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ROLE AND RELEVANCE OF POISON INFORMATION CENTRES IN INDIA

Poisoning due to chemicals, pharmaceuticals, plants and animal toxins is a world-wide phenomenon and has a heavy social and economic impact on a country's health care system. The poisonings may be intentional, accidental or occupational; acute or chronic. Acute poisonings present as medical emergencies at all levels of health care and the personnel involved in health care should be aware of the critical care and management required by such cases.

Mass chemical poisonings have occurred due to accidental contamination of food, medicines and consumer goods. Some well known examples include the Minamata Bay episode in Japan of mercury poisoning during the 1950s. Extensive episodes of mercury poisoning have also been reported to be due to contamination of bread made from cereal grains treated with alkyl-mercury fungicides[1]. In Spain, the toxic oil syndrome of 1983 killed 340 people and caused permanent disability in 20,000 persons[2]. Large scale poisoning due to diethylene glycol used in place of propylene glycol in many pharmaceutical formulations has been reported from many countries[3]. Adulteration of illicit liquor with methanol resulting in mass poisoning is often reported in India. In Vietnam, baby talc containing warfarin killed many infants and caused serious sickness in others[2].

A number of industrial disasters have occurred during the manufacture, storage and transport of chemicals. The worst chemical disaster occurred at Bhopal where methyl isocyanate and other reaction products released from the Union Carbide plant manufacturing carbaryl, caused more than 2500 deaths and disabled nearly 150,000 people[2].

In India, as in other countries, mass poisonings due to any cause receive a great deal of media coverage, but it is the individual patients of poisoning seen by physicians which in reality make up the bulk of poisoning cases. Though it is mandatory to report all cases of poisoning due to their medicolegal nature, the official figures often do not reflect the extent of the problem on account of under reporting. Since many cases of poisoning are suicidal in nature, the relatives often consult private practitioners. Industrial poisonings though notifiable, are also under reported as compensation has to be paid to the workers. Under these circumstances only the very serious patients go to the hospitals, and it is mostly through publications of such case reports that the types of poisonings prevalent in India are known.

The commonest cause of poisoning in India and other developing countries is pesticides[4,5], the reasons being agriculture based economies, poverty and easy availability of highly toxic pesticides. Occupational poisoning due to pesticides are also common in developing countries, due to unsafe practices, illiteracy, ignorance and lack of protective clothing.

In India, organophosphates form the largest bulk of pesticide poisonings[6-8]. Since 1985, the problem of aluminium phosphide poisoning, a grain fumigant, is reported

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as the commonest cause of intentional poisonings in northern parts of India *viz.* Haryana, Punjab and Rajasthan[9,10].

Pesticide poisoning is associated with high morbidity and mortality. Education of the pesticide handlers about safe practices can prevent accidental poisoning to a large extent. Immediate first-aid can be life saving in most cases of poisoning and can be carried out at the primary health care level.

The problem of low dose chronic exposure to chemicals is as important as that of acute poisoning. In India, a great deal of concern is being shown about the harmful effects of environmental pollution on human health. A number of legislations have also been enacted or ammended to exercise stricter controls and contain the harmful effects of chemicals on human health and environment.

International Concern About Chemical Safety

In the 1970s, international concern about the dangers of chemicals led to the United Nations Conference on the Human Environment in 1972 at Stockholm, Sweden[11]. In 1977, the World Health Assembly, decided to develop long-term strategies to control and limit the impact of increasing manufacture, use, storage, transport and disposal of chemicals. The International Labour Organisation (ILO) and United Nations Environment Programme (UNEP) joined WHO in setting up the International Programme on Chemical Safety (IPCS) in 1980. The IPCS provides guidelines for assessing the risk of chemicals to human health and gives technical support to different countries to strengthen their chemical safety programmes. One of the major thrust areas in chemical safety is the development and strengthening of Poison Information Centres especially in developing countries.

In 1992, the United Nations Conference on Environment and Development (UNCED), the Earth Summit, held at Rio de Janeiro, recognised the need for an international strategy to achieve sound management of chemicals which led to the Intergovernmental Forum on Chemical Safety (IFCS). The IFCS provides a mechanism for co-operation between governments for chemical risk assessment and environmentally sound management of chemicals. The IFCS has also identified a number of priority areas including the establishment and development of Poison Information Centres world-wide as a means of collecting harmonized data on a global basis on the impact on human health of deliberate and accidental exposures to chemicals[12].

