

GUIDELINES FOR ESTABLISHING A POISON CENTRE



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This publication is the update of the Guidelines published in 1997 entitled "Guidelines for poison control".

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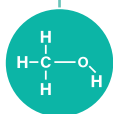
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PREFACE

This publication is an update of the *Guidelines for poison control*, published by WHO in 1997 under the auspices of the International Programme on Chemical Safety. The stimulus for the original publication was recognition that poisoning by chemicals was a significant and growing risk in all countries but that relatively few countries had well-established facilities for the prevention and management of poisoning (1). The need to strengthen such capacity in countries, particularly through establishment of poisons information centres, was highlighted at a joint meeting of the World Federation of Associations of Clinical Toxicology Centres and Poison Control Centres, the International Programme on Chemical Safety and the European Commission held at WHO headquarters in October 1985. One of the outcomes of that meeting was a recommendation for preparation of guidance for countries on establishing or strengthening capacity for the prevention and management of poisoning. An international working group was convened to prepare such guidance.

The publication *Guidelines for poison control* was part of a larger WHO project, the INTOX programme, to support countries in establishing and strengthening poison centres. The INTOX programme included a project to evaluate antidotes and other substances used in the treatment of poisoning, development of a multilingual information package and data management system to help new poison centres get started and establishment of a global network of medical and analytical toxicologists and poison centre specialists.

In the years since the *Guidelines for poison control* were published, there have been developments in the roles and activities of poison centres and also in information technology (IT) and communication. Of particular importance is a renewed emphasis on the role of poison centres in public health after revision of the International Health Regulations in 2005 (IHR). The Regulations now take an all-hazards approach to protecting public health and require that countries have the capacity for surveillance, detection and response to public health events caused by chemicals. Much of this capacity can be provided by a well-resourced poison centre.

This update of the *Guidelines for poison control*, entitled *Guidelines for establishing a poison centre*, reflects the development of the role of poison centres in public health and the sound management of chemicals, described in section 1, and the opportunities provided by new technology. Assessments carried out under the IHR show continuing gaps in capacity for managing chemicals (2). In particular, many countries still lack access to poison centre services (3). There is therefore demand for updated guidance.

The update was prepared as follows. In May 2018, WHO convened a group of specialists in poison centres and medical and analytical toxicology from all the WHO regions. The group was asked to examine the *Guidelines for poison control* to identify where updates were needed and any additional information that should be included. The WHO Collaborating Centre for the Public Health Management of Chemical Exposures, part of Public Health England, commissioned the National Poisons Information Service (NPIS) units in Birmingham, Cardiff, Edinburgh and Newcastle to update individual sections and annexes. Personnel from the WHO Collaborating Centre made additional contributions, and the Team Leader at the Surveillance Coordination Unit in the Chemical Emergency Management and Toxicovigilance Division, Health Canada, provided significant material for section 5.

Each updated section was reviewed by members of the WHO expert group, who made further revisions. The complete document was reviewed at a meeting of the expert group on 9–10 July 2019, hosted by the NPIS (Edinburgh Unit) in Edinburgh, Scotland. After further revision, the document was reviewed at a small editorial group meeting on 4–5 December 2019, hosted by Public Health England in London. That revision was circulated to the WHO expert group and also to environmental health focal points in the WHO regional offices for comments.

The first section describes the history of poison centres and the policy background. It then provides an overview of the services that may be offered by a poison centre and the considerations to be taken into account in planning a poison centre. Subsequent sections address the more practical aspects of poison centre services and operations. Sections 2–4 give guidance on setting up a poisons information service, a clinical toxicology service and an analytical toxicology service. Section 5 describes the role of poison centres in toxicovigilance and the prevention of poisoning, and section 6 outlines their role in preparedness and response to chemical incidents. Section 7 presents issues in improving the availability of antidotes. Sections 8 and 9 present databases and reference sources for poison centres. Section 10 gives practical guidance on the training of poison centre staff and quality management. Section 11 discusses potential funding sources for poison centres, as experienced in various countries.

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LIST OF CONTRIBUTORS

The project was led by Nicholas Brooke, Principal Environmental Public Health Scientist, Chemicals and Environmental Effects Department, Centre for Radiation, Chemical and Environmental Hazards, Public Health England, London, England, and Joanna Tempowski, Department of Environment, Climate Change and Health, World Health Organization, Geneva, Switzerland.

The main contributors are as follows:

Amber Bryce, trainee clinical scientist, All Wales Medical Genomics Service, University Hospital Wales, Cardiff, Wales

Lydia Izon-Cooper, Principal Public Health Scientist, Centre for Radiation, Chemical and Environmental Hazards, Public Health England, London England

Ted Cheung, Bornnali Das, Des Henke, specialists in poisons information, National Poisons Information Service (Birmingham Unit), Birmingham, England

Michael Beddard, Alexander Capleton, Talan Parnell, specialists in poisons information; and James Coulson, honorary consultant physician, National Poisons Information Service (Cardiff Unit), Llandough Hospital, Cardiff, Wales

Sonia Bradley, Information Services Manager; and Dacia Jones, Medical Information Scientist, National Poisons Information Service (Newcastle Unit) and Regional Drug and Therapeutics Centre, Newcastle-upon-Tyne, England

Victoria Eagling, specialist in poisons information; Gill Jackson, TOXBASE Manager; and Euan Sandilands, Director, National Poisons Information Service (Edinburgh Unit), Royal Infirmary of Edinburgh, Edinburgh, Scotland

Richard Wootton, team leader, Surveillance and Coordination Unit, Chemical Emergency Management and Toxicovigilance Division, Health Canada, Ottawa, Canada

The following people provided expert review of the content of the book:

Mohammedsali Hassen Ahmed, Assistant to Chief Executive Officer, St Peter's Specialized Hospital, Addis Ababa, Ethiopia

Kamal Al Hadidi, Director, National Drug and Poison Information Center, Amman, Jordan

Ryan Chuang, emergency physician, Alberta Health Services, Calgary, Canada

Sam Collins, Principal Public Health Scientist, Chemicals and Environmental Effects Department, Centre for Radiation, Chemical and Environmental Hazards, Public Health England, Chilton, England

Meghan Cook, IHR Strengthening Project Officer, Chemicals and Environmental Effects Department, Centre for Radiation, Chemical and Environmental Hazards, Public Health England, Chilton, England

Carissa Paz Dioquino, Head, University of the Philippines Manila, Philippine General Hospital National Poison Management and Control Center, Manila, Philippines

Nina Dobbin, epidemiologist, Surveillance and Coordination Unit, Chemical Emergency Management and Toxicovigilance Division, Health Canada, Vancouver, Canada

Gabija Dragelyte Laubner, Head, Acute Poisonings and Toxicology ICU Departments, Republican Vilnius University Hospital, Vilnius, Lithuania

Raquel Duarte-Davidson, Head, Chemicals and Environmental Effects Department and National Poisons Information Service Commissioning Services, Centre for Radiation, Chemical and Environmental Hazards, Public Health England, Chilton, England

Nick Edwards, consultant, London, England

Muhammad Elamin, consultant physician and clinical toxicologist, National Poisons Information Service (Birmingham Unit) and West Midlands Poisons Unit, City Hospital, Birmingham, England

Ligia Vêras Gimenez Fruchtengarten, Medical Director, Poison Control Centre of São Paulo, São Paulo, Brazil

Najla Khoja, Chairperson, Poison Control Department, King Fahad Medical City, Riyadh, Saudi Arabia

Marc Lafontaine, science advisor, Chemical Emergency Preparedness and Response Unit, Chemical Emergency Management and Toxicovigilance Division, Health Canada Ottawa, Canada

Royal Kai Yee Law, epidemiologist, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta (GA), United States of America

Carlo Alessandro Locatelli, Director, Toxicology Unit and Pavia Poison Centre, National Toxicology Information Centre, Pavia, Italy

Ann-Maree Lynch, Head of Department, Western Australia Poisons Information Centre, Nedlands, Australia

Carine Marks, Director, Tygerberg Poison Information Centre, Cape Town, South Africa

Monique Mathieu-Nolf, Director, Centre Antipoison et de Toxicovigilance, Lille, France

Tom Menge, Office of the Chief Pharmacist, Kenyatta National Hospital, Nairobi, Kenya

Shekoufeh Nikfar, School of Pharmacy, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

V.V. Pillay, Chief, Poison Control Centre, Amrita Institute of Medical Sciences and Research, Cochin, India

Sandy Remer, epidemiologist, Surveillance and Coordination Unit, Chemical Emergency Management and Toxicovigilance Division, Health Canada, Toronto, Canada

Mahmoud Lofty Sakr, Director, Poison Control Center, Ain Shams University, Cairo, Egypt

Eleri Thomas, specialist in poisons information, National Poisons Information Service (Cardiff Unit), Llandough Hospital, Cardiff, Wales

Winai Wananukul, Director, Ramathibodi Poison Center, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Deborah Weiss, epidemiologist, Surveillance and Coordination Unit, Chemical Emergency Management and Toxicovigilance Division, Health Canada, Ottawa, Canada

Sherika Whitelocke-Ballingsingh, Poison Information Coordinator, Caribbean Poison Information Network, Kingston, Jamaica

Stacey Wyke, group leader (Chemicals and Poisons), Chemicals and Environmental Effects Department, Centre for Radiation, Chemical and Environmental Hazards, Public Health England, Chilton, England

Abdool Yasseen, epidemiologist, Surveillance and Coordination Unit, Chemical Emergency Management and Toxicovigilance Division, Health Canada, Ottawa, Canada

Mark L. Zammit, advanced pharmacy practitioner, Ministry of Health, Valletta, Malta

Zaw Lynn Aung, Head, Department of Medicine, University of Medicine 1, Yangon, Myanmar

All the above contributors and reviewers completed a WHO declaration of interests form, which was reviewed by the WHO technical officer. No conflicts of interest were identified.

The following WHO staff reviewed this publication: Ana Boischio, Advisor Chemical safety, Climate Change and Environmental Determinants of Health Unit, Pan American Health Organization and Irina Zastenskaya, Technical Officer, WHO Regional Office for Europe, WHO European Centre for Environment and Health. Section 7 and Annex 5 were reviewed by Klara Tisocki, Medical Officer, Essential Drugs and Other Medicines, WHO Regional Office for South-East Asia.



1 POISON CENTRES: THEIR ROLE IN THE PREVENTION AND MANAGEMENT OF POISONING



1.1 INTRODUCTION

There are estimated to be 40 000–60 000 industrial chemicals in commerce globally, of which about 6000 account for most of the total volume (1). In addition, there are over 6000 approved drugs (2), about 730 new psychoactive substances (3), an estimated 2000 poisonous plant species, 1200 species of poisonous and venomous animals (4) and countless household and industrial products and cosmetics. Humans may be exposed to many of these substances and products, resulting in illness or death. The human toxicology of many chemicals and natural toxins is, however, poorly understood.

Poisoning is a significant global public health problem. WHO estimates that, in 2016, unintentional poisoning caused 106 683 deaths and the loss of 6.3 million years of healthy life (disability-adjusted life years) (5, 6). It has also been estimated that 81 410–137 880 people die each year from snakebite (7). In addition, it is estimated that about 20% of global suicides are due to pesticide self-poisoning, mostly in rural agricultural areas in low- and middle-income countries (8). In many countries, poisoning is one of the main causes of emergency attendance at hospitals. Poisoning is a time-dependent emergency and, like infectious diseases, may require a specialist for appropriate diagnosis and treatment.

Poison centres were established in countries as sources of specialized expertise to address the fact that health professionals could not be expected to know about the toxicity of every substance and product and also to provide a focus for toxicological research. A short history of poison centres is provided below.

1.2 WHAT IS A POISON CENTRE?

A poison centre is a specialized unit that advises on and assists in the prevention, diagnosis and management of poisoning. Its primary role is clinical: advising on and, in some cases, providing treatment for poisoning cases. The structure and function of poison centres varies around the world; however, at a minimum, a poison centre is an information service. Poison centres may also include a clinical treatment unit and/or a laboratory that can provide toxicological analyses.

The data collected by poison centres in the delivery of their duties can be used for public health purposes and to support the sound management of chemicals through toxicovigilance (see section 5). Other potential roles of a poison centre include organizing antidote supply, involvement in research, education and training, and advising on environmental exposure to chemical substances. Community interaction may be an important activity and helps raise the profile of poison centres. These elements are summarized below and described more fully in other sections.

In some countries, poison centres may deal with toxicological problems that affect both animals and humans. As poisoning of animals can have important economic consequences, veterinary poisons information centres have

been established in some countries, including Australia, France, the United Kingdom and the United States of America (USA).

1.3 TERMINOLOGY

Different terms are used globally to describe services that provide information and advice on the management of poisoning and, in some cases, treatment and laboratory services. These include “poisons information centre”, “poisons information service”, “poison control centre”, “poisons information and support centre”, “antipoison centre”, “poison centre”, “toxicology information service” and “toxicology centre”. In this guidance, the following terms are used:

- *poisons information centre*, when referring to an establishment that provides only information and advice; and
- *poison centre*, when referring to an establishment that is both a poisons information centre and has a clinical treatment unit and/or a toxicological laboratory. This term is also used more generically when the discussion could apply to a poisons information centre or a combined poisons information centre and treatment unit or laboratory.

The following terms are used to describe the specialist staff working in poison centres:

- *specialist in poisons information*: a health service professional who is trained to work in a poisons information centre to provide information and advice about the diagnosis and management of poisoning; and
- *medical toxicologist*: a medical doctor who has received specialized training in clinical toxicology.

1.4 HISTORY

After the Second World War, there was an enormous increase in the development of new chemical products, including pharmaceuticals and pesticides (9), with a corresponding increase in the number of poisonings (10). As most health professionals were unfamiliar with the clinical management of poisoning, the need for specialist toxicology advice became evident, and this was the primary stimulus for the establishment of poison centres. A prerequisite for their establishment is a cadre of health care professionals interested in human and clinical toxicology and motivated to extend their knowledge in this area.

The development of clinical toxicology treatment units preceded that of poisons information centres. One of the earliest treatment centres was established in 1949 at the Bispebjerg Hospital in Denmark (11), which mainly treated patients with psychotropic drug overdose. The experience gained by centralizing the treatment of poisoning and the focus on clinical monitoring to provide good symptomatic and supportive care were considered to be responsible for a decrease in mortality from poisoning.

In the USA, a major factor in the evolution of poisons information centres was the scale of fatal poisonings of young children revealed by an epidemiological study conducted in 1949–1950 (11, 12). The American Academy of Pediatrics established an Accident Prevention Committee in 1950, which found that 49% of the reported “accidents” treated by its members involved poisoning (12). The first poisons information centre in the world was established in Chicago (IL) in 1953 (13). The centre provided professional telephone advice and used a standard data collection form. The first poisons information centre in Europe was founded in the Netherlands in 1960 (14, 15). More centres were established subsequently, particularly in Asia, Australasia, Europe and North America.

The early poisons information centres drew from a variety of medical specialities, including paediatrics, intensive care, forensic medicine, occupational health, analytical toxicology, pharmacy and pharmacology. To some extent, the original character of many centres has been maintained, and there is considerable heterogeneity in their

structure and organization. Poison centres have historically provided advice in response to telephone enquiries; however, more recently, Internet-based databases have taken on a prominent role in some countries (see section 9).

When poisons information centres began offering their services, they also started collecting data on the cases referred to them in order to characterize the frequency and pattern of poisoning in the population and for medico-legal purposes (16). Developments in information technology have enabled the establishment of poison centre surveillance systems for aggregating, analysing and interpreting national data on poisoning. The data sets can form the basis for poisoning prevention and harm reduction initiatives in public health and in regulatory and health security domains (see section 5).

1.5 INTERNATIONAL POLICY FRAMEWORK

The services provided and the data collected by poison centres can contribute to both public health and the sound management of chemicals. The establishment of poison centres has therefore been recognized as a priority in successive intergovernmental environment and health forums. The start was Agenda 21, a non-binding action plan to further sustainable development, which was agreed at the 1992 United Nations Conference on Environment and Development in Rio de Janeiro, Brazil (17). The Intergovernmental Forum on Chemical Safety, which was established in 1994 to coordinate international implementation of Chapter 19 of Agenda 21, reiterated the priority of establishing and strengthening poison centres in its Priorities for Action beyond 2020 (18). In 2006, the First International Conference on Chemicals Management, which adopted the Strategic Approach to International Chemicals Management, included poison centres in the Global Plan of Action (19).

The IHR (see Box 1) require countries to be capable of detection, alert and response to public health events caused by chemicals (20, 21). The core capacities identified as necessary for countries to meet their IHR obligations include a poisons information centre and access to toxicology laboratory services (22). The establishment and strengthening of poison centres is also a priority action for governments in the WHO Chemicals Road Map to reinforce the role of the health sector in reaching the goals of the strategic approach to international chemicals management (23), which was approved by the Seventieth World Health Assembly in 2017 in decision WHA70(23) (24).

Box 1. International Health Regulations (2005) (21)

In 2005, the WHO Member States adopted the revised International Health Regulations (IHR). Their purpose is to prevent, protect against, control and provide a public health response to the international spread of disease. The scope of the IHR is not limited to a specific disease or manner of transmission, as was the case under the previous Regulations. Instead, the IHR cover illness and medical conditions, irrespective of etiology, that present or could present significant harm to humans, including those of chemical origin.

The IHR oblige States Parties to have certain minimum core public health capacities, with a focus on early detection and response for public health events. Countries must inform WHO of events, chemical or otherwise, that are assessed as possibly constituting a public health emergency of international concern, taking into account the context in which the event occurs, including the availability of response capacity.

To help countries decide whether WHO should be notified of an event, a decision instrument is provided in Annex 2 of the Regulations. The instrument lists four criteria by which countries should assess events in their territories: (i) if the public health impact of the event is serious; (ii) if the event is unusual or unexpected; (iii) if there is a significant risk of international spread; and (iv) if there is a significant risk of restriction on international travel and/or trade. Countries that determine that an event meets any two of these four criteria should inform WHO under the Regulations through their national IHR focal point.

1.6 FUNCTIONS OF POISON CENTRES

The functions of a poison centre can vary among and within countries, but, as mentioned above, they can include a poisons information centre, a clinical toxicology unit and a toxicology laboratory.

1.6.1 POISON INFORMATION CENTRE

A poisons information centre is a specialized unit for answering enquiries, usually by telephone, about exposure to chemical agents, including products, pharmaceuticals, substances of abuse, natural toxins, pesticides and industrial chemicals. The roles and functions of a poisons information centre are described in more detail in section 2 and are only summarized here.

Poisoning incidents can occur in the home, at work or in rural areas at some distance from a medical facility. Callers who seek advice from a poisons information centre may be health professionals, other professionals (such as police, schools) or members of the public. From the information they provide, a specialist in poisons information assesses whether the exposure is hazardous and provides information on whether and what kind of treatment should be given. The information is tailored to the circumstances and should be appropriate to the enquirer's level of knowledge and understanding. The poisons information centre provides evidence-based advice on management and advises against ineffective or unnecessary treatment. When a case is complex or severe and requires more detailed clinical advice, the specialist in poisons information can usually refer the caller to a medical toxicologist, who can discuss clinical management with the treating physician.

A poisons information centre can also advise on whether laboratory analyses are necessary and can provide information on the availability and location of antidotes. As a centre of expertise on toxicology, the poisons information centre can assist in diagnosis for patients with acute symptoms of unknown origin.

In some countries, including New Zealand, South Africa and the United Kingdom, poison centres have developed Internet-based clinical toxicology databases for use by health professionals in dealing with straightforward cases of poisoning (see section 9). A small number of online resources are also available for use by the general public. In the USA, an online and smartphone application provides members of the public with basic first aid and advice on poisons (25) and serves as a triage mechanism to reduce or prevent unnecessary medical referrals for exposure of low toxicity and to ensure that urgent medical referral is sought when necessary. In South Africa, information on low-toxicity substances is available from the AfriTox website (see section 9).

Poisons information centres have pioneered teleconsultation, and the use of other telemedicine techniques, such as audio-visual consultation with patients, is becoming more common (26). These techniques are particularly useful when there is no medical toxicologist at the location to assess the exposed patient or when a consultation with a specialist adviser such as a snakebite expert is required. In these cases, a telemedicine consultation could prevent transport of a patient to a distant hospital and may speed up diagnosis and treatment and save associated health care costs (25, 26). Where telecommunications infrastructure is poor and telephone services are inadequate, the centre can conduct direct consultations with those who visit in person, although this is not a common means of accessing the service. Poisons information centres can also provide written material on some topics, such as treatment algorithms in poster form. Other communication channels that can be used for non-urgent enquiries include e-mails, letters and social media.

In addition to providing information, a poisons information centre collects information on the poisoning cases referred to it, such as the circumstances and severity of poisoning. The collection and analysis of these data are part of the toxicovigilance activities of the poisons information centre, facilitating identification of unanticipated hazards of chemicals and products and the emergence of new toxicological hazards. These data may also be used to increase knowledge about the toxicity of different agents, to identify failures in risk management and to form the basis for prevention. More information on toxicovigilance and prevention is given below and in section 5.

In collaboration with other responsible bodies, a poisons information centre can play an important role in detection, preparedness and response for chemical incidents, as further described in section 6. In fulfilling its role and functions,

each centre must cooperate not only with similar organizations but also with other institutions concerned with the prevention of and response to poisoning. In some countries, poisons information centres may be required to provide a broad range of information on toxic chemicals, including on risks to the environment and on safe levels in food and environmental media as well as in the workplace. This information may be provided to a wide range of users, including medical and other professional personnel, other concerned groups, government authorities, the media and the public.

Severely poisoned patients may require rapid transportation to an appropriate hospital, or a specially trained doctor might have to be brought to patients if they cannot be moved immediately. Depending on the local circumstances and resources, a poisons information centre might have to be aware of the availability of paramedics and forms of transport. A formal arrangement for communication between the poisons information centre and the ambulance service may be helpful, particularly in the case of large-scale poisoning incidents, to assist with triaging patients for ambulance transport.

As poisoning can occur at any time, the information service should ideally be available 24 h a day, 7 days a week, throughout the year. This may not be essential when the poison centre first opens and there are few enquiries, but it should be the goal as the centre develops.

1.6.2 CLINICAL TOXICOLOGY UNITS

In addition to a poisons information centre, some poison centres have a clinical toxicology unit to provide treatment to poisoned patients. Patients may be admitted directly to the unit or transferred from another hospital for specialized treatment. A dedicated clinical toxicology unit provides a specialized medical function in the management and treatment of poisoning, helping to improve the identification of toxic substances and evaluation of their effects, to elucidate the mechanisms and kinetics of different kinds of toxic action and to assess new diagnostic and therapeutic techniques.

The clinical toxicology unit will usually be staffed by specially trained nurses and medical toxicologists. In some settings, the nurses may also be required to answer enquiries on poisons. In such circumstances, it is important to ensure that there are sufficient staff so that the quality of the advice and the clinical care of patients are not compromised.

One advantage of having both treatment facilities for poisoned patients and a poisons information centre in one unit is the opportunity for clinical staff at the poisons information centre to be involved in the treatment of poisoning cases, thus building their knowledge and expertise. It also provides training opportunities for poisons information specialists, who can sit in on case reviews. The association between information centres and treatment services facilitates updating and expansion of information on the diagnosis and treatment of local poisoning cases, encourages detailed follow-up of patients and stimulates essential research on human toxicology and patient management. Clinical facilities are described in detail in section 3.

1.6.3 LABORATORY SERVICES

Access to a laboratory service for toxicological analyses and biomedical investigations is important for the diagnosis, assessment and treatment of certain types of poisoning, particularly when a differential diagnosis with other causes of disease is required. Clinical units for treating poisoned patients must have access to a toxicology laboratory, as analytical data may be required rapidly for diagnosis and to support therapeutic decisions, such as the use of antidotal therapy or enhanced elimination techniques, and to determine the end-point of such therapy. After a large-scale chemical event or novel exposure, a toxicology laboratory should be able to process samples rapidly and identify the chemical of concern.

