for example) appear be diminishing? What are the other medical and health consequences of these deficienceis? And what are e new problems coming to fore with life style changes and changes in the kinds of food available? *(See so note on nutritional security at the end by S.Sridhar)*

ole of State Policies, Markets, Technology and Ecology

lsewhere, increasing nutritional insecurity seems to be related to increasing deforestation; loss of control ver common natural resources such as forest, water and land; the decrease in the availability and variety vegetables (for instance greens), cereals (decrease in millets), food grains and edible oils; major shifts in riculture from cash to commercial crops and the consequent ecological imbalance and scarcity of food id animal fodder.

practice we need to examine the feasibility of distributing free food to people who are unemployed or ndless and poor and subject to droughts, cyclones and other natural calamities. In fact many of these tural events, including earthquakes, need not end up as livelihood and nutritional calamities. What can e do to prevent such catastrophic consequences?

hat are the new roles of the state, the market and civil society in ensuring food and nutritional security ith a "reforming" Government of India? This is of concern especially as the one of the major nutritional olicy interventions, the PDS, is being diluted. What and how effective have been the other policy terventions -- the ICDS and the mid-day meal schemes and Take Home Ration schemes. What will be the

MK/office/room

Please be careful when printing out — half the sentence is in there in the last few pages — it has become a waste

Please discuss & look at the problem in your office room meeting & get back to me on Monday 18/6/01 TN 15/6

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fect of the slow winding up of the Food Corporation of India? There is talk also of toning down the role the Agricultural Prices Commission, the one which fixes procurement prices.

f extreme concern are suicides among farmers and the apparent increase in immiserisation of all kinds of rsons, poor and not so poor. Some of these seem to be related to rapid shifts in government policies of port-import, the increasingly adverse terms of trade for the indigenous producer, the dumping or herwise of food and other industrial items of (what used to be) local production and consumption.

ow many of these are indeed related to the green revolution technology of farming and how many to other ctors out of control of the farmer, for instance spiraling debt and lack of farm insurance? A closely related sue is the kinds of rural and urban indebtedness and its long-term effect on nutrition, health and food vailability at the house hold level. Are Grameen bank type solutions (banking for the poor), increasingly lvocated by Indian NGOs, the answer?

f special interest are gender differentials and any new insights coming out of recent studies including the test round of census.

Vith the inroads of WTO, or rather the easy succumbing to WTO logic by our policy makers (for instance, e hasty removal of QRs on a host of items), we need to worry about what are the practical crop rotation ternatives for farmers in the tussle between the market, growing more cash crops, soil nutrient depletion id self-dependence. Can India afford to buy food in the international markets using money earned from ports. Is it moral to export food (as we have recently done with rice, wheat and sugar) when our own poor e starving? Why have prices of agricultural commodities fallen post-WTO while food prices have not llen?

A similar look at the inroads made by shrimp farming in states like Tamil Nadu is in order, as the additional reliance on growing cereals for sustenance seems to have been sacrificed, and therefore more rectly assured food security. A related issue is the investment of high technology fishing/trawling in the astal areas (blue revolution?) over the past 20 years and the actual effects on food and nutritional status of e fishermen, especially the poorer among them.

t another area of related interest is an examination of the 30-year old romance with soya beans, especially / farmers in M.P.. Now what has been the real life consequences of this dedication to soya beans pecially as pulse production seems to have come down (not the only reason for pulse production decline owever). What also has been the nutritional consequences of emphasis on wheat and rice as "prestige" reals as compared to say ragi, jowar, maize and other millets and the consequent decline in production of e latter? What is happening to our combined resource base of ground water, soil and pest ecology, thanks the Green Revolution and now the market? People have shifted to cash crops. Is there any alternative ossible?

lso of interest is to ask why in spite of the many warnings about impoverishment, both rich and poor eople still subscribe, at least in Gujarat, to the Operation Flood led dairy farming? Some other data, from ajasthan and West Bengal, however seem to indicate dairying actually results in per capita decline of the vailability of milk in villages and therefore likely to have adverse nutritional consequences.

'e need to think of different nutritional and food security policies across classes and cultures and as well
: across geo-climatic zones.

ood Security and Ill Health Promoting Work

ow do we resolve the apparently obvious health-related tension between campaigns against tobacco and
n masala on the one hand and the unemployment of so many tobacco growing farmers and labourers,
eedi workers, tendu leaf collectors -- many of them being really poor -- if all of them were to shift from
bacco? (Beedi making is one of the largest sectors of employment after agriculture and construction).

ood Security and Ideology of Self-Reliance

national self-reliance as an ideology, which was a major theme of our independence movement and our
dy politic till the seventies, out of fashion? Or rather, we need to ask why has something so
mmonsensical become out of fashion. Are we hurtling towards a market-led economy in the name of
st and, now second generation, reforms without perfecting our act as a welfare state? (It is to be
membered most of the highly industrialised states of Europe have sound welfare mechanisms in place so
at people do not go hungry.) What kind of food security are we providing with increase in hire and fire
olicies (as per the recent budget of 2001, firms up to 1000 workers need not take permission to get rid of
orkers), of mindless disinvestment of PSUs.? We are told by economists that it is good for all of us in the
ng-term. How true is this assertion?

related issue of interest is, why has China, once touted as an example of a society with high equity, given
collective farming and communes and gone for market-led mechanisms? Closer home, what has been the
lance sheet at the end of the day of land reforms in West Bengal (Operation Barga)?

hat indeed are the nutritional consequences of the market-led economy, of the Mcdonalds, Pepsis and
okes, Cargill salt and Monsanto seeds? Do we leave it to the wisdom of the system, some new invisible
nd to take care of all the damage? What are the implications of patents, biotechnology, genetically
odified foods and organisms, and the onrush of MNCs in "value-added" food industry? Is free trade fair
ade?

as nutritional quality and food security really increased on the whole even as the percentage of people
elow poverty line seems to have decreased? Is there any special role for health activists in all this? Is the
ny solution to go back to an ecoconscious, welfare society -- if so how do we do it?

ince the major concern of the meet is to be food security, a number of issues in nutrition can be identified at should contribute to a better understanding of food security and a rational approach for achieving the me. It may be enough to limit discussion on nutrition to background papers, especially if these are refully conceived. The issues that I can think of as meriting attention are:

1. Major nutritional deficiencies in India: nutritional anemia, protein-energy malnutrition (child and adult), selected micronutrient deficiencies (vitamin A, iodine, etc): trends, current status, contribution to morbidity / mortality / quality of life.

2. An examination of the regional / sociocultural differences in nutritional status (both under- and over-nutrition).

3. An examination of the changes over the last few decades in the understanding of the pathogenesis of specific nutritional derangements, and implications of these on for policies related to agriculture and food security.

4. The nutritional impact of PDS, ICDS, MDM, TINP and other such programs - expected and actual. The possible and actual effects of their dilution.

5. Potential and actual nutritional implications of recent policy changes related to food production, procurement, distribution, etc.. Evidence for changes in nutritional status in vulnerable populations of countries opting for major macroeconomic policy changes.

6. Evidence for regional and gender differences in health indicators attributable to differences in traditional dietary practices. Urbanisation and improvement/decrease in food security. Potential and actual effects of a host of macro and micro factors on nutritional and health indicators: recent rapid changes in lifestyles, particularly diets, availability of processed foods, worsening fuel crisis, availability of cooking time, availability of time for cooking and differential calorie requirements at different stages in life starting from weaning; Evidence for factors that influence such changes.

7. Evidence for diminishing biodiversity in food sources. Potential or actual impact of this specifically on local / regional health indicators, and generally on other biodiversity including human diversity, if any.

8. Genetically modified foods and their potential impact on nutrition and health.

9. Any relevant studies available on traditional concepts of evaluating food value vis-a -vis variations in food / nutritional needs of different individuals / families / communities, and prescriptions and proscriptions that follow: their correlates in modern nutrition, and relevance of loss of such traditional practices for nutrition / health status. Intrafamily food distribution over the years across various classes and castes; Research needs in nutrition in its relation to food / agriculture policies.

've gone through your background paper and
dlict that you have laid out a very broad framework,
id a whole range of issues have been raised which
ay be classified into the following:

Access to food.
Wages and Food
Nutritional problems in relation to a large no. of
ariables
Famine and Food security
Other Calamities
Role of the state eg. Nutritional Programmes,
DS., ICDS., Procurement prices ,
Agriculture related, such as cash cropping, WTO.
xport Markets
WHO campaigns against tobacco and and it's effect
i food security and livelihoods.
Land reforms, collective farming. Indebtedness,
id its impact on food security
). Right to food.
1. GM foods, Biodiversity and implications for food
curity.
. Problems of procurement, storage, and
stribution.
. Others

suppose each of these areas are important and need
scussion and lend themselves to activism, however I
onder about our strengths, and how do we handle the
roblem.

ne way out is to identify papers or paper writers,
id then structure the theme around the topics
overed. We could try to avoid issues which are of
etorical value and /or common knowledge, such as
cology, environment., and our great past kind of
apers., unless there is some compelling evidence.
ven Sridhar's note starts off with
pecificities,but ends up covering all the above
sues. Please do comment and let me know whether I'm
isreading the problem.

Padmini Swaminathan's Comments

I have the following suggestions to offer:

1] Let us use the MAM to discuss the theme of Food Security & Nutrition

in each of the Cells. Cells may decide to discuss it jointly or separately or both. At the Meet we could also zero in on a few key issues and take responsibility for presentations, getting papers, etc.

2] The Note on Nutrition issues that have been circulated sketches a wide canvas. At the MAM we need to attempt some form of synthesization so that the issues are not only put in perspective but also in a manageable form. To this I have the following extremely tentative format to suggest:

a] Conceptual and Methodological Issues:
Here I have in mind the debate generated by the two main methods that have been used to assess the extent of undernutrition in different parts of the world, namely, the FAO approach and the WHO approach. The FAO approaches the problem through food availability statistics; the WHO proceeds to study the problem through observed conditions of human body and basic functionings-the so-called anthropometric approaches. The consequences and limitations of relying on these approaches have to be analytically and empirically delineated with their differential implications for policy.

b] Issues related to Data on Nutrition, both qualitative and quantitative:
Few would disagree with the notion that habitual intake below the calorie expenditure required is inadequate. The problems arise when this general definition is to be operationalized.
It would be interesting to learn from scholars like Veena Shatrughna how the Indian State , has, through Bodies like the NMMB, defined and operationalized the undernutrition/malnutrition question. The questions of data can themselves be split up into the following:

i] The What question--what constitutes under/malnutrition
ii]The Who question--Identification of the population or segments of the population who are undernourished.Is there a disproportionate emphasis on small children and women as victims of undernutrition to the exclusion of adolescents and men?
iii]The When question-When in life is the risk of undernutrition highest? Do we have longitudinal observations of the same individuals to answer the question, to what extent anthropometric failure early in life is the explanation for short stature in adulthood and other complications.
iv] The Where question- location of undernutrition geographically and among segments within a geographic population.
v] The Why question-explanation for undernutrition [food availability failures only or more substantively, income or entitlement failures]

[i] Consequences of Undernutrition: Do we have concrete case studies linking nutrition to particular debilitating diseases. Additionally how does one go about looking for and generating such data.

IV Policy Implications of Approaches adopted

I am stressing the aspect of Approach adopted since the policy implications can be diametrically different depending on what approach we adopt. Therefore we need to be aware of the possibility that the fundamental reasons for undernutrition are different in different parts of the world and also across countries. For example, literature shows that in Sub-Saharan Africa the chief human problem is not low supply of food and primary undernutrition but rather grossly inadequate health care for large sections of the population. In South Asia on the other hand, where the anthropometric status of the population is far worse than in Africa, and where mortality is considerably lower, primary undernutrition is a chief aspect for the overall deprivation. Action plans that fail to recognise such differences over space and time are doomed to fail

Ritu Priya's Comments

I see the last section of the draft Outline, that on Nutritional Security, along with the formulation of issues by Padmini, as forming the format for the Annual meet. I say this for three reasons:-

1) that this section of the draft provides an overview of all the issues, the other sections only detail those issues.

2) that many of the conceptual and methodological issues which were objects of debate in the '60s and '70s (eg those raised by Sukhatme and Gopalan), and settled in favour of the more holistic and pro-poor perspective, are again being restated in reverse arguments, almost ignoring the earlier debates. They are currently providing the 'technical' justification for 'medicalisation' of the nutrition problem and for narrow, technocentric policy approaches.

3) mfc has the onus of debating and taking positions on the 'technical' issues of 'nutrition science' and its inherent concepts and methodologies. Padmini's note points to these very clearly.

Therefore I would suggest that the Note on Nutritional Security in the draft be at the beginning of the Outline paper rather than at the end. Also or it incorporate points II (on conceptual and methodological issues) and

/ (on policy implications) of Padmini's note.

NUT-1.

MORE DEATHS DUE TO VITMIN A IN ASSAM

Subject: MORE DEATHS DUE TO VITMIN A IN ASSAM
Date: Sun, 18 Nov 2001 04:28:13 +0000
From: "umesh kapil" <kapilumesh@hotmail.com>
To: secy.wcd@sb.nic.in
CC: kapilumesh@hotmail.com

Respected Sir
I am enclosing furthur update on deaths due to Vitamin A administration in Assam.

Dr. Umesh Kapil
Additional Professor
Department of Human Nutrition
AIIMS, New Delhi, 110029
kapilumesh@hotmail.com

==========

3 more Vitamin A deaths in Assam
TIMES OF INDIA 18.11.2001

P P SINGH

TIMES NEWS NETWORK

GUWAHATI: At least three more children have died in Assam after taking Vitamin A dose in a Unicef-sponsored programme, taking the toll to seven though unofficial reports put the figure at eight, said state Health Minister Dr. Bhumidar Barman.

Barman, while talking to this correspondent said that there have been three more deaths in Kokrajhar district in Balagaon Relief Camp under Gosaigaon sub-division, but he felt these were too late for any reaction to the Vitamin doses.