The IPCS/INTOX project has developed a computerised information management package which will help the Poison Information Centres in harmonized collection and analysis of toxicological data on a global basis. Thus multicentric toxicological studies can be undertaken to evaluate the effectiveness of preventive and therapeutic interventions. The project involves about 100 toxicologists from 60 centres based in 45 countries[12]. Two centres from India, one at the All India Institute of Medical Sciences (AIIMS), New Delhi and the other at the National Institute of Occupational Health (NIOH), Ahmedabad are participating in this project.

Poison Information Centres

The Poison Information Centres are specialized units[13] with the objective of—(i) reducing morbidity and mortality from toxic exposures of any kind, be they intentional or accidental; single or multiple; acute or chronic and by any route of exposure; and (ii) carrying out intervention programmes for prevention of poisoning.

Reduction of Morbidity and Mortality

Emergency information service

This is the most important activity of a poison information centre. By accessing a number of information sources and databases, the centre can quickly identify the agent involved in any kind of toxic exposures and provide information on its toxicity and risks. In instances of acute poisoning, the centre provides immediate advice on first-aid, management, antidotes and investigations needed for patient care. Personnel at the centre would require training to respond to telephonic enquiries which is the commonest mode of communication. Since many exposures are non-toxic and need only reassurance or minor first-aid, unnecessary visits to the already overburdened emergency departments can be avoided. In developing countries, the poison information centres may also provide a range of information on the environmental risks of chemicals and safe levels of chemicals in food and at the workplace.

Analytical laboratory investigations

The poison information centres can also provide laboratory service for analyses of the toxicants and biochemical investigations for diagnosis of certain types of poisoning and for patient management. Simple tests such as spot tests, immunoassays or thin layer chromatography may be undertaken by emergency services attached to a

clinical toxicology unit. More detailed analyses using sophisticated instrumentation for confirmation of screening results and studies on the kinetics of the toxin can be undertaken by reference laboratories.

Clinical toxicology services

In many countries poison information centres are integrated with clinical units which carry out treatment, follow up of poisoned patients and evaluation of treatment efficacies.

Teaching and training of health professionals

These centres being an important source of human toxicology data, can provide updated information on new treatment modalities to health professionals.

Chemical accidents and disasters

Poison information centres make an important contribution in the handling of chemical disasters by providing appropriate information at the time of an accident and by taking part in contingency planning.

Preparation of information material

This may be specially important for developing countries where communication and transport facilities are not well developed in the rural areas. Information cards, brochures on locally prevalent poisonings may be prepared as quick reference materials for health professionals.

Prevention of Poisonings

Toxicovigilance

This is an active process of identification and evaluation of toxic risks in the community. All enquiries addressed to a poison information centre are regularly analysed to determine the possible toxic agents and circumstances of poisoning. The regulatory or health authorities can be alerted to take appropriate preventive measures, if poisoning related to a new product, improper packaging or wrong labelling is observed.

Public education and awareness

Educational programmes either for the whole community or for certain high risk groups *eg.* on prevention of poisoning in toddlers, safe use of pesticides for rural workers, dangers of self medication in the elderly, prevention of exposures to chemicals at work, *etc.* may be undertaken through various information material and campaigns.

POISON INFORMATION CENTRES: THE INTERNATIONAL SCENARIO

Clinical toxicology became a specific branch of medicine in the early 1950s in developed countries in response to the proliferation and use of chemicals in everyday life. The first poison centres were started in America in the mid fifties and by the early eighties there were nearly 400 centres some of which were in the emergency departments of hospitals. The American Association of Poison Control Centres (AAPCC) established in 1958, has developed standards for the certification of such centres[14]. The Poison Prevention Packaging act of 1972 in USA which led to child resistant packaging and a marked reduction in childhood poisonings was largely due to the efforts of the AAPCC.

The organization of Poison Information Centres in various countries is varied. In the USA, most of the centres provide 24 h information and are not associated with any diagnostic laboratories or treatment units. In Ireland, Spain and Netherlands the information centres are integrated with diagnostic laboratories. In other countries such as the UK, France and Germany some poison centres work in conjunction with acute poisoning treatment units and diagnostic laboratories. The European data indicate an annual incidence of human poisoning of 0.2-2.9/1000 inhabitants[15].

The National Taiwan Poison Control Centre reported an annual incidence of human poisoning ranging between 0.16-0.22 exposures per 1000 population[16]. Among countries of the Asia Pacific region, Australia, New Zealand, Indonesia, Singapore, Phillipines, Hongkong, Pakistan, Sri Lanka, Iran and Turkey have already established poison information centres. Among Latin American countries, Brazil has 30 poison control centres, while Uruguay has one well established centre. Very few countries in the African continent with the exception of South Africa, Zimbabwe and Kenya have poison information centre facilities. Some East European countries have started developing poison control facilities recently[17]. In 1993, the Toxicology Information and Advisory Centre (TIAC) was created in Moscow and there is a plan to create 20 information toxicology centres in different regions of Russia by 1998.