Toxicology laboratory services can be cost-effective, as one laboratory can serve a large territory or population. The services can reduce health service expenditure by confirming whether a patient has been exposed to or poisoned by a substance and whether specific treatment is indicated. In addition, use of a laboratory service can help avoid unnecessary treatment, overtreatment or unnecessarily prolonged hospital admission. Laboratory analyses can also be used to monitor the effectiveness of treatment. A toxicology laboratory can support research on, for example, determining the pharmacokinetics (absorption, distribution, metabolism and elimination) of a toxicant.

In addition, toxicology laboratory services can generate information useful for pharmacovigilance, toxicovigilance and surveillance and in early identification of new public health threats.

At a minimum, a toxicology laboratory should be able to identify, characterize and, ideally, quantify toxic substances in samples of biological fluids. Capacity to test other tissues, such as hair or nails, and analysis of environmental samples and residues may be developed later, or such testing may be done by other laboratories, such as forensic, environmental or research laboratories.

In view of the importance of laboratories for the identification and confirmation of toxic exposure, access to a toxicology laboratory is considered a required core capacity under the IHR (28). In many low- and middle-income countries, however, there are very few toxicology laboratories in which clinical samples can be analysed for a range of toxic substances. In such cases, it may be necessary to combine the services providing clinical analytical toxicology with those for forensic medicine, occupational toxicology, therapeutic drug monitoring, food contaminants, substance abuse or veterinary toxicology.

The development of laboratory networks and mutual assistance agreements should be considered in preparedness planning. For instance, after a large-scale chemical or mass poisoning incident, local toxicological laboratories may have insufficient capacity to conduct the necessary analyses and may require assistance from other laboratories, including in neighbouring countries. Such an arrangement might also be beneficial in low-resource countries more generally to ensure access to rarely required toxicological assays. Laboratory networks might be able to support development of new analytical methods, training and the provision of reference standards.

A laboratory should have adequate staff and equipment to conduct the analyses that are essential in cases of poisoning in the country or region. This is discussed further in section 4. The proximity of laboratories to the poisons information centres and treatment services can promote interdisciplinary collaboration.

1.7 OTHER ROLES OF POISON CENTRES

The poison centre may also be involved in other activities and have other responsibilities, which are outlined below and discussed in more detail in other sections.

1.7.1 TOXICOVIGILANCE

Surveillance was first undertaken in poison centres in the USA in 1957, when the National Clearinghouse for Poison Control Centers was established. The centre obtained information on the ingredients of different products and began to track exposure to poisons (16).

Toxicovigilance is an essential function of poisons information centres and is an important public health activity. Analysis of enquiries received by the centres permits identification of the circumstances in which the poisoning occurred, the populations at risk and the toxic agents most likely to be involved; it may also allow detection of previously unidentified hazards. The role of a poison centre in toxicovigilance is to alert public health and other authorities so that the necessary preventive and regulatory measures are taken. For example, the centre may identify:

- a large number of cases of poisoning by a product newly introduced onto the local market;
- new patterns in harmful use of psychoactive substances (for example, new psychoactive substances);
- new problems occurring in a particular population group (for example, analgesic poisoning in children);
- use of a herbal or traditional medicine resulting in poisoning;
- contamination of pharmaceutical preparations;
- cases occurring in particular circumstances (for example, carbon monoxide poisoning from misuse of heating stoves after a natural disaster);

- cases occurring at particular times of the year (for example, seasonal mushroom or plant poisonings, drug misuse during music festivals); or
- concern about product safety or labelling.

Illustrative examples are given in section 5. In some cases, the poison centre may conduct research to better understand such exposure.

A poisons information centre also plays an important role in the surveillance of chemical incidents and mass poisoning. In certain circumstances, the poisons information centre may be the first to detect an unusual pattern of poisoning, for example, if numerous individuals present to different hospitals with similar symptoms, which could be a sign of a contaminated product or covert release of a chemical. By communicating these signs to public health authorities, poison centres contribute to health security.

Such signs can be detected by mechanisms for automatic alerts in clinical toxicology databases if access to information on the same agent increases in a particular geographical region. In a country with several poisons information centres, a mechanism for pooling and sharing data from poisons enquiries enhances the ability to identify potential public health issues and to alert relevant authorities. Section 5 provides further details on toxicovigilance.

1.7.2 PREVENTION

The prevention of poisoning is an important goal for both public health and sound chemicals management. Staff at a poison centre can use their data, observations and experience to alert responsible authorities and manufacturers to circumstances in which the risk of poisoning is high, so that appropriate preventive measures can be taken. These measures may be regulatory, such as codes of practice or legislation that require precautionary labelling of toxic products, special packaging to reduce the risk of exposure to toxic substances, or modification or withdrawal of products from the market. Once risk management measures have been introduced, poison centres can assess their impact on the incidence and severity of exposure.

Another aspect of prevention is direct communication with the public through mass and social media, the production of brochures, leaflets or posters, and educational activities. Communication may be seasonal, for example, a winter campaign on prevention of carbon monoxide poisoning from heating appliances, or may be targeted at a specific group, for example, new parents or gardeners.

An example of a successful prevention intervention to which poisons information centres contributed was the introduction of child-resistant packaging in the USA in the 1970s. Data collected from poison centres were important in demonstrating that children were prone to accidental ingestion of pharmaceuticals and household products. This finding facilitated collaboration between the Government and industry, which resulted in introduction of the 1970 Poisons Prevention Packaging Act, many of the regulations coming into effect between 1973 and 1978 (29). Subsequent studies demonstrated that, during this period, the annual number of children under 5 years of age who were treated for accidental ingestion in hospital emergency rooms decreased incrementally, from 125 560 children in 1973 to 81 127 children in 1978. The introduction of child-resistant packaging was considered to be an important factor in this reduction. More recently, data collected by the National Poison Control Centre in Milan, Italy were used to demonstrate the need for and effectiveness of child-resistant packaging for liquid laundry detergent capsules (see section 5, Box 5). The role of poisons information centres in prevention of poisoning is described further in section 5.

1.7.3 CHEMICAL INCIDENT PREPAREDNESS AND RESPONSE

Poison centres have expertise in the diagnosis and management of exposure to a wide range of substances and also have databases on the toxicity of chemicals and products. They are therefore equipped to support the management of chemical incidents in a variety of ways. Whether the chemical incident is large-scale contamination of food or water, accidental industrial spillage, deliberate release of toxic industrial chemicals or chemical warfare agents or a contaminated product, the poison centre can advise first responders and those who are managing

exposed people, as well contribute to public health risk assessment. The toxicovigilance activities of the poison centre can alert public health and other authorities to emerging problems. In some cases, after release of an unknown chemical, the poison centre may be able to assist in diagnosis through its toxicology laboratory or by identifying a specific toxidrome.

Responses to chemical incidents are multidisciplinary, involving emergency services and government agencies, such as public health, environmental, agricultural and regulatory bodies. Private businesses and industry may also assist after chemical releases, such as water utility companies in the event of a water-borne hazard. The role of the poison centre in responding to incidents is strengthened if the centre is also involved in preparedness planning, so that all stakeholders become familiar with the poison centre and understand how it can contribute. The poison centre should be included in chemical incident response plans, and it should have clear internal procedures, backed up by training, for notifying public health authorities of and responding to events. The role of poison centres in chemical incident response is discussed more fully in section 6.

1.7.4 COORDINATION OF ANTIDOTE AND ANTIVENOM SUPPLIES

Information on the frequency and pattern of poisoning collected by poison centres is useful for evaluating the antidote and antivenom requirements in a country. In addition, poison centres can advise on the most cost-effective antidotes and antivenoms that should be prioritized for stocking by the health system. In some countries, poison centres are centralized holding centres for antidotes and antivenoms, particularly those that are not frequently used, and are responsible for dispatching these medicines as needed for the treatment of cases. Some poison centres are responsible for maintaining an inventory of the holdings of antidotes and antivenoms in major hospitals and elsewhere to facilitate their provision in an emergency. Further information on antidote and antivenom supplies is provided in section 7.

1.7.5 TEACHING AND TRAINING

As focal points of toxicological expertise, poison centres should engage in teaching and training of medical practitioners and other health professionals who are likely to encounter cases of poisoning. Indeed, building up a cadre of trained medical toxicologists is critical for the sustainability of the poison centre. Some poison centres have well-established 3- or 6-month training programmes for medical staff on a rotation basis. Poison centres can also provide training for first responders and telephone helpline staff. Poisoning prevention activities may involve some teaching, for example, in schools or to new parents. Section 10 describes training for poison centre staff.

1.7.6 RESEARCH

Poison centres are in a unique position to carry out and publish research based on the data they generate from enquiries and from the treatment of cases. Examples include:

- analysis of enquiries over time to identify trends in, for example, the impact of a new poisoning prevention measure;
- follow-up studies on the evolution and outcome of poisonings of interest; and
- studies of the circumstances of poisoning as a basis for preventive measures.

Research findings should be published regularly in peer-reviewed journals. In addition, staff should actively seek to participate and present at national and international conferences and workshops. The role of poisons information centres in research is discussed further in section 2.

1.7.7 MEDICINE (DRUG) INFORMATION, TERATOLOGY AND PHARMACOVIGILANCE

The provision of information on medicines (drugs; the terms are often used interchangeably) supports safe, effective, efficient use of medicines. The medical profession should have access to advice on the therapeutic use, contraindications, interactions and adverse effects of pharmaceutical agents, including traditional medicines. Most developed countries have medicines information centres that provide such information. When there is no such service or it is provided only during office hours, the poisons information centre may be contacted. In some settings, a poisons information centre may be integrated with a medicines information service, although it may be accessed through separate telephone enquiry lines and may be available only to health care professionals.

Although poisons information centres usually take relatively few enquiries about medicines (usually out of office hours), they can contribute to pharmacovigilance by sharing information on cases with other institutions, such as pharmaceutical companies or medicine information services. If a medicines information service is limited or absent, the poisons information centre may receive significantly more enquiries about medicines. As such calls are usually less urgent than those for poisons information, the centre should have a policy on triaging such calls or referring them.

The potential effects of medication taken by a breastfeeding mother are usually considered medicines information, particularly when related to the use of therapeutic drugs, although some situations may be the remit of a poisons information centre. For example, if a mother who is breastfeeding takes an overdose, there might be concern that the substance is secreted into the breast milk, resulting in exposure of the infant.

A few teratology information services provide advice on the potential effects on the fetus of exposure to chemicals and drugs, both in terms of therapeutic dose and overdose. In Europe, information on such services is provided by the European Network of Teratology Information Services (30). In certain cases, a poisons information centre is combined with or linked to a medicine and/or a teratology information service. This is the case of the United Kingdom Teratology Information Service, which is linked to the National Poisons Information Service (NPIS) (31) and the Centro antiveleni e tossicologia in Bergamo, Italy (32). This may be a useful model for low- and middle-income countries, to maximize use of limited resources and of appropriate sources of teratology information (see section 9).

1.7.8 ENVIRONMENTAL AND OCCUPATIONAL TOXICOLOGY

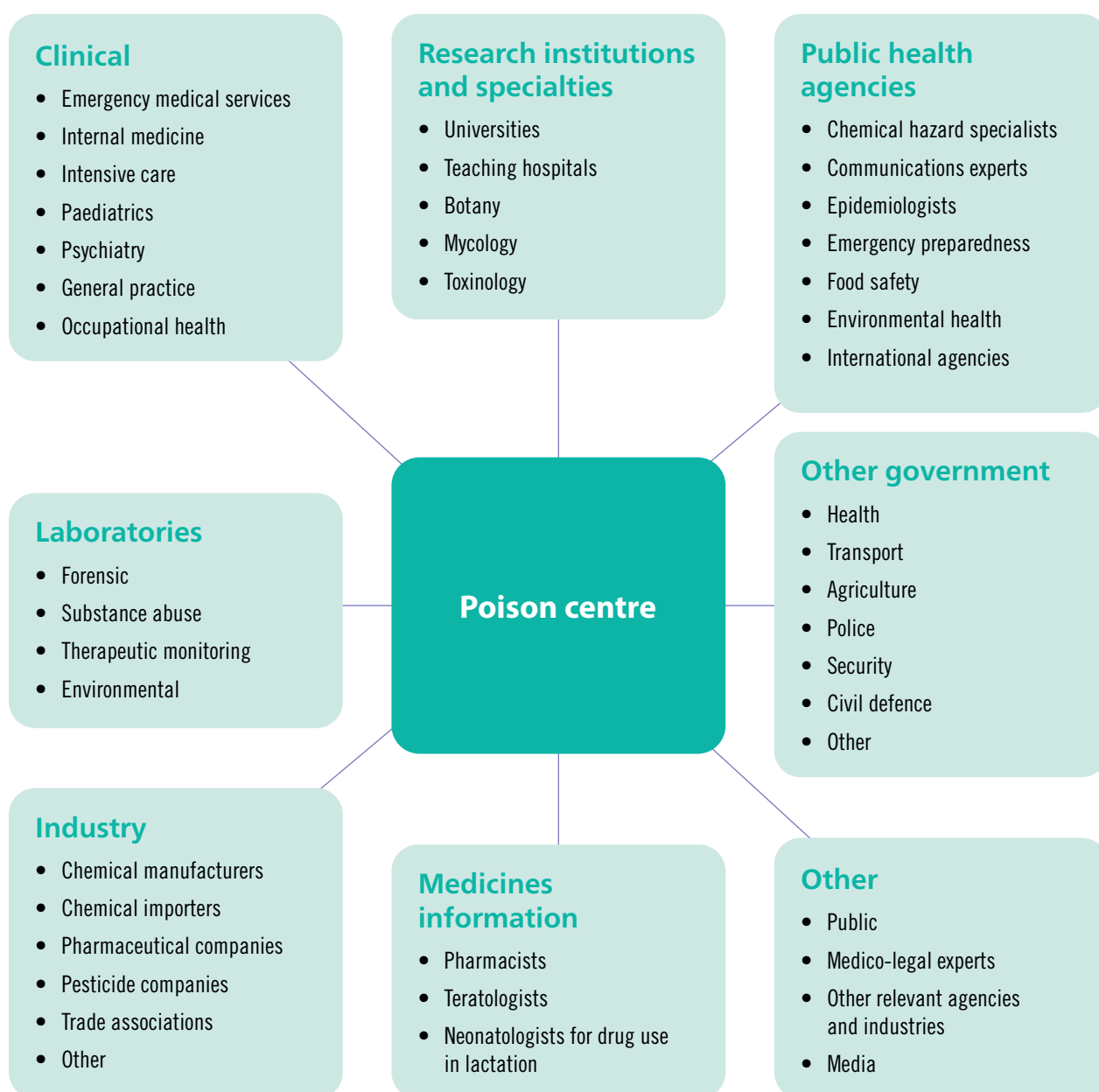
In the broad scope of enquiries that a poisons information centre should be prepared to receive, there may be questions about the health impact of toxic chemicals in food, toxic wastes, consumer goods such as cosmetics and the environment (air, water and soil) and from occupational use. These queries may concern whether a chemical can give rise to chronic poisoning, whether the effects of exposure are cumulative and whether there are long-term sequelae. Although these enquiries are less frequent than more conventional calls, poisons information centres can provide an important public health role in answering them and identifying concerns that should be referred to public health authorities.

Some poison centres may be linked to occupational medicine and industrial hygiene activities and laboratories and provide toxicological expertise in these fields.

1.7.9 COOPERATION AND INTERRELATIONSHIPS

To provide an effective service and to maximize their roles in the prevention and management of the effects of toxic chemicals on human health and the environment, poison centres should maintain contact and cooperate with a wide range of partners, both within and outside the health sector. These include various medical specialities, academic and research institutions, experts in toxicology and mycology, industry, government departments and the mass media. Figure 1 indicates the typical contacts a poison centre should consider maintaining to operate successfully, although they may vary by country.

Figure 1. Key stakeholders in poison centres



Good relations with the mass media play a key role in bringing information to the public. The publishing or broadcasting of educational messages (usually in conjunction with public health agencies) on the prevention of poisoning can form part of general health education; poisons information centres can provide the media with appropriate information and material. Hence, collaboration with communications experts and appropriate media training are important. The media have an even more significant part to play in the event of a major chemical incident, and they must be kept fully and properly briefed by public health agencies, poisons information centres and emergency services, so that essential, balanced information is provided to the public without causing undue panic and alarm.

Of equal importance is contact among poisons information centres themselves, both nationally and internationally. This may be established directly or through membership in national and international scientific and professional associations and participation in congresses and meetings. Examples of associations with international membership that organize regular scientific congresses are:

- American Academy of Clinical Toxicology (33)
- American College of Medical Toxicology (34)
- Asia Pacific Association of Medical Toxicology (35)
- European Association of Poisons Centres and Clinical Toxicologists (36)
- International Union of Toxicology (37)
- Latin American Association of Toxicology (Asociación Latinoamericana de Toxicología) (38)
- Middle East & North Africa Clinical Toxicology Association (39).

Important areas for international collaboration are in the exchange of data on cases, products and substances in comparable formats, evaluation of antidotes, quality control, training, response to major accidents and research.

1.8 HEALTH AND ECONOMIC BENEFITS

The subsections above describe the contributions that poison centres can make to public health and to improving the clinical management of poisoning by providing targeted information and advice. Poison centres also have economic benefits in terms of savings in health care costs and to individuals, mainly due to avoided use of health care services and of ineffective or unnecessary treatments, shorter hospital stays and fewer days of lost work.

Consultation with a poisons information centre can quickly identify exposures that carry no or minimal toxic risk and can be managed at home or at primary care level, thereby avoiding unnecessary transport and hospital treatment. Severe poisoning cases, which may require specialized facilities and equipment for treatment, can be directed immediately to a suitable hospital, thus reducing delays. Specific antidotes, therapeutic agents and specialized medical equipment are made more readily available by coordination of stocks, and their use can be rationalized, thereby reducing costs and saving lives.

A number of studies have addressed the cost-effectiveness of poison centres (summarized in Annex 1), although most were conducted in high-income countries. In some studies, interviews were conducted with callers to the poison centre to determine how they would have managed the exposure if they had not had access to the service. These studies showed that people with low-toxicity exposures would have been referred or would have self-referred to physicians or hospitals, which would have cost more than contacting the poisons information centre. Cost-benefit estimates showed that use of a poisons information centre by the public led to significant net savings in health care costs as compared with the costs of funding the poisons information centre.

In two studies in the USA, the actual impact on use of medical services when poison centre services were temporarily suspended was assessed (40, 41). These showed an increase in health care costs, mainly because of more self-referrals to medical services. In one study, the increase amounted to more than three times the state funding for the poison centre. In 2012, the American Association of Poison Control Centers commissioned a report on the cost-effectiveness of US poison centres, which found a near 1:14 benefit for each US\$ spent, amounting to an estimated saving of US\$ 1.8 billion per year (42). The analysis took into account savings due to avoided use of medical services, shorter hospital stays, in-person outreach and fewer days of work lost. It did not include other benefits such as the provision of surveillance data to federal agencies, training of health care professionals in toxicology or involvement of the centre in local, state and federal emergency preparedness and response.

A study in the United Kingdom, where calls are not taken directly from members of the public, also found significant benefits, with the avoidance of an estimated 41 000 referrals to an emergency department per year (43).

The contribution of poison centres to the prevention of poisoning provides a health benefit in reducing exposures and therefore morbidity, as well as saving costs to the health system, the community and individuals. An example is the identification by numerous poison centres of the toxicological hazards of liquid laundry detergent capsules, which led to improvements in their packaging and labelling and a subsequent reduction in exposure (44) (see Box 5 in section 5).

1.9 ESTABLISHING A POISONS INFORMATION CENTRE

Access to a poisons information centre should be available in every country, irrespective of its size or population. The optimum population size that a poison centre should serve and, therefore, the number of centres that a country should have is not established. Some variables that could influence such a decision include whether the centre will be available to the public or just to health professionals, the geography and its impact on communications infrastructure, the language(s) spoken in different regions in the country and the level of government that is responsible for health services (for example, national, federal or regional). Another factor is provision by a poison centre of online clinical toxicology information, as use of online information to deal with straightforward poisoning cases can reduce the number of telephone enquiries to a poisons information centre, thereby potentially increasing the population size that can be served by a single centre.

A balance must be found between ensuring enough centres for complete coverage of the country and a good response time for enquiries and having so many centres that the service is not cost-effective. Another consideration is that specialists in poisons information should handle a sufficient number of calls to develop and maintain competence but not so many that the quality of the service suffers because there is insufficient time to respond to each call adequately. In small countries, access to a poison centre in a neighbouring country may be sufficient, especially if the countries share a common language. If a country is to receive the full toxicological and public health benefits from a poison centre in another country, however, certain requirements must be met, which are described in section 2.

When there are several poison centres in a country, they must collaborate to pool resources, provide consistent advice and collect harmonized data.

Poison centres should be officially recognized by government authorities. They should have independent status, stability and neutrality to enable them to carry out their functions effectively. A poison centre can achieve recognition by contributing to mitigation of poisoning through policy recommendations, research and providing treatment protocols for the medical community. A centre may have a governing body that includes representatives of various government and other authorities to provide policy guidance and assist in fund-raising (see section 11). This body should not, however, interfere with the daily operation of the centre or compromise its independence. Like other health care providers, a poison centre should maintain the confidentiality of its patient data and of commercially sensitive data on product composition. Funders of the centre should respect its independence and neutrality. Information should be provided free of charge to enquirers, particularly in emergencies, although charges may be levied in certain circumstances (see section 11).

1.10 CONCLUSIONS AND RECOMMENDATIONS

This section presents information on the various ways in which poison centres can improve the management of poisoning, strengthen the public health response to chemical exposures and contribute to the sound management of chemicals. Ideally, every country should have access to poison centre services. The subsections below describe the national and international actions that should be considered by authorities to strengthen the establishment and maintenance of poison centres.

1.10.1 ACTION BY NATIONAL, REGIONAL AND LOCAL AUTHORITIES

The prevention and control of poisoning could be made more effective by a number of actions by national and local authorities:

- official recognition by government authorities of the role of poison centres in toxicovigilance and of their contribution to prevention, with provision of adequate financial support;
- ensuring that poison centres are appropriately integrated into chemical emergency preparedness and response structures;

- ensuring that poison centres are integrated into public health services and systems to ensure cooperation in sharing information and data;
- ensuring that poison centres have the resources to fulfil the requirements of the IHR, including the provision of a 24-hour service;
- ensuring that, when there are several poison centres in a country, they have sufficient resources to work as an efficient network and work together to standardize their treatment advice and harmonize their data collection;
- ensuring that the community is aware of, and has ready access to, the services provided by poisons information centres, either directly or through health care professionals;
- establishing a robust channel of communication between the poison centre and the public health authority, so that alerts and advice on appropriate response are communicated;
- ensuring that centres have access to adequate information on the composition of commercial and other products on the local market (on the understanding that the confidentiality of the information will be respected);
- establishing clinical toxicology services and building capacity for laboratory-based toxicology analysis when indicated;
- providing courses on toxicology and appropriate facilities in order to establish certificates or other appropriate qualification for poisons information specialists and for nurses and paramedical staff working in poison treatment units;
- ensuring official recognition of clinical toxicology as a discipline to encourage academic institutions to establish appropriate teaching units or departments;
- promoting sub-national and international exchanges of staff and experts;
- ensuring rapid access to antidotes and essential supplies for the treatment of poisoned patients in the event of an emergency;
- establishing mechanisms and facilities for systematic recording and long-term follow-up of patients exposed to toxic chemicals; and
- considering a requirement that certain poisonings be notifiable, according to the epidemiology of poisoning in the country.