However, according to sources, the two infants -- Duler Hasda aged five and Bali Hasda aged three -- both daughters of Saran Hasda had died on 15th of November. The vitamin doses were administered on 12th and 13th of this month. It is learn that the district administration exhumed the bodies and has sent them to Kokrajhar hospital for post-mortem.

Another child, Vijay Topo, aged three, son of Etua Topo also died on Saturday morning in the same relief camp according to sources in Kokrajhar. His body has also been sent for post mortem.

When contacted the DC Kokrajhar, Dr. Ashish K Bhutani, while confirming the news informed that he has seized all the used and unused bottles of Vitamin A. He said the much talked of five ml cups were not seized with these indicating normal two ml spoons were used for administering the vitamin. This may mean that the deaths were not due to over doze as has been suggested by the state health minister.

Dr. Barman said though originally he had also opined that the deaths might be due to overdose it seems the contents of the bottles could also be responsible thus bringing the manufacturers of the Vitamin A also into the picture.

for Nutrition Resource file

He said that orders for the suspension of two doctors and one pharmacist who were in charge of three booths where deaths took place earlier in the three districts of Cachar, Sonitpur and Nalbari have been issued.

However, Cachar DC P K Das said that no medical officer there has so far been suspended.

Dr. Barman said with the latest deaths being reported action against more medical staff would be taken. According to the Health Minister two nurses and one Anganwadi worker have also been suspended in the three districts of

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MORE DEATHS DUE TO VITMIN A IN ASSAM

Cachar, Sonitpur and Nalbari.

===

Vitamin A deaths: Screening was not done
SHANKHADEEP CHOUDHURY

TIMES NEWS NETWORK

GUWAHATI: Were enough precautions taken by the state government-Unicef combine in Assam during the now-tainted Pulse Vitamin A programme?

Not really, it seems, if the minutest of risks are taken into consideration.

The basic public health question that has been raised in the aftermath of the tragedy is whether a screening should have been done before Vitamin A drops were administered to children to eliminate all risks, whatsoever.

Already, seven children have died after consuming Vitamin A drops in various parts of Assam under a joint Unicef-Assam government programme. Red faced authorities, while suspecting that it happened because of an overdose, have ordered a enquiry besides suspending six health officials till now.

Nutritionists and child specialists here feel that a screening should have been made mandatory, even though some of them agree that this might be physically impossible in a public health programme for the masses.

The logic, as city-based nutritionist Nahid Pasha says, is very simple. "Vitamin is given in the form of retinol. If the child has a liver disorder and the retinol binding capacity is reduced, then it can cause toxicity and he is not fit to receive Vitamin A. Therefore, a screening by medicos is needed to ensure that a child is not suffering from a liver disorder or diarrhoea", she feels.

Agrees another prominent Guwahati paedetrician, Dr Rajkumar Kayal: "Sometimes, children are intolerant to a megadose of Vitamin A either per se or because of some underlying ailments, and hence, theoretically speaking, a screening would eliminate all such risks of ailments."

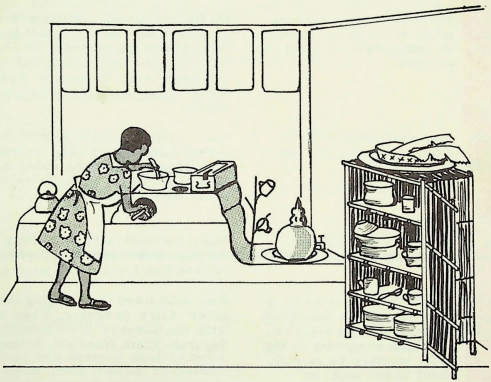
However, he added: "Of course, I understand that this might be practically impossible. Hence, the next best thing to do would be to adhere to strict guidelines on dosage, and at the same time, to preferably impart this Vitamin A only to really vulnerable sections -children with malnutrition, or with clinical Vitamin A deficiency, or with measles, or with chronic diarrhoea."

However, Unicef authorities - while agreeing that no screening was conducted - have a different opinion. Pat Engle, Unicef's chief of child development and nutrition, when contacted over telephone in New Delhi, pointed out: "Globally, children are generally not screened, except for age, for a public health campaign, including Vitamin A. Children are screened for age, but there are no other criteria mentioned in the Government of India policy for Vitamin A. Preventative supplementation of Vitamin A, in fact, has been on in India for the last twenty years."

TN.

19/11/01

PREPARE AND SERVE SAFE MEALS



As a homemaker, you have the important job of preparing and serving safe wholesome meals for your family. There are many things you can do to make food safe.

When you prepare and serve food it is important to--

- select good quality food
- keep yourself clean
- keep dishes and equipment clean
- keep the cooking and eating area clean.

Food can become unsafe to eat if it is--

- served by a person carrying disease germs
- served in soiled dishes
- eaten with dirty utensils and hands.

Keep everything clean. Cleanliness helps to keep away disease germs. Clean food is likely to be safe food.

MAKE MEALS SAFE

Some foods are eaten raw, others are cooked. Either way, they should be clean. You can prepare foods to make them safe for you and your family.

Some foods spoil quicker than others.

Foods made of milk, eggs, meat, poultry, fish or shellfish may contain harmful bacteria that grow rapidly. These bacteria can cause food to spoil. Spoiled foods will make you sick.

When preparing these foods:

- store them for a very short time
- prepare in clean containers
- cook thoroughly
- serve immediately
- don't save leftovers.

Some Illnesses Are Caused by Food

ILLNESS	FOODS USUALLY INVOLVED	WAYS TO PREVENT SPREAD BY FOOD
Bacillary dysentery	Moist or prepared foods; milk, other dairy products or water contaminated with excreta.	Strict personal cleanliness in food preparation; keeping moist foods cool during storage periods; cooking foods before serving; getting rid of flies. Persons with dysentery should not handle food. Dispose of human wastes safely.
Brucellosis (Undulant fever, Malta fever, Bang's disease)	Raw contaminated milk, dairy products, or meat.	Get rid of brucellosis from livestock by vaccinating young animals and slaughtering infected older animals. Boil milk used to drink or to make other dairy products.
Diphtheria	Milk contaminated by humans with the illness.	Make the milk safe by boiling. Search for the person carrying the illness and isolate him from other people.
Scarletfever or septic sore throat	Foods contaminated by a discharge from the mouth or nose of a person who has disease germs in his body, whether he is sick, about to get sick, or immune. Milk from cows with udder infections caused by these organisms.	Boil milk used for drinking or to make other dairy products. Keep persons with the disease from handling food. Separate them from other people.
Botulism	Home canned foods, or sometimes commercially prepared foods.	Cook canned meat and vegetables thoroughly before serving. Boil 15 minutes and stir to make sure you heat all parts.
Amoebic dysentery	Water contaminated with sewage. Moist food contaminated with human excreta.	Protect your water supply. Use safe drinking water. If you are not sure water is safe, boil it for 10 minutes. Be clean in preparing food. Dispose of human excreta properly.
Trichinosis	Raw or undercooked pork and pork products.	Cook these foods thoroughly. Cook garbage fed to swine. Get rid of rats in hog lots.
Salmonellosis	Cracked or dirty eggs contaminated with poultry excreta, meat meal, bone meal, or fish meal. Poultry meat contaminated by unsanitary handling.	Use only clean eggs with sound shells. Soiled eggs should be washed. Handle poultry meat and eggs under clean conditions. Store them in a cold place. Cook thoroughly and refrigerate if not eaten at once. After handling raw eggs or poultry, wash your hands thoroughly.

USE SAFE WATER

You need safe water to prepare foods and beverages. Water is likely to be safe when it comes from a city water supply or a sanitary well. Your local health officials can tell you how to make a sanitary well.

If you are not sure water is safe, boil it at least 10 minutes in a clean container. Store in a clean covered container.

Use this boiled water for:

- drinking
- preparing dried, condensed or evaporated milk
- making cold beverages
- making ice
- washing fruits and vegetables
- washing dishes.

Foods Eaten Cooked

Cooking food will destroy most harmful bacteria. Most foods should be washed before cooking. Wash them before cutting into small pieces.

Wash meat, fish, and poultry with a clean damp cloth to remove dirt or chipped bones. Do not let them soak in water. They will come out soft and may lose some of their natural juices.

Green leafy vegetables may need to be washed several times to remove dirt, insects, and worms. Lift leafy vegetables from the water. The dirt and sand settles to the bottom of the container.

Foods Eaten Raw

All fresh fruits and vegetables that are to be eaten raw should be washed thoroughly in safe water.

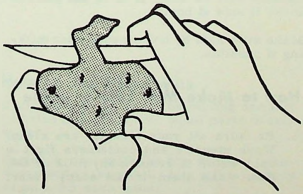
Washing fruits and vegetables helps remove any sand, dirt, or pesticides that might be on them.

If there is mold, bruised or spoiled spots, or insect damage, cut away these spots before eating the food.

Foods Grown in Night Soil

Some foods such as fruits and vegetables may come in contact with human excreta or night soil. These foods need special care.

Untreated night soil may carry disease germs. There is no known way to treat night soil at home so that it is safe. Never use it to fertilize your garden.



Protect yourself and your family from germs in human waste:

If there is a danger any night soil has gotten into your garden, cook your vegetables. Do not eat them raw.

Any fruit that falls on ground that has been fertilized with night soil should be cooked, particularly if it cannot be peeled.

Sometimes water from irrigation ditches contains night soil. This water is not safe. If you have to use this water for watering your garden and fruit trees, cook vegetables and fruits to make them safe.

Foods Sprayed with Pesticides

In many countries, gardens and fruit trees are sprayed with pesticides to get rid of insects. Washing fruits and vegetables will help remove these sprays.

Ask your health department sanitarian or other health officials to tell you how to get rid of these sprays on food.

Leftover Foods

All leftover foods should be stored in a clean covered container.

If the food has been cooked, cool it quickly. Place the container in cold water. Do not cover tightly until it is cool. Put a clean cloth over the container until the food is cooled.

After food is cooled, cover the container tightly. Place the container in a cool place. If possible, store it in an iceless or mechanical refrigerator or a cave.

Foods made with milk, eggs, meat, fish, or poultry spoil rapidly. In hot climates without refrigeration, never save them for another meal.

All cooked leftover foods should be reheated to make them safe to eat. Heat well for 15 minutes.

USE SAFE MILK

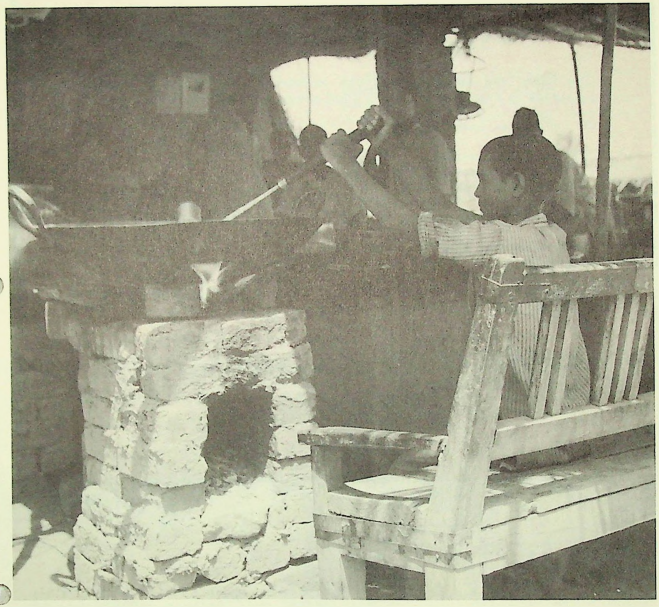
Milk is one of our best foods. Fresh milk can have harmful bacteria in it. To make fresh milk safe, bring it to a boil.

Milk that you buy from a modern dairy usually will be safe. If it is not you can make it safe at home.

Make milk safe by boiling soon after milking if possible.

How to Make Milk Safe at Home

1. Be sure all your utensils are clean. Wash utensils and containers first in cold water to remove any milk or fat, then wash them in hot soapy water. Rinse with water that has been boiled for 10 minutes. Be sure to wash the cloth strainer.
2. Pour milk through the strainer into the container for heating. It is best not to heat more than 2 quarts at a time.
3. Place the container over the fire and bring the milk to a boil. Stir with a ladle or a wooden spoon.
4. As soon as the milk boils, remove the container from the fire.
5. Place the container in a basin of cold water. Change the water often to cool the milk quickly.



Boy in Pakistan is boiling milk to make it safe.

6. Put the cooled milk into clean bottles or pottery jars that have been washed in safe water, and cover.

7. Keep milk in a cool place. Iceless or mechanical refrigerators or caves are ideal places for storing milk.

How to Use Dried Milk

Fluid milk is prepared by mixing one part of dried milk with four equal parts of safe water.

Sprinkle dry milk on top of safe, lukewarm water. Mix well. Mix a fresh supply of milk for each meal.

Keep Meat, Fish and Poultry Covered

These foods should be kept covered--

- in the market
- on the way to your home
- in your home.

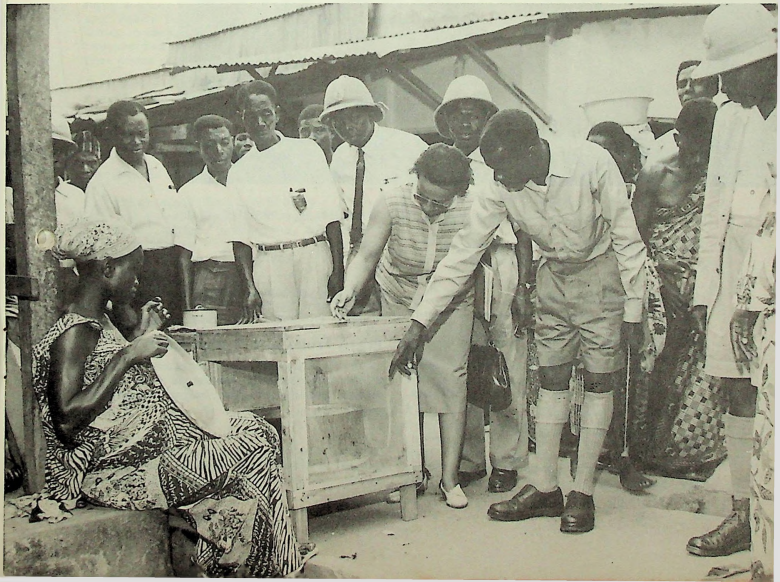
They should be wrapped loosely to allow air to circulate. Flies and other insects like to feed on these foods.