In two of the most populated and rapidly industrializing countries *viz.* China and India, poison information centres have yet to make an impact on the health care system.

Present Status of Poison Information Centre Activities in India

Poison information centres should become an integral part of the health care delivery system and chemical information services in India. These centres need expertise in a wide range of areas which include pharmacology, toxicology, clinical sciences, preventive medicine, occupational health, environmental sciences, biology and computer sciences. Special skills in telephonic consultation, data search and risk assessment are also needed. It is essential, that before a network of such centres is set up, the infrastructural needs, human resources and the training requirements are thoroughly understood. Guidelines for Poisons Control have been prepared by a group of experts following a joint meeting of International Programme on Chemical Safety (IPCS), Commission of the European Communities (CEC) and the World Federation of Associations of Clinical Toxicology Centres and Poison Control Centers at Geneva in 1985[13].

The need for poison information centres has been felt in India for quite some time. Following the Bhopal gas tragedy, an Inter-ministerial Group on Prevention and Control of Chemical Accidents met in 1986 and strongly supported the idea of setting up poison control centres in India. In 1991, the existing facilities in India for diagnosis, management and prevention of poisoning were identified at a workshop organized in New Delhi[4]. The IPCS/WHO through its INTOX project provided technical help and training to two centres from India (AIIMS, New Delhi; NIOH, Ahmedabad).

Poison Information Centre at AIIMS, New Delhi

The National Poisons Information Centre set up in the Department of Pharmacology in December 1994, provides information by telephone and fax, on poisoning by drugs and chemicals on a 24 h basis, seven days a week, throughout the year, to hospitals, doctors in practise and the general public in the event of poisoning/suspected poisoning. The Centre has up-to-date information on toxic substances (drugs and chemicals). In difficult cases, information from other countries can be collected and transmitted to the concerned hospital/individual. The Centre has also made about two dozen treatment cards on common acute poisonings which provide information on prehospital and hospital management of the poisonings; the doses of various drugs to be used are also given. The Centre has also published two monographs on the "Management of Plant Poisonings" and "Management Guidelines for Pesticide Poisonings". The Centre has also prepared booklets giving information about "Management of Various Poisonings" and sources from where the antidotes can be obtained. A card for "Prevention of Household Poisoning" has also been publised. Further, the Centre has developed facilities for detection of common poisons.

Poison Information Centre at NIOH, Ahmedabad

This Centre provides expert guidance and treatment recommendations to medical personnel handling patients of poisoning. Initially, patients were being referred only from few hospitals of Ahmedabad city but now private hospitals, nursing homes, general practitioners of not only Ahmedabad but from other parts of Gujarat seek help from the NIOH Poison Centre. Investigations for identification of pesticide and metal posonings are also undertaken at the NIOH. The Centre also carries out market surveys for common poisons and availability of antidotes. Teaching in clinical toxicology and toxicovigilance are the other main activities of the Centre. Based on the types of poisoning reported to the NIOH centre, poison information cards have been prepared on pesticides and industrial chemicals to serve as quick reference material for health personnel.

The following are the main observations of the Centre:

1. Acute poisonings are very common and patients are admitted to the emergency wards almost daily. The patients often arrive very late when referred from rural areas leading to high morbidity and mortality.
2. Pesticides, both household as well as agricultural, are the commonest cause of poisoning. Mortality is much higher with agricultural pesticides. Though organoposphates are responsible for the bulk of pesticide poisonings, other pesticides such as organochlorines, synthetic pyrethroids and herbicides are frequently encountered. A variety of industrial chemicals are also responsible for many instances of poisoning.
3. Simple diagnostic tests such as plasma cholinesterase levels are not done in any of the hospitals. Most pesticide poisonings are treated as organophosphate poisonings. However, with the establishment of the Poison Information Centre at NIOH, physicians avail its services for the identification of the pesticides and also request for cholinesterase assays.
4. Teaching or training in clinical toxicology, both at the undergraduate as well as at the postgraduate level is limited in some medical colleges.

5. Simple remedies such as syrup of Ipecac and activated charcoal which is recommended for most ingested poisons are not easily available in India. Very few antidotes are available even in big cities in India.
6. Many of the pesticide formulations are sold unlabelled in the market making it difficult for patient management. Some of the pesticide containers had incorrect information about antidotes which led to complications in many patients.
7. Occupational poisonings are quite common but are not reported due to various reasons.