1.10.2 ACTION AT THE INTERNATIONAL LEVEL

Cooperation at the international level among poison centres, their national and regional associations, relevant professional bodies, governments and international organizations could do much to improve the prevention and control of poisoning by:

- improving international communication and exchange of information and experience in the field of poison control (including personnel, particularly for education and training);
- harmonizing, to the extent possible, the definitions, coding and criteria for clinical signs, symptoms and sequelae of poisoning, including severity grading;
- ensuring comparability among methods of collecting, storing, transporting and analysing biological and other samples and monitoring exposure to toxic chemicals;
- establishing internationally agreed mechanisms for the collection, validation and analysis of data on exposure to toxic chemicals;
- undertaking collaborative research projects with agreed protocols (for example, for evaluating new antidotes, elucidating the mechanisms of poisoning and improving treatment regimens);

- establishing channels of communication among countries so that antidotes, other therapeutic agents, medical equipment and samples (where necessary) can be made available or exchanged rapidly on request in the event of a chemical incident or emergency;
- establishing channels of communication among countries for rapid access to information about chemical incidents or emergencies for deciding whether a toxic alert should be called (see section 5); and
- facilitating collaboration among countries for the supply of technical equipment, including laboratory equipment.

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Entrance to Ramathibodi Poison Centre, Bangkok Thailand / Credit: Puangpak Promrungsri

2 POISONS INFORMATION CENTRES



2.1 INTRODUCTION

The roles, functions and establishment of a national poison centre are described in section 1 of these guidelines. This section provides more detailed guidance on the operational aspects of a poisons information centre, including considerations for starting a new centre. The location, facilities, equipment, staffing, financial aspects, legal framework and governance of a poisons information centre are also addressed.

Poisons information centres provide specialized advice on the diagnosis and management of poisoning in patients of any age, exposed by all routes and in any circumstance (accidental, intentional, unintentional, occupational or environmental). The agents include consumer products, pharmaceuticals, substances of abuse, environmental chemicals, natural toxins, pesticides and industrial chemicals. Poisons information centres may also assist in poisoning prevention strategies, public outreach, response to chemical incidents, training and public health toxicovigilance.

Poisons information centres promote the cost-effective, evidence-based management of poisoning and avoidance of unnecessary or ineffective treatment. These centres provide a service to both health professionals and, in many countries, the public. Other users may include government bodies, emergency services, regulatory agencies, public health services, academia and industry.

2.2 ORGANIZATION AND OPERATION OF A POISONS INFORMATION CENTRE

The structure and functions of poisons information centres depend on local requirements and resources, although there are some core similarities. A poisons information centre is typically staffed by specialists called, for the purpose of these guidelines, “specialists in poisons information”. These staff may have a variety of biomedical or health care professional backgrounds and receive specific training for work on poisons information. Their task is to provide timely, accurate information and advice on a broad spectrum of toxicology-related issues, including verification of and information on products and ingredients, clinical features that may follow exposure, the likelihood of toxicity and its potential severity, whether treatment is required and advice on clinical management and decontamination.

To be effective, poisons information staff should have access to extensive toxicological and product databases. Ideally, the centre should be supported by physicians trained and experienced in clinical toxicology who can provide additional specialized advice and clinical discussion on severe, complex or unusual cases.

Every poisons information centre should be able to operate independently and impartially so that it can provide an authoritative service without any perceived conflict of interest. The safeguarding of confidentiality and data storage should conform to national legal, clinical and ethical standards.

Poisons information centres should be formally recognized by government authorities to ensure the sustainability of the service. For example, the roles and responsibilities of poison centres in France and Italy are defined by statute, particularly with respect to toxicovigilance. In other countries, for example, Algeria, medical practitioners are required to contact the poisons information centre about all cases of poisoning.¹ Such a requirement is not however, universal, and a decision by a health care provider to contact a poisons information centre is often based on their toxicological knowledge and experience, the agent involved, the severity of poisoning and ease of access to the service.

2.3 REQUIREMENTS FOR A POISONS INFORMATION CENTRE

2.3.1 LOCATION

Most poisons information centres are associated with a health care facility, usually a hospital; however, some are based in public health institutions, toxicology laboratories or universities. The decision on the location of a poisons information centre will depend on local circumstances and certain considerations, which are discussed below.

As poisons information centres provide health-related information and advice, they should ideally be located within or close to a hospital with emergency and intensive care facilities. This also has the advantage of ready access to a network of medical disciplines to support and enhance the work of the centre and to give staff the opportunity to extend their knowledge of the clinical aspects of poisoning. Furthermore, hospitals are open 24 hours a day and therefore have the necessary infrastructure to support a 24-hour a day poisons information centre.

If the centre is located within a teaching institution such as a medical school or university, it will have easier access to, for example, libraries, research facilities and educational activities. Location within a public health institute or ministry will permit more activities for the prevention of poisoning and closer relationships with decision-making authorities. In these settings, it is essential that the medical staff of the centre still have some clinical responsibilities and, ideally, are involved in the care of poisoned patients. There should be provision for the poisons information centre to operate 24 hours a day once it is fully established.

The poisons information centre should have dedicated space for its operations and for the secure storage of its information and records. If the number of enquiries is such that staff must be present 24 hours a day, the centre should be a self-contained, secure facility.

2.3.2 STAFF

Poisons information centres are centres of expertise, and the staff should be recruited and trained accordingly. The staff can include physicians, nurses, scientists (for example, biochemists, biologists, chemists), pharmacists or a mixture of these. Key members of staff are the director, administrative and operations manager, specialists in poisons information, medical toxicologists and support staff.

A fully operational centre that provides 24-hour service and adequate medical advice requires at least one medical toxicologist and a sufficient number of specialists in poisons information to ensure that at least one person is on duty at any time. In practice, a poisons information centre should have an adequate number of dedicated, trained specialists in poisons information to ensure coverage of staff absences for illness, holidays and professional training.

The number of staff required depends on several factors, including the operating hours of the centre and the volume and complexity of the calls. The latter are influenced by whether the service is available to the public or only to the medical profession and the penetrance of service, i.e. the number of calls per 1000 population served. Furthermore, as the frequency of enquiries is likely to vary each day and week, additional staff may have to be on duty at busier times. Patterns vary throughout the world, and each centre must ensure that its service is adequate for local needs. As the poisons information centre develops, the number of staff required may increase, and, when specialists in

¹ Professeur Hadjadj-Aoul Fatma Zohra, personal communication, December 2018

poisons information are expected to undertake other work such as researching and writing substance datasheets and treatment protocols or conducting follow-up studies or other research, additional staff may be required.

DIRECTOR

The poisons information centre should ideally be headed by a director experienced in clinical toxicology; however, if the director's role is administrative, a dedicated medical toxicologist should support the director. The director is wholly responsible for the operation of the centre and should be employed full-time. The director should have personal leadership qualities and the ability to supervise staff and maintain good relations with colleagues and other stakeholders. The director should also be able to promote research, raise funds and undertake further development of the poisons information centre. The director or the supporting medical toxicologist should also take responsibility for clinical governance and for defining research priorities.

ADMINISTRATIVE OR OPERATIONS MANAGER

Depending on the size and requirements of the centre, it might also be desirable to have an administrative or operations manager who is qualified to manage and supervise the centre's financial resources and equipment and operational requirements, including staff rotas and dealing with routine personnel matters. The respective responsibilities of the director and the administrative manager should be clearly defined.

SPECIALISTS IN POISONS INFORMATION

A specialist in poisons information is usually the first point of contact with the service. This person deals directly with enquirers and provides timely responses to their requests for information and advice. Specialists in poisons information are skilled clinical toxicologists drawn from many different disciplines, including various branches of medicine, pharmacy, nursing, chemistry, life sciences and veterinary science. In some countries, only physicians are permitted to provide medical advice, so that the specialist in poisons information must be a specially trained medical doctor. When they are nurses, they should ideally have some experience in clinical management of poisoned patients, particularly if there is an associated clinical toxicology unit.

The knowledge and skills required for providing information on poisons are highly specialized and not generally taught in other clinical and scientific fields; therefore, an in-house programme for training and assessment is essential. Training should be continuous, so that staff maintain up-to-date knowledge of new developments in toxicology. Training should result in an officially recognized certificate or other qualification, such as designation as a clinical specialist, when this exists. Consideration could be given to liaison with other poison centres to develop a transferable qualification that would enable staff to work at another centre. Training is discussed in more detail in section 10.

Once trained, specialists in poisons information should be able to provide tailored information and advice to enquirers, using the databases and other sources of information at the centre and in accordance with agreed patient management protocols. In addition to scientific knowledge, specialists in poisons information should be proficient in operating computer systems and relevant software. They should be able to record details of all enquiries, cases and consultations in a standardized way, which may include entering data into a poisons enquiry database (see section 8). When information is not immediately available at the centre, for example about a specific product, specialists in poisons information should know how to obtain it. They must also use agreed protocols to recognize when to consult a medical toxicologist, senior colleague or specialist adviser and when to alert the public health agency. In many situations, specialists in poisons information help to analyse the data collected for service improvement and contribute to the wider research base for toxicology.

Each specialist in poisons information should take part in all the activities of the centre, including answering enquiries, preparing documentation, reports and monographs, evaluating and interpreting data and regularly searching the literature. These tasks all contribute to building knowledge and can increase job satisfaction. Regular discussions among the team of interesting cases and toxicological problems should be encouraged

as a means of making each member aware of new developments and promoting a harmonized approach to poisoning and patient management. The development of networks to facilitate periodic meetings and information exchange among poisons information centres within a country or in other countries in the region should also be encouraged in order to discuss topics of common interest and strengthen links among the centres.

Specialists in poisons information should be encouraged to participate in research in the field of toxicology to engage and update them. They should also have the opportunity to present their work at appropriate scientific meetings and should be encouraged to attend and contribute to national and international conferences and to develop as scientists in the field of toxicology.

THE MEDICAL TOXICOLOGIST

Clinical toxicology is the discipline that addresses the harmful effects of chemicals, including natural substances, on humans, although its scope is broader than the clinical aspects of poisoning. A poison centre should have a medical toxicologist, i.e. a qualified physician with training and several years' experience in treating cases of poisoning. A medical toxicologist may also have a grounding in aspects of emergency medicine, paediatrics, public health, internal medicine, intensive care or forensic medicine. Clinical experience in occupational diseases and in diseases caused by chemicals of environmental origin is also relevant. Experience in the clinical management of poisoned patients is essential, and experience in toxicological research is also valuable. All countries do not recognize clinical toxicology as a medical specialty, with a training path and accreditation, and it may, instead, be included as a sub-speciality of clinical pharmacology or occupational medicine. This is discussed further in sections 3 and 10.

In low- and middle-income countries with inadequate medical staffing overall, it may be particularly difficult to recruit a trained medical toxicologist, and it may be possible to recruit only other types of health care professional, such as nurses or pharmacists with some training or experience in clinical toxicology. In countries that lack medical toxicologists, the poison centre should nurture development of this speciality through training, research and collaboration with colleagues both locally and internationally.

In some countries, medical toxicologists provide the front-line poisons information service, whereas in centres in other countries they deal only with more complex cases of poisoning referred to them by specialists in poisons information. As an expert, the medical toxicologist should be involved in training specialists in poisons information and trainee medical toxicologists. They are also usually involved in training in hospitals and medical faculties and sometimes in multidisciplinary teaching of toxicology at university level.

Medical toxicologists must keep abreast of the latest developments in all areas of clinical toxicology, including analytical and experimental toxicology. They must be able to organize and compile comprehensive dossiers on poisons and their effects from the available material and personal experience. It is particularly important that they systematically collect and evaluate clinical observations, which are a major source of clinical data for the poisons information centre and for the evidence base for practice.

SUPPORT STAFF

A poisons information centre may require the support of at least one administrator to assist the director, manager and medical toxicologists with appointments, meetings and administrative duties.

As most poisons information centres rely on electronic databases, they are likely to require the support of a computer specialist. Depending on the needs and resources of the centre, this may be a dedicated member of staff or an IT specialist. Support may be provided by the host institution, such as the IT department in a hospital.

Provision should be made for the maintenance and cleaning of equipment and facilities at the centre. This is often the responsibility of the administration of the building in which the centre is located; however, it may be the responsibility of the poison centre if, for example, it is located in a non-clinical area of a hospital.

The security of staff and the poison centre premises is important, particularly when staff members work alone at night. The centre might require its own security guard or a guard in the building in which it is located to ensure a rapid response in case of a security incident.

SPECIALIST ADVISERS

A poisons information centre requires a variety of specialist help and advice, which may be medical or non-medical and may be provided by independent experts or representatives of specialized organizations or local agencies. As the centre acquires more experience and the scope and volume of its work expand, it may become necessary to employ extra staff with some of the various kinds of expertise indicated below, part- or full-time.

Various kinds of specialist help may be required in the management of certain cases. Poisons information centres should therefore have rapid access to a network of external specialists, such as in paediatrics, psychiatry, teratology, veterinary medicine and toxinology. For example, if a poisons information centre decides to offer a service for poisoning in animals, the support of trained veterinarians might be necessary to ensure that appropriate advice is given. A centre in a country where envenoming or poisoning by snakes, spiders, scorpions and marine animals is common should have access to experts in this field to advise on management and on use of antivenoms. Botanists and mycologists can identify venomous plants and fungi, respectively.

Specialist advisers need not be permanent members of staff, but formal agreements should be in place defining what is expected of the specialist and how and when they should be contacted. Close relations should be established with these external experts. They are unlikely to require specific training, but they should be introduced to the work of the centre and the way in which it functions. Periodic joint scientific meetings and activities may help to strengthen relations between the centre and its specialist advisers, who may also train poison centre staff in their areas of competence. Access to epidemiological expertise is helpful for surveillance and toxicovigilance. The staff of a poisons information centre may include an epidemiologist, or it may be able to access expertise from elsewhere, for example, a public health agency.

2.3.3 DATABASES

To function, poisons information centres must have access to databases containing information on substances and products and a database of enquiries. These databases are described briefly below and in more detail in sections 8 and 9 and Annex 2.

DATABASE ON SUBSTANCES

In order for a poisons information centre to answer enquiries about exposures, it must have data on the substances about which it may be consulted, i.e. consumer products, professional products, chemicals, pharmaceuticals, substances of abuse and natural toxins (flora, fungi and fauna). A small number of databases are available for poison centres on subscription that contain information on a wide range of substances and products, on their toxicity and on managing exposure. A potential limitation is that the content is mainly geared towards the country of origin of the database, and there may be no or only limited data on the agents of concern to a poisons information centre in a different country. Further information on these databases is given in section 9. Data on locally important agents may therefore have to be compiled by the poisons information centre, and this will be one of the first tasks of a new centre. For each agent or group of agents, the poisons information centre should include an evaluation of toxicity, features of poisoning and treatment. This activity will require literature researches and reviews of case data, including those collected by the poison centre.

Product information is an important component of these databases. Information can be sourced from the Internet, local pharmacopoeias and government registries or directly from pharmaceutical firms and

manufacturers and suppliers of household, agricultural and industrial products. It is helpful if there is a regulatory requirement for manufacturers to provide product information to poison centres; otherwise, the poison centre should establish mechanisms for obtaining adequate data from manufacturers and suppliers. In the absence of information from manufacturers, some information can be found on product labels, either online or by visiting retailers.

Substance databases should be supplemented by reference books and subscriptions to relevant journals (see Annex 2). As poisons information centres may be expected to identify tablets, capsules, plants, fungi, insects and animals, pictorial information is also useful.

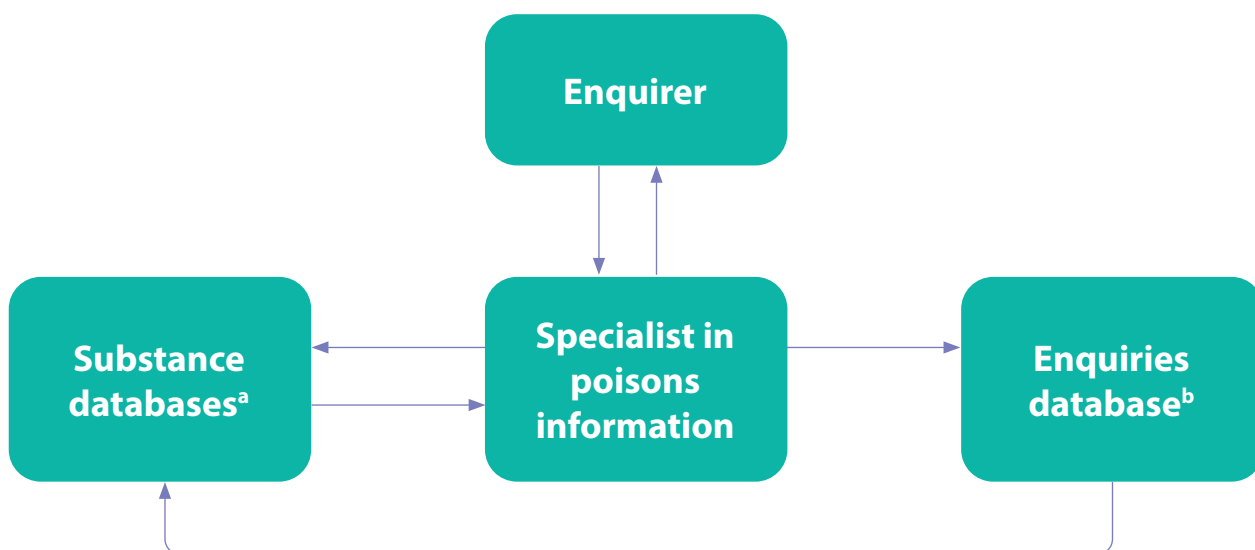
Additional information on compiling substance and product databases is given in section 8.

DATABASE OF ENQUIRIES

Systematic collection of data from poisoning enquiries is a key function of a poisons information centre. These data should cover not only telephone enquiries pertaining to clinical cases of poisoning but every kind of enquiry received at the centre, including general requests for information (for example, poisoning prevention), as these all contribute to the workload of the centre.

Standardized recording of each poisoning enquiry is very important, as it is both a record of the transaction between the enquirer and the specialist in poisons information or medical toxicologist and a unique source of information on the circumstances and effects of exposure to a wide range of substances. This information should be used to refresh and update the substance database so that accurate, up-to-date advice is provided for future cases (see Figure 2). When cases are followed up after the initial enquiry, valuable information can be collected on the outcome of exposure, including the type and efficacy of treatment. While enquiry data can be captured on paper, computerizing the information will greatly facilitate subsequent analysis. Information to be included in an enquiries database is listed in Annex 3.

Figure 2. Flow of information on cases and substances in a poisons information centre



^a Data derived from various sources, including product databases, scientific journals, textbooks, reports, safety data sheets and evaluated enquiries.

^b Data obtained in the course of the centre's information work and its follow-up of reported poisoning cases. Data on exposures and outcomes for specific substances can be fed back into the substance database, for example, to help establish the toxic dose.

OTHER INFORMATION SOURCES

Poisons information centres should also collect (and regularly update) information on health and other relevant resources and facilities in the region or country. This information should cover services that provide diagnosis and treatment, including specialized treatment facilities such as dialysis and transplant centres, clinical toxicology units, analytical facilities and the types of analyses they provide, facilities for emergency transport of patients, antidotes and their availability and other medical and non-medical services with related areas of responsibility.

A poisons information centre should also have ready access to a medical library with scientific publications and literature review services. While many publications are available online, access may require payment. The poisons information centre should determine which reference books and other publications should be accessible at all times in the centre itself and which could be accessed in a local medical library. Annex 2 lists a selection of books, journals and electronic resources that are useful for poisons information centres.

2.3.4 FACILITIES AND EQUIPMENT

ROOMS

The poisons information centre should have a sufficient number of spacious rooms to perform its functions. One room should be allocated to the “answering service” and should contain the telephones assigned to it, plus the books and other information materials required by the specialists in poisons information and physicians on duty, basic administration files and standard operating procedures. This room should be free of external distractions and background noise and exist as an area of confidential space. Staff on duty should have a private area located close by, with the basic facilities for personal hygiene and rest breaks, including for preparing refreshments and eating meals.

A space for secure storage of documents may be required, such as paper-based case records and product information. A separate area should be set aside in which scientific literature can be read. This area or room should ideally be at least large enough to allow all staff to attend departmental meetings, training and discussions or meetings with external advisers or visitors.

The medical director and administrative manager should each have an office or suitable private area, including space for additional administration staff if necessary. When medical staff carry out consultations with patients, a suitable private consultation room should be available.

As the activities of the poisons information centre expand and new functions are added, additional space may be required. The location should therefore allow for future expansion.

OFFICE FURNITURE AND COMPUTERS

The minimum furniture required for a new poisons information centre consists of ergonomic desks and chairs, large work tables, lockable filing cabinets and bookshelves. As the centre develops and the working area grows, further appropriate office and library furniture should be provided. There should be specially designed work stations with computer terminals and monitors and both Internet and telephone access points. If the centre begins to function 24 hours a day, staff on duty must have a private area with suitable office furniture to accommodate long working hours and to take rest breaks.

COMMUNICATIONS EQUIPMENT AND INFORMATION TECHNOLOGY

A poisons information centre must have adequate telecommunication and IT resources, in particular telephones and computers. As a poisons information centre receives most of its enquiries by telephone, a reliable telephone service that covers the geographical area served is essential. Access to the poisons information centre should be by at least one or more dedicated telephone numbers. Two telephones are a

minimum to allow for calling out at the same time as calling in. Use of mobile phones or voice-over Internet may be preferable in locations where landline infrastructure is absent or unreliable. In some countries, the poisons information centre is automatically connected with the emergency services telephone network, and all calls for toxicological emergencies are directed straight to the poison centre. The emergency number of the poison centre should ideally be easy to remember and accessible from all telephones in the region served by the centre. A toll-free line or, at a minimum, a local call-rate number is also desirable, especially in low-income countries, to ensure easy access to the centre.

As the poisons information centre develops and enquiries increase, use of a call management system should be considered, if it has technical infrastructure to host it. These systems accept a call, reroute it if necessary and let the caller know their position in the queue. An on-hold recorded message can provide useful information. The system can also generate statistics for quality control, such as the average waiting time for the caller to be answered by a poisons information specialist or the number of callers who disconnected rather than waiting.

Equipment for recording each telephone enquiry, while not essential, provides a more complete record of each enquiry. The recordings may also be useful for training and quality control (see section 10).

The poisons information centre must have access to a reliable, dependable Internet connection to allow access to online databases (see section 9) and the possibility of cloud-based information storage, retrieval and sharing. Electronic mailing systems (e-mail) provide fast communication among individual poisons information centres and other sites. Dependable communication is essential not only for the information service but also for necessary contacts with other poison centres, external advisers, manufacturers and others. The poison centre should have a dedicated e-mail address that is accessible to all the specialists in poisons information and is frequently checked. A fax machine may be useful as a back-up for sending written information.

The importance of worldwide communication networks for toxicology is widely recognized. Ideally, the poison centre should be equipped with the most practical advanced communication system appropriate to the country and to the centre's functions. These systems may also include teleconferencing or video conferencing for the purposes of telemedicine. Provided there is adequate telecommunications infrastructure, telemedicine offers the possibility of providing a toxicology consultation service to remote populations, which may be beneficial in isolated or low-resource communities with limited access to specialized poisons information advice.

Telecommunication systems must be well maintained and financially supported by the appropriate authorities or government ministry. Robust back-up systems should also be in place in the event of Internet or telephone service outage to ensure the continuity of the service.

From the outset, a poison centre should be adequately equipped with computers linked to a good-quality printer, scanner and photocopying equipment. Computers are required for data storage and retrieval, for electronic communication and to run toxicological databases. While most subscription databases are used online, some providers make versions available that can be run from a standalone computer. This is useful in low-resource settings where regular interruptions to Internet connection may be common. The centre should have the capacity to back up all databases regularly and, ideally, to store the back-ups at a different physical location. The provision of tablets or large-screen smartphones would enable staff to access a variety of relevant toxicology-related mobile phone applications that cannot be accessed via desktop computers, or for the purposes of telemedicine.

As the poison centre should be involved in education and training, it might find it useful to have its own projector and screen or equivalent equipment. Poisons information centres should consider producing their own brochures, posters, websites and social media pages for publicizing and circulating information on poisoning prevention and advertising the centre to the public (if it is publicly accessible). If a poisons information centre does set up a website and social media presence, some resources should be dedicated to keeping them active and up to date.