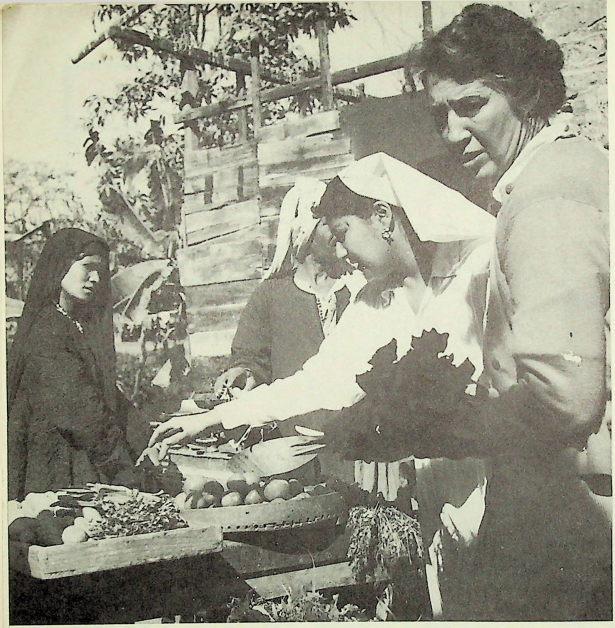
In the market, cheese cloth or other loosely woven cloth could be used. In some countries, food is protected from flies by screened containers.

On the way from the market to your home, these foods should be wrapped. If the seller does not wrap them, take wrappings with you. You may use paper, large clean leaves or clean cloths.

At home, keep foods covered. If they are wrapped with paper, leaves or a clean cloth, loosen the wrapping. Air needs to circulate around these foods. Store in a cool place until used.

Food sold in the market is protected by a screen.--Ghana.





Homemakers choose fresh vegetables in a market in Egypt.

Cereals and Breads

Select cereals free from weevils, dirt, and stones. When you pick the grain up in your hand, it should feel heavy. If it feels light, insects may have eaten some of the grain. Insects eat the best part of grains.

Bread should be free from mold.

Keep bread covered at the market, on the way home, and in your home. Covering bread helps to avoid dirt, flies, and other insects.

Fresh Fruits and Vegetables

When selecting fresh fruits and vegetables, avoid wilted, shriveled or decayed ones.

Green leafy vegetables should have a fresh and attractive color, no yellow streaks or spots, or damage by insects or worms.

Milk and Cheese

Fresh milk should be free of insects and dirt. It should have a fresh, not a sour smell. Be sure it is in a clean covered container. Sour milk is sold in many markets.

Dry milk that has a strong flavor and is lumpy may be old or may have been stored in a damp place. Look for insect and rodent damage.

Some kinds of cheese are made with a mold in them. This type of cheese is safe. Mold that forms on the outside of cheese is not safe to eat.

Do not buy cheese that has been damaged by insects or rodents.

STORE FOOD IN A CLEAN PLACE

Whether you buy food or grow it, you must have a place to store it properly until you are ready to use it. Good storage saves time, money, and food. Select suitable containers and plan to keep foods cool, dry and free from dirt, insects, and rodents.

Dry foods such as grains, salt and sugar may be stored in pottery or glass jars, tin cans or bottles. These containers with tight covers may be kept on open shelves in a cupboard.

Perishable foods like--

- fresh meat, fish and poultry
- some fresh fruits and vegetables
- milk, butter, margarine, cream and leftovers

should be kept in a cool place.

When possible, store these foods in covered containers in an iceless or mechanical refrigerator, food safe, cave, or window box.

In cool climates, some fruits and vegetables may be stored from 4 to 6 weeks in cellars or in outdoor pits dug in the ground.

Remember--

- keep foods cool
- keep foods covered.

Food that is not carefully stored attracts insects and rodents. They may carry disease germs.

To control these pests you should--

- keep your home and surroundings clean
- keep all food in covered containers
- keep garbage in a covered container
- feed garbage to animals or burn or bury it
- burn or bury trash
- use a sanitary latrine
- ask government officials about the use of pesticides.

You may need to use pesticides to get rid of household pests. Ask your sanitarian of the health department or other officials to help you. They can tell you how to control them.

Keep poisons for killing insects and rodents away from children, food, dishes, and cooking utensils. Mark containers which hold poisons clearly, and store in a safe place. Poisons can make you and your family sick.

KEEP YOURSELF CLEAN

Develop good personal habits. Wash your hair every 10 days or 2 weeks. Do not let hair fall into food--wear a scarf, net or cap. Never comb or fix your hair where food is being prepared.

Wear clean clothing. Wash your clothing often. Use clean aprons to protect your dress. Change clothing when it becomes dirty.

Don't cough, sneeze, or spit near food or dishes. You could spread disease germs.

Never lick your fingers or thumbs. Wash your hands.

Don't scratch your head or touch your face when preparing food.

When tasting foods for flavor, use a separate fork or spoon.

Remember, harmful germs are all about you. They are on your body, hair, face, and clothes. If you do not keep clean and healthy, you can spread germs.

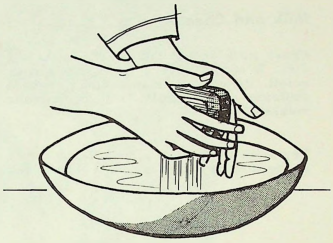
Several ways you can spread disease germs when preparing and serving food are by having:

- infected sores on your hands
- unwashed hands
- a contagious disease.

Scratches and Cuts

The sore on your hand may have disease germs. Those germs can get into the food you are preparing.

Later you eat this food. In awhile you may get a stomach ache. The germs traveled from your hand to your food and then to your stomach. If your family eats the same food, they will be sick too.



If you have a cut or scratch, wash it with soap and water, cover with a clean cloth.

Keep sores covered so that flies and dirt cannot get on them.

If possible, you should see a doctor if you have sores or ulcers.

Wash Your Hands Often

Disease germs of amoebic dysentery, food poisoning and typhoid fever can be spread by unwashed hands. Get into the habit of washing your hands often with soap and clean safe water.

Wash your hands before you:

- handle food, dishes or other eating utensils
- set the table
- eat
- feed the children.

Wash hands after you:

- go to the latrine
- use a handkerchief
- handle animals
- clean animal pens
- work in gardens
- cough or sneeze
- wipe your eyes, even when you use a cloth
- handle a baby or sick person.

Keep your fingernails cut short. Dirt and disease germs gather under long nails.

Care of a Person with a Contagious Disease

Such diseases as diptheria and scarlet fever are contagious. This means they can be spread from one person to another.

See a doctor if possible.

A person with a contagious disease should not prepare food. Have some other member of the family do it.

KEEP EQUIPMENT AND DISHES CLEAN

Equipment and dishes used for preparing and serving meals must be:

- kept clean
- stored in a clean, safe place.

Remember, if equipment and dishes are cleaned immediately after they are used, it will take less time and the job will be easier for you.

Care of Dishes, Pots and Pans

Dishes, glasses, silverware, pots, pans and other cooking utensils used for preparing food should be washed after each use.

Washing and rinsing dishes carefully helps to prevent the spread of disease germs to you and your family.

To wash dishes, use water as hot as your hands can stand. Use soap in the wash water. Pour hot water that has been boiled for 10 minutes over the dishes to rinse them. This rinse water should not contain soap and should be clear and clean.

Let the dishes dry in the air. Air drying is the safest and easiest way if the dishes are protected from dust, flies, insects, and animals.

If you use towels to dry dishes, be sure the towels are clean.

Burned-on food, smoke, rust and other stains need special cleaning with a scouring material. Wood ashes, sand and pebbles, salt, and other local materials can be used. Commercial scouring powders are good, if available.

Store clean dishes in a clean, ventilated place, free from insects and rodents.

Care of Babies' and Sick Person's Dishes

Babies' dishes and dishes for the sick need special care. Wash these dishes separately with hot soapy water and rinse with clear water.

Then place each person's dishes in a separate container. Cover the dishes with clean water. Boil for 10 minutes. Drain. Air dry. Store separately from the dishes the rest of the family uses.

Care of Large Equipment

The stove and oven should be thoroughly cleaned at least once a week. Food that has spilled should be wiped off after each meal.

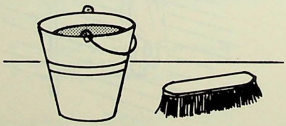
Other equipment, such as the iceless or mechanical refrigerator, stools, chairs, and cupboards, need to be cleaned often to keep them clean and safe. Scrub with soapy water and rinse with clear water. If you have a sink, it should be cleaned thoroughly at least once a day.

Store Dishes, Pots and Pans in a Clean Place

All eating and cooking utensils should be stored in a clean, dry place. Dishes and glasses should be stored in an enclosed cupboard, if possible. Store eating utensils in a drawer, if possible.

Large pieces of cooking equipment, such as pots and pans, can be turned upside down on open shelves, a table or counter to help keep out dirt, insects and rodents.

KEEP THE COOKING AND EATING AREA CLEAN



Take pride in keeping the place where you cook and eat clean and orderly. Keeping these areas clean will help to keep away household pests and avoid sickness. Keep all animals, dogs, cats, pigs, and chickens out of this area. They can spread disease germs.

Painting or whitewashing the walls helps keep the place clean. It will be a more attractive and pleasant place to work.

Have good air circulation to remove odors, grease and smoke. A stove with a chimney will help to keep out smoke.

Some people screen windows to keep out mosquitoes and other insects. They use metal screening, mosquito netting, or other available material.

Scrub the table and chairs often.

A clean kitchen is a more pleasant place to work. When your kitchen is clean, you will be proud of it and the food you prepare in it.

Keep the Working Surface Clean

After each meal is served, clean the work surface or table with soap and water. If water is scarce or expensive, cover the work surface with clean paper or large clean leaves.

Be sure the leaves have not been sprayed with insecticide. After you are through preparing the meal, burn the paper or leaves. Then the work surface will not need to be cleaned each time.

Keep the Floor Clean

Sweep the floor after meals to pick up food scraps that have fallen to the floor.

Sweep after food is prepared and served, not while food is being prepared or served. Dust rises in the air and will fall on the food and on work tables. Dampen the broom when sweeping to avoid scattering dust.

If the floor is made of washable material such as wood or cement, or is covered with linoleum, wash it with soap and water to keep it clean.

Dispose of Garbage and Waste Water

Put all good scraps in a covered garbage container. Do not let them fall on the floor. They attract household pests and pets.

Waste foods can be fed to animals, used for fertilizer, burned or buried. When garbage is used to feed pigs, boil it for 30 minutes. This keeps pigs healthy and prevents spread of trichinosis from food scraps. Be careful that there are no bones, glass, or metal in garbage fed to pigs.

Wash the garbage container with soap and water each time it is emptied.

Don't throw garbage in the yard. It attracts insects and animals.

You can use waste water on your garden. Some homes have a sink with septic tank and a cess pool for disposing of waste water.

If you do not have a sink, dig a hole in the yard and fill it with rocks. Empty the waste water into this hole. The water will seep through the rocks into the earth.

Use a separate container for trash. When the container is full, burn or bury the trash.

MAKE EATING A PLEASANT TIME

Almost everyone enjoys eating. To help make eating time pleasant, serve food in clean containers, in a clean, cheerful place.

In many countries, all members of a family sit down together to eat. Each person should have his own dishes and utensils to eat with at a table.

If flies or other insects are a problem, the serving dishes should be kept covered. Remove the cover just long enough to serve each member of the family.

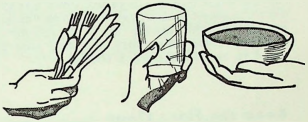
Use serving forks, spoons, spatulas or ladles to serve food to each member of the family. Do not touch the prepared food with your hands.

Sometimes there are not enough dishes and utensils so all members of a family can eat at one time. No one should eat out of the same container or use utensils that another person has used until they have been washed. Washing helps to destroy disease germs.

If cloth or paper napkins are used, each person should have his own. Paper napkins should be burned after use. Cloth napkins should be washed in very hot soapy water. Rinse in clean water and, when possible, hang in the sun to dry.

When setting the table--

- keep your hands off the tines of forks, the blades of knives, the bowls of spoons
- do not touch the rims of glassware or cups
- keep fingers off the inside of bowls and plates.



EQUIPMENT IS IMPORTANT

Good equipment helps you to:

- prepare and serve safe meals
- keep your home clean.

A piece of equipment needed in one country may not be practical in another. The kind and amount of equipment needed will depend on the jobs you do in your own kitchen.

When you have good equipment to store, prepare and serve food, you are helping to avoid the spread of harmful bacteria.

Storing foods in covered containers off the floor or ground helps to protect them from dirt, insects and rodents.

An iceless or mechanical refrigerator helps to keep perishable foods such as meat, fish, poultry, milk and eggs for a longer time.

Containers for garbage and trash help to keep your home clean.

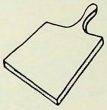
Find out what equipment is available in the markets. Buying commercial equipment may cost less than making it.

If you do plan to make equipment, you should find out if the materials you need are available. You should figure the costs to make the equipment before you start the project. Your husband can help you make the heavy pieces of equipment.

Do not have more equipment than you can use.

EQUIPMENT FOR PREPARING FOOD

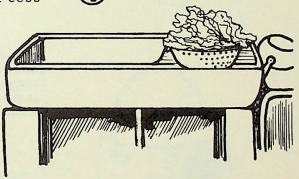
Your work area can be a table or a counter over a cupboard. Although food is sometimes prepared on a board on the floor or ground, a table or a counter is better because dirt and dust cannot get into the food so easily.