In a country as large as India, it may be necessary to have a number of regional poison information centres. Many research institutes in India not only have the expertise in human toxicology, but also have fully equipped analytical laboratories. Such facilities could be upgraded and the institutes encouraged to develop liasion with emergency care services. By extending service to the hospitalized patients, unnecessary duplication of expensive laboratory facilities can be avoided and at the same time close observation and follow up of patients exposed to a variety of toxicants will encourage research in clinical toxicology and provide a wealth of knowledge (minimizing animal experimentation).

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This write-up has been contributed by Dr. A. Dewan, Deputy Director, National Institute of Occupational Health, Ahmedabad.

ABSTRACTS

Some Research Projects Completed Recently

Evaluation of citrate therapy in the management of oxalate lithiasis with special reference to renal tubular acidosis

A total of 181 (164 male and 17 female) radiologicaly proven renal stone formers (SF) and 30 normal subjects with no history of renal disorders were evaluated for total distal renal tubular acidosis (dRTA) defects by acid challange (150 mg ammonium chloride/kg body weight) test. Potassium citrate therapy in the management of stone formers with dRTA defect and recurrent calcium oxalate stone formers with hypocitraturic defect, was also evaluated.

Nephrolithiasis had occurred for the first time in 120 patients while in 61 it was recurrent. dRTA defect was found in 3.3 per cent normals and in 30.3 per cent SF; only one SF had complete dRTA defect. The prevalence of dRTA was 28.6 and 47.1 per cent in males and females

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respectively. In the first episode SF, dRTA was found in 29.0 per cent males and 61.5 per cent females while in recurrent SF, dRTA was found only in males (28.1%).

In normals and SF without dRTA defect a progressive fall in the urinary pH was seen after acid (ammonium chloride) loading. The initial pH in SF was slightly higher than in normal subjects. In SF with incomplete dRTA defect, the pre-acid load pH was higher than in those without dRTA defect and it did not fall below 5.0 after acid load. In the only patient with complete dRTA the urine did not become acidic even after acid load. No differences were observed in urinary creatinine excretion in normals and various groups of the SF. However, calcium excretion increased after acid load in both groups of subjects; the calciuric effect of acid load being greater in SF without dRTA defect. A progressive decrease in the excretion of citric acid after acid load was observed in normals and SF without dRTA defect. Comparatively the hypocitraturic effect was milder in SF with incomplete dRTA defect, and was negligible in SF with complete dRTA defect. No significant differences were observed in pre-load ammonium excretion in normals and different groups of SF. Increasing pattern of ammonium excretion after acid load was observed in all the subjects.

No significant differences were observed in the acid-base status of normals and SF and in patients with the first and recurrent episodes of nephrolithiasis. The base excess tended to be lower in recurrent SF. After acid load the bicarbonate, base status and base excess of extra cellular fluids reduced in SF with and without dRTA defect.

Potassium citrate therapy for the management of renal stones was evaluated in 58 stone formers (32 first episode and 26 recurrent). Urine chemistry (24 h sample) was studied pre-therapy and 1,3,6 and 12 months after therapy. Urinary pH increased progressively during therapy. Calcium excretion decreased significantly and reached normal levels after one year in all hypercalciuric patients. Hypocitraturia was also corrected in all the stone formers. Twenty four h urine output, creatinine, magnesium, inorganic phosphorus, uric acid and oxalic acid remained unaltered during this period. Serum chemistry and acid base status also remained unaffected. Recurrence of the disease was not observed in any of the patients during one year of therpay.

The results of the study thus indicate that dRTA defect is a significant factor in the etiopathogenesis of urinary calculi. Recurrence does not appear to be related to this defect. Potassium citrate therapy was found to be an effective remedy for aleviating hypercalciuria and hypocitraturia.

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In situ hybridization studies of Epstein-Barr virus in Hodgkin's disease

The study was carried out on 40 patients of Hodgkin's disease to demonstrate the presence of Epstein-Barr viral (EBV) RNA in the malignant cells by a sensitive non-isotopic *in situ* hybridization and to localize the EBV encoded latent membrane protein-1 (LMP-1) in the malignant cells. Efforts were also made to correlate the results of *in situ* hybridization with immunohistochemistry for EBV-encoded LMP-1 and analyse the percentage of positivity in relation to various subtypes of Hodgkin's disease.