ANTIDOTE STORAGE

If the poison centre is responsible for holding stocks of antidotes and antivenoms (see section 7) and other substances used in the treatment of poisoning, it will usually require a refrigerator. A lockable cabinet for storing pharmaceutical agents may also be required. Local guidelines for storage and dispensing such products should be adhered to.

BACK-UP POWER SUPPLY

In settings where the electricity supply is unreliable, the poison centre should have its own back-up system, such as an uninterruptable power supply, in order to maintain its operations. Back-up power is particularly important for refrigerators containing antidotes, antivenoms and antitoxins.

2.4 OPERATIONAL CONSIDERATIONS

The evolution of a poisons information centre will depend on local circumstances, needs and resources. Ideally, all the staff of a poison centre should have career opportunities, and each should have the opportunity for additional training and advancement in his or her area of competence. Contact should be made with other agencies that address various aspects of the prevention and treatment of poisoning, both within the country and abroad. Where appropriate, professional staff should be encouraged to undertake relevant research and contribute to the medical and scientific literature to identify gaps and improve knowledge.

2.4.1 FINANCIAL ASPECTS

As poisons information centres deliver a public good, it is appropriate that they be funded from government resources; however, in practice, many poison centres have mixed funding sources, including a range of non-governmental sources. Social community groups, fund-raising campaigns, philanthropic groups and associations of industry and commerce are all possible sources of financial or other support. Funds for specific projects received from national and international organizations concerned with chemical safety may be useful for investigating areas of joint interest and support some staff costs. Private funding has proven to be effective in many countries and should not be discouraged, particularly for new services. Further information on some common sources of funding used by poison centres around the world is provided in section 11, which also describes the infrastructure required to access those sources. Whatever the source of funding, governance mechanisms must exist to ensure that the poison centre remains neutral, independent and, preferably, autonomous in order to carry out its functions effectively.

It is an important principle that information should be provided free of charge, at least in an emergency. Some payment to the centre might be appropriate, however, for special reports or expertise requested by private institutions or individuals.

Although the bulk of a poison centre's budget will be used for salaries, there should also be adequate funding for the maintenance of up-to-date information systems and technology, for example, the telephone system, computers and associated peripherals and database and journal subscriptions. Funds should also be available for the development of outreach materials and staff training.

2.4.2 SERVICE CONTINUITY

As a poisons information centre is a 24-hour, 7-days a week emergency service, it should have measures and procedures in place to ensure service continuity in case of an event such as a steep rise in the number of calls because of a chemical event; a failure of the power supply, telephone system or computer system; a fire on the premises; a natural disaster that damages infrastructure; or civil unrest. Every poisons information centre should have a written service continuity plan, including measures such as storing duplicates of key databases off-site and a pre-arranged agreement with another poisons information centre to take over the call service temporarily.

2.4.3 GOVERNANCE

Clinical governance is a framework for medical services that is also applicable to poisons information services. Its principles are that the service be accountable for continuous improvement of its quality and safe-guarding high standards of care by creating an environment in which excellence will flourish. Developing a robust system of clinical governance is a key task of leadership, and operation of an effective system is the responsibility of all members of the poison centre team. An effective clinical governance system requires defined standards of quality and safety, a method for monitoring performance, quality assurance (such as clinical audit), quality improvement and a framework for risk and incident management.

2.4.4 CONFIDENTIALITY

For ethical and commercial reasons, much of the information handled by poisons information centres, notably that relating to individual patients, must be considered confidential. Should there be a breach in data confidentiality, the risk to the patient and to the reputation of the centre, resulting in loss of stakeholder engagement, may be substantial. The director should be aware of national legislation regarding data protection and ensure that the poisons information centre has the required technical measures in place and that all staff are aware of their responsibilities with respect to secure data storage and avoiding breaches. Patient enquiry databases contain the most sensitive data and should be password protected and accessed only by the staff of the poisons information centre. Procedures should be in place to ensure that all hard copies of patient-identifiable data (such as patient notes) are securely stored when not in use. All staff should be aware of their duty to protect the confidentiality of the information held by the centre and should understand the limits of how they may use the data. If a data breach occurs, procedures should be in place to deal with it and to identify the individuals and information affected.

2.4.5 HARMONIZED DATA COLLECTION

Research should be conducted on human exposures to chemicals, pharmaceuticals and natural toxins for better understanding of their toxicity and to determine the most effective management procedures. Some research can be based on reviews of cases of poisoning referred to poisons information centres. All poison centres collect the same basic information about cases; however, they may use different terms to document the cases, identify the agents concerned and describe clinical features, treatments and outcomes. Such differences may exist among poison centres in the same country and are very likely among poison centres in different countries. Differences in terms and definitions can make it difficult to compare case data among centres.

In principle, adoption of harmonized terminology facilitates comparison and pooling of case data collected by different centres to improve knowledge on the toxic effects of chemicals, pharmaceuticals and toxins. Experience with the WHO INTOX Data Management System project has revealed challenges to achieving internationally harmonized data collection by poison centres. While the project has resulted in a multilingual data collection format, defined terminologies (“authority lists”) and classifications of substances and products, in practice, each poisons information centre that uses these tools has found it necessary to adapt them to its own needs by adding or removing terms or modifying the classifications. Thus, international harmonization exists at the broader levels of classification (for example, “rodenticide” as a category of pesticide) but not necessarily at a detailed level (for example, type of rodenticide). Management of any harmonized system, whether national or international, requires mechanisms for agreeing changes and developments and maintenance of a data manual; this in turn requires sustained resources. Such resources may be easier to obtain at a national than at an international level.

Internationally harmonized data collection is more readily achievable when the scope is limited, such as for a specific type of information or when it is planned for specific projects. The “poisoning severity score” is an example of a tool for recording specific information, namely grading the severity of poisoning in cases referred to the poisons information centre. This tool was developed in a joint project between WHO and the Swedish Poisons Information Centre and with the support of the European Association of Poisons Centres and Clinical Toxicologists and the European Commission (1). It is used by poisons information centres in many countries. Other schemes for coding clinical effects and diagnoses are described in section 8.

When starting a new poisons information centre, it is a good practice to study the data collection formats and terminology used by other poison centres in the same country or region. It is also useful to consider the WHO terminology and classifications, which are available from the WHO website (2), as these have been used as the basis for poison centre databases in a number of countries, such as Argentina, Australia, Brazil, Chile, South Africa, Thailand and Uruguay.

2.4.6 RESEARCH

Poisons information centres are important sources of information on human toxicology. In particular, the information can be used to identify the emergence of new toxicological hazards. It can also broaden the scientific database on human toxicology through regional and international cooperation. Their research function should be recognized and encouraged by the relevant authorities. In addition, poison centres are well placed to conduct or coordinate observational studies and clinical trials.

2.5 POISON CENTRE MODELS

There is no single model for a poison centre: the location, associated services and scope of service provision can vary considerably. This section describes the most common types of model in operation in various countries (3).

2.5.1 POISONS INFORMATION CENTRE ONLY

Some centres function exclusively as poisons information centres, providing information to health care professionals and, in many cases, the general public. The staff of such centres are not actively involved in the medical management of poisoned patients and only give advice over the telephone or otherwise. Ideally, as described above, at least one medical toxicologist with clinical experience should be attached to the centre. This model is most common in low- and middle-income countries, although not exclusively, and is the easiest to set up with relatively limited resources. Although the majority of poisoning enquiries can be managed in this model, it may lack the clinical input developed through practical experience in the management of poisoned patients, which is an advantage in advising on more serious or complicated poisonings.

2.5.2 POISONS INFORMATION CENTRE ATTACHED TO A CLINICAL UNIT

Another model of a poison centre provides both information and a clinical service. In these centres, medical staff are involved in clinical management of poisoned patients. These poison centres are usually located within a hospital. The centre may have a dedicated treatment unit, or physicians at the poison centre may have allocated beds in the hospital to which poisoned patients can be admitted. Alternatively, the medical staff of the poison centre may jointly manage patients admitted to hospital departments such as a paediatric unit, emergency department or intensive care unit.

This model provides the opportunity for poison centre medical staff to gain direct experience in the management of poisoning, sharing evaluation of cases with other specialists and maintaining general clinical skills. The clinical expertise thus acquired is the basis for the advice given to physicians who consult the poisons information centre about complicated or serious poisoning cases. This model also provides the opportunity for research on the management of poisoning.

2.5.3 POISONS INFORMATION CENTRE ASSOCIATED WITH AN ANALYTICAL TOXICOLOGY LABORATORY

A further model is one in which the poisons information centre has, or is closely linked to, an analytical toxicology laboratory in which samples from poisoned patients can be analysed. Information is provided by dedicated trained staff, and there is the opportunity for sharing knowledge and experience with laboratory staff on the types of analyses that should be offered and interpretation of the results of toxicological analyses.

2.5.4 POISONS INFORMATION CENTRE THAT PROVIDES INFORMATION, ANALYTICAL TOXICOLOGY AND TREATMENT

Some poison centres provide a comprehensive service for the management of poisoned patients, with dedicated, integrated units providing information and clinical advice, clinical management of poisoned patients and an analytical toxicology service. This model is less common, but it offers good opportunities for training and research. The laboratory usually specializes in toxicological analyses and may therefore provide services at district, regional or national level.

2.5.5 COMBINED POISON AND MEDICINES AND/OR TERATOLOGY INFORMATION SERVICE

A relatively common model for poison centres is a combined medicines and poisons information service staffed by pharmacists. Such a service may start with medicines information then extend its scope to cover poisoning to fill a gap. A variation is inclusion of therapeutic drug monitoring in addition to the medicines and poisons information service. Such centres are usually overseen by a pharmacist with specialist toxicology training or knowledge. Some centres may also include a teratology information service to advise on exposures during pregnancy.

2.5.6 CROSS-BORDER POISONS INFORMATION SERVICES AND POISON CENTRE NETWORKS

Most poisons information centres offer a service in a single country, but there are a few cross-border poisons information services. One example is the National Poisons Information Centre in Dublin, Ireland, where out-of-hours service is provided by the United Kingdom NPIS (4). The two services use the same databases for providing toxicological advice and recording enquiry data, which ensures a consistent approach to poisons information enquiries.

A cross-border toxicological consultancy system has been established by an Italian poison centre with industry support for the management of poisonings and chemical accidents in countries where there are large Italian industrial installations but no national poisons information centres. The system is based on telemedicine techniques and on targeted preparation of local health services, for example through provision of standard operating procedures, toxicological evaluations for occupational health services and an antidote supply.²

Short-term cross-border arrangements have also been made. For example, the London Centre of the NPIS handled overnight telephone enquiries to the New Zealand National Poisons Centre for 4 months to cover a staffing shortfall (5). In preparation for this partnership, the New Zealand Centre provided the London Centre with New Zealand medicine formularies, pharmaceutical schedules, medicines guides, access to the New Zealand Internet-based poisons database TOXINZ and the contact details for New Zealand hospitals. The London Centre completed reports for all New Zealand calls and sent them to the New Zealand Centre daily for auditing and medico-legal purposes. In another example, the poison centre in Lille, France, works with the Belgian Poisons Information Centre to coordinate antidote supplies. The two poison centres also have an arrangement to transfer telephone enquiries to the other centre in case of service discontinuity, due for instance to an IT failure, fire, natural disaster or terrorist attack.³

Most poison centres also handle a small number of ad-hoc enquiries from other countries. For example, during the 4-year period 1 June 2015 to 14 May 2019, the Poisons Information Helpline of the Western Cape, South Africa, answered 199 calls from other countries, accounting for 0.5% of their total calls.⁴ Most of the calls (28%) were from a neighbouring country, but calls were also taken from 10 other African countries. Poison centres may also take a few calls from overseas nationals, for example, from the armed forces or clinicians working abroad where a local poisons information centre is not available.

² C. Locatelli, personal communication, January 2019

³ M. Mathieu-Nolf, personal communication, July 2019

⁴ C. Marks, personal communication, July 2019

The possibility of a sub-regional poison centre in East Africa that would serve several countries was examined in a feasibility study led by WHO in 2014 (3). Various options were examined, for example, a sub-regional centre that belonged to one country and offered services to other countries on a contractual basis or an international centre hosted by one country and run by an international steering group. Some requirements to ensure that a cross-border service is operational were identified (Box 2).

Box 2. Requirements for a sub-regional poisons information centre (3)

1. The sub-regional poisons information centre should serve countries with a common language in order to maximize accessibility.
2. There should be good telecommunications infrastructure linking the countries to the poison centre.
3. There should be strong political support and an institutional and legal framework agreed by the ministries of health, environment, finance, trade and justice of all the countries concerned. This framework should cover issues such as funding for the service, the scope of the service and its terms of use (e.g. who can use the service, response times, quality standards and procedures for alerting about chemical events).
4. There should be agreement on how issues of accountability and medical liability would be handled, and, ideally, there should be harmonized legislation between the countries on such issues.
5. There should be agreement on the handling of confidential information such as patient data and commercially sensitive information on products.
6. The sub-regional centre should have collections of information about the pharmaceuticals, products, plants and venomous animals in each of the countries that the centre serves, including local names.
7. The centre should have information on clinical and laboratory services in the other countries and, if available, the contact details of specialist toxicologists in the countries served.

Potential obstacles and disadvantages in setting up a sub-regional poisons information service were also identified (3), including:

- difficulty in allocating responsibility for procuring funding (both to establish the centre and for maintenance);
- language barriers between countries;
- significant administrative overheads to ensure that all user countries paid their share for the service;
- political instability in the host country, which could threaten continuation of the sub-regional service;
- potential unwillingness to share information about poisoning events, patients and products;
- regulations and laws relating to standards of medical care, confidentiality and liability that could create medico-legal barriers;
- reduced accessibility by all rural communities to a single sub-regional poison centre; and
- more benefit to the host country in professional training and toxicological experience than to other countries.

These considerations are likely to apply to other regions or sub-regions.

2.6 NETWORKING AND TWINNING

As the global community of poison centres and clinical toxicology is relatively small, it is worthwhile for poisons information centre staff to join a national or international poison centre or clinical toxicology association, as this provides opportunities for learning, networking and obtaining assistance or support from well-established centres in other countries. Networking among poisons information centres is particularly relevant in a specific geographical region, in which countries may have common toxicological problems. WHO supports regional poisons information centre networks, such as in the African and Eastern Mediterranean regions. In addition, WHO maintains an international poison centre network in the form of a global directory of poison centres (8) and a Listserv called INTOX-General that enables members to share information and pose questions.

Twinning arrangements between poisons information centres in developing and developed countries can be valuable, permitting exchanges of documentation, including data on unusual types of poisoning, exchanges of staff for teaching and training and the provision of antidotes, especially in emergencies. An example of a long-standing twinning arrangement that led to establishment of the National Poison Management and Control Center in Manila, Philippines, is described in Box 3.

Box 3. Twinning support for the National Poison Management and Control Center in the Philippines⁵

In 1975, the National Poison Management and Control Center in Manila, Philippines, began to receive support from the Australian Capital Territory Poisons Information Centre and the Norwegian Poison Information Centre, facilitated by WHO. Copies of scientific journals and reports in the field of toxicology were sent to the Center to strengthen its library and to better enable it to address toxicological issues in the Philippines. Training placements were organized that provided a variety of experience in the epidemiology and management of poisoning, the logistics of poisons units and the different challenges faced by other regions or countries.

This poison centre is now well established with a 24-hour poisons information service, a treatment unit, a clinical toxicology fellowship programme and a training programme for nurses. The poison centre also assists with the risk assessment and management of chemical incidents and organizes an annual poisons prevention week.

For effective twinning, centres must have facilities for rapid communication, such as telephone, e-mail and possibly videoconferencing. If arrangements are made as an emergency preparedness measure, the centre can benefit from rapid importation of antidotes and other essential supplies in emergencies.

2.7 PLANNING A POISONS INFORMATION CENTRE

The main prerequisites for the success of a poisons information centre are enthusiasm and interest in human toxicology by a group of health care professionals who recognize the problem of poisoning in their country and are committed to addressing it. The official support (including financial) of the government is also very important. The requirements for establishing a national poison centre are discussed in detail in section 1; the information aspects of the service are discussed below.

A poisons information centre can start as a small operation, but, if it is successful in building a large user base and increasing its activities, it should have scope for expansion. If possible, future need should be considered

⁵ C. Dioquino, personal communication, July 2019

at the planning stage. During planning of a poisons information centre, the questions listed below should be considered carefully.

- Where will the poisons information centre be located? Which of the available options meet the criteria outlined in these guidelines?
- Which model of poison centre will be used?
- How will the poisons information centre operate?
 - To whom will the service be offered initially (for example, medical professionals only, the public, veterinarians)?
 - Will it offer service 24 hours a day?
 - If it is not a 24-hour service initially, how will it be extended subsequently?
 - In what languages will the poisons information centre provide advice (i.e. should the advice be multilingual)?
 - How will the poison centre and its services be advertised to the user population?
- Who will provide the poisons information service?
 - What category of staff will be recruited (for example, scientists, nurses, physicians)?
 - What are the initial and subsequent staffing requirements?
 - How will the poison centre contact and recruit the necessary expertise?
- Are the telephone, Internet and other communication systems adequate and reliable?
 - How can any deficiencies be overcome?
- What requirements and procedures should be in place for data management?
 - How will the poison centre collect the full range of data required to operate the information service?
 - How will the reliability, accuracy and usefulness of the data be evaluated, and how often will it be revised and updated?
 - How will the necessary toxicological data be compiled, recorded and stored for rapid retrieval?
 - How will the enquiry data be managed and updated? Who will have access to what type of data, and who will have the authority to modify data files?
 - What support staff are needed, for example, for equipment maintenance, cleaning, security?
- What are the requirements for training?
 - Are the necessary toxicology training materials and equipment available, such as dual headsets for listening into calls during training, training files and example case reports to work through?
 - Who will provide and continually assess the basic training of the staff who will work in the centre?
- What are the risks to the sustainability of the poisons information centre in both the short and the long term?

Before a poisons information centre becomes operational, the following should be ensured and perhaps tested.

- The poisons information centre can function competently once its policies, practices and processes are established and fully operative.
- Clinical governance elements such as risk management, clinical effectiveness, clinical information and clinical audit are well established and function appropriately.
- Means of collecting information on local consumer products, recording enquiries to the centre and follow-up of enquiries (see section 8) are established and operating effectively.

- The poison centre has begun to compile documents on the chemicals used in local commercial products (such as pharmaceuticals) and locally relevant natural toxins and on relevant medical and analytical services available in the country (see section 8).

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Poisons treatment in ICU Ramathibodi hospital, Bangkok Thailand / Credit: Puangpak Promrungsri

3 CLINICAL SERVICES FOR THE MANAGEMENT OF POISONING



3.1 INTRODUCTION

Acute poisonings can be time-critical, life-threatening emergencies for which expert management is often essential to a good outcome. Ideally, poisoned patients should be managed in consultation with specialists in poisons information at a poison centre, and all potentially serious cases should involve a medical toxicologist. Medical toxicologists have expertise in the diagnosis, clinical risk assessment, prognosis and management of exposure to a wide range of substances.

Poisoned patients may be treated in many places, including the scene of exposure, during transport, in a primary care setting and in secondary and tertiary medical facilities. Regardless of the sophistication of the services available, fundamental rules for the management of poisoned patients apply in all scenarios and in all settings. Basic resuscitation skills, particularly in airway management and maintaining respiratory and cardiac function, can be life-saving.

Not all cases of poisoning are life-threatening. Patients who exhibit minor features of toxicity who are unlikely to deteriorate may receive adequate care at home, at the workplace or in primary care. A poisons information centre can advise on first aid and whether hospital attendance is required after evaluating the history of exposure, including the agent(s) to which the patient was exposed, the amount, when and by which route. In countries where members of the public do not have direct access to a poisons information service, they may obtain initial advice by contacting a primary care facility, a hospital or a telephone health helpline.

When secondary care is required, it should be provided in a hospital with a wide range of medical facilities, including a critical or intensive care unit. In some countries, clinical toxicology units are available to give specialized care. Clinical toxicology units are usually situated in larger hospitals with direct access to other specialized services such as critical care, nephrology and hepatology. Hospitals with clinical toxicology units offer the optimal care for poisoned patients and provide a range of additional functions, which are described further below.

3.2 CLINICAL REQUIREMENTS FOR TREATING A POISONED PATIENT

Even in settings with a clinical toxicology unit, in practice, most cases of poisoning are treated in normal health service facilities, usually at a general hospital, with information and advice from a poisons information centre. Depending on the requirements of each case, treatment may be provided by various departments, including those listed below. Ideally, medical staff in these departments have had some training in clinical toxicology.

- *Emergency department.* In practice, emergency services receive a relatively large number of poisoning cases, as they function round the clock and have trained personnel and equipment for decontamination, resuscitation and life support.

- *Intensive care units* usually have highly specialized personnel and equipment for resuscitation and life support for the care of critically poisoned patients.
- *General medical units.* Basic medical care of non-critical poisoning cases can be provided in general medical units.
- *Specialized services.* Specialized services offer the advantage of well-trained medical staff and appropriate equipment for the management of poisoning cases in which specific organ systems are affected; they include nephrology, hepatology, gastroenterology, neurology, cardiology and haematology services.
- *Paediatric departments,* including paediatric emergency departments, provide treatment for poisoned children.

To treat poisoned patients effectively, hospitals require the following resources:

- qualified health care personnel, ideally with some training in clinical toxicology;
- equipment and staff to resuscitate and provide initial management of poisoned patients, including cardiopulmonary resuscitation;
- facilities to decontaminate at least a few patients (for example, a designated area for disrobing and showering) to prevent secondary contamination of staff or the hospital, and eyewashes for ocular exposure;
- equipment and staff to perform basic and advanced gastrointestinal decontamination and elimination, for example, single-dose activated charcoal, whole bowel irrigation, multiple-dose activated charcoal or endoscopic imaging and elimination;
- antidotes for immediate use in adequate quantities for local needs (see section 7), in adherence with national guidelines;
- equipment and staff to provide supportive measures indicated by the patient's clinical condition in the appropriate setting, for example, intravenous fluid therapy or pharmacotherapy; in cases of severe poisoning, endotracheal intubation, assisted and controlled ventilation, cardiac pacing or mechanical cardiac support and therefore access to critical or intensive care facilities;
- equipment for continuous cardiac and circulatory monitoring (for example, electrocardiograms, blood pressure measurement) and monitoring of other vital functions; extracorporeal removal techniques for severely poisoned patients, such as haemodialysis, and modalities for continuous renal replacement therapy such as continuous venovenous haemofiltration; and other specialized procedures, such as extracorporeal membrane oxygenation;
- access to best-practice protocols for the treatment of common poisonings, rapid access to toxicological information and expertise and access to a poisons information centre or a clinical toxicology database (see section 9);
- access to laboratory facilities for initial and repeated general biomedical laboratory analyses (for example, acid–base balance, blood gases, electrolytes, blood glucose, liver and kidney function and coagulation tests);
- access to specialist laboratory facilities for initial and repeated toxicological analyses of body fluids such as blood, urine and stomach contents (the choice of analyses will depend on local patterns of poisoning) and for toxicological screening;
- facilities to perform other investigations as appropriate, for example, X-ray, computed tomography, endoscopy; and
- access to specialized services such as nephrology, hepatology and psychiatry.

Emergency departments should have plans for dealing with disasters and major chemical accidents (see also section 6).

3.3 IMPROVING CLINICAL MANAGEMENT OF THE POISONED PATIENT IN THE HEALTH SECTOR AS A WHOLE

Ensuring good clinical management of poisoned patients requires that health care professionals have ready access to good-quality poisons information and advice. In addition, all health care professionals involved in the initial and further care of poisoned patients should have some training in clinical toxicology (1), including paramedics, pharmacists, telephone triage nurses, emergency department and critical care nurses and physicians, paediatricians and anaesthetists. The extent and type of training should be tailored to the roles of these personnel. At a minimum, all health care professionals involved in treating poisoned patients should have training in advanced life support techniques and in decontamination, finding poisons information, the common toxidromes and, if appropriate, where to find information on measures for personal protection.