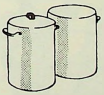
Use a hardwood board to cut or chop foods on. Cover with a clean cloth to use for rolling out pastry.

A paddle, a long, flat board 4 or 5 inches wide and tapered at one end, can be used for stirring large containers of food and for removing foods from the oven.

A sink with a drain connected to a septic tank or a cess pool is a sanitary way to get rid of waste water.



Vegetable brushes can be made of coconut shells and other local materials.



You will need several containers of wood, pottery, metal, or enamel to prepare and mix foods, and several to wash and peel fruits and vegetables into. Gourds or calabashes may be used.

A rotary beater or wire whip is used to beat eggs and mix powdered milk with water. A wire whip can be made at home.

Funnels made of metal, wood, or plastic are used to pour liquids into containers with small openings.

A sieve can be made by punching holes in a large tin can. It can be made of metal or screening.

A bottle opener is a hook used to remove caps from bottles. A can opener is made of metal with a sharp cutting edge. There are many different types.

You may need several types and sizes of knives. Keep the blades sharp. Store out of the reach of children.

Ladles made of metal, wood, or gourds are used to take foods such as rice, flour, sugar and beans out of cans and to serve juicy foods.

Measuring cups made of aluminum, tin, glass or gourds can be used to measure ingredients for cooking. Measuring spoons, usually made of metal, wood, or plastic, are to measure salt, pepper, spices, sugar and flavoring.

A mortar is a heavy vessel to put grain in. A pestle is used to crush grain in the vessel. It is important to keep them clean. Wash them after each use and set in the sun to dry.

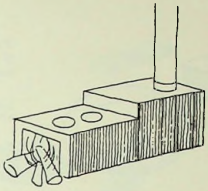
A grater can be made from one long side of a can by punching holes of different sizes on the can. Bind the edges with small strips of wood. Use it to grate cheese, vegetables and spices. It may also be used to grate soap for dish washing or laundry. Keep it clean. Store it where children cannot reach it.

A hand-operated grinder can be used to grind foods at home. They are available in many countries.

Grinding stone. Used in many countries for grinding grains, peppers and other spices.

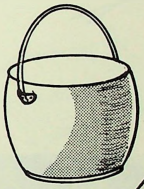
EQUIPMENT FOR COOKING

Many different types of stoves are made in countries around the world. When the stove is inside your house, try to have one with a chimney. This will keep the smoke out and help to keep your home clean.

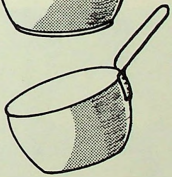


An oven can be made of oil drums, kerosene cans, mud, clay or bricks. Many times the oven is separate from the stove. If the oven is placed inside your house, be sure it has a chimney.

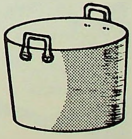
A double boiler may be made from two cans, one smaller than the other. It should have a cover. The bottom can is filled with water and the smaller can containing food is placed inside the can with water. Cook sauces or other foods which need to be cooked very slowly in a double boiler.



Pots for cooking can be made of aluminum, cast iron or clay. The number and size you need depends on the amount and kinds of food you prepare. They should have lids and handles. A lip makes pouring easier. They should not be too heavy to lift when full.

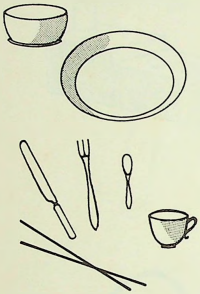


Pans for baking may be made of tin, aluminum or stainless steel. They are used for baking breads, casseroles, meats, cakes, pies, and cookies.



Pot holders are used to handle hot pots, pans, spoons and other hot utensils. You can make them by sewing several thicknesses of cloth and binding the edges. They should be about 6 inches square.

EQUIPMENT FOR SERVING



Food is placed on the table in large serving dishes. From these, the food is taken to put on each person's own dish.

Cups or glasses are used to drink from. Each person should have his own.

Knives, forks, spoons or chopsticks made of stainless steel, aluminum, tin, silver or wood are used to eat with. Each person served should have his own.

Tablecloths or place mats are made of closely woven washable material. You can make them at home. They are placed between the dishes and table to keep the table clean.

Napkins may be made of cloth or paper. They are placed on your lap to protect your clothing while you are eating, you can also wipe your hands or face on them.

A table can be made at home. It should be made of material that is easy to clean.

Stools or chairs can be made at home. Place them around the table to sit on when eating.

EQUIPMENT AND SUPPLIES FOR CLEANING UP

Dish pans are used for washing and rinsing dishes, glassware, silverware, and cooking utensils.

A brush, dishmop, or cloth is used for washing dishes, pots and pans, etc. They may be made of local materials.

Tongs made of metal or wood can also be used to lift dishes out of hot rinse water.

Dish baskets made of wire mesh or woven fibers are used to dip dishes into boiling hot rinse water.

Put dishes on a shallow drain pan made of metal or plastic when they are lifted from boiling hot rinse water.

Dish towels can be used to dry dishes, pots and pans. They can be made at home. But it is more sanitary to air dry dishes.

A dish drying rack can be made of wood, bamboo, metal or plastic.

Wash pans are used to wash hands often when preparing foods. Towels for drying hands are made of closely woven cloth or paper.

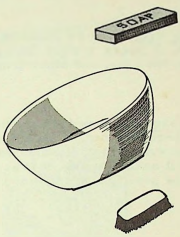
Use a towel drying rack or line to air towels well and raise them from the ground. This keeps them out of the reach of children.

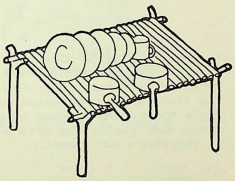
A broom may be bought or made of tough grass or palm leaves tied firmly to a wooden or bamboo pole.

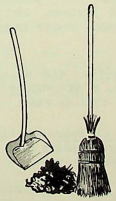
A dust pan may be made of an oblong tin can and a long stick. Use it to collect dust and any waste food or trash that has fallen on the floor.

You need cleaning cloths for washing work areas. Keep a separate one to clean the stove.

A scrub pail can be used to hold water and soap for washing the floor or large equipment. An oil can with the top cut off may be used.



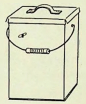




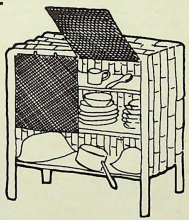
A soap dish is used to save bar soap. It needs to be dried from time to time.

Trash can. May be made of metal, wood, or cardboard. It needs a tight fitting cover. Used to collect paper, tin cans, and other trash.

A garbage can may be made from a large tin can, such as a kerosene can. It should have a tight fitting cover and be waterproof. Handles on each side and the cover make it easier to use. It is used to collect food wastes such as peelings, scraps, and bones.

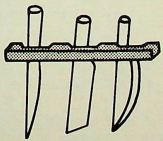


STORAGE EQUIPMENT



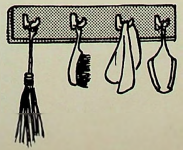
Cupboards can be hung on the wall or stood on the floor. They are made of wood, packing cases, bamboo, or other local materials. Storing food, dishes and eating utensils in a cupboard saves space. It also protects them from dust and animals. A cupboard placed above the washing up area will save time and effort in carrying clean utensils.

Containers of metal, pottery, glass, or coconut shells are used to store dry foods such as sugar, salt, flour, or spices. They should have tight fitting covers to keep out insects, rodents and dirt. Containers for storing safe water may be made of pottery, metal or wood.



Knife holder will store knives safely out of reach of children. A drawer is better because it keeps knives clean as well as safe.

Storage shelves are used to store small covered containers holding food. Shelves should be attached to a strong wall.



Hooks made of bamboo, wood pegs, a nail or wire are used to hang equipment on. They are useful in a small space because they keep the kitchen tidy.

Subject: "Magic Cup " for VA administartion is Guilty
Date: Sat, 24 Nov 2001 07:33:40 +0000
From: "umesh kapil" <kapilumesh@hotmail.com>
To: nfi@bol.net.in

Dera Sir
I hope you find this information useful
kapil

USE OF NEW CONTRAPTION IN THE VA DISTRIBUTION

No one owns up, all blame cups and spoons
In Assam, paramedics contradict each other on how they gave Vitamin A to village kids

SAMUDRA GUPTA KASHYAP

The commonly held theory is that the children fell ill from an overdose of Vitamin A, apparently because medical staff were using cups for the first time, instead of the usual spoons, to dole it out.

His boss Dr Ashok Kumar Choudhury, sub-divisional medical officer and in charge of the Bihdiya PHC, echoed Basumatary, adding ruefully that despite this ''care taken by us for fear of overdose'', seven children were diagnosed with complaints of vomiting and loose motions. One of those who attended the training session and administered the dose was Sanika Begum, a fourth grade female attendant (FA, in official parlance). Sanika, who's been with the health department for over 20 years, said

"she'd been shown neither medicine nor cup the hour-long session, held three days before the actual programme. She and the 25 others were just told, in theory, how to go about the dosage."

Lab note file - VIT A
for
29/11 TM

26/11

Subject: Fwd: Vit A related deaths in Assam , India from the BMJ: (http://bmj.com)
Date: Fri, 23 Nov 2001 11:11:02 +0000
From: "umesh kapil" <kapilumesh@hotmail.com>
To: secy.wcd@sb.nic.in

Dr.R.V. V. Ayyar
Secretary
Government of India
Department of Women and Child Development
Ministry of Human Rsource Development
Shastri Bhawan
New Delhi

Respected Sir,

Here is an update for you on deaths in assam related with Vitamin a administration from "The British Medical Journal " one of the most reputed medical journal in the world

with regards
Dr Umesh Kapil
Additional Professor Public Health Nutrition
Department of Human Nutrition
All India Institute of Medical Sciences,
New Delhi 110 029, INDIA
Phone O: +91-11-6593383, R: 6195105,6185105
Fax: +91-11-6862663
email: kapilumesh@hotmail.com

>*From: "umeshkapil" <kapilumesh@hotmail.com>*
>*To: <kapilumesh@hotmail.com>*
>*Subject: Vit A related deaths in Assam , India from the BMJ:*
>*(http://bmj.com)*
>*Date: Thu, 22 Nov 2001 22:52:03 -0800*
>
>---
>
umeshkapil (kapilumesh@hotmail.com) has sent this article to you from BMJ:
>
>
>*Deaths trigger fresh controversy over vitamin A programme in India*
>
>*http://www.bmj.com:80/cgi/content/full/323/7323/1206?eaf*

WB - Under fwd - Vit A

TN

26/11

Subject: UN vitamin A campaign in India under fire :Lancet, Vol. 358, No.9295, 24 Novembe
Date: Tue, 27 Nov 2001 04:41:44 +0000
From: "umesh kapil" <kapilumesh@hotmail.com>
To: ayyar@hub.nic.in
CC: kapilumesh@hotmail.com

Subject: UN vitamin A campaign in India under fire
Lancet, Vol. 358, No.9295, 24 November, 2001.
Author: Marcie_Francis@americanchemistry.com
Date: 11/26/01 7:00 AM
UN vitamin A campaign in India under
fire

Indian public-health experts have criticised a UNICEF campaign to treatchildren with vitamin A deficiency after 15 infants died in Assam allegedly after an overdose ofvitamin A administered during a state-wide campaign on Nov 11. According to the Assam state government 700 children of 3·2 million who were given the vitamin A dose, are ill. The federal and state governments and UNICEF are investigating the deaths. "The figures being reported are all overestimates. We will first share our findings with the government", said Pat Engle, a UNICEF official. Umesh Kapil (Human Nutrition Unit, All India Institute of Medical Sciences, New Delhi)questioned the need for the campaign. "Surveys conducted by Indian Council of Medical Research in 1999 in Dibrugarh and Nagaon districts of Assam revealed that only 0·3% of children were suffering from Bitot's spots, a marker of vitamin A deficiency", he said. The "campaign approach is wholly uncalled for . . . Mild forms of vitamin Adeficiency are seen in highly deprived pockets and this does not justify a programme of universaldistribution of vitamin A supplements", said C Gopalan, Director General, Nutrition Foundationof India, who pioneered vitamin A prophylaxis in India in the 1970s.However Kapil noted that since 1970 government trained health workers used spoons with a 2ml marking for administering vitamin A doses. "In Assam, a 5 ml cup was provided,instead of a spoon. Health workers were possibly not properly trained . . . and overdose of vitamin A occurred", said Kapil.
Assam's health minister, Bhumidhar Barman, has warned UNICEF that legal actionwill be taken if tests show the syrup was contaminated. It has also been suggested that the syrup may have been out of date. However UNICEF has said that the syrup has an expiry date of March, 2003, and passed independent quality control checks in India.

Dinesh C Sharma

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hb. nutr file - VitA

GH

B
27/11

Dear Dr Kapil, Please send us the GOI guidelines for Vit A administration circulated in Sept 2000. & any update. We would also be interested in the ICMR 18 district study of Vit A deficiency. Do you have any recent data from Karnataka? Best wishes & thanks
Thelma Narayan 21/11

Subject: **Experts wonder whether all children need Vitamin A**
Date: Mon, 19 Nov 2001 14:03:13 +0000
From: "umesh kapil" <kapilumesh@hotmail.com>
To: secy.wcd@sb.nic.in

Guwahati, Monday, November 19, 2001

Experts wonder whether all children need Vitamin A
NEW DELHI, Nov 18 - Even as authorities try to find out what went wrong causing the death of some children after Vitamin A administration in Assam, questions are being raised whether all children need to be administered Vitamin A doses, reports PTI. Experts agree that overdose of Vitamin A cannot be fatal although it can cause some problems like diarrhoea and vomitting. UNICEF, the agency involved in the State programme, said it had sent a team to Assam which would re-examine the quality of Vitamin A used.