Of the 40 patients studied, 30 were adults and 10 children; male: female ratio being 37:3. The most common histological subtype was nodular sclerosis (24/40; 60%), followed by mixed cellularity (12), lymphocyte predominance (3) and one case of lymphocyte depletion.

EBER-1 transcripts were identified in 28 of the 40 (70%) patients (18 adults and 10 children). In the positive cases, EBER-1 positivity was confined to the Reed-Sternberg and mononuclear Hodgkin's cells. A higher rate of EBER-1 positivity was observed in mixed cellularity (83.33%) and lymphocyte depletion (100%) followed by nodular sclerosis (70.83%). No positivity was observed in lymphocyte predominance.

Twenty six of the 28 patients (except one with mixed cellularity and the only case with lymphocyte depletion) showing positivity with *in situ* hybridization, showed reactivity for EBV encoded LMP-1.

The 100 per cent EBER-1 positivity in paediatric patients strongly support the role of EBV in the etiopathogenesis of Hodgkin's disease. The demonstration of

LMP-1 along with the detection of EBER-1 sequences has important implications since it is one of the latent gene products which produces B lymphocyte transformation. The data thus strongly support the hypothesis, that when present, EBV is not merely a silent passenger in Hodgkin's disease but contributes directly to the pathogenesis. The results also indicate that the procedures used in this study can be applied on archival material allowing retrospective analysis of many neoplasms suspected to be EBV related.

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ICMR NEWS

The following meetings of various technical committees/groups of the Council were held:

Meetings of the Project Review Committee (PRC)/ Project Advisory Committee (PAC) and Annual Review Meeting held at New Delhi:

Annual Review Meeting of the National Cancer Registry Programme	April 21, 1997
PRC on Oncology and Gastroenterology	May 5, 1997
PAC on development of a scale for measuring psychosocial stress	May 9, 1997

Brain Storming Session/Meeting of the Scientific Advisory Committee (SAC):

ICMR–DBT Brain Storming Session on Research in Haemoglobinopathy	April 19-20, 1997 (at Mumbai)
SAC of the Centre for Advanced Research for Health Consequences of Earthquake Disaster with special reference to Mental Health, Pune	May 15-16, 1997 (at Pune)

Participation of ICMR Scientists in Scientific Events:

Dr. Rani Balasubramanian, Dy. Director, Tuberculosis Research Centre (TRC), Chennai, participated in the XXIII Middle East Regional Congress of the International Union against Tuberculosis and Lung Diseases at Tehran (April 21-24, 1997).

Dr. Manjula Datta, Dy. Director, TRC, Chennai, participated in the meeting of the WHO Steering Committee on Immunology of Mycobacterial Diseases, Vaccine Research and Development Unit of the Global Programme for Vaccine and Immunization at Geneva (April 23-25, 1997).

Dr. V. Kumaraswami, Dy. Director, TRC, Chennai, participated in the meeting of the WHO Task Force on Community Directed Treatment of Lymphatic Filariasis and Onchocerciasis at Geneva (April 28-30, 1997).

INDIAN COUNCIL OF MEDICAL RESEARCH

Grant-in-aid for organising Seminars/Symposia/Workshops

The Council provides partial financial assistance for organising Seminars/Symposia/Workshops. Applications for grant of financial assistance (complete in all respects in the prescribed proforma), will be considered only if furnished **at least four months before the date of commencement of the Seminar/Symposium/Workshop**, *etc.*

COUNCIL'S TRAINING PROGRAMMES FOR 1997-98

Leprosy

At the Central JALMA Institute for Leprosy, Agra:

- Training Course on National Leprosy Eradication Programme for Medical Officers (September 15-26, 1997).

Virology

At the National Institute of Virology, Pune:

- Diploma in Medical Virology (June 1997-May 1998).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

- Workshop on Genotoxicity (August 18-29, 1997).
- Workshop on Basic Molecular Biology for Clinicians (December 2-11, 1997).

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Applications (August 1-September 15, 1997).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 1, 1997-February 28, 1998).
- Postgraduate Certificate Course in Nutrition (December 1, 1997-February 28, 1998).

Occupational Health

At the National Institute of Occupational Health, Ahmedabad:

- Orientation Course on Occupational Health for Industrial Medical Officers (September 30-October 11, 1997).
- Training Course on Environmental Hygiene Practice (November 10-14, 1997).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 16-July 31, 1997).
- Training Course for Laboratory Animal Supervisors (September 1-November 29, 1997).

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 27-October 24, 1997).
- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August 27-September 26, 1997).
- Training Course in Advanced Haematology and Immunohaematology (October 6-24, 1997).

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