While the necessity for clinical toxicology services is becoming increasingly obvious, the growing demand for adequate, trained personnel is often not met. Clinical toxicology is not recognized as a medical speciality everywhere and is therefore not included in medical and nursing curricula or in professional training programmes (2–4). In low- and middle-income countries, where there are severe shortages of medical staff of all kinds (5), there may be no trained medical toxicologist. In such settings, it is especially important that health care professionals have some knowledge of the main toxidromes, recognize situations that require the immediate application of life-saving measures and know how to find poisons information.

3.4 TRAINING IN CLINICAL TOXICOLOGY

Hospitals with established clinical toxicology units are uniquely placed to offer training in this discipline because of their association with consultant toxicologists, the opportunity offered to gain practical experience in the management of poisoned patients and their close proximity to a poisons information centre. Nevertheless, poison centres without clinical units can also provide training.

Training in clinical toxicology can be at various levels, from short training placements for physicians planning to make a career in a related speciality such as emergency or intensive care medicine, to a full 1- or 2-year training fellowship programme leading to qualification or accreditation as a medical toxicologist (6, 7). Section 10 outlines a curriculum for training in clinical toxicology. Such training is not readily available in every country, particularly in low-resource settings (2, 3, 8); however, online postgraduate toxicology courses and other online training opportunities are available. Doctors in countries with limited facilities for training in clinical toxicology will benefit from inclusion in training programmes by visiting experts. Alternatively, trainees could take placements at poison centres abroad to supplement or extend their practical experience.

Some clinical toxicology units or poison centres may be able to provide training and, in some cases, accreditation for medical toxicologists from other countries. The objective should be to provide experience in every aspect of the work of the unit, which can then be used to initiate or develop a clinical toxicology unit or poison centre in the trainee's own country. Trainees should know the problems and risk profiles associated with poisoning in their countries so that these can be addressed during training.

Ideally, trainee physicians should have experience in related disciplines, such as emergency medicine, internal medicine, paediatrics or intensive care medicine, and some knowledge of chemistry, biochemistry, statistics, epidemiology, pharmacology and IT. Training should cover all the main areas of clinical toxicology in general, with emphasis on local factors such as prevalent types of poisoning and envenoming.

3.5 ESTABLISHING A SPECIALIZED CLINICAL TOXICOLOGY UNIT

General clinical wards and various specialized services treat both poisoned patients and other types of patients, whereas a clinical toxicology unit exclusively manages poisoned patients. Ideally, all countries should have at least one clinical toxicology unit, which should be a separate department in an advanced multi-disciplinary hospital, close to a poisons information centre. It should preferably be located on the ground floor to facilitate rapid transfers, with access that can be controlled. Regular interaction among the unit, psychiatric services, the poisons information centre and the laboratory is essential to establish a partnership for the diagnosis and management of poisoned patients.

Clinical toxicology units should be staffed with consultant medical toxicologists and specially trained nurses so that patients admitted to the unit receive optimal care. Consultant medical toxicologists may also assist in the management of severely poisoned patients admitted to the intensive care unit or other specialized units in the hospital.

Clinical toxicology units have three principal functions besides patient management, namely toxicosurveillance, education and research. Depending on the organization and resources available, a clinical toxicology unit may undertake the following activities:

- ensuring optimal treatment of poisoned patients (resulting from intentional or unintentional poisoning, therapeutic excess or recreational abuse);
- assessment of new developments in clinical and analytical methods of diagnosis and treatment;
- development of specific therapeutic management modalities;
- evaluation of cause–effect relationships in cases of poisoning;
- identification of the effects of pharmaceuticals, chemicals and natural toxins on health;
- appropriate follow-up and surveillance of cases for identification and assessment of sequelae; and
- study of the circumstances of the poisoning and predisposing factors (data may then be used for planning preventive action).

Clinical toxicology units should record data on poisoning cases and toxicological consultations in a standard format, preferably compatible with that used by poisons information centres (Annex 3). Full case data, including outcomes, should be recorded.

3.6 ADDRESSING CHALLENGES

The requirements listed above may not be easy to meet within the financial or political constraints of a country. Policy-makers should nevertheless endeavour to establish and fund facilities that can provide the optimum evidence-based care for poisoned patients. In the interim, health care professionals may work towards optimum care for poisoning cases by:

- learning where to find poisons information and access to a clinical toxicology database (see section 9 for information on databases that may be available free of charge or at a discounted cost to low-income countries) (Note that a clinical toxicology database is not a replacement for clinical judgement by appropriately trained and qualified health care professionals specialized in clinical toxicology.);
- collecting data on poisoning cases to demonstrate the prevalence and severity of poisoning in the locality;
- establishing a national network for data collection on poisoning;
- identifying common poisonings that require antidotal treatment and trying to obtain the antidotes as a priority;
- identifying common poisonings that require specific toxicological assays and clinical investigations, and working with the laboratory service to access the tests (see also section 4); and

- training small local groups in managing common poisonings.

3.7 RECOMMENDATIONS

Clinical toxicology is still not acknowledged as a separate medical discipline in many countries. Its full acceptance by medical schools and public health services is desirable, and active collaboration among scientists and professionals in this area is important. Every effort should be made to ensure that the relevant human resources are developed as quickly and effectively as possible. Measures to harmonize approaches to clinical toxicology throughout the world and to coordinate the work of international organizations and other international bodies in this area should be reinforced.

At national level, the following measures should be taken to support and promote clinical toxicology.

- Clinical toxicology services should be established wherever they are required. They should be accessible in every country.
- The discipline of clinical toxicology should be recognized officially, as should the trained professionals who are already working in this field.
- Academic institutions should be encouraged to develop clinical toxicology as a discipline in its own right, for example, by establishing a department within a teaching hospital that has an intensive care unit, outpatient clinic and laboratory for toxicological analyses. This would be a step towards institution of a specific career structure for medical toxicologists.

Internationally coordinated measures that would promote clinical toxicology include establishment of:

- mechanisms for ensuring unimpeded communication and exchange of information and experience;
- collaborative research projects in clinical toxicology;
- international collaboration in establishing protocols for the treatment of poisoned patients and for evaluation of antidotes;
- international mechanisms for ensuring adequate availability of antidotes and early warning of toxic hazards; and
- appropriate international educational programmes and exchanges.

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Toxicology Laboratory, Pontificia Universidad Católica de Chile, Santiago / Credit: Alejandra Andrea De Lucca Valderrama

4 ANALYTICAL TOXICOLOGY AND OTHER LABORATORY SERVICES



4.1 INTRODUCTION

Analytical toxicology is the detection, identification and measurement of drugs and other foreign compounds (xenobiotics) in biological and other specimens to help in the diagnosis, treatment, prognosis, and prevention of poisoning. Analytical toxicology laboratory services are an important component of a fully functional poison centre operation; however, as discussed below, analytical toxicology can also be provided as a standalone service or by other types of laboratory.

An analytical toxicology laboratory should be capable of undertaking analyses of both biological and nonbiological materials (such as soil). The laboratory service should develop its analytical capabilities in partnership with physicians dealing with poisoning cases to ensure that the necessary services are available.

Because of the specialized nature of analytical toxicological investigations, the laboratory may find difficulty in having a sufficient workload and sustainable funding. In order to provide a service to support the management of poisoning, many laboratories offer other services, such as testing for drugs of abuse, specialized therapeutic drug monitoring, trace element analysis, biological monitoring of occupational or environmental chemical exposure and forensic toxicology, in which similar equipment and expertise are used (1).

4.2 FUNCTIONS OF AN ANALYTICAL TOXICOLOGY SERVICE

The main functions of an analytical toxicology service are to provide the following:

- emergency qualitative and/or quantitative assays for common poisons, especially when knowledge of the plasma, serum or urine concentration may influence treatment;
- more complex analyses, such as screening when the cause of illness is unknown but poisoning is suspected (Even if such analyses are not available immediately, they may be helpful in identifying the cause of poisoning and guide further treatment.);
- analyses to monitor the efficacy of certain treatment or elimination techniques (such as chelation therapy, haemoperfusion, haemodialysis, multiple-dose activated charcoal);
- analyses for biological monitoring of populations exposed to chemicals occupationally or environmentally and environmental monitoring (such as soil, air, water);
- advice on the collection, storage and transport of specimens and on the interpretation of results of analyses;
- research into the toxicokinetics and mechanisms of toxicity of drugs and chemicals, in collaboration with clinical services and poisons information centres; and
- training in analytical methods and laboratory procedures and in interpretation of analytical data.

4.3 LOCATION, FACILITIES AND EQUIPMENT

4.3.1 LABORATORY TYPE

A toxicology laboratory may be located within a poison centre, or other laboratories may offer analytical toxicology services (at least partially). These include forensic, government agency, occupational health, general health service, medical college, university research and private laboratories. The service provided will depend on the core function of the laboratory, its facilities and location. Some may provide a limited service and not be equipped to handle potentially infectious specimens. Others may be well equipped and offer a large repertoire of tests and/or an emergency 24-hour service.

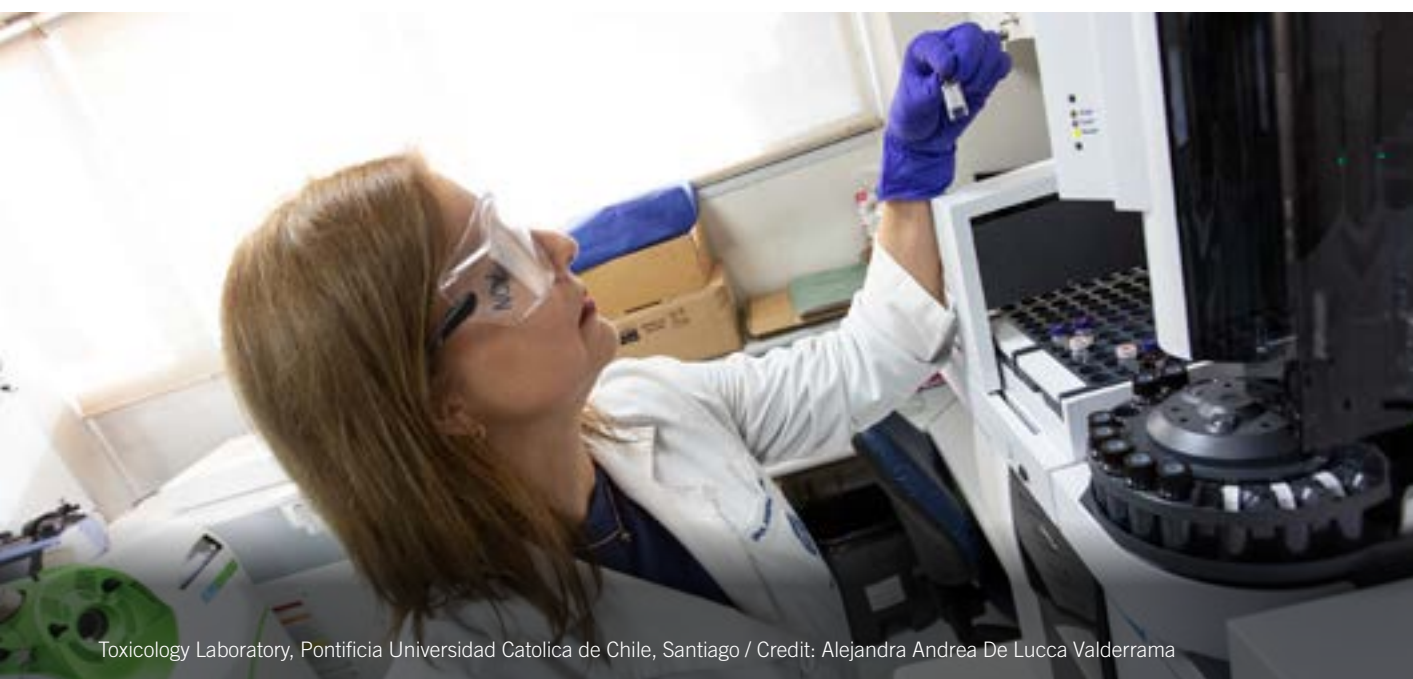
4.3.2 LOCATION

The location of an analytical toxicology laboratory will depend on its purpose and where it is based, such as in a hospital or university or on its own premises. Close proximity to a poison centre or a clinical service in which poisoned patients are treated facilitates rapid transport of samples and consultation with clinicians.

4.3.3 EQUIPMENT

The basic equipment required includes scales, centrifuges, vortex mixer, pH meter, water-bath, refrigerator, freezer and fume cupboard. Although the analytical equipment will depend on local requirements and circumstances, certain basic equipment should be available for techniques such as colorimetry, spectrophotometry and thin-layer chromatography, even if only in the local hospital laboratory. Other, simple analytical techniques and instruments that can be used for rapid screening are discussed below.

More sophisticated analytical techniques, such as immunoassay, gas chromatography, high-performance liquid chromatography, atomic absorption spectrophotometry and mass spectrometry, require specialized support such as servicing, spare parts and consumables. Expertise in both the use and maintenance of such equipment is essential. It is recommended that investment in and use of such equipment be undertaken only as part of a comprehensive development programme for analytical facilities. Table 1 lists examples of the types of analytical equipment that might be used in a toxicology laboratory.



Toxicology Laboratory, Pontificia Universidad Catolica de Chile, Santiago / Credit: Alejandra Andrea De Lucca Valderrama

Table 1. Techniques and associated instrumentation used in a toxicology laboratory

Technique	Type of Instrumentation	Comments
Rapid screening tests (can include point-of-care testing)	Spectrophotometer	Can be used for initial screening for “unknowns”
	Rapid immunoassay	
	Simple colour test, colorimetry	
N.B. Equipment listed is not exclusive to rapid screening	Portable anodic stripping voltammetry	For point-of-care measurement of blood lead concentration
	Blood gas analyser with pulse co-oximeter	Widely available. Results may indicate the poison, e.g. substances that cause metabolic acidosis. Addition of a pulse co-oximeter allows measurement of carboxyhaemoglobin and methaemoglobin
Chromatography	Thin-layer chromatography	
	Gas chromatography Detectors: <ul style="list-style-type: none"> • Flame ionization • Nitrogen–phosphorus • Electron-capture • Mass spectrometry 	
	High-performance liquid chromatography Detectors: <ul style="list-style-type: none"> • UV/diode array UV • Fluorescence • Mass spectrometry • Time-of-flight mass spectrometry (accurate mass) • Electrochemical 	
Spectrophotometry	Direct-reading spectrophotometer	
	UV/visible light recording spectrophotometer	
	Atomic absorption or emission spectrometry	
	Inductively coupled plasma mass spectrometry	
	Infrared spectrometry	
Immunoassay	Radioimmunoassay	May be highly sensitive but poorly selective, i.e. cross-reaction with structurally similar molecules
	Enzyme-multiplied immunoassay	
	Fluorescence immunoassay	
	Enzyme-linked immunosorbent assay Fluorimetry	
Electrophoresis	Capillary electrophoresis	

4.3.4 REFERENCE STANDARDS

Certified reference standards for a range of analytes, such as controlled drugs, pesticides and other chemicals, must be available in any analytical toxicology service. Reference standards are used to validate analytical methods and to calibrate analyses. They may be purchased from chemical suppliers or included in commercial kits. Some reference standards may be obtained from other laboratories, either locally or internationally.

An analytical toxicology laboratory may be required to identify substances involved in poisoning cases for which no reference standards are yet available (such as new psychoactive substances). In such cases, the laboratory may be involved in developing new analytical methods, which may be formally validated only later, when analytical standards become available.

4.3.5 REAGENTS AND CONSUMABLES

A variety of reagents and consumables will be required, depending on the assays offered by the laboratory. The reagents may include solvents, purified water and gases. Consumables include general items such as pipette tips and specialized items such as chromatography columns and injection syringes. Replacement parts such as detector lamps must be stocked. A reliable supply of consumables must be ensured to prevent the stocks from becoming a limiting factor, especially in lower-resource countries (2).

4.3.6 REFERENCE WORKS

Annex 2 provides a list of reference books on laboratory investigations.

4.4 SELECTION OF ASSAYS TO BE OFFERED BY THE LABORATORY

Decisions on which assays should be offered by a toxicology laboratory depend on the pattern of poisoning in the population served, the requirements for therapeutic drug monitoring and the equipment and trained staff available to the laboratory. A further consideration is whether the laboratory will or has the resources to provide a 24-hour service.

Certain assays are frequently needed to guide the management of poisoning and should be readily available, ideally in all hospitals in which poisoned patients are treated. Assays that are less frequently requested or that can be provided with a longer turnaround time, may be offered only by a specialized toxicology laboratory.

Detailed lists of routine and specialized assays required for the management of poisoning have been drawn up by national clinical biochemistry associations in conjunction with clinical toxicologists (4, 5). These can provide a useful guide but should be adapted to the circumstances in each country and in particular to the local epidemiology of poisoning. Examples of laboratory assays that might be required urgently and those that can be provided after hours or days are listed below.

- Assays that might be required urgently to guide clinical management:
 - carboxyhaemoglobin
 - methaemoglobin
 - iron
 - lithium
 - toxic alcohols (methanol, ethanol, ethylene glycol)
 - formate concentration (a proxy for methanol)
 - paracetamol
 - salicylate

- paraquat (qualitative urine test)
- general urine drug screen.
- Assays that might be required less urgently for management:
 - cholinesterase (plasma and erythrocyte)
 - lead
 - mercury
 - methotrexate
 - thallium
 - general toxicology screen.

Some of the assays required urgently may also be offered by a standalone analytical toxicology laboratory; however, their clinical utility will depend on the proximity of the laboratory to the treating hospital and the speed with which the samples can be transported to the laboratory and the results returned.

4.4.1 POINT-OF-CARE TESTING

“Point-of-care testing” refers to testing carried out in close proximity to the patient in order to obtain a result within a few minutes. The samples for these tests require minimal manipulation before the analysis, and the tests can be carried out by personnel who are not trained laboratory technicians (3). Such tests are commonly performed with small portable handheld devices, such as simple spot tests, or in small bench-top analysers. They include:

- qualitative urine screening tests with dipsticks or cassettes for drugs of abuse and other drugs of interest (6);
- measurement of blood lead concentrations with venous or capillary samples (7);
- measurement of cholinesterase activity from a finger-prick sample (8);
- diagnosis of ethanol intoxication with a breath alcohol test (9); and
- use of a pulse co-oximeter fitted to a blood gas analyser for the measurement of carboxyhaemoglobin and methaemoglobin (10).

Such tests are useful for screening and provisional diagnosis. They can assist a quick decision, allowing faster treatment, and are particularly useful in emergency departments. As the results may be less accurate than those of laboratory testing, laboratory confirmation should be sought when possible. As for all laboratory equipment, these instruments must be regularly calibrated, checked and maintained. It is also important to establish who is responsible for this, for example, the laboratory or the clinical team.

4.5 INTERPRETATION OF DATA

Analytical results should be interpreted in the context of other information and in particular the patient’s clinical status, the history of exposure, the treatment given and other pathological conditions that might influence the results (for example, renal or liver dysfunction). The analytical toxicologist and the poison centre clinical toxicologist play critical roles.

4.6 QUALITY MANAGEMENT

The analytical data provided by a laboratory service must be reliable. This is best ensured by a robust quality management system, defined as “coordinated activities to direct and control an organization with regard to quality” (11). The system involves integration of all aspects of laboratory operation, including the organizational structure,

processes, procedures and resources, in order to ensure that the service provided is of high quality (11). The components of a quality management system are quality assurance and quality control.

Quality assurance is concerned with processes and procedures. It includes documentation requirements, standard operating procedures for all laboratory operations (such as the receipt, storage and handling of specimens, analytical techniques, recording and reporting of results), instrument maintenance records, calibration records and methods for validation and verification.

Quality control refers to the control of errors in the performance of tests and verification of test results. It has two components: internal and external quality assessment. Internal quality control typically involves analysis of control material known to contain the analyte of interest that is not used in assay calibration. Usually, low, medium and high concentrations of each analyte are prepared in analyte-free human serum, and the results are compared with predetermined acceptance limits. For quantitative work, the sample for internal quality control should be run with clinical samples in order to validate the procedure. External quality control is a system for objective checking of laboratory performance by an external agency. The laboratory is sent “blind” test samples by another laboratory, in which the identity and/or quantity of the analyte(s) is unknown. The results are returned to the central coordinating laboratory, which assesses the performance of the receiving laboratory.

Training and participation of laboratory staff in quality assurance and quality control are crucial to maintenance of good analytical performance. Further guidance on quality management can be found in the WHO handbook on laboratory quality management systems (11). A training toolkit (12), a template for a quality manual (13) and guidance for implementation of a laboratory quality management system in resource-limited settings (14) are also available.

4.6.1 QUALITY STANDARDS, CERTIFICATION AND ACCREDITATION

Compliance with recognized quality standards is required for high levels of quality and competence in a laboratory. Compliance with laboratory standards may be voluntary or required by law or by another authoritative body. Standards may be local, national or international and may therefore differ between countries. Examples of international standardization bodies are the International Organization for Standardization (ISO), the Clinical and Laboratory Standards Institute and the European Committee for Standardization.

Processes to indicate that a laboratory complies with defined standards include:

- certification: the provision by an independent body of written assurance (a certificate) that the product, service or system meets specific requirements;
- accreditation: the procedure by which an authoritative body formally recognizes that the laboratory is competent to carry out specific tasks; and
- licensure: the laboratory may require a licence, usually from a government agency, to store or use controlled drugs (in accordance with national legal requirements).

It is recommended that every analytical toxicology laboratory (whether standalone or affiliated with a hospital or institute) be accredited by an independent, impartial accreditation agency that can assess its technical competence and integrity. The agency may provide written evidence of the laboratory’s compliance (certification) and competence (accreditation) with a standard, providing additional assurance about the consistency and reliability of test results. Commonly used accreditation standards are ISO 15189 and ISO 17025 (15, 16). ISO 15189 outlines requirements for quality, competence and the quality management system. This standard is specific for medical laboratories and applies to the laboratory as a whole. ISO 17025 outlines requirements for competence to carry out tests and/or calibrations and can be used for individual tests (11).

It is important to note that ISO status is not accreditation, only certification. Every test performed by a laboratory need not be accredited, and only a few tests might be subjected to the accreditation process, which exposes the infrastructure, staff and testing methods laboratory to overall scrutiny. This will be sufficient to ensure that a basic standard of functioning is met.

Most countries have accreditation agencies for various kinds of laboratory. In the absence of a national accreditation agency, a laboratory can seek accreditation by a reputable international or foreign accrediting body. Examples can be found on the website of the International Accreditation Forum. They include the Asia Pacific Accreditation Cooperation and the International Laboratory Accreditation Cooperation (17).

4.6.2 LABORATORY SAFETY

A laboratory safety programme is a key component of a quality management system, and staff must be familiar with and adhere to safety policies and procedures (11). There are risks associated with handling certain reagents, such as chemical burns and systemic toxicity, and with handling biological samples, such as exposure to blood-borne viruses (particularly hepatitis B and C and HIV). Preventive measures must be in place, including ensuring that staff vaccinations are up to date, treating all samples as potentially high-risk and having designated decontamination and eye-wash facilities. Personal protective equipment should always be used, which includes a laboratory coat, gloves and eye protection. There may be legal requirements to be observed, such as storage of controlled drugs (usually in a locked cabinet). Guidance on health and safety in the laboratory is available from various sources (18, 19).

4.7 STAFF AND TRAINING

4.7.1 STAFF

The staffing requirements of an analytical laboratory service depend on the volume and type of toxicological and other tests to be performed, which in turn is guided by local circumstances, such as the requirement for a 24-hour service. Every analytical toxicology laboratory should have an experienced analytical toxicologist to provide an effective service and interpretation of data. Ideally, there should be at least two such staff to cover staff sickness and annual leave. A central analytical toxicology service requires considerably more staff because of the wide range of clinical and research work it performs. It will also require administrative staff and possibly a documentalist.