"We have sent an expert to the State to know the factual position regarding this incident. The postmortem report is also awaited and by Monday all reports are likely to be available", A R Nanda, Secretary Family Welfare, told PTI. It was not a Centre-sponsored programme but a State government programme in collaboration with UNICEF. The administration was done in "campaign mode" in which effort is made to administer a particular drug of vaccine to all the children of a specific age group, he said. Clarifying that the Centre was not against the campaign mode with regard to Vitamin A administration, Nanda said, "We favoured combining of this programme with immunisation programme".

Guidelines on administering Vitamin A as micronutrient which have been circulated to the States say that it can be given along with measles vaccine and should be repeated after six months. The guidelines also prescribes the age of children and the appropriate dose. Dr Umesh Kapil from AIIMS Gastroenterology and Human Nutrition Department, who was among experts who framed guidelines last September on Vitamin A administration, came out heavily against the international agency involved saying Government of India guidelines should be followed in national programmes. "These agencies are going to the States, which can make modifications in Government of India guidelines according to their needs, and convincing them for switching over to campaign mode", Kapil said. In India, campaign mode was not needed for Vitamin A administration which should be given as part of routine health care programmes, he said.

Kapil said campaign mode was needed only in areas which had large number of cases of illness associated with Vitamin A deficiency. But there is no such epidemic in the country. Comparing Vitamin A administration with polio programme, being followed in campaign mode, Kapil said polio was a communicable disease and if 90 per cent children are immunised against it, it would lead to development of herd immunity. Vitamin A-related problems were non-communicable and all children did not require Vitamin A supplementation, he said. For example, Kapil said, a child having half a kilogram of milk every day did not need additional Vitamin A. Even an ICMR study in the country's 18 districts, including two from Assam - Dibrugarh and Nagaon - did not find Vitamin A deficiency as a public health problem, Kapil said. But UNICEF insisted that all children in India needed Vitamin A supplementation. Covering all the children by combining Vitamin A doses with immunisation programme was difficult. [16 per]

According to the data available, only 17 per cent children in India have received any Vitamin A dosage during past six months, it said. The agency, however, admitted that Indian government had requested it not to combine Vitamin administration with campaign. On the quality of Vitamin A used, UNICEF's chief of Child Development and Nutrition in India, Pat Engle said the agency uses locally produced Vitamin A doses which were tested beforehand. "Our team is right now in field and samples would be tested again. We do not need risk contamination" Engle said, adding there was a "fierce response" to the incident. There was always a small risk with Vitamin A administration but it was shortlived, she said, adding one per

cent children globally show symptoms like vomitting and diarrhoea. While about 3.2 million children were scheduled to be administered Vitamin A in the campaign, only 720 were hospitalised which comes to even less than point 25 per cent, she said. So far death has not been reported by an overdose of Vitamin A, Engle said. Kapil also agreed saying reactions can occur in children who already have some health problems and are severely malnourished.

However, Kapil cautioned that there might be some "commercial interests" in pursuing Vitamin A programme in campaign mode as there was only one company in the world which was producing Vitamin A. The best method was to supply Vitamin A through other sources like green leafy vegetables, Kapil said. But, UNICEF said studies in India indicated that only 50 per cent of Vitamin A need was met through fruits and vegetables. While in developed countries, Vitamin A needs are met through foods which are fortified with this vitamin, in countries like India there was hardly any food fortification. Besides, the poor would not be able to afford such food items, Engle said. Speaking against fortification of food products with Vitamin A, Kapil said what was true for developed world might not be suitable to India. The country had to set priorities as to whether it would provide Vitamin A which costs about Rs four, cost of administration included, or other essential drugs like that for Malaria, which causes many deaths in the country, he said. Meanwhile, Government now plans to reiterated earlier guidelines on Vitamin A administration and would advise States to be cautious in the administration of the vitamin.

NUT-1.

Blaming the dispenser

The Assam Human Rights Commission indicts the State government for the vitamin A-related deaths of 23 children in November.

R. RAMACHANDRAN

THE Assam Human Rights Commission (AHRC) has held the Government of Assam responsible for the vitamin A related deaths of 23 children after a "high dose vitamin A supplementation" campaign in the State in November last. In its inquiry report submitted to the State Chief Secretary on January 17, it said that a *prima facie* case exists that the deaths occurred owing to lapses on the part of the "agencies or instrumentalities or public functionaries" of the government, whether the children died "due to vitamin A poisoning or toxicity or allergy or coincident with the administration of vitamin A".

The mass administration campaign in the "pulse mode" approach, conducted to combat vitamin A deficiency (VAD) with the assistance and support of the United Nations Children's Fund (UNICEF), targeted 3.17 million children in the one to five age group. The high dose supplementation involved administering 2 ml (0.2 million International Units, or 60 mg) on a single day on November 11 and covered 2.8 million children. This resulted in 23 deaths and several hundred children suffered adverse toxicity effects (*Frontline*, December 21, 2001). Unlike two earlier rounds in Assam, which were linked to pulse polio campaigns, the one conducted on November 11 was a stand-alone vitamin A campaign as per the recommendations of the National Consultation of December 2000 that vitamin A supplementation should not be linked to pulse polio campaigns.

Significantly, the report has refrained from blaming UNICEF. One of the suspected causes for the deaths was the unilateral switch by UNICEF to the use of a 5 ml dispenser. The Government of India's stated norm is a 2 ml dose. The dispensing health workers were reportedly not warned of this or trained adequately. The Report, however, takes cognisance of the fact that a change in methods of dispensing in some areas might have resulted in the administration of a higher dose and that some children may have suffered side effects due to the plastic cup measuring out a mega dose.

According to AHRC Chairman Justice R.K. Manisana Singh, the Commission undertook a *suo motu* inquiry into the episode which, in its view, amounted to a *prima facie* case of human rights violation. However, since its jurisdiction was governed by the Human Rights Act of 1993, which is in respect of human rights violations by a public servant, and not a private individual, irrespective of any pending litigation – civil or criminal – in any court of law among the contending parties, the Commission did not have the authority to investigate the roles of NGOs like UNICEF.

Twenty-two children died within a week of administration. One child died on November 19. According to the report, 15 of these were in the one to three age group. Significantly, two cases were outside the target group – seven-month-old infant and a five-and-a-half year old child. Under the Central government recommended vitamin A intervention programme, the target age group is nine months to three years.

The AHRC considered two questions. One was whether the deaths were coincident with the vitamin A administration, and not due to vitamin A – a view expressed by some experts, given the high under five mortality rate (U5MR) in Assam. The second question was whether there was any violation of human rights by any public servant, and if so what steps should be taken by the government.

In order to substantiate the theory of coincidence, in his submission to the Commission the Director of Health Services of Assam had provided a statement detailing the cases of 31 children who died in the first post-week of the campaign. Of these eight had not received vitamin A.

However, having considered the causes of death from a medico-legal perspective, the Commission has rejected this premise on the grounds that the signs and symptoms preceding the deaths of several children were attributable to vitamin A toxicity or allergy, and distinct from other causes of common poisoning.

Further, a forensic examination of the viscera (stomach, kidney and liver) of two cases (of two years and three years respectively) was positive for vitamin A poisoning. The Commission has requested the authority concerned to preserve the viscera for future investigations. It also said that the opinions of experts were too theoretical and could not be accepted in the context of the case. Based on these considerations, the report has argued that there exists a strong *prima facie* case that some of the children died owing to vitamin A administration.

The Commission's conclusion with regard to the second question brings a better perspective to its conclusion with regard to the first. It has pointed out that the pamphlet (in Assamese) distributed to the health workers as part of the training did not contain any warning to the workers and the parents or guardians of the children about the possible side effects of high dose vitamin A administration. Also, the training did not give any consideration to the health status of the child and the pamphlet did not caution workers against giving vitamin A to sick or ailing children. Nor did it indicate whether vitamin A should be administered to a child suffering from chronic vitamin A toxicity, as even 2 ml may be a mega dose in such a case. Vitamin A may have precipitated the death of children already suffering from gastroenteritis, viral fever and other childhood diseases, the report has said.

It has pointed out that, significantly, the leaflet also did not warn the workers against exceeding the 2 ml limit while measuring out with a 5 ml cup. The supervision provided, in the form of one doctor for 10 booths, was also not sufficient to ensure safe administration. The Commission has also drawn attention to the report of the government analyst, the State Drug Testing Laboratory, Assam, in respect of the quality of vitamin A drawn from Batch No. VSD 22, which indicated "possible loss of potency on storage".

Acknowledging the importance of the vitamin A supplementation programme, it has made a set of recommendations for future campaigns, which includes examination of the quality of vitamin A, exclusion of sick and ailing children, supervision with one doctor per booth, warning against exceeding the dosage of 2 ml and that the dispenser should not have a capacity in excess of 2 ml.

The Chief Secretary and the Commissioner and Secretary of Health and Family Welfare Department will have to respond to the AHRC report, as well as state the actions taken, within two months. ■

Policy and perspective

A critique of the Science and Technology Policy–2001.

R. RAMACHANDRAN

FOR the last three months, the draft of a new science and technology (S&T) policy document has been under discussion among the science administrators of the country. Called the Science and Technology Policy–2001 (STP–2001), this draft of October 29, 2001, was prepared by a drafting committee set up by the Ministry of Science and Technology under the chairmanship of Goverdhan Mehta, Director of the Indian Institute of Science (IISc), Bangalore, and the then president of the Indian National Science Academy (INSA). The Mehta Committee has also come out with a document outlining the Action Plan and Implementation Strategy framework along with the STP-2001.

However, the pertinent question is: what necessitated the enunciation of a new policy? In terms of past policy enunciations in S&T, what we have today is the expression of a political commitment to science in the form of the Scientific Policy Resolution (SPR) of 1958 and the Technology Policy Statement of 1983 (TPS-1983). The development of S&T in the country has been guided all these years by these basic documents. In 1992-93, Minister for S&T Rangarajan Kumaramangalam proposed a Technology Policy. The Technology Policy Statement of 1993 (TPS-1993) was "aimed at giving a renewed sense of purpose to indigenous technology for its accelerated development and use in the context of the Industrial Policy Statement of 1991 and keeping in view the need to adhere to international quality systems as well as preserve the environment." Following the processes of economic reforms and industrial liberalisation that were initiated during the same period, it was a political initiative on the part of the Minister, rather than an initiative from the scientific community. The draft TPS-1993, as a revision to TPS-1983, was circulated among scientific institutions, Central and State level scientific departments, scientocrats and technocrats and the public for discussion. The draft was discussed at various levels but the policy, for reasons best known to the government, the change of party in power certainly being one, never saw the light of day.

Later, the Scientific Advisory Committee to the Cabinet (SACC), under the chairmanship of the Principal Scientific Adviser (PSA) to the government, A.P.J. Abdul Kalam, resurrected the TPS-1993 document to give it a new shape in the light of the ongoing process of globalisation and the emerging ground realities that indigenous technology development will have to face in the wake of trade regimes under the World Trade Organisation (WTO) system. The draft document prepared by the SACC was submitted to Human Resource Development Minister Murli Manohar Joshi after it was discussed and approved by the advisory committee comprising eminent scientists and the empowered committee comprising essentially secretaries to the government that function under the PSA.

The Minister called a discussion meeting to consider the SACC draft at the end of which he, in his wisdom, decided to set up yet another drafting committee under the IISc director. (Informed observers say that this provided evidence of the chasm that had developed between the Minister and Abdul Kalam, as a fallout of which the scientist is believed to have quit office.)

According to reliable sources, the Mehta Committee includes scientists whose views are close to the Bharatiya Janata Party's perspective on S&T development. In fact, one component of the new draft, pertaining to integration of science teaching with the "extensive knowledge acquired over long civilisational experience", is susceptible to the interpretation that it legitimises subjects such as Vedic Mathematics and Astrology. Although the SACC draft was not made public, people in the know said that the Mehta Committee's draft was somewhat different from the SACC draft.

The draft has been put up at the websites of various scientific departments and the scientific academies in a bid to solicit comments from the scientific community. The comments are to be considered by the new SACC headed by R. Chidambaram, the new PSA. The original idea was to evolve a final policy document to be announced at the December 2001 session of the Indian Science Congress in Lucknow. Politically speaking, this was to parallel the announcement of TPS-1983 by Prime Minister Indira Gandhi. However, it appears that the process could not be completed in time.

Besides the imperatives warranted by the process of globalisation and the impact of the WTO regime, the apparent aim of the SACC was to integrate both the S&T policy statements in a single document instead of the earlier separate documents of 1958 and 1983. In fact, in the otherwise excellently phrased SPR, the importance given to technology development was only secondary. It said: "...technology can only grow out of the study of science and its applications." While the truth of the statement cannot be denied, the focus of the wording of the SPR was to foster and nurture science in the country. The sharp distinction between science and technology is no longer possible with the advances currently in evidence, especially in the emerging field of biotechnology where the time and space difference between discovery and application has become extremely short. Conversely, high technology is increasingly being used in the laboratory to do modern basic research. From such a perspective, a single document may seem reasonable.

However, the way the SPR was worded did not imply that technology development itself was not on the same footing as science. In fact, following the clearing of the SPR, the identification of the steps involved in the implementation of the SPR and the task of working out a plan of action was taken up by the government, resulting in three national level conferences (in 1958, 1963 and 1970) that brought together scientists, educationists and industrialists. Moreover, a round-table conference of young scientists was called by the Prime Minister in 1967 to get their perspectives on critical issues.

The setting up of the National Committee on Science and Technology (NCST) in 1971, at the initiative of C. Subramaniam, was an important step towards systematic planning in the S&T sector. In 1973, the NCST brought out a policy document titled "An Approach to Science and Technology Plan". It was a classic document that addressed all the relevant issues concerning the demand and supply components of S&T development – forward, backward and horizontal or inter-sectoral linkages, fiscal issues and funding patterns, industrial participation and investment in research and develop-

Community Health Cell

From: "umesh kapil" <kapilumesh@hotmail.com>
To: <kuber_routela@hotmail.com>
Sent: Saturday, April 26, 2003 2:51 PM
Attach: IDA-India.txt
Subject: Fwd: iron deficiency anemia-India

Dear colleague,

I am sending you a recent publication as an attachment entitled "Prevention and control of iron deficiency anemia amongst young children". I hope you will find it informative and useful.

With personal regards
Umesh Kapil
(Dr Umesh Kapil)
Additional Professor Public Health Nutrition
Department of Human Nutrition
All India Institute of Medical Sciences,
New Delhi 110 029, INDIA tel No. (R) 91-11-26195105, (Off) 26593383
For All details of Past , Present and Future of IDD in India-Please Visit Web Site iddindia.20m.com
From: "umesh kapil"
To: kapilumesh@hotmail.com
Subject: Iron deficiency anemia-India
Date: Fri, 25 Apr 2003 07:10:43 +0000

Dear colleague,

I am sending you a recent publication as an attachment entitled "Prevention and control of iron deficiency anemia amongst young children". I hope you will find it informative and useful.

With personal regards
Umesh Kapil
(Dr Umesh Kapil)
Additional Professor Public Health Nutrition
Department of Human Nutrition
All India Institute of Medical Sciences,
New Delhi 110 029, INDIA tel No. (R) 91-11-26195105, (Off) 26593383
For All details of Past , Present and Future of IDD in India-Please Visit Web Site iddindia.20m.com

TN
28/4

Do you want to print out the attachment.
Yes - for Nutrition Resource file in Library
29/4

4/28/03

Indian Pediatrics 2003; 40:293-295

Prevention and Control of Iron Deficiency Anemia Amongst Young Children

Iron deficiency remains a major nutritional problem among infants and young children in India. The National Family Health Survey II, conducted in 1998-99, documented that about 74 per cent children between the ages of 6-35 months were anemic(1). Earlier studies from different regions in the country during the last three decades have also reported a similar high prevalence(2-7).

Since 1990, outstanding progress has been made towards eliminating iodine deficiency through universal salt iodization. Vitamin A deficiency is being aggressively addressed through nationwide biannual distribution of vitamin A solution to infants, young children and fortification of foods. However, during this same period, little progress has been made towards elimination of iron deficiency. Iodine and vitamin A deficiencies receive far greater attention and support due to more intense advocacy efforts by international and bilateral organizations. Simultaneously, an erroneous perception exists amongst the health adminis-trators and planners that effective and practi-cal interventions are not available for prevent-ing iron deficiency. Iron thus continues to remain the most "neglected micronutrient" in spite of it's greater burden on health.

Evidence indicates that iron deficiency anemia is associated with impaired performance on a range of mental and physical functions in children including physical coordination and capacity, mental development, cognitive abilities, and social and emotional development(8). Other health consequences include reduced immunity, increased morbidity, increased susceptibility to heavy metal (including lead) poisoning. The precise effects vary with the age groups studied. Recent studies have documented that the iron supplementation at a later age may not reverse the effects of moderate to severe iron deficiency anemia that occured during the first 18 months of life(9-12).

It is true that National Nutrition Anemia Control Program (NACP) was launched in the country in 1970. It was supposed to cater to children between 1-5 years of age. Under this program, fifty per cent of children were to be given 100 tablets of iron and folic acid (IFA) per year for prophylaxis against nutritional anemia(13). However, the children below 24 months can not swallow the tablets and there is no provision of IFA liquid preparation in the program. Consequently, the children in this age group largely remained uncovered.

The health consequence of iron deficiency during first two years of life are not only serious but also irreversible. Paradoxically, during this critical "window" no effectively functioning supplementation program is in place to prevent iron deficiency. It is evident that strong concerted efforts need to be undertaken to improve the scenario(14). Some of the possibilities in this context are enumerated below (i) inclusion of IFA liquid under the NACP and targeting iron supplementation to children in the age group of 6 35 months on a priority basis (ii) initiating iron supplementation of all anemic and non anemic women/adolescent girls in the community so that they can enter pregnancy with adequate iron stores, (iii) promotion of exclusive breast feeding for all infants as it plays a significant role in preventing iron deficiency in both infants and their mothers, (iv) full term infants (of mothers with adequate iron stores), who are exclusively breastfed do not need supplemental iron until they are 6 months of age. After this age, breastfed infants should be given extra iron in the form of iron-fortified home made complementary foods. Where

iron-fortified complementary foods are not widely or regularly consumed by young children, all infants should receive iron and folic acid supplements after six months of age.

It is often argued that the liquid iron supplements are costly to transport and store, and require packaging to enable caregivers to provide it in an effective, correct, and safe manner. However, no attempt has been undertaken to prove this assumption. Even if this approach is costly, there is a strong need to experiment with it on a pilot basis.

IFA supplementation should be done through the peripheral health and integrated Child Development Services Scheme functionaries at the village level. Home visit once in a month is a part of the routine responsibilities of Anaganwadi Worker and Auxiliary Nurse Midwife, which can be utilized for distribution of the IFA. Various contact points like measles immunization (9 months), DPT booster (16 months) and take home ration day in ICDS scheme (where ever followed) should be utilized for distribution of IFA. Other village level developmental functionaires/voluntary persons available in the community may also be utilized for IFA supplementation, monitoring the compliance and side effects and for counseling the mother about the benefits of IFA. An effective step would be to make the IFA available at the village level through the net work of health sub-centers and anganwadi centers.

In conclusion, there is an urgent need to initiate specific public health action to prevent iron deficiency in young children. The time for meticulous planning is over, what is needed is immediate action.

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AN INDIAN VIEW POINT FROM A COMMUNITY HEALTH PERSPECTIVE

1. At the dawn of the new millennium, with all its new wealth, knowledge and technology base, it is critical we take an honest and hard look at the hunger and food security situation of the poorest among us. They continue to suffer and be marginalised even while government commitments are made in global UN conferences that reaffirm their fundamental human rights and their access to adequate food.
We here offer an evidence-based synthetic situation analysis of India...which holds one fifth of the world's population.

2. A 1996-97 survey (NIN, 1999) revealed the disturbing magnitude of the problem in comparison with earlier surveys in the country. **Smaller studies and news reports reinforce the findins.** 48% of households had chronic energy deficiencies; in two decades, the proportion of well-nourished children under 6 years increased only from 5.9% to 8.9%; stunting was at 57%; a decreasing trend in intake of protein, energy, iron and calcium was also documented as was a lower consumption of cereals, millets and pulses in all states plus inadequate consumption of milk, milk products, sugar, and green leafy vegetables; the IMR in 10 states has stagnated or even worsened during the past 5 years; the proportion of low birth weight babies continues to be a high 30%.
However the most significant finding was that nutrition and food security was being severely compromised by the economic development policies being applied:
The proportion of landless households increased from 30-41% in ten years and there was a fragmentation of the landholding size contributing to increased food insecurity; (prices of agricultural commodities were crashing causing distress among poor farmers;) during the same 10 years, the average per capita income per month increased by the equivalent of only approximately 50 pence at constant prices. Other sources report that an increase in suicides, indebtedness, unemployment and migration is being seen; lack of money is causing delayed marriages, mass marriages, pawning of household assets and overall impoverishment.

3. In the state of Karnataka, where we live, hunger and hidden hunger remains widely prevalent, adversely affecting children's physical and intellectual development with the consequent negative impacts on households/families, affected communities and the nation.

4. This situation is symptomatic of deep societal disparities and compels us and the international community to address the root causes of poverty and hunger, namely social, economic and political injustice.
Broader people-centred policies, access to markets, the lifting of agricultural subsidies in the North and greater social security in the South, the removal of barriers to developing countries international trade, a halt to the negative effects of globalization and trade liberalization are all needed to reverse the negative social effects we are seeing, including adverse nutritional effects.
Public distribution systems which make essential food grains available to people are being forced to rise prices and reduce coverage rather than helping to increase equity and act as genuine safety nets.

5. Development strategies wich changed agricultural practices in India are
depleting the soil of micronutrients; this is passed on to foods. In the meantime pharmaceutical houses aggressively market vitamins and minerals and influence government agencies to introduce them into mass-based health programmes for women and children. Genetically modified crops and foods are being quietly introduced as well.

6. The role of the state is being eroded. Between 1990 and 2000, in Karnataka, expenditure on nutrition interventions declined 4.3% a year (in real terms) adversely affecting nutrition support services. World Bank loans are being taken for health and nutrition while structural adjustment and global trade agreements increase economic vulnerability and food insecurity of a large majority.

7. In this context, the Indian Peoples Health Charter adopted by a widely representative countrywide group in a National Health Assembly in Calcutta in December 2000, expressed strong concerns and made concrete demands regarding agriculture, trade, pricing and public health . The global Peoples Charter for

Health adopted by the Peoples Health Assembly in Dhaka in December 2000 also raised these concerns (www.phamovement.org) and a worldwide movement is now being organised to systematically follow-up on these issues.

8. Given this reality --at the end of 2001 and five years after the WFS-- we have more unanswered questions than answers. **W**here exactly are we in relation to its 1996 Plan of Action? and Where do we see economic and social rights taking central stage in the struggle against hunger and malnutrition? What is being done to address the root causes of malnutrition and the **ineffectiveness** of nutrition programmes we currently see being implemented? Can collective peoples rights (as much as individual human rights), as well as the social accountability of the big players be more clearly put on the agenda? These seem to be urgent agenda issues for a more **assertive** and better inter-connected civil society.

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ORIGINAL ARTICLES

Efficacy of vitamin A in reducing preschool child mortality in Nepal

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Community trials of the efficacy of vitamin A supplementation in reducing preschool childhood mortality have produced conflicting results. To resolve the question, a randomised, double-masked, placebo-controlled community trial of 28 630 children aged 6–72 months was carried out in rural Nepal, an area representative of the Gangetic flood plain of South Asia. Randomisation was carried out by administrative ward; the vitamin-A-supplemented children received 60 000 retinol equivalents every 4 months and placebo-treated children received identical capsules containing 300 retinol equivalents. After 12 months, the relative risk of death in the vitamin-A-supplemented compared with the control group was 0·70 (95% confidence interval 0·56–0·88), equivalent to a 30% reduction in mortality. The trial, which had been planned to last 2 years, was discontinued. The reduction in mortality was present in both sexes (relative risk for boys 0·77; for girls 0·65), at all ages (range of relative risks 0·83–0·50), and throughout the year (0·76–0·67). The reduction in mortality risk was not affected by acute nutritional status, as measured by arm circumference. Thus, periodic vitamin A delivery in the community can greatly reduce child mortality in developing countries.

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Introduction

Vitamin A deficiency is associated with an increased risk of childhood morbidity[1–3] and mortality[4] in developing countries. Community trials of vitamin A supplementation in Indonesia[5,6] and India[7] reported annual reductions in preschool child mortality of 34% to 54%. However, another field trial in India failed to confirm a reduction in child mortality with vitamin A;[8] thus, concern was raised about the potential impact of improved vitamin A nutrition on child survival across different cultures.[9–11]

As a follow-up to the original large-dose vitamin A trial in Indonesia,[5] a community trial in rural Nepal was undertaken to assess the efficacy of vitamin A supplementation every 4 months in reducing preschool child mortality. Such supplementation is recommended by the World Health Organisation for prevention of xerophthalmia[12] and may represent an achievable delivery schedule for child survival.

Study population and methods

A randomised, double-masked, placebo-controlled vitamin A supplementation trial was carried out from September, 1989, to December, 1990, in the rural, plains (Terai) district of Sarlahi. This area was selected because it has endemic vitamin A deficiency,[13] no previous vitamin A supplementation programme, and ecological, cultural, and demographic similarities to the Gangetic floodplain communities of South Asia, with which it is continuous; the factor enhances the general applicability of the findings.

29 local development units, each containing 9 administrative wards, were selected for the trial. In 1988 the area had a population of 144 000 with about 28 000 children (19·0%) under 5 years of age (Census Report of the District Public Health Office, Sarlahi, Nepal,

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TABLE I—BASELINE CHARACTERISTICS OF STUDY CHILDREN

	No (%)	
—	Control (n = 12 264)	Vitamin A (n = 12 541)
Sex		
Male	6265 (51·1)	6479 (51·7)
Female	5999 (48·9)	6062 (48·3)
Age (mo)		
6–11	1290 (10·5)	1356 (10·8)
12–23	2806 (22·9)	2827 (22·5)
24–35	2696 (22·0)	2827 (22·5)
36–47	2624 (21·4)	2595 (20·7)
48–60	2848 (23·2)	2936 (23·4)
*Measles during previous 4 mo**	759 (6·2)	639 (5·1)
Morbidity ≥ 1 day during previous week†		
Diarrhoea	1214 (11·0)	1244 (11·0)
Dysentery	506 (4·6)	508 (4·5)
High fever	1882 (17·0)	1936 (17·1)
Persistent cough	1609 (14·5)	1720 (15·2)
Arm circumference (cm)		
< 11·5	420 (3·8)	380 (3·4)
11·5–12·4	1032 (9·4)	1109 (9·9)
12·5–13·4	2859 (26·1)	2836 (25·3)
≥ 13·5	6652 (60·7)	6890 (61·4)
Total‡	10 963	11 215
Xerophthalmia§	66 (3·5)	52 (2·6)

*Data missing for 69 controls and 42 vitamin A children.
†Assessed only for children reported to be at home for all of the previous 7 days (about 90% of children).
‡Not measured on 2627 (11%) children at baseline.
§Nightblindness, Bitot's spots, corneal xerosis, keratomalacia; assessed in a random 15% sample of 40 wards (n = 4274 children: 1871 control, 2024 vitamin A, 379 not examined). There were 2 corneal cases, 1 in each group.

TABLE II—HOUSEHOLD CHARACTERISTICS AT TIME OF ENTRY

	No (%)	
—	Control	Vitamin A
Mother's age (yr)		
<20	860 (8·6)	873 (8·7)
20–29	5586 (55·9)	5662 (56·1)
≥30	3540 (35·4)	3551 (35·2)
Total	9986	10 086
Mother's education (any)	912 (9·1)	1018 (10·1)
History of ≥ 1 child death	4177 (41·9)	4200 (42·0)
Occupation of head of household		
Farmer	5218 (58·0)	5288 (58·1)
Labourer	2250 (25·0)	2174 (23·9)
Other	1536 (17·0)	1636 (18·0)
Total	9004	9098
Household owns radio	1832 (20·3)	1942 (21·3)
Preschool child/infant death in previous year	355 (3·9)	374 (4·1)

1989). Signed statements of consent were obtained from all 29 chairmen on behalf of their communities. Participation of wards, households, and children in the trial was voluntary at all times.