Laboratory technical staff should be educated in a science subject and have practical laboratory experience. Rotation of analytical personnel with, for example, the staff of a local hospital laboratory could help in establishing a pool of experience. The laboratory technical staff will undertake most practical laboratory testing and oversee laboratory assistants.

A further qualification, such as a doctorate, and relevant experience that includes a high standard of practical analytical work are advantages for the head of an analytical toxicology laboratory. Knowledge of aspects of toxicology other than analytical toxicology is also desirable. Individuals recruited for analytical toxicology posts must be committed to their work, and a career structure should be provided to encourage them to remain in their posts after training and to pass their experience on to others.

4.7.2 TRAINING

Training of staff for a central analytical toxicology service must be considered in the context of the country. Training for all staff should be competence-based and recorded in a personal training log to document evidence of training and achievement. Training must be viewed as a continuous process, and competence should be reassessed after a defined period (such as every 2 years). Training should be both practical and theoretical, as determined by the requirements of the service and the equipment and facilities available. The duration of training may depend on the individual's previous education and experience.

When possible, training should lead to a recognized qualification. Individuals will continue to gain practical on-the-job experience, particularly as the work of the analytical toxicology service expands. Continuing education, such as participation in research and development projects, case presentations and attendance at international meetings, should be encouraged, as should membership in national and international toxicological and pharmacological societies.

The training required by the head of a laboratory will also depend on local circumstances. If a country does not yet have a suitable training programme, help should be sought from countries with well-established analytical toxicology services, which should be encouraged to provide training fellowships. In a country that already has an analytical toxicology service but requires additional expertise in some fields, experts may be invited from other countries to provide the necessary training. Sample criteria for laboratories that provide training in analytical toxicology are given in Table 2.

Table 2. Criteria for training in clinical analytical toxicology

Component	Criteria
Staff	<ul style="list-style-type: none"> The laboratory head should have appropriate experience in clinical analytical toxicology. In addition, he or she should have suitable academic qualifications (e.g. a doctorate), have published original research and have teaching experience. Ideally, at least two experienced analytical toxicologists should also work in the laboratory to ensure comprehensive coverage.
Organization	<ul style="list-style-type: none"> The laboratory should be associated with a multifunctional poison centre that provides information and patient care to facilitate contact between the clinical and analytical services. It may also offer a 24-hour emergency service. A wide range of analyses should be available, and special investigations should be possible when necessary (e.g. occupational exposure to toxic metals and certain pesticides; monitoring of drug use).
Techniques	See Table 1 for a list of techniques for which instructions should be readily available.

Training should be provided in:

- good laboratory practices and quality assurance procedures;
- basic pathology related to clinical toxicology;
- toxicokinetics, metabolism and human toxicology of the substances analysed, with emphasis on interpretation of results;
- laboratory management (handling and storage of specimens, reporting and recording results, health and safety requirements); and
- teaching and oral presentation of cases, reviews of the literature and the results of research projects.

Laboratory staff should be encouraged to participate in continuing professional development, which includes attendance at regular meetings, for example in a multifunctional poison control centre, in order to:

- review case reports and, in particular, discuss medical interpretation of analytical results with clinical personnel;
- review developments in analytical toxicology published in the literature;
- examine the results of research conducted in the laboratory to identify areas for cooperative investigation or further research; and
- discuss laboratory management in relation to overall work on poison control.

Laboratory staff should also be encouraged to present papers at and participate in scientific meetings relevant to their work.

4.8 CONSIDERATIONS IN ESTABLISHING AN ANALYTICAL TOXICOLOGY SERVICE

If suitable general laboratory facilities already exist, they can form the basis for a comprehensive toxicology service. The requirement for particular analyses will depend on local circumstances. Two levels of operation may be envisaged. The first would be to offer a relatively restricted but more widely distributed service based mainly on simple spot tests, immunoassays and thin-layer chromatography. Field-tested techniques to be used at this first level are listed in a WHO manual, *Basic analytical toxicology (2)*.

The second level would support the first but be more advanced, offering a full range of analyses with a wide variety of techniques. Certified laboratories at this level could act as reference laboratories, confirming the results of screening tests and developing methods. Links should be formed between laboratories for areas such as training, research and quality assurance. The assays to be used should be selected according to proven clinical need and the availability of:

- a supply of appropriate, certified reference compounds;
- a supply of consumables and reagents and satisfactory arrangements for maintenance;
- practical analytical techniques that can provide results within a reasonable time;
- clearly defined standard operating procedures for all activities and analyses; and
- internal quality control and external quality assurance systems.

4.9 CONCLUSIONS

An analytical toxicology service provides essential support for the management of poisoning cases and also for investigations into the health effects of exposures resulting from chemical incidents or environmental contamination.

Establishing an analytical toxicology service requires significant investment and planning. Important considerations include whether a new laboratory is necessary or whether the services of an existing laboratory can be extended and ensuring the sustainability of the laboratory service. Challenges that must be faced, particularly in limited-resource settings, include recruitment and maintenance of a cadre of trained, motivated laboratory personnel, ensuring supplies of good-quality reagents and consumables and meeting the cost of maintaining and, when necessary, upgrading laboratory equipment.

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5 TOXICOVIGILANCE AND PREVENTION OF POISONING



5.1 INTRODUCTION

The global increasing dependency on chemicals requires the health sector to expand its traditional roles and responsibilities to be able to address the public health and medical issues associated with the use of chemicals and their health effects (1).

Harmful acute exposure (either unintentional or deliberate) to toxic substances and products results in a significant health burden. This health burden can be reduced by early recognition of new or developing trends in exposure and preventive measures. This activity is known as “toxicovigilance”. To be most effective, it requires enhanced information-sharing and collaboration among disciplines and jurisdictions.

Toxicovigilance is active identification and assessment of the risk of toxicity from exposure of a community or population to consumer products, pesticides, pharmaceuticals, environmental and industrial chemicals, controlled substances and natural toxins (2). It involves monitoring to identify trends in poisoning and the emergence of new risks associated with toxic substances and also to assess the effectiveness of preventive measures. Toxicovigilance may also provide an alert for a more sudden event, such as deliberate or unintentional contamination of a product.

The goal of toxicovigilance is to provide information for timely action to prevent, treat, reduce harm and manage risks of toxic exposures of public health concern, which are suspected or confirmed exposure to hazardous substances, regardless of source, that may require timely, coordinated multi-jurisdictional or multi-sectoral actions, often going beyond routine or normal operations, in order to minimize adverse outcomes.

In some countries, the term “toxicosurveillance” is used rather than “toxicovigilance” to describe the same activities (2). A distinction can be made between the two terms, “toxicovigilance” being defined as general monitoring for all potential toxic threats and “toxicosurveillance” as focused on specific substances or toxidromes (2). For the purposes of these guidelines, the term “toxicovigilance” is used to cover both toxicovigilance and toxicosurveillance.

Toxicovigilance has parallels and potentially some overlap with pharmacovigilance; however, it has a broader scope. “Pharmacovigilance” is defined as the science of and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (3). Hence, it refers largely to pharmaceuticals in normal use. Toxicovigilance is concerned with any toxic hazard, which can include abuse, misuse and overdose with pharmaceuticals and other health products and also toxic exposure to a broad range of other, non-pharmaceutical substances (such as pesticides, drugs of abuse).

5.2 PERFORMANCE OF TOXICOVIGILANCE

Toxicovigilance involves collaboration among poison centres, toxicology laboratories, public health agencies, health authorities, regulatory agencies, health security agencies and others. Toxic risks can be recognized in a community by several methods, including assessment of environmental factors such as air quality, reporting by toxicology laboratories and physicians under mandatory disease notification (see below), surveillance of hospitalizations and health care use, poison centre data and reports from drug abuse agencies and civil society organizations (1, 2, 4–6). The range of toxicovigilance activities can be adapted to the available resources.

Toxicovigilance comprises the detection and management of toxic exposure events of public health concern, including:

- exposure to novel or rare drugs or other xenobiotics;
- unusual exposure patterns or trends that can signal an emerging toxicological problem;
- suspected poisoning outbreaks caused by, for example, contamination of food, water or pharmaceuticals;
- mass chemical exposure, for example, resulting from chemical incidents or environmental health disasters;
- exposure to toxic chemicals that are considered to be of health security concern, for example, military warfare agents; and
- terrorism or criminal threats and acts suspected or confirmed to involve deliberate use of toxic chemicals.

The response to such events, depending on their nature, magnitude and scope, may benefit from joint assessment and investigation, with support from specialized resources. These include medical and analytical toxicologists, epidemiologists, regulatory authorities, public health experts and public safety and health security practitioners. They contribute to timely, comprehensive risk assessment and management by:

- identifying the agent that is causing harm;
- identifying the source, intensity and location of the exposure;
- identifying populations who might have been exposed;
- proposing action to mitigate risks to human health; and
- evaluating the effectiveness of mitigation and intervention measures.

5.3 MANDATORY NOTIFICATION OF POISONING

One form of toxicovigilance is mandatory notification of poisoning cases to public health authorities. Mandatory notification of cases of specific infectious diseases is well established in many countries, including diseases caused by natural toxins, such as botulism or paralytic shellfish poisoning. Its purpose is to enable public health services to collect, analyse and act on information to reduce the risk of disease. Many countries have schemes whereby health care professionals report adverse reactions to therapeutic doses of medicines. Although notification of poisoning cases to a public health authority is not a universal requirement, some countries have notification systems or systems in which there are thresholds of severity above which specific cases must be reported. Examples are described below.

In New Zealand, poisoning arising from chemical contamination of the environment or the finding of a blood lead concentration $> 10 \mu\text{g/dL}$ after a non-occupational exposure must be reported to the Medical Officer of Health (7). In the United Kingdom, exposure to certain chemicals (such as lead, mercury, carbon monoxide) that may have public health implications is notifiable (8). In Brazil, notification of poisoning attributed to pesticides and highly toxic substances, severe poisoning cases requiring hospitalization and suicide attempts has been mandatory since 2012 (9). In addition, notification of snakebite is required so that designated health care facilities can obtain further stocks of antivenom.⁶ South Africa, as part of implementation of the Rotterdam Convention on

⁶ Dr L. Fruchtgarten, personal communication, December 2019.

Prior Informed Consent, requires reporting of pesticide poisonings, especially due to street-sale pesticides, which is a significant public health issue. It is the legal responsibility of the first health care professional who becomes aware of the exposure to report it to the relevant authorities (10). In Germany, the Chemicals Act requires that a physician who is consulted for treatment or about the sequelae of exposure to a chemical substance or product must send information to the Centre for Documentation and Assessment of Poisonings at the Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung) (11).

These examples show that notification schemes for poisoning cases can be either broad or closely targeted. Notification systems can assist in planning the provision of countermeasures. For example, in countries where reporting of snake envenoming is poor, making snakebite a notifiable condition could improve the collection of epidemiological data to support antivenom development and provision.

A notification system requires a physician or other health professional to take additional action beyond that required to manage the patient. Experience from adverse drug reaction reporting suggests that, for various reasons, there is likely to be significant underreporting (12). Such systems are therefore complementary to rather than a replacement for poison centre data.

5.4 ROLE OF POISON CENTRES IN TOXICOVIGILANCE

Poison centres play a key role in toxicovigilance (2, 6). For the general public in most countries and for health care professionals, poison centres are a focal source of advice on toxic exposures. A single national centre may serve a large population and numerous health care facilities, or there may be several poison centres, each covering a specific geographical area in a country. Whatever the arrangement, poison centres as recipients of enquiries about poisoning are well placed to identify trends or signals of emerging toxic hazards and public health threats. They can collect data on demographics, patterns of use and exposure, clinical features, management of poisoning and, in some cases, clinical outcomes in the population served. By regular, systematic analysis of such data, poison centres can identify unexpected shifts in the recorded causes of poisonings and rapidly detect adverse health consequences.

Integration of poison centres into the public health infrastructure increases the collective capacity and capability for timely detection, assessment and management of toxic exposure events of public health concern (6).

Through toxicovigilance, poison centres can collect data to:

- identify serious poisoning risks in the community and the substances, circumstances and population groups involved;
- identify trends in poisoning, such as different substances of abuse, application of new pesticides and seasonal variations in the pattern of poisoning, such as carbon monoxide poisoning from heating appliances;
- monitor the toxicity of commercial products, such as household, industrial and agricultural chemicals and pharmaceuticals, for acute, medium-term and chronic effects; for example, overuse of analgesics, occupational exposure to solvents;
- characterize the toxic effects of exposure to chemicals and drugs;
- monitor introduction of a new product or a change in the formulation, packaging or recommended use of a product to determine any associated health impact;
- identify substances that cause significant morbidity and mortality and specific effects on target organs, such as a high incidence of renal insufficiency or fetal malformations;
- detect signals that demand preventive or corrective action and report them to health authorities and other relevant bodies;

- generate statistics (ad hoc or routine) and trends to provide evidence for decisions on poisoning prevention; and
- support monitoring and evaluation of prevention and harm reduction activities.

When a poison centre identifies new patterns of poisoning, the data should be verified and evaluated before being reported to the relevant authorities or organizations to take action. Action may be required by public health authorities, regulators, or manufacturers of the chemicals or products involved. The responsibility of alerting and notifying the relevant authorities or the general public will depend on local or national guidelines and responsibilities. It may not be the responsibility of the poison centre to manage a public campaign, and the centre should liaise with the public health authorities if such action is required. Box 4 gives a case study that illustrates the involvement of a poison centre in a multi-agency response to a counterfeit pharmaceutical.

Box 4. Outbreak of poisoning by fentanyl in Georgia, USA (13)

On 5 June 2017, an emergency department in Georgia North Central Health District notified the Georgia Poison Center of six opioid overdoses, including one death, that had occurred the previous day. All the patients had severe opiate toxicity that required high doses of naloxone to reverse the symptoms. The case histories indicated that the most likely cause of the poisonings was potentially counterfeit Percocet tablets.

The Georgia Poison Center notified local hospitals and the Georgia Department of Public Health, which sent the information to hospitals and health care professionals through epidemiological links and the Office of Emergency Medical Services. The Georgia Bureau of Investigation was also notified, which then performed drug testing and confirmed that the tablets contained illicit fentanyls. The High Intensity Drug Trafficking Area office was also alerted, which contacted law enforcement officers and local coroners to identify additional deaths under similar circumstances.

The coordinated multi-agency response led to two press conferences on 6 June to notify the public about the risks of the counterfeit pills. Epidemiologists established a case definition based on the opiate toxidrome and a history of buying illicit tablets, which led to syndromic surveillance. Among the 37 possible cases initially reported (including five deaths), 27 cases (one death) that occurred between 4 and 13 June met the case definition of the counterfeit Percocet cluster. The multi-agency response contributed to control of this outbreak of poisoning through rapid identification, notification and public messaging, in which the poison centre played an important role.

As a similar toxic hazard could arise in other countries, such as from a product sold internationally, information and alerts should also be disseminated widely, especially to other poison centres and professional toxicology bodies (see Annex 4 for a description of a European alert network of poison centres). When an event that might meet the criteria defined in Annex 2 of the IHR, the poison centre should follow local procedures to inform the IHR national focal point (see section 1 for more information).

Examples of toxic risks that have been identified by toxicovigilance in poison centres are:

- exposures to new drugs and medications, for example, novel oral anticoagulants (14);
- reformulated or repackaged household products with unanticipated toxic effects (for example, liquid laundry detergent capsules (see also Box 5) (15);
- abuse of new recreational drugs, including new psychoactive substances (NPS) such as synthetic cannabinoids (16, 17);
- exposure to natural toxins (such as mycotoxins, plant toxins, marine and freshwater toxins) (18) and poisoning associated with food, water and livestock feed;

- adulteration or contamination of products, such as alcoholic drinks contaminated with methanol (19); and
- severe poisoning with cosmetic products (20).

Poison centres may not only raise alerts but also provide access to scarce specialized medical toxicology expertise to support response activities.

The strengths of poison centres in toxicovigilance are:

- near-real time detection of toxic exposure events of public health concern;
- trained, experienced medical toxicologists and specialists in poisons information, who can identify, assess and advise on unusual events;
- structured, systematic enquiry data; and
- a large amount of data on exposures, including demographics, circumstances of exposure, clinical outcomes and management.

Poison centres that take calls from the public have the unique ability to capture data on exposures that are managed outside of a health care facility. They can conduct targeted monitoring of emerging issues and provide an indicator of the burden of poisonings.

While all poison centres can conduct effective toxicovigilance, they are not always recognized for the role they play in detecting and responding to public health threats. This has limited the integration of many poison centres into public health, regulatory, health security and other toxicovigilance communities and has limited their access to resources for their operations and surveillance. Other challenges in toxicovigilance are listed below.

- In most countries, there is no requirement that physicians contact the poison centre about poisoning cases, and some physicians choose not to consult about poisonings with which they are familiar or may use another source of information.
- Poison centres may not be used to their full potential because of limited awareness of their availability or because they do not operate 24 hours a day (for example, new and/or under-resourced poison centres).
- Exposures are rarely validated by analytical confirmation, except in special projects.
- When several poison centres aggregate information or upload data to a single repository, the comparability of data quality within and among poison centres may be limited, reducing the usability of the data. This may be due to differences in case management systems, interpretation of coding, training, regional practices and communication infrastructure.
- The outcomes of exposures may be unknown, as the number and types of cases that are followed up differs (for example, limited in some countries to severe cases of poisoning).
- It might be difficult to obtain information on product formulations from manufacturers and suppliers. Furthermore, product labels may not include a unique product identifier that all centres can use consistently.
- Communication and relations with public health and other partners may be sub-optimal.

5.5 TOXICOVIGILANCE NETWORKS

Toxicovigilance activities can be enhanced through a toxicovigilance network, a collaborative group of agencies, institutions and bodies involved in the identification of and response to toxic exposures. These could include:

- poison centres and their associations;
- local, state, national and international public health, health security and regulatory programmes;

- toxicology laboratories;
- medical examiners and coroner's offices;
- medical professionals;
- first responders;
- civil society organizations that collect data on injury prevention and harm reduction;
- national security, public safety and border services;
- academia;
- industry; and
- communications specialists.

The aim of a toxicovigilance network is to provide information for timely poisoning prevention, treatment, harm reduction and management of risks associated with toxic exposures of public health concern. This is achieved by building relations among toxicovigilance partners for information exchange and collaboration and identifying and bridging gaps. Electronic communication tools such as e-mail distribution groups and a shared electronic workspace for posting documents and for discussion forums can advance toxicovigilance activities.

For a network to function effectively, there must be a common understanding of each member's roles, responsibilities, strengths, limitations, priorities and needs. The development and maintenance of a toxicovigilance network require significant investments of time and resources.

5.6 PROGRAMMES FOR POISONING PREVENTION

Activities for preventing poisoning are the counterpart to toxicovigilance. As for toxicovigilance, the responsibility for poisoning prevention is shared by organizations such as health bodies, poison centres, government agencies, industry and civil society (21).

Poisoning prevention programmes require good information about the local situation, including details of acute and chronic poisoning cases, environmental contamination, substance abuse patterns and the circumstances that give rise to a high risk of exposure. Through toxicovigilance, poison centres are well placed to identify priorities for poisoning prevention. Box 5 describes the role of poison centres in the prevention of children's exposure to liquid laundry detergent capsules.

Box 5. Role of poison centres in reducing paediatric exposure to liquid laundry detergent capsules (15)

An example of effective prevention due to poison centre activities is the identification by numerous centres of the toxicological hazards of liquid laundry detergent capsules, which led to improvements in their packaging and labelling. These capsules were introduced in France, Ireland and the United Kingdom in 2001 as a convenient pre-measured dose of detergent. Poison centres soon began to receive reports of cases of eye and throat injuries in children. Nevertheless, the capsules were introduced onto the Italian market in 2010 without child-protective packaging. Shortly afterwards, the National Poison Control Centre in Milan identified an increase in enquiries about paediatric exposure, including reports of respiratory and ocular effects associated with the new product. After alerting the manufacturers and public health authorities, the National Poison Control Centre collaborated with the National Centre for Epidemiology, Surveillance and Health Promotion in the National Institute of Health to further monitor the potential problem and conducted a study to compare the severity of poisoning by traditional laundry detergents and by liquid laundry detergent capsules in children under 5 years between 2010 and 2015. The study demonstrated that the capsules were more likely to be associated with multiple-route exposure, the development of symptoms, more severe symptoms and a greater likelihood of hospitalization. By publishing these trends, the Poison Centre provided evidence to encourage manufacturers to adopt voluntary preventive measures, including more visible warnings on packaging, opaque packaging, child-resistant closure and a public information campaign. Use of these measures (particularly opaque packaging) resulted in a steep decrease in the number of enquiries to the Poison Centre about the capsules, and the protective measures became mandatory in Italy. Shortly afterwards, similar measures became mandatory in the European Union, with additional requirements for use of aversive agents, slower dissolution of the capsule in water and increased mechanical resistance. Engagement in toxicovigilance and active surveillance made the Poison Centre central in identifying a novel pathway of exposure to poisons, proposing measures to address the issue and demonstrating the effectiveness of risk management measures.

The principal types of preventive action that can be initiated by poison centres are:

- monitoring: investigating trends in toxic exposure to both well-known agents and emerging threats to public health by collecting data from enquiries and from other sources, such as attendance at hospital emergency departments to identify local risks;
- analysing and interpreting data generated by monitoring;
- reporting to and collaborating with other organizations and institutions on the development of safer products, safety measures in packaging, design, labelling, transport and handling of hazardous products and withdrawing or limiting the availability of selected toxic substances;
- education of particular groups at risk as well as the general public and professional health care workers, including dissemination of leaflets, social media messaging, articles in the mass media, education sessions and targeted outreach as well as organization of regular poisons prevention campaigns (21); and
- evaluation of effectiveness, which should be planned for any preventive activity, with poison centre data, market share data and other data to demonstrate the effectiveness of prevention and harm reduction measures (15, 21).

Box 6 illustrates the use of poison centre data to provide evidence for strengthening regulation of nicotine refill products for electronic nicotine delivery systems.

Box 6. Poison centre data and regulation of electronic nicotine delivery systems in the USA

Nicotine, a pharmacologically active compound in tobacco products, is toxic, particularly for young children, and high concentrations can result in death (22). Children's exposure to nicotine has usually been a result of ingesting conventional cigarettes and other tobacco products, such as chewing tobacco and snuff. Since its development and release, however, nicotine replacement therapy such as nicotine chewing-gum has also resulted in poisoning in infants. In 2010–2011, electronic nicotine delivery systems (ENDS) such as e-cigarettes and vape pens and solutions of nicotine in cartridges or as refills entered the market in the USA, with no regulation requiring child-resistant closures on refill products or standardized concentrations. As ENDS became more widely used, poison centres started to receive calls about young children ingesting nicotine solutions. An analysis of cases documented in the National Poison Data System between January 2012 and April 2015 showed that the number of children under 5 years of age who were exposed to nicotine cartridges and refill products had increased by approximately 1500% during the study period (23). Children who were exposed to these products were 2.6 times more likely than children who were exposed to traditional tobacco products to have severe symptoms and 5.2 times more likely to be admitted to a health care facility (22). Researchers noted that the packaging, colours and flavours of these products might have increased their appeal to children (23). The American Association of Poison Control Centers used the data collected in the National Poison Data System to advocate for stronger regulation of these products (6). Amendments to the Federal Food, Drug, and Cosmetic Act in 2016 gave the Food and Drug Administration authority to regulate ENDS and associated products, which has resulted in the introduction of industry requirements for marketing, packaging and sales (24, 25).

Examples of educational and campaign activities for prevention include:

- general campaigns on poisoning prevention, perhaps at fixed dates during the year (such as a regular “poisoning prevention week”) or at high-risk periods, for example, warning against eating wild mushrooms during the autumn;
- posters demonstrating the dangers of poisoning by household products;
- booklets identifying poisonous fungus, plant and animal species; and
- booklets identifying specific groups at risk (such as pregnant women, or rural workers who use pesticides).