The ward served as the unit of treatment allocation. Local development units were ordered by geographic areas and wards by population size within each local development unit. After a random start, each of the 261 wards was systematically allocated to one of four coded batches of supplements. Two codes contained a standard 60 000 μg retinol equivalent (200 000 IU) dose of vitamin A and two served as control, containing 300 retinol equivalents (1000 IU) of vitamin A (retinyl palmitate in arachis oil; Roche, Basel, Switzerland). All supplements contained 40 IU vitamin E as an antioxidant. The supplements were given as single-dose gelatin capsules of identical taste and appearance. Every 4 months two capsules of each code, sampled from the study area, were analysed for vitamin A potency by a local laboratory unaware of their code. The mean retinol contents were 53 300 (SD 3513) and 246 (27) retinol equivalents, which is equivalent to 89% and 82% potency for the vitamin A (n = 19) and control (n = 20) capsules, respectively.

All households in a ward were visited by trained field staff every 4 months for a year. At baseline, children of 60 months and younger were enrolled; at follow-up visits only infants born during the study were later enrolled. Birth dates of children were determined by means of local events and Nepali astrological calendars. At each visit infants aged 6–11 months received half the contents of a capsule (6 drops of oil), equivalent to either 30 000 or 150 retinol equivalents, respectively, and children of 12 months and older received the whole contents of the capsule. After repeated household visits when children were absent, capsules were left in the home and the parents were asked to administer them. Families and childen who moved within a ward were followed at each visit; those who moved out of a ward (less than 2% per round) were declared withdrawn at the next household visit. At each visit, a child's capsule receipt and vital status were recorded, left mid-upper arm circumference was measured with an insertion tape,[14] and 7-day morbidity and 4-month measles histories were taken. Children of 12 months and older with an arm circumference below 11·5 cm were referred to local health posts. At the time of enrolment household and demographic indicators were assessed, including maternal histories of previous child mortality by the Brass method.[15]

At baseline an ocular survey was carried out in a 15% random sample of wards (n = 40). Children were examined for xerophthalmia at a central site by an ophthalmologist (S. K. K.) or a senior ophthalmic assistant. Chance-corrected inter-observer agreement,[16] based on 1001 independent replicates, was excellent (κ = 0·93). A history of night blindness ("ratandho/ratauni") was elicited from parents for children of 12 months and older. All xerophthalmic and severely ill children were treated with vitamin A and referred to local health posts for follow-up, as indicated. These children are included in the analysis. Full details of this substudy will be published elsewhere.

Child deaths were identified by means of the regular 4-monthly census and by an independent vital events surveillance every 2 months in every ward. A "verbal autopsy" interview was carried out, usually within 2 months of death, for all children who died. Data were reviewed and probable causes of death were assigned independently by two physicians. Differences in assignment were discussed and a consensus cause of death assigned.

Capsule codes were broken and the four groups merged into control and vitamin A treatment groups. Baseline differences were tested by chi-square.[17] All analyses were carried out on an intention-to-treat basis. Computed mortality rates were based on child-years of observation. Relative risks were derived with all variance and 95% confidence interval estimates[17] adjusted to account for the design effect[18]—ie, the ward rather than individual serving as the unit of treatment allocation. Mortality rates and

TABLE III—INTERVAL-SPECIFIC AND ANNUAL MORTALITY OF CHILDREN 6–72 MONTHS OF AGE

	Time interval (x to x + 4)			
	0–4 mo	4–8 mo	8–12 mo	0–12 mo
No entered at x	24 805	1807	2018	28 630
Control	12 264	834	1045	14 143
Vitamin A	12 541	973	973	14 487
Withdrawals				
Control	174	207	152	533
Vitamin A	154	201	214	569
Child deaths				
Control	62	72	76	210
Vitamin A	48	51	53	152
*Child-years**				
Control	4049	4241	4505	12 795
Vitamin A	4147	4395	4633	13 175
Mortality (per 1000 child-years)				
Control	15·3	17·0	16·9	16·4
Vitamin A	11·6	11·6	11·4	11·5
Relative risk	0·76	0·68	0·67	0·70
(95% CI)	(0·50–1·15)	(0·45–1·00)	(0·45–0·99)	(0·56–0·88)

*Children who were withdrawn or who died during an interval were assigned ½ months of observation.

11·6
15·3

TABLE IV—ANNUAL MORTALITY OF CHILDREN AGED 6–72 MONTHS BY AGE AND SEX

	Control			Vitamin A			Relative risk (95% CI)
	Child-years	Deaths	MR	Child-years	Death	MR	
Sex							
Male	6531	89	13·6	6821	72	10·6	0·77 (0·55–1·09)
Female	6263	121	19·3	6354	80	12·6	0·65 (0·48–0·89)
Age (mo)							
6–11	1315	47	35·8	1393	39	28·0	0·78 (0·49–1·25)
12–23	2725	75	27·5	2790	53	19·0	0·69 (0·47–1·01)
24–35	2592	31	12·0	2724	27	9·9	0·83 (0·47–1·50)
36–47	2633	28	10·6	2657	18	6·8	0·64 (0·33–1·24)
48–59	2573	25	9·7	2649	13	4·9	0·51 (0·24–1·07)
60–72	956	4	4·2	964	2	2·1	0·50 (0·08–3·29)

MR = mortality rate (per 1000 child-years).

relative risks were calculated across strata of age, sex, and nutritional status. A Poisson regression model[19] was fitted to estimate the effect of vitamin A on mortality with simultaneous adjustment for each of these factors.

The study protocol was approved by the Nepal Health Research Council in Kathmandu, Nepal, and by the Joint Committee on Clinical Investigation at the Johns Hopkins University School of Medicine in Baltimore, USA.

Results

24 805 children aged 6–60 months entered the trial at baseline (12 264 in the control group and 12 541 in the vitamin A group), which represented more than 96% of all children of eligible age in the study area. The two groups of children were very similar in their distributions of demographic and clinical characteristics (table I). The pooled prevalence of xerophthalmia in the random subsample of wards was 3·0%.

Treatment groups were also practically identical on more than 25 characteristics assessed in all participating households, including risk factors commonly associated with preschool child mortality (table II). In both treatment groups, at least one of the liveborn children of 42% of mothers had died, and 4% of households reported at least one preschool child death during the previous year. During the year before the trial in both treatment groups, the estimated infant mortality rate was 82 per 1000 livebirths and the 1–4-year-old mortality rate was 12–13 per 1000 children per year. Thus, the two groups showed no differences in many risk factors for mortality and by reported past mortality at the outset and were taken to represent the same population.

Capsule coverage remained high and equal in each group throughout the trial—about 88% of children in each group received the capsule contents from the staff at each visit. Capsules were left in the home for about 10% of children at each visit, of whom about 65% were estimated (by history on follow-up of a subsample) to have received the capsule contents from the parents. Thus, about 93% of all eligible children in each group received a supplement at each visit. At least 74% of all enrolled children in each group were known to receive their full quota of supplements; only 2% failed to receive any supplement.

TABLE V—ANNUAL MORTALITY OF CHILDREN AGED 6–72 MONTHS BY NUTRITIONAL STATUS AND AGE

Arm circumference (cm)	Control			Vitamin A			Relative risk (95% CI)
	Child-years	Deaths	MR	Child-years	Death	MR	
Children aged 6–11 mo							
<11·5	132	14	106·3	126	12	94·9	0·89 (0·37–2·12)
11·5–12·4	261	12	45·9	267	6	22·5	0·49 (0·17–1·41)
12·5–13·4	392	8	20·4	432	10	23·1	1·13 (0·40–3·16)
⩾13·5	346	6	17·3	387	6	15·5	0·89 (0·25–3·11)
Unknown	184	7	38·0	179	5	27·9	0·73 (0·20–2·62)
Children 17–72 mo							
<11·5	208	61	293·3	191	33	172·6	0·59 (0·39–0·90)
11·5–12·4	721	15	20·8	759	24	31·6	1·52 (0·75–3·08)
12·5–13·4	2132	30	12·9	2371	16	6·7	0·52 (0·27–1·00)
⩾13·5	6986	35	5·0	7150	29	4·1	0·82 (0·48–1·41)
Unknown	1232	22	17·9	1310	11	8·4	0·47 (0·21–1·03)

MR = mortality rate (per 1000 child-years).

The initial 24 805 children plus 3825 infants who entered the 6–11 month age range at the first or second 4-monthly visits (1879 controls, 1946 vitamin A) provided a total of 28 630 children who contributed 25 970 child-years of observation for this analysis (table III). There were 362 deaths during the 12 month period. The annual mortality rate was 16·4 per 1000 child-years in the control group and 11·5 per 1000 child-years in the vitamin A group, which gives a protective relative risk of 0·70 (95% CI 0·56–0·88) for a 30% reduction in child mortality. This CI and all others reflect a 23% increase in the estimated variance due to the design effect. The difference in risk increased from the first to the second interval of dosing and then remained stable during the third interval, which indicates a sustained effect.

The effect of vitamin A was evident across sex and age strata (table IV). There was a slightly greater reduction in mortality in girls than in boys. The excess female/male mortality ratio was somewhat smaller in the vitamin A than in the control group (relative risk 1·19 *vs* 1·42). The protective effect of vitamin A was consistent at each age and, except for children aged 24–35 months, became stronger with age (table IV).

The effect of acute nutritional status on the impact of vitamin A during a subsequent 4-month interval was examined separately in infants and older children (table V). Although arm circumference was measured at least once in 97% of the children, only 89% were measured at each visit, thus reducing by 11% the number of child-intervals for this analysis. In 8 of 10 age-status-specific strata, including the most malnourished and the best nourished children, vitamin-A-supplemented children had lower mortality ($p < 0·05$ by Wilcoxon signed rank test). No trend in the effect was observed with severity of wasting.

Multivariate analysis did not change the effect estimate. The relative risk of death in the vitamin A group, after simultaneous adjustment for the effects of sex, age, and

nutritional status by Poisson regression, was 0·72 (95% CI 0·55–0·95).

Based on 358 completed verbal autopsy reports, vitamin A seemed to reduce mortality ascribed to diarrhoea or dysentery (relative risk 0·61), wasting malnutrition (0·65), uncertain (infectious) causes (0·52), and measles (0·24). These "probable causes" accounted for 28%, 20%, 19%, and 4% of all deaths, respectively, in the combined groups. There was no apparent effect on mortality due to acute lower respiratory infection (1·29) or other miscellaneous causes (1·01), which accounted for 18% and 11%, respectively, of all deaths.

Discussion

Since the initial report from Indonesia on the effectiveness of periodic, large-dose vitamin A supplementation in reducing child mortality,[5] there have been several attempts to clarify the effect of vitamin A on child survival in different populations. Most trials have reported a profound effect, but one trial did not show a significant reduction in child mortality,[8] for reasons which remain unclear.[9-11]

More frequent supplementation of children with vitamin A may have a greater effect on child survival than less frequent dosing—supply of about half of a preschool child's daily requirement by way of fortification reduced mortality by 46% in Indonesia,[6] and weekly vitamin A doses of 2500 retinol equivalents reduced mortality by 54% in south India.[7]

The reduction in mortality was slightly greater in girls than in boys, which accords with the south Indian study.[7] As in Indonesia,[5] the effect of vitamin A in Nepal was stronger with age, reaching a 50% reduction in mortality in the fifth and sixth years of life. By contrast, the south Indian trial found the greatest effect among infants 6–11 months of age.[7] This variability may reflect differences in the age specificity and severity of vitamin A deficiency and other determinants of child mortality in different populations. Given the wide confidence intervals for all age-specific findings in all studies, it may also be chance variation.

A very small arm circumference (less than 11·5 cm) at the start of each interval was associated with a very high risk of mortality (table v), despite referral of such children to local health posts. However, acute nutritional status did not seem to modify the protective effect of vitamin A. A consistent effect of vitamin A across categories of wasting was also observed in south India, although its effect was stronger in stunted children.[7]

It is likely that vitamin A modifies the incidence, duration, or severity of life-threatening infectious illness, as seen with severe measles.[20,21] The verbal autopsy suggested that vitamin A had no effect on mortality attributed to acute lower respiratory infection. This finding is surprising, because there is evidence that vitamin A deficiency is linked to increased risk of respiratory infection.[22] However, the 40% reduction in deaths attributed to diarrhoea and dysentery is consistent with evidence that closely links mild xerophthalmia to risk of protracted diarrhoea.[23-25] The substantial reduction in mortality from measles (76%) is consistent with vitamin A measles intervention trials[20,21] from Africa and the weekly supplementation trial from India.

This trial provides a firm estimate of the efficacy of large-dose vitamin A prophylaxis in an endemically vitamin-A-deficient population. The large sample size, the similarity of the treatment groups, the high coverage while minimising visits to avoid a "contact" effect,[7] the checking of capsule potency, and the high level of ascertainment help to support the validity of the findings. A 30% reduction in preschool child mortality predicts that, in Nepal alone, where 2% or more of preschool children are xerophthalmic,[26] more than 15 000 deaths could be averted each year by adequate nourishment of children with vitamin A. In south Asia 0·7–1·1 million child deaths could probably be prevented annually by adequate vitamin A nourishment in the preschool years (J. Humphrey and colleagues, unpublished).

Although periodic, large-dose delivery may lead to a more modest reduction in child mortality than more frequent, smaller doses, this approach is a feasible strategy for most developing countries seeking to reduce child mortality with vitamin A by means of immediately available and affordable delivery systems.[27]

Periodic dosing should not preclude, or compete with, efforts to improve the local food supply and dietary vitamin A intake by vulnerable groups (eg, by means of gardens, dietary counselling, and fortification). However, there may be a compelling reason, in terms of child survival, to control vitamin A deficiency quickly through periodic supplementation while longer-term solutions are pursued.