The methods used for preventing and generating awareness of poisoning should be adapted to the national situation and circumstances. Media and communications experts can ensure that the messages used are clearly understandable and attractive. Establishment of a multidisciplinary group of professionals to review data on poisonings and to prioritize and plan poisoning prevention activities can be valuable. See Annex 4 for a description of the Canadian community of practice for toxicovigilance and prevention.

5.7 REQUIREMENTS FOR TOXICOVIGILANCE AND PREVENTION

As toxicovigilance and poisoning prevention are linked, this subsection addresses both. It describes the requirements for data collection and handling for toxicovigilance and the staff and other resources required. Conditions that support toxicovigilance and prevention based on poison centre data include contacts with experts such as poison centre scientists, epidemiologists and biostatisticians in a strong community of practice. The activities often depend on provisions for sharing information securely, on the availability of electronic records and on ensuring that the data are handled sensitively by the whole team.

5.7.1 DATA REQUIREMENTS

For toxicovigilance and poisoning prevention, the poison centre should collect a minimum set of data on each exposure. A comprehensive list of data elements is given in Annex 3; however, each centre should decide on its priorities for toxicovigilance.

5.7.2 DATA QUALITY AND COMPARABILITY

The value of poison centre data for toxicovigilance depends on accurate reporting of an exposure by the caller and accurate recording of the information by the poisons information specialist (6). Poison centres should have procedures for monitoring and ensuring good history-taking and documentation, including training (see below) and regular audits of call records. Methods for ensuring data quality are further described in section 10.

Poison centres should also have measures to ensure data comparability, such that the name of an agent or a clinical feature is documented in the same way by each poisons information specialist. This is important both within a poison centre and among poison centres in a country and is essential when centres pool their data in a single repository. Tools to improve data comparability include data dictionaries or manuals with definitions of terms and the use of classification schemes, for example, for agent types and symptoms and signs. Examples of defined terminologies and product classification can be found on the WHO website (26). Ensuring data comparability among poison centres may require dedicated resources to identify differences in practice, development and maintenance of common coding manuals and definitions, and training of poisons information specialists.

5.7.3 IDENTIFICATION AND ESCALATION OF POTENTIAL THREATS

Recognition of signs and symptoms indicative of toxic exposure is the cornerstone of toxicovigilance, and identifying signals from background noise is an important challenge. As the front-line professionals dealing with enquiries about poisoned patients, experienced poisons information specialists can detect unusual cases and patterns. The “human in the loop” is a crucial element of toxicovigilance, particularly in the early stages of an emerging threat; however, signals that are not obvious may not be detected immediately in the mass of other poisoning cases.

Use of electronic, rather than paper, case records enables use of automated surveillance to identify signals of potential threats. Surveillance algorithms applied to electronic records can more readily identify temporal trends, geographical and seasonal clusters and complex syndromic relations between toxic exposures and demographic factors. These systems can then highlight the issue to subject matter experts for follow-up.

Manual, paper records or simple spreadsheet databases can also be used, including:

- daily or weekly review of records by one staff member, who thus has an overview of the poisoning cases reported to the centre;
- regularly tabulating summary information from call records to identify trends;
- using a notice board to flag potentially suspicious events to staff; and
- listing events of potential interest that should be flagged if they occur.

The practicality of these methods depends on the number of calls handled by the poison centre. These methods are likely to be less efficient and more prone to error and human bias than automated systems.

Once a signal or emerging trend has been validated by the poison centre, appropriate stakeholders should be notified and the data used in a dynamic risk assessment. As mentioned above, a procedure should be in place to determine when and how an event is to be notified.

5.7.4 SETTING UP AN ELECTRONIC SURVEILLANCE SYSTEM

The availability of electronic records facilitates the storage, handling and rapid analysis of poison centre data and use of electronic-based surveillance techniques. Such surveillance systems should cover a large reference period so that expected rates can be established and secular trends and seasonal patterns in exposure and exposure risks can be identified. Surveillance analyses can be performed statistically or heuristically, and subject matter experts can aid in interpreting the results. Ideally, poison centre data should be securely housed in a centralized location on a platform that allows ready access by authorized users, frequent reporting and data upload capability. Such a platform requires significant investment for development and maintenance.

The development, operation and maintenance of a poisons surveillance system require a multidisciplinary team of subject matter experts, such as poisons information specialists, medical toxicologists, epidemiologists and IT and systems development personnel. The group should have relevant expertise in toxicology and epidemiology to design, revise or refine case definitions. With these case definitions, epidemiologists can develop signal detection algorithms to scan poison centre data continuously and generate automated notification responses to the surveillance team for validation. During validation, an epidemiologist evaluates the identified signals for data quality, correctness and consistency. Subject matter experts then evaluate the identified signals for clinical relevance and potential impact before notifying the relevant authorities. Examples of surveillance systems in operation in selected countries are given in Annex 4.

5.7.5 DATA GOVERNANCE

Data governance is important to ensure responsible, ethical use of poison centre data for toxicovigilance and surveillance. It may be necessary to establish a committee or steering group for this purpose. Members should include representatives of contributing poison centres, custodians of the central repository and data users (as required). The committee could oversee the development and maintenance of privacy assessments and information-sharing agreements, manage requests for data and disclosure, mediate the information flow from poison centres to end users and maintain privacy and protocols for security breaches.

5.7.6 STAFF

A poison centre should have not only well-trained poisons information specialists but also staff with other skills for a full-scale programme of toxicovigilance and prevention. They include staff with epidemiological and biostatistical knowledge or timely access to such experts to assess cases in the context of underlying patterns and limitations of the data and to determine whether cases should be reported to public health partners. Staff trained in risk communication, health promotion, media communication and the use of social media will enhance the poison centre's capacity for toxicovigilance and prevention.

Other specialists who can contribute to toxicovigilance and poisons prevention include:

- health educators, to design programmes, communicate with the mass media and ensure effective, continuous distribution of educational material;
- primary health workers, to promote prevention in communities;
- psychiatrists, to evaluate the incidence and severity of certain types of poisoning (such as suicide attempts) to determine possibilities for preventing or minimizing them;

- social workers, to evaluate social conditions that might determine some types of poisoning and to advise on getting clear messages to target populations;
- experimental toxicologists, to conduct studies to confirm or refute apparent links between newly identified hazards and clinical effects and to determine mechanisms of toxicity;
- IT specialists, to initiate and improve electronic capture, integration and analysis of data (if electronic systems are available); and
- toxicovigilance network partners.

Toxicovigilance and poisoning prevention programmes also require adequate administrative and secretarial personnel.

The director of the poison centre should be familiar with the concepts and implementation of toxicovigilance and prevention, supervise the analysis of data and ensure that the relevant authorities are informed about identified toxicological hazards. The director should also ensure funding for prevention activities, for example, for publication of brochures or posters and for campaigns.

5.7.7 TRAINING

Eliciting a complete, accurate history from a caller is a skill that should be addressed in training, and this is described in detail in section 10. Ensuring that poisons information specialists understand the importance and value of data quality for toxicovigilance may help to ensure that they collect and code data to a high standard. When there are several poison centres in a country, standardized training might help to improve data quality and comparability. Additional training might be required for poisons information specialists (for example, in epidemiology and statistics) to support toxicovigilance activities.

All front-line staff at a poison centre should be trained in reporting cases that might signal an emerging hazard, outbreak or other event of public health significance. Training can be based on a standard operating procedure to ensure that the process is followed correctly. More advanced training may be required to prepare for large-scale public health emergencies that require rapid deployment of several agencies, as described in section 6.

Staff should be familiar with legislation and regulations on the safety of chemical products and pharmaceuticals and of local toxicological problems, for example relating to environmental contamination or use of psychoactive substances. Training should also include dealing with the public, the mass media and professionals in other fields in order to communicate prevention messages.

5.7.8 DOCUMENTS AND FACILITIES

Section 2 describes the documentary resources and physical facilities that a poison centre requires to operate to a good standard. Some additional resources useful for toxicovigilance and prevention activities are:

- up-to-date lists of contacts, protocols and procedures to share information and for joint assessments, coordinated management of events and general collaboration among stakeholders;
- reports of surveys and monitoring by other poison centres;
- an established programme and resources for the production and distribution of educational and instructional materials (brochures, leaflets, posters, slides, videos, websites, mobile apps); and
- educational material produced by other poison centres.

Increased use of social media and virtual forums to share information on the misuse of medications and on substances of abuse make them useful sources for new and developing trends. Poison centre staff should therefore develop expertise in the use and analysis of these media. Automatic approaches, such as supervised classification and natural language processing, hold promise for future monitoring and interventions (27).

5.8 RECOMMENDATIONS

Efficient communication and coordination among all partners in toxicovigilance and prevention are essential for effective planning of these activities. The efficacy of toxicovigilance and measures for the prevention of poisoning is considerably improved by both national and international agreements.

5.8.1 RECOMMENDED ACTION AT NATIONAL LEVEL

Health ministries and public health agencies should support toxicovigilance and poisoning prevention activities in the form of advocacy, facilitation, endorsement and funding. As toxicovigilance requires data, improving the availability and accessibility of data on exposures and on products is fundamental. The use of electronic records can facilitate the storage, handling and rapid analysis of data.

Official support for and recognition of the role of poison centres in toxicovigilance and prevention of poisoning adds authority to the preventive actions instituted by a centre and makes it easier for the centre to obtain complete data on the composition of toxic and potentially toxic products. Furthermore, consultation of the data and experience of poison centres can strengthen regulatory risk management measures. For example, a medicines regulatory agency that is proposing to change restrictions on the availability of a pharmaceutical should seek the advice of the poison centre about the potential impact of such a change on the incidence of poisoning with that agent. The poison centre can also monitor exposure after the change to provide data on the impact.

The following measures by health ministries and by poison centres would improve national toxicovigilance and poisons prevention.

Health ministries:

- Strengthen systems for the collection of data on morbidity in poisoned patients treated by health care professionals (with diagnostic codes), with mechanisms for following-up patients to identify and evaluate any medium- and long-term sequelae.
- Strengthen systems for the registration and collection of mortality data by ensuring precise certification of death by cause (for example, from public health systems and forensic departments).
- Introduce mechanisms for mandatory notification of selected poisoning incidents to public health authorities.
- Advocate for regulations that require manufacturers and industry to provide product information to a national database that can be accessed by poison centres and other health partners for treatment and surveillance.
- Implement a procedure for communication between poison centres and the national IHR focal point.

Poison centres:

- Maintain contacts with industry for exchange of information on the chemical and industrial products they manufacture and use and the circumstances and effects of poisoning by these chemicals and products.
- Promote integration of information collected from related areas of mutual interest (such as experimental toxicology, analytical toxicology and occupational medicine).
- Contribute to a national toxicovigilance network supported by electronic communication tools such as list servers, e-mail distribution groups or a virtual community of practice to facilitate information exchange and collaboration.

5.8.2 RECOMMENDED ACTION AT INTERNATIONAL LEVEL

As poison centres may detect a chemical threat that might have international implications, a protocol should be in place to ensure that the national IHR focal point is informed so that the information can be shared with WHO and with other national focal points.

Poison centres in different countries may arrange to share data on toxic risks to permit early warning of potential problems. Pooling of information and expertise in respect of case data on rare, limited or new phenomena and of data on new hazardous products would ensure that preventive measures were taken at an early stage. For useful exchange of information, collaborators should standardize the terminology and agree on format, content and the procedures for exchange.

International collaboration is necessary to:

- promote use of poison centre networks, for example, the WHO INTOX network, and professional poison centre associations to enhance information exchange and collaboration on toxicovigilance objectives;
- establish a mechanism for rapid notification of toxic alerts called in any country and exchange of experience in dealing with such alerts; and
- exchange of education and training in the field of toxicovigilance and prevention of poisoning and of educational materials to be adapted by each centre for local use.

5.9 CONCLUSIONS

Poison centres are vital in improving toxicovigilance globally, as their services are usually available 24 hours a day, and they are uniquely equipped to collect, analyse and disseminate toxicovigilance data. Collaboration with other stakeholder organizations offers the possibility of near real-time detection of health threats and the provision of expertise to guide the best course of management and the prevention of further harm.

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Spill of toxic red mud from alumina plant, Ajka, Hungary / Credit: David Russell

6 ROLE OF POISON CENTRES IN THE PUBLIC HEALTH MANAGEMENT OF CHEMICAL INCIDENTS AND EMERGENCIES



6.1 INTRODUCTION

A chemical incident can be defined as the uncontrolled release of a toxic substance resulting in potential or actual harm to public health and the environment. Once detected, chemical incidents usually trigger a public health response, which requires collaboration among many stakeholders to assess exposure and risk and to provide advice to authorities and to the public when applicable (1).

Box 7 lists some common types of chemical release, which may be accidental or intentional and occur in and affect any setting, including industrial and commercial sites, public spaces and the home. Chemical incidents can have many manifestations due to various technological and natural events. Technological events include an explosion at a chemical factory, spillage during transport or storage or a release resulting from conflict or from criminal or terrorist activity. Incidents with a natural source include groundwater contamination with arsenic or fluoride, exposure to natural toxins such as aflatoxin and marine toxins and release of chemicals during wildfires, volcanic eruptions and other natural disasters.

Box 7. Common sources of chemical hazards

Technological (non-natural) sources	
Industry (formal and informal)	Agriculture (industrial and small-scale)
<ul style="list-style-type: none"> Emissions to air, land and water resulting from both normal operations and accidents Loss of chemical containment due to accidents or ineffective management of emissions 	<ul style="list-style-type: none"> Emissions to air, land and water resulting from both normal operations and accidents Loss of chemical containment due to accidents or ineffective management of emissions
e.g. mining and processing; chemical manufacturing industries; industries that use chemicals	e.g. pesticide and fertilizer use; stubble burning; livestock emissions
Transport (road, rail, air and water)	Storage (commercial and domestic)
<ul style="list-style-type: none"> Loss of chemical containment due to accidents or ineffective management Absence of suitable labelling 	<ul style="list-style-type: none"> Loss of chemical containment due to accidents or ineffective management Absence of suitable labelling
e.g. after a collision or derailment; leakages or breaches of pipelines (e.g. fuel)	e.g. poor storage practices such as leaking containers, unsecured or inappropriate storage sites; excessive volumes of chemicals; storage of obsolete chemicals

Technological (non-natural) sources		
<p>Waste disposal (commercial and domestic)</p> <ul style="list-style-type: none"> Emissions to air, land and water resulting from normal operations and accidents Loss of containment of chemicals during accidents or ineffective emissions management <p>e.g. poorly constructed and managed waste sites; illegal dumping and uncontrolled disposal of waste, including chemical waste; in-country and imported wastes</p>	<p>Conflict, crime and terrorism (covert or overt)</p> <ul style="list-style-type: none"> Emissions to air, land and water resulting from intentional use or incidental release of chemicals Loss of containment due to physical damage <p>e.g. weapon strike on an industrial site; covert contamination of a consumer product with a chemical; use of chemical weapons</p>	
<p>Food (in-country and imported; small-scale or commercial)</p> <ul style="list-style-type: none"> Accidental contamination during production or from raw materials Adulteration with non-consumable or contaminated substances Use of chemically contaminated containers <p>e.g. contamination by re-use of pesticide containers for storage of food or drinks; use of poor-quality or contaminated ingredients in food production.</p>	<p>Consumer products (in-country and imported; small-scale or commercial)</p> <ul style="list-style-type: none"> Accidental contamination or adulteration during production with poor-quality or incorrect substances Incorrect or excessive use of chemical-containing consumer products <p>e.g. medicines manufactured with poor-quality or incorrect ingredients; cosmetics containing toxic substances; toys made from or coated with toxic materials; cleaning products and household chemicals; traditional remedies containing toxic substances</p>	
Fire (accidental or intentional, in urban or rural areas)		
<ul style="list-style-type: none"> Release of products of combustion into the air Loss of containment and/or combustion of chemicals resulting in contamination of air, land or water <p>e.g. fires at: industrial sites; densely populated areas; developed areas liable to wild-fire</p>		
Natural sources		
Volcanoes	Earthquakes	Wildfires
<ul style="list-style-type: none"> Loss of chemical containment due to physical damage Smoke, dust and fumes 		
Storms		Flooding
<ul style="list-style-type: none"> Loss of chemical containment due to physical damage Displacement of chemicals Run-off and overland flow 		
Marine toxins		
<ul style="list-style-type: none"> Accidental contamination of seafood by marine toxins, such as algal blooms 		

The chemicals industry is the second largest manufacturing industry globally and is continuing to grow rapidly, particularly in emerging economies (2). The rapid growth in the production, trade and consumption of chemicals, coupled with increasing urbanization and a lag in the development of the necessary regulatory capacity increase the risk of technological incidents resulting in human exposure, particularly in developing countries and those in economic transition (2).

Humans can be exposed to chemicals in contaminated air, land, water, food and consumer products (1). Chemical incidents may be acute, with a sudden release of chemicals, or chronic, when they occur over a longer period. An acute incident that remains undetected or uncontrolled for some time may result in a chronic longer-term incident. Exposure may also be considered in terms of acute (short-term), for example, a single accidental exposure to a contaminated consumer product, or chronic (longer-term), for example, regular consumption of a contaminated drinking-water supply. Acute exposure may also occur against a background of chronic exposure. Poison centres may most commonly expect to be involved in acute incidents and exposure but also play an important role in the detection of and response to chronic incidents and exposure.

Chemical incidents can affect people's health in several ways, in addition to the obvious burden of morbidity and mortality, for example, through environmental and economic damage and psychosocial impacts. Efficient, effective detection and response to chemical incidents is therefore essential to reduce these impacts.

This section considers the potential role of poison centres in the response to chemical incidents, with reference to the five stages of disaster management: prevention; preparedness; detection and alert; response; and recovery.

6.2 GENERAL CONSIDERATIONS FOR PREPAREDNESS AND RESPONSE

Many countries have frameworks for emergency management that include strategic emergency management plans and policies for all hazards, including natural, human-induced and technological vulnerability. The aim of emergency management is to allow identification of shared responsibility in all sectors of society, thereby strengthening the way governments and stakeholders assess risks and work together to prevent, mitigate, prepare for, respond to and recover from the threats and hazards that pose the greatest risk.⁷ As part of emergency preparedness, all-hazards and hazard-specific plans, such as ones to address chemical incidents, should be developed to guide response, manage consequences and transition to recovery. These should include a “concept of operations”, which is an important aspect of emergency preparedness, resilience and response that defines arrangements among stakeholders for responding to incidents and emergencies.

Other activities of preparedness include mutual assistance agreements among different agencies or administrative regions (for example, states, counties), inventories of resources (supplies and expertise), public awareness-raising, training and exercises. Countries should consider the possibility of serious cross-border threats, including chemical hazards, and seek to activate international agreements strategically to ensure multi-stakeholder public health preparedness and response.⁸

Emergency responders, who may be personnel of fire, police or ambulance services, paramedics, civil protection, military or voluntary services, are often the first to the scene of a major chemical incident. To fulfil their roles safely and effectively, first responders need information on the hazards and toxicity of the chemicals concerned. Ensuring access to such information is an important part of preparedness planning. In some countries, a poison

⁷ Modified from the purpose statement of the Emergency Management Framework for Canada (<https://www.publicsafety.gc.ca/cnt/rsrscs/pblctns/2017-mrgnc-mngmnt-frmwrk/index-en.aspx>).

⁸ For example, Decision No 1082/2013/EU of the European Union lays out the requirements for dealing with serious cross-border health threats, including epidemiological surveillance, monitoring, early warning, preparedness and response planning, to coordinate and complement national policies. It also establishes a mechanism for joint procurement of medical countermeasures by member states.

centre may be the only authoritative source of information and advice on toxic substances and should, ideally, be available 24 hours a day, 7 days a week. The poison centre may therefore play a central role in managing chemical emergencies.

6.3 ROLES AND RESPONSIBILITIES OF POISON CENTRES IN CHEMICAL INCIDENTS

The roles and responsibilities of a poison centre in chemical incidents depend on its operational capacity and institutional or administrative arrangements and its financial resources. Some poison centres focus on providing information and advice on toxicology and treatment for the management of exposed people, while others are fully integrated into the public health infrastructure and support preparedness planning and training as well as risk assessment and management after a chemical incident. As the toxicity of all chemicals is not fully known, poison centres should also consider initiating and contributing to research and follow-up studies when appropriate.

Poison centres have a clear role to play in the identification and thus notification of emerging threats and can also contribute to international alert and response. Emergency preparedness may include participation in international rapid alert systems. An example is the Rapid Alert System for Chemical incidents (RASCHEM), a European Union system to link poison centres in member states to allow exchange of information on incidents, including chemical agents relevant to terrorism, and consultation and coordination of countermeasures (3) (see also Annex 4).

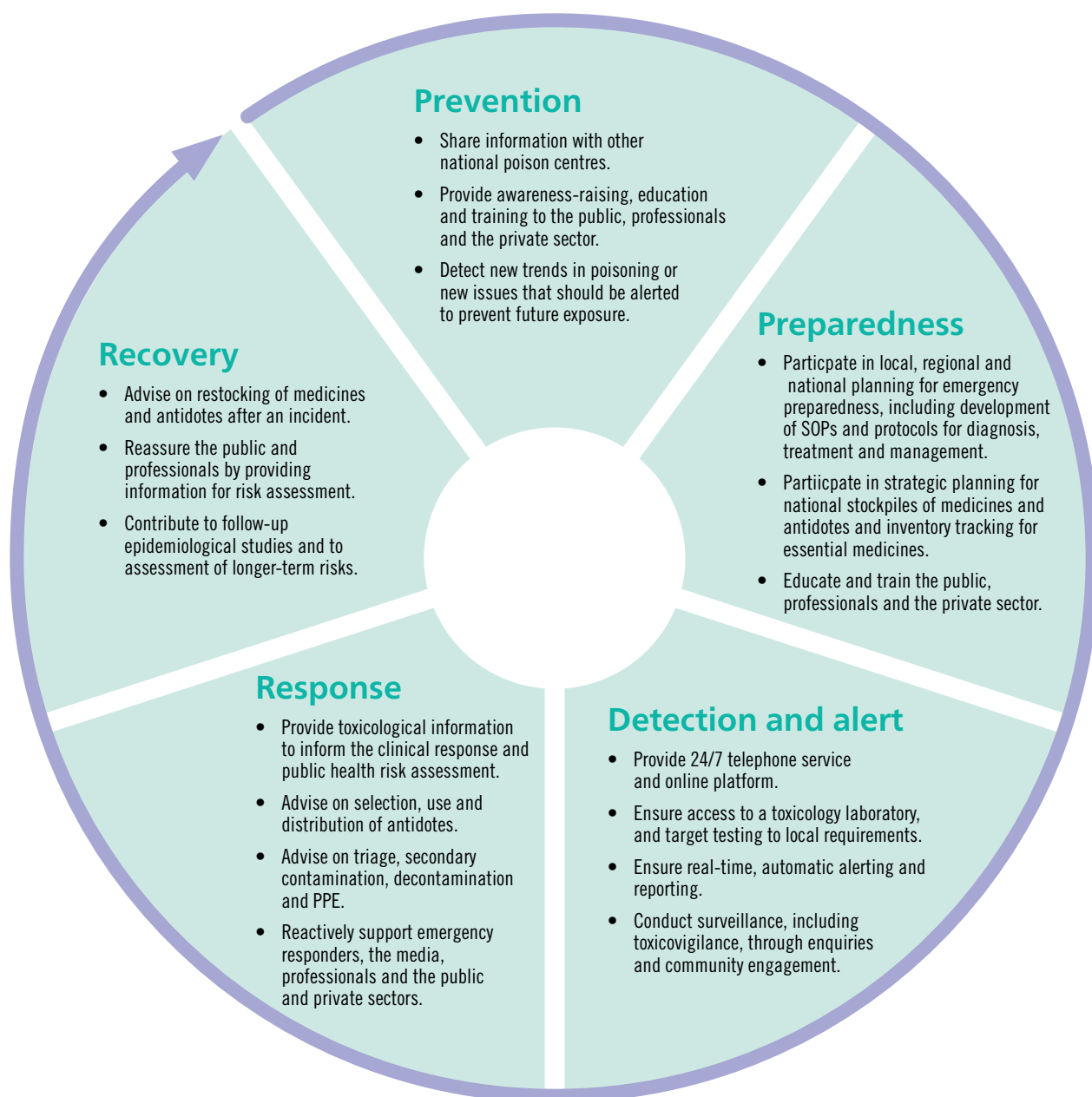
Poison centres are recognized as an important resource for implementation of the IHR, as discussed in section 1. The IHR Joint External Evaluation tool includes the core capacities required for a country to detect and respond to chemical events, indicating the importance of an adequately resourced poison centre that operates 24 hours a day, 7 days a week (4).