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Automated Perimetry: A Study of the Glaucoma Hemifield Test for the Detection of Early Glaucomatous Visual Field Loss

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Summary: In order to verify the ability of the Glaucoma Hemifield Test in detecting early glaucomatous alterations, as well as its sensitivity, specificity, and reproducibility, 78 glaucoma patients, glaucoma suspects, and normals were selected. In those eyes who presented alterations of the optic disc suggestive of glaucomatous damage, but with no typical lesions in the visual field, the test was positive in 18.4% of the cases. The sensitivity, specificity, and reproducibility of the test were 100, 100, and 83.3%, respectively. Key Words: Automated perimetry—Optic disc—Glaucoma Hemifield Test.

One of the major objectives of perimetry in glaucoma is to detect any possible evidence of lesion at the earliest possible stage in order to prevent its progression by using the appropriate therapeutic treatment. In this sense, the automated perimetry has been helpful, allowing the detection of visual field defects at an earlier stage than manual perimetry (1–5).

Numerous strategies have been developed in computerized perimetry with the objective of increase its sensitivity in the detection of early glaucomatous alterations (6–9). In 1985, Duggan et al. (10) proposed a test in which the visual sensitivity thresholds were compared across the horizontal field meridian. Preliminary studies (10) have shown that the specificity and sensitivity of the detection of early glaucomatous lesion by this method reached 94% and 92%, respectively, based on Goldmann perimetry. Such a fact is based on the observation, originally described by Hart and Becker (11) and confirmed by Mikelberg and Drance (12) and by Drance et al. (13) that the loss in the visual field in glaucoma occurs asymmetrically along the horizontal meridian.

Later, in 1989 (14), a similar test is incorporated to the Humphrey Field Analyzer (STATPAC 2) with the name Glaucoma Hemifield Test (GHT), which provides an analysis based on difference of probability scores across the horizontal field meridian and also detects alterations if the two corresponding clusters have a total depression of sensitivity (Fig. 1).

The present study was done in order to verify how early the GHT detects glaucomatous alterations and also its specificity, sensitivity, and reproducibility.

PATIENTS AND METHODS

A total of 160 patients who have done at least three perimetric examinations with the Humphrey's C30-2 automated perimetry program were studied.

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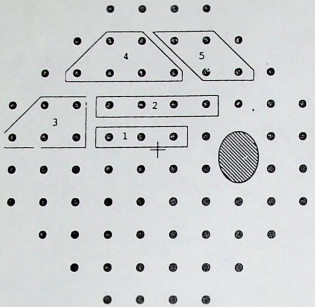

FIG. 1. A scheme of the Glaucoma Hemifield Test, with the five superior clusters of points which are compared with their mirror image clusters in the inferior meridian. (From ref. 14, with permission.)

In each case, maximum intraocular pressure (IOP) presented during the follow-up period was noted. The vertical cup to disc ratio (C/D) was analyzed from stereoscopic photographs of the optic disc by two experimental observers who didn't know other data from the patients.

The eyes were classified into three groups, the first being further subdivided into three. Eyes that could not be classified in these three groups were excluded. Only patients who had the same size of optic disc were considered. When two eyes of the same patient matched the criteria to be included in this study, we selected only one eye randomly. Also, patients with retinal or optic nerve disease besides glaucoma were excluded. No patients were under pilocarpine or other miotic medication. Only visual field tests performed with pupil diameter of ≥3 mm were considered.

The following groups were defined:

Group 1. Consisting of those eyes in which there is a clinical impression of glaucomatous damage of the optic nerve head without, however, exhibiting typical glaucoma perimetric defects (as defined in group 2). 1A: Those which presented C/D of >0.5, showing an asymmetry with the contralateral eye of ≥0.2 and IOP of >22 mm Hg. 1B: Primary open angle glaucoma patients with one eye with CD of >0.5 independently of the IOP levels in which the contralateral eye showed typical glaucomatous visual field defect. 1C: Those with CD of ≥0.7 associated with an IOP of >22 mm Hg.

Group 2. Consisting of those eyes with a typical visual field defect, characterized by a nasal step and/or a paracentral or arcuated scotomas, consisting in two or more adjacent points shown in the probability graph ($p < 0.05$) of pattern deviation, and reproducible in at least two perimetries.

Group 3. Consisting of those eyes in which there isn't the clinical impression of glaucomatous damage of the optic nerve head, which was defined by a C/D of <0.4 and contralateral asymmetry of ≤0.1 and no typical visual field defect.

The last two visual field examinations of each patient were considered for the study of reproducibility of the GHT. Only the last visual field of each patient was considered for the studies of sensitivity and specificity, and also to study how early the GHT is able to detect glaucomatous alterations.

RESULTS

Seventy-eight patients matched the criteria established above. They were 39 males and 39 females. The interval between the last two visual field examinations of each patient ranged from three to 26 months (average of 10.4 ± 5.9 months).

Group 1 consisted of 38 eyes from 38 patients, nine eyes belong to subgroup 1A, 20 eyes to 1B, and nine eyes to 1C. Thirty-seven patients had visual acuity of ≥20/30, and only one patient had visual acuity of 20/40. From a total of 38 eyes, the GHT was positive in seven eyes (18.4%; confidence limits from 12.4 to 24.4%[a]). Table 1 shows the data from group 1.

Group 2 consisted of 23 eyes belonging to 23 patients. The visual acuity of these patients ranged from 20/20 to 20/100, and 17 patients had visual acuity of ≥20/30 (73.9%). The GHT was positive in all eyes from this group.

Group 3 included 17 eyes from 17 patients without clinical evidences of optic nerve damage and no typical visual field defect. The GHT was negative in all eyes of this group. The visual acuity of all patients was equal to or better than 20/25. Table 2 shows the data from groups 2 and 3.

Table 3 shows the distribution of visual acuity in the three groups. There wasn't a statistical difference between the visual acuity of patients from

[a] For a coefficient of 95%.

TABLE 1. *Data from group 1*

	No. patients	Sex M	Sex F	Age (mean ± PD)	GHT N	GHT % pos.	GHT CL (%)
Subgroup A	9	5	4	50.7 ± 10.1	1	11.1	1.2–21
Subgroup B	20	14	6	56.3 ± 13.6	4	20.0	11.5–28.5
Subgroup C	9	5	4	52.8 ± 16.3	2	22.2	8.4–36
Total	38	24	14	54.2 ± 13.8	7	18.4	12.4–24.4

M, male; F, female; PD, pattern deviation; N, number of positives GHT; % pos., percentage of positive GHT; CL, confidence limits, for a coefficient of 95%.

groups 1 and 3, but the visual acuity of both was statistically different from patients of group 2 ($p < 0.0001$, χ^2 test).

There was a high statistical difference between the groups 1 and 3 in respect to the positivity of the GHT ($p = 0.0055$, Student's t test).

The results of the GHT obtained in the two visual field tests were the same in 65 eyes of the 78 eyes studied (83.3%). From the 33 eyes in which the first GHT was positive, 25 remained positive in the second test (75.8%). From the 45 eyes in which the first GHT was negative, 40 eyes remained negative in the second test (88.9%).

The average interval of time between the two GHT of each patient in the group in which they were reproducibles and in the group in which they were not were 10.71 ± 6.02 and 8.69 ± 5.40 months, respectively. This difference was not statistically significant ($p = 0.13$, Student's t test).

DISCUSSION

Perimetric study is essential for the early diagnosis of glaucomatous lesion as well as in the evaluation of its progression. However, some authors suggest that the visual field damage appears only when a significant number of nerve fibers was lost (15–18). In this sense, the automated perimetry offers a great help, because it can detect the damage at an earlier stage than the manual perimetry (1–5). Furthermore, several analytic strategies have been developed with this objective (6–10).

TABLE 2. *Data from groups 2 and 3*

	No. patients	Sex M	Sex F	Age (mean ± PD)	GHT N	GHT % pos.
Group 2	23	8	15	66.1 ± 12.2	23	100.0
Group 3	17	7	10	50.5 ± 12.6	0	0

M, male; F, female; PD, pattern deviation; N, number of positives GHT; % pos., percentage of positive GHT.

One of these methods, the GHT, is based on the observation that the damage on the visual field occurs asymmetrically along the horizontal meridian (11–13). In this test, clusters of points located superiorly are compared with their mirror image below the horizontal meridian. The comparisons are based on the pattern deviation probability map. A visual field is considered "outside normal limits" when the difference between any mirror image is larger than is found in 1% of the normal population, or when the total depression in any two corresponding clusters is greater than is found in 0.5% of the normal population. A visual field is considered "borderline" when the difference or the total depression of any mirror image clusters is greater than is found in 3% of the normal population. The result "generalized reduction of sensitivity" is when the sensitivity of the most normal region of the field is lesser than is found in 0.5% of the normal population. Another possible result is "abnormal high sensitivity," which is when the sensitivity of the field is higher than is found in 0.5% of the population. In this study, the results "outside normal limits" and "generalized reduction of sensitivity" were considered a positive test.

To study how early this test would detect incipient perimetric alterations in glaucoma, we selected eyes in which there was a clinical impression of glaucomatous damage of the optic disc without any typical alterations in the visual field.

TABLE 3. *Visual acuity from patients*

	Group 1 No.	Group 1 (%)	Group 2 No.	Group 2 (%)	Group 3 No.	Group 3 (%)
20/20	29	(76.3)	8	(34.8)	15	(88.2)
20/25	5	(13.16)	7	(30.4)	2	(11.8)
20/30	3	(7.9)	2	(8.7)	—	
20/40	1	(2.6)	4	(17.4)	—	
20/60	—		1	(4.3)	—	
20/100	—		1	(4.3)	—	

No., number of eyes; %, percentage of eyes.

In the general population, few eyes with a CD >0.5 and a contralateral asymmetry bigger than 0.2 are encountered. Weisman et al. (19) verified that a vertical asymmetry >0.2 occurs in only 4% of the population. When associated with a CD >0.5, it occurs in 31% of glaucomatous eyes and in only 0.7% of eyes without this condition. Shin et al. (20) showed that 32% of patients with a high IOP and a CD >0.5 developed perimetric alterations. Wilensky (21), studying a group with an IOP of >25 mm Hg, observed the appearance of visual field loss in 27.3% of cases in a 6-year follow-up.

It is also known that the percentage of perimetric alterations encountered in eyes whose contralateral eye already has glaucomatous lesion is significantly greater than in other patients (22), principally when associated with a CD bigger than 0.5 (23).

Another group of patients suspected of presenting alterations in the optic disc due to glaucoma are those which show a cup disc >0.7. Cup discs of such magnitude occur in only 1–2% of the population (24,25) and, when associated with high IOP, have an even greater possibility of being pathological. There is the possibility that these eyes have a large congenital scleral rim or even a congenital asymmetry, which may cause a false impression of a pathological cup disc (26). However, the association with high IOP suggests glaucomatous damage.

Thus, it is likely that certain number of eyes which we selected for Group 1 present anatomic lesions of the optic nerve disc due to glaucoma, without presenting characteristics perimetric alterations detectable by the GHT.

In this group, the GHT was positive in 18.4% of the cases. When we study the three subgroups isolated, we notice that in the subgroup A the GHT was positive in 11.1% of the eyes, in the subgroup B in 20.0%, and in the subgroup C in 22.2%.

Among the seven positive GHT in group 1, four showed the result "outside normal limits" and three showed "generalized reduction of sensitivity." Although there was a small number of patients, it seems that both criteria have the same sensitivity to detect the first alteration in patients from group 1. It's important to emphasize that these patients haven't been treated with Pilocarpine or other miotic drugs, which could reduce the global sensitivity of the visual field, and all patients with positive GHT had visual acuity ≥20/25.

In order to test the sensitivity of the method, we apply it in patients already known to present glaucomatous perimetric alterations. The GHT was positive in all 23 eyes studied (sensitivity of 100%). Katz et al. (27) reported the GHT's sensitivity of 92%, slightly lower than our result. Also Duggan et al. (10) and Sommer et al. (28) reported a sensitivity of 94 and 97%, respectively, using a test similar to the GHT, called the differential threshold test.

To verify specificity, eyes with vertical cup disc of <0.4 without asymmetry, that is to say eyes with no clinical evidences of lesion, were chosen. In this group the GHT proved negative in all eyes (specificity of 100%). Katz et al. (27) reported for the GHT a similar result. Comparing the results of this group with those of the first one, a high statistical difference was found, showing that the glaucoma suspect population (group 1) differs from the normal population (group 3).

The reproducibility of a test is also of considerable importance in establishing its reliability. In the present study, the general reproducibility was 83.3%. When we divide the eyes in two groups, those where the first GHT were positive showed a reproducibility of 75.8%. Those where the first GHT were negative showed a reproducibility of 88.9%. It would be possible that the time between the tests might influence its reproducibility. This was not the case in our study, as the average interval between the tests in the group where it was reproducible compared with the group where it was not reproducible was not statistically different.

This study showed that 18.4% of the patients who present clinical impression of damage of optic disc without typical visual field defect showed a positive GHT. As we were interested only in studying the GHT, we disregarded the value of MD (mean deviation), SF (short-term fluctuation), and other criteria to detect visual field defects. It is possible that if we considered them, the number of eyes with visual field defects would increase. In contrast, all eyes without this clinical impression of damage of the optic disc showed a negative GHT. Therefore, the GHT seems to be an important tool in the detection of visual field damage in glaucoma suspects. However, 81.6% of the eyes that had clinical evidences of lesion of the optic disc showed a normal GHT. Although it's possible that some of these eyes might have only an apparent glaucomatous damage of the optic disc, this is unlikely to occur in all of these eyes. These data are in agreement with the findings reported by Quigley et al. (29) that a substantial loss of nervous fiber is necessary before the first visual field defect can be detected.