The following sections describe how poison centres can contribute to each stage of the disaster management cycle, reflecting the breadth of their possible functions.

6.4 DISASTER MANAGEMENT CYCLE

The disaster management cycle is the continuous process by which government, industry, the health sector and civil society plan for and reduce the impact of chemical incidents (1). The cycle comprises five stages: prevention; preparedness; detection and alert; response; and recovery (1). The potential contribution that poison centres can make at each stage is summarized in Figure 3; however, the extent to which a poison centre fulfils these tasks will depend on its defined role and the country situation and capacity.

Figure. 3. Roles of poison centres in the disaster management cycle



Key: SOP, standard operating procedure; PPE, personal protection equipment; 24/7, 24 hours a day, 7 days a week

6.4.1 PREVENTION

As poison centres are often one of the first points of contact after an exposure, they are well placed to detect new and re-emerging trends in poisoning as well as rare or unusual exposures and the circumstances that give rise to them. This information can guide prevention and harm reduction. This activity is described in more detail in section 5 on toxicovigilance and prevention, but some examples are given below.

- As it is known that the incidence of carbon monoxide poisoning increases during power outages, for example following a natural disaster, poison centres can include information on the safe use of barbecues and diesel generators in their poisoning prevention programmes.
- An increase in the number of enquiries about health effects after use of a specific product can provide evidence to trigger withdrawal of the product.
- Some poison centres may provide a commercial service to industries by writing or reviewing chemical safety data sheets and thus promote the sound use of chemicals.

6.4.2 PREPAREDNESS

To be the most effective in supporting response, poison centres should be involved in contingency planning for chemical incidents locally, nationally and internationally and should be proactive in establishing relations with emergency medical facilities, the national public health institute or equivalent and, where appropriate, any national disaster management organization that operates separately.

The role of the poison centre(s) should be clearly stated in national emergency response plans (for example, in the concept of operations) and ideally in the chemical incident emergency response plan. Local, regional and even site-specific chemical incident response plans might be appropriate, in which the role of the poison centre should also be defined. If the roles and responsibilities are not clear, poison centres and other national stakeholders are advised to undertake a gap analysis to identify needs and corrective actions for effective planning. This should ideally be followed by national, regional or local assessments of vulnerability, to identify chemical hazards of concern. The distribution of poison centres and geographical factors such as transport times and access to analytical services, which affect preparedness, should be considered in vulnerability assessments and in local, regional and national plans.

The plans of emergency medical facilities and hospitals should also include chemical incidents, in close collaboration with the poison centre. The poison centre should contribute toxicological expertise and be involved in establishing guidelines on issues such as:

- measures for risk assessment
- isolation and decontamination in situ and in hospitals
- personal protective equipment
- first-aid measures
- general and specific therapy
- measures to ensure the availability of antidotes.

Poison centres should also be aware of the medical facilities available for caring for large numbers of casualties in terms of the number of beds, pharmaceutical supplies and availability of specific antidotes. They should assist in the development of standard operating procedures, protocols and memoranda of understanding for diagnosis, treatment and access to additional resources, as required. The reporting of diseases of unknown etiology should be included in standard operating procedures, as they may be an indicator of chemical poisoning.

Poison centres should be involved in planning strategic national stockpiles of medicines and antidotes and, ideally, also in preparedness planning to ensure distribution and maintenance of supplies regionally and locally (see section 7). They should also participate in establishing arrangements for accessing additional supplies (through national and international agreements, as necessary) should these be required in an incident, and they should track inventories of essential medicines.

All these activities require financial planning and identification of sources and means of accessing financial support from the national government and, if required, internationally. Financial considerations should be included in emergency response plans, including responsibility for funding the purchase and movement of medical supplies and staff.

When developing toxicological analytical capacity, it is advisable to consider the requirements of the country or region (on the basis of toxicovigilance, surveillance or previous chemical incidents) and focus resources on the relevant tests and programmes. For example, in a country with a known problem of exposure to organophosphate pesticides, testing and reporting on acetylcholinesterase activity may be appropriate for monitoring and research. When chronic exposure to chemicals such as lead or mercury is identified, the relevant detection and measurement methods should be introduced. Practical issues such as transport of samples and financial support should be considered in the emergency preparedness stage so that appropriate laboratory capacity can be planned. When laboratory capacity is lacking, samples might have to be sent to a laboratory in another country, and making arrangements in advance will facilitate sample transfer in an emergency.

6.4.3 DETECTION AND ALERT

Detection of a chemical incident can be broadly categorized as detection of health effects that result in identification of chemical exposure (including cases of disease of unknown etiology and those for which there is no robust evidence of the source of exposure) or detection of environmental contamination, which results in identification of an exposed or potentially exposed population.

Detection and alert should ideally be both proactive and reactive. Activities for the detection of a chemical incident are known as toxicovigilance (see section 5). Briefly, this involves analysis of poison centre enquiries to identify any specific circumstances or agents that give rise to poisoning or certain populations with a higher incidence of poisoning. Toxicovigilance can also indicate whether a toxicological problem is emerging from, for example, a product or environmental contamination.

An effective public health plan should require that all stakeholders who observe a potential public health issue share their observation with relevant bodies so that the necessary preventive and public health management measures can be taken. Poison centres can identify potential issues and should therefore be part of a procedure to alert the appropriate authorities.

Depending on feasibility and the importance to the local community, a system for reporting sentinel events⁹ could be established. After an incident has occurred, clinical reporting systems for sentinel health events could be established near sites of contamination, with routine reporting systems such as through death certificates or cancer registers. Follow-up monitoring may be important for tracking the effects of a chemical incident on a population during the incident and over time. Local poison centres might contribute to these activities (1).

Poison centres may detect chemical incidents reactively from direct reports by the public, clinicians, workers or industries. This system is most effective when the poison centre provides a robust telephone service 24 hours a day, 7 days a week. In countries in which the telephone number of the poison centre is on the labels of chemical products, such as pesticides, reporting from a range of users or stakeholders is increased.

As described in section 5, poison centres may collect data that result in real-time alerts to a public health authority. When the poison centre does not assess public health risk itself, arrangements should be made for real-time reporting of certain syndromes (syndromic surveillance) and chemical exposures. Such reporting may be automated, for example, through a toxicological database or an electronic rapid alert system, or the poison centre may telephone the public health authority, which will conduct appropriate investigations and follow-up.

Ideally, poison centres with clinical toxicology units will have access to a toxicology laboratory for biomedical investigations, diagnosis and monitoring of treatment. Toxicology laboratories can contribute to toxicovigilance by drawing attention to unusual findings, such as an increase in the number of cases of high blood lead concentrations

⁹ An observance of a preventable disease, disability or untimely death the occurrence of which serves as a signal that a hazardous environmental exposure may have occurred or may be occurring. Within health surveillance and reporting (e.g. by a poison centre), the purpose of monitoring local sentinel health events is to identify chemical releases that have not been reported or noticed or have been considered harmless.

or detection of thallium in samples. Laboratories also identify and measure chemicals to validate treatment and for long-term follow-up studies.

Although huge numbers of chemicals are used regularly throughout the world and there is a wide range of natural toxins, there are few sensitive, specific biomarkers to confirm individual exposure. Methods of analysis might have to be developed during an incident, which may be complicated, as testing often requires specific equipment, specific sampling and handling techniques for certain chemicals and classes of chemicals, significant skill and expertise on the part of laboratory staff and sometimes specialized toxicology laboratories.

6.4.4 RESPONSE

Poison centres can support response activities in a number of ways. As sources of information and expertise on the toxicity of chemicals and management of exposure, poison centres can contribute to:

- public health risk assessments, including information on protective actions, such as removal of a product, sheltering or evacuation, depending on the nature of the incident;
- developing case definitions for surveillance;
- patient triage and clinical management;
- prevention of secondary contamination by advising on the need for appropriate personal protective equipment, isolation and decontamination of exposed people;
- medical treatment, including accessing and using antidotes; and
- preparing and distributing information to health professionals and the public, either directly or through the public health authority.

The level of involvement of poison centres and toxicology services will depend on their defined roles and responsibilities in preparedness and in emergency response plans, including financial, geographical and administrative considerations. For instance, in some settings, clinical toxicologists at a poison centre may attend the scene of an incident to assess and treat patients or to obtain and transport samples. This is the case in the poison centre in the Philippines, for example.¹⁰ Poison centres with clinical toxicology units may also admit and treat patients exposed during chemical incidents.

After a large-scale incident, a poison centre may see a rapid increase in the volume of enquiries, especially if calls are taken from members of the public. To prevent overwhelming the poisons information service, and as a contingency measure, the poison centre should have dedicated back-up telephone lines that can be activated to receive enquiries from separate groups, such as the public, health care professionals and public health managers. Poison centres that provide advice to private organizations (usually by commercial contract) may also be responsible for providing advice on the health and safety of workers in the event of an incident.

6.4.5 RECOVERY

Recovery comprises rebuilding and rehabilitating a population after an emergency (5). The recovery phase of a chemical incident could include restoring food and drinking-water supplies, restoring medical services if they have been disrupted, remediating contaminated areas, medical follow-up of exposed people and providing psychosocial support.

The actual role of poison centres in recovery may be defined in the recovery plan. They may also contribute to:

- public health risk assessments and post-incident messaging, such as food and drinking-water advisories and information for self-protection;
- epidemiological studies on chemical hazards;

¹⁰ C. Dioquino, personal communication, July 2019

- determining the need for activities such as land decontamination or removal of populations from contaminated areas; and
- advising on restocking of medicines and antidotes, by mechanisms, including financing, that should be agreed upon during planning.

It may be difficult to establish public health mechanisms and planning for environmental remediation after chemical contamination because of lack of clarity or complexity in identifying the responsibility and financing for decontamination and recovery of natural and built environments. Recovery of individual, community and population health and well-being may also be difficult. Poison centres can contribute by instigating or collaborating in follow-up studies of chemical incidents, either major and minor. In some cases, poison centre personnel might be able to collect information from the scene. These activities may provide valuable information on the impact of such events in terms of exposure and burden of disease and on requirements for recovery, which should ultimately be used in planning prevention.

6.5 CAPACITY REQUIRED FOR POISON CENTRES

In order to contribute to the detection, preparedness, response and recovery of chemical incidents, poison centres must have adequate information and trained staff. Section 2 describes the resources required to provide reliable, high-quality service. This section describes the resources required specifically for chemical incidents.

6.5.1 INFORMATION

The poison centre should be prepared rapidly to provide adequate information in the acute phase of chemical incident response and must therefore have its own toxicological information. Various toxicological databases and databanks are available free of charge or on subscription (see section 9 and Annex 2). The poison centre may also compile its own resources on the chemicals that are likely to be involved in accidents, including less frequently used industrial chemicals and reactive intermediates. The chemicals can be identified in vulnerability assessments conducted in preparedness planning for location-specific chemical hazards and risks. Information should be available on toxic chemicals and their effects; high-risk areas, processes and activities; chemicals that might be released, in what forms and in what quantities; and possible protective and remedial measures. In countries where there is a legal requirement to notify authorities of highly hazardous activities involving the use or transportation of chemicals and of the location of stored chemicals, this information could also be made available to the poison centre.

Experience in industrial accidents involving chemicals is often available at the plants concerned but not always elsewhere. This kind of information is very valuable for poison centres to understand the consequences of chemical incidents and provide advice. Therefore, an effort should be made to encourage exchanges of information and experience with occupational health services in industries.

As described in sections 2 and 8, poison centres routinely collect data from enquiries. The data on exposures resulting from chemical incidents will increase knowledge about the chemicals concerned and should be included in the case database. Internationally agreed mechanisms for collecting, validating and analysing data on exposure to toxic chemicals and observations of the features of poisoning, including long-term sequelae, would also improve knowledge about the chemicals.

Through contacts with poison centres in other countries, a poison centre might be able to obtain information on the availability of antidotes and facilitate emergency access to antidotes for a chemical incident. This is discussed in section 7.

6.5.2 STAFF AND TRAINING

In the event of a major chemical accident, poison centres may expect a significant increase in the number of telephone enquiries. They should have a plan for surge response and increase the number of staff available to answer calls and conduct other response activities.

Training for poison centre staff should include the principles of chemical incident management, including issues related to secondary contamination, decontamination and personal protective equipment, and professional techniques to prevent contamination. The staff of the poison centre should receive specific instructions on what to do in the case of a chemical incident. They should be prepared to provide relevant information on the chemicals involved to those responsible for handling the emergency or alert procedures, as well as to decision-makers and the media. They should know how to recognize the extent or level of the incident (operational, local, regional or international) and should alert authorities at appropriate levels, as defined in emergency preparedness activities. At least some staff should be trained in chemical risk assessment and crisis communication in order to respond appropriately to the concerns of responders and the public. There should be a clearly understood communications policy, with designated staff to deal with the media.

Poison centres should be included in debriefs and after-action reviews to ensure that any gaps in training are identified and filled. Participation in multi-sectoral exercises or simulations is a good basis for training staff and for contingency planning with other stakeholders.

Further information on staff and training is included in sections 2, 5 and 10.

6.6 CONCLUSIONS

Poison centres have databases and expertise in the toxicology of chemicals and toxins and in the management of exposure to these substances. Their services are usually available 24 hours a day, 7 days a week. Some poison centres have facilities for patient management and toxicological analyses. They can therefore play a vital role in the response to chemical incidents. In order to ensure that their services are used most effectively, poison centre personnel should be involved in planning, training and exercises for emergency preparedness and response. Poison centres must have sufficient resources to fulfil their roles adequately.

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Antidote store, Ramathibodi Poison Center, Bangkok Thailand / Credit: Puangpak Promrungsri

7 ANTIDOTES AND ANTIVENOMS



7.1 INTRODUCTION

Antidotes and antivenoms are substances used to treat poisoning, with a specific action against the toxic substance concerned. Antidotes modify the kinetics or elimination of a toxic substance or interfere with its effects at receptor sites, thereby improving the outcome of poisoning. Antivenoms are immunoglobulins that bind to and neutralize the effects of specific animal venoms, for example, from snakes or spiders.

While many cases of poisoning can be managed with good supportive care and, sometimes, elimination techniques, appropriate use of antidotes and antivenoms is essential for certain poisonings to rapidly improve the patient's condition and prevent death. Use of these agents can also significantly reduce the medical resources required to treat a patient and can shorten the period of therapy, thereby reducing the overall burden on the health service of managing cases of poisoning. In areas that are remote and far from good hospital services, particularly in low-resource settings where adequate facilities for supportive care are lacking, certain antidotes may be particularly important for the treatment of poisoning.

The availability of antidotes and antivenoms differs from one country to another, and in many low- and middle-income countries they may be difficult to obtain, either because they are not authorized for use or because of cost or limited availability on the global market. Access to antivenom immunoglobulins used in the treatment of snakebite faces particular problems, including poor regulatory frameworks, lack of appropriate reference standards for manufacture, inadequate investment in research and development, poor-quality products and inadequately trained staff. These factors affect the availability, efficacy and use of antivenoms; therefore, snakebite presents a significant global health burden (1).

This section outlines the requirements and challenges for the provision of antidotes and antivenoms and some approaches used to increase their availability, including the role of poison centres.

7.2 DEVELOPMENT OF ANTIDOTES

Studies on the mechanisms of toxicity and the kinetics of toxic substances and of ways to improve the management of poisoning may lead to the development and use of specific antidotes. In addition, manufacturers of new drugs may develop an antidote at the same time, particularly if the drug is one for which rapid reversal of its clinical effects is required.

The efficacy of a newly developed substance as an antidote must be validated scientifically, initially in experimental animals, preferably in species in which the pattern of toxicity is similar to that in humans. The clinical efficacy of an antidote in humans may be more difficult to ascertain and document than that of other pharmaceutical agents, as

there is limited opportunity for clinical trials (2). Often, data on the efficacy of antidotes come from a combination of sources, including experimental research, biochemical data and clinical observations (3).

Comprehensive scientific studies facilitate approval by regulatory authorities for registration of useful, effective antidotes. Governments are responsible for ensuring the availability of antidotes and should recognize the importance of this group of therapeutic agents and of supporting scientific studies on them.

7.3 TECHNICAL ASPECTS

7.3.1 REGISTRATION

Antidotes and antivenoms are pharmaceutical products, for which almost all countries have an official body for registration and approval. Some antidotes are drugs that have undergone a full range of tests before registration and are authorized for distribution and use in many countries. Nevertheless, pharmaceutical agents that have been evaluated for other uses may require additional authorization for use as antidotes.

In order to register an antidote or antivenom in a country and obtain marketing approval, the manufacturer must submit extensive documentation, including data on the product's physicochemical properties, the stability of the formulation and its toxicity and efficacy as determined in experimental animals, pharmacological studies and clinical trials. Some pharmaceutical manufacturers are disinclined to register antidotes and antivenoms, because the cost involved exceeds the expected return from the small production volume required to meet market demand (4). While a manufacturer may register an antidote in a country in which a market has been identified, it may be reluctant to navigate multiple regulatory systems to register the antidote in other countries.

Incentives can be provided, such as recognizing an antidote as an "orphan drug"¹¹ or a "common drug", for which the registration procedure is less complicated. The registration procedure could be modified for a new pharmaceutical substance that will be used only as an antidote, so that it is less comprehensive than that for a standard pharmaceutical. Authorities often accept different criteria for the registration of specialized pharmaceutical substances, such as anticancer drugs, because of the particular conditions of their use. A new antidote could be considered similarly, thereby facilitating its registration and encouraging manufacturers to make it more widely available. An approach used in the USA for an antidote for which clinical data were lacking was to require the manufacturer to collect data on use of the antidote after marketing, as a condition for approval (4).

A means for facilitating registration of new antidotes and antivenoms in a country that has limited regulatory capacity is participation in the WHO certification scheme on the quality of pharmaceutical products moving in international commerce (5). Under this scheme, a pharmaceutical company can request the competent authority of a participating country that has registered its product to provide a "certificate for a pharmaceutical product" that can be presented to the competent authority of another country. The certificate attests that marketing of the pharmaceutical product is authorized in the certifying country and that the manufacturing facilities and operations conform to good manufacturing practice as recommended by WHO.

When considering registration of antidotes and antivenoms, manufacturers and regulatory authorities can refer to the WHO Model List of Essential Medicines (6). This is a list of medicines that are selected on the basis of their public health relevance, evidence of efficacy and safety and comparative cost-effectiveness to medicines with similar actions. A separate list covers medicines considered essential for children (7). These medicines should be available at all times, in adequate amounts and appropriate dosage forms. Antidotes that correspond to the WHO definition of an essential medicine have been included on the WHO Model List of Essential Medicines (see Annex 5). Countries develop their own essential medicines lists or a national formulary list. Therefore, it is important that

¹¹ Drugs for diseases or conditions that occur so infrequently that there is no reasonable expectation that the costs of developing and marketing will be recovered in revenues from sales. Some jurisdictions, e.g. the European Union, Japan and the USA, provide incentives for the production of such drugs.

they list antidotes relevant to their needs to facilitate their procurement and availability in government-funded health facilities.

7.4 ECONOMIC ASPECTS

The economic considerations relating to antidotes and antivenoms include the costs of their development and of their purchase and use. Developing and registering a new pharmaceutical product is costly, and, as stated above, there is little financial incentive for the development of new antidotes for less common poisonings or those that occur primarily in low-income countries or regions. The situation is therefore similar to that of orphan diseases (3). In general, pharmaceutical companies manufacture and supply antidotes only if they are encouraged by an adequate economic return on their investment and by simplified registration procedures, as described above.

In considering the cost of purchasing antidotes, governments should take into account the social and medical consequences of failure to treat poisoned patients appropriately and the continued economic burden on local or national resources that may ensue. Thus, purchase of a relatively expensive antidote or antivenom that shortens the course of poisoning or prevents sequelae may be more cost-effective than prolonged in-patient treatment with standard supportive care or a cheaper alternative antidote that has more adverse effects or is less effective (8).

Funding is required to maintain a stock of antidotes. Many antidotes, particularly those for less commonly observed poisonings, may not be used and must be disposed of once their shelf life expires. As antidotes are usually expensive, the possibility that they may expire unused is a disincentive for stocking them (9). The risk of wastage can be reduced by a regionally or nationally coordinated system of procurement, distribution and monitoring of use (see below) (9, 10).

If antidotes cannot be supplied by the local pharmaceutical industry, other means of obtaining them should be considered, including establishment of government manufacturing facilities, a manufacturing pharmacy laboratory or a system to allow importation of antidotes registered elsewhere.

7.5 AVAILABILITY OF ANTIDOTES AND ANTIVENOMS: PRACTICAL CONSIDERATIONS

Demographic, geographical and economic factors may limit the availability of antidotes and antivenoms in health care facilities. The high cost due to infrequent demand and a short shelf-life may limit widespread distribution of these medicines.

7.5.1 PROCUREMENT

Many countries have a centralized procurement system for importing pharmaceutical agents. Decisions on what to purchase depend partly on what is known about the prevalence of disease in the country. The institutions concerned should therefore consult and cooperate with national poison and clinical toxicology centres or networks of such centres, so that the antidotes and, if necessary, antivenoms that are imported correspond to local needs. When certain antidotes are not available from either local manufacturers or as imports, the central institution may cooperate with poison centres in recommending local manufacture in hospital pharmacies.

A clinically oriented poison centre might take responsibility for procuring and distributing antidotes and antivenoms in a country. In the event of an emergency or chemical disaster, an arrangement among poison centres in different countries might ensure a supply of antidotes that are commercially available elsewhere, provided a mechanism is in place to fast-track approval for importation and use.

7.5.2 STOCKING AND DISTRIBUTION

As many antidotes are expensive, infrequently used and have a short shelf-life, central stocking of antidotes is a practical and economic approach. This makes inspection easier and ensures a supply of products that have not expired. Such a central “bank” of antidotes should be organized by the health authorities in such a way that any poisoned patient may be assured of receiving an antidote in the appropriate time. The level of use of each antidote and antivenom should be determined, with agreement on the timeframe for its administration. Antidotes used frequently or required quickly should be stocked at or near hospitals or other treatment centres, while others can be kept in a central location. The recommended minimum stocking levels should be determined according to local trends in poisoning (11).

A decision about which antidotes and antivenoms to be stocked by hospitals may be taken at national level, as for example in Abu Dhabi (12). In many countries, however, such decisions are taken locally. Consensus guidance has been issued by professional associations of clinical toxicologists to assist decisions on antidote stocking (11, 13), with antidotes classified into those required immediately and those for which timing is less critical. For example, naloxone and atropine are immediately life-saving in cases of severe poisoning with opioids and organophosphates, respectively, whereas acetylcysteine is still effective in treating paracetamol poisoning after a delay, provided it is given within 8 hours of ingestion. According to this classification, antidotes that are required immediately should be stocked at all hospitals, ideally in the emergency department or the area where poisoned patients are treated and in health centres or doctors’ surgeries if the nearest hospital is some distance away. Certain antidotes might have to be available at workplaces for use under medical supervision (for example, in factories in which cyanide is used).

Antidotes that are required less urgently can be stocked at certain main hospitals, to which patients can be taken for treatment, or the antidotes can be transported – within the time limit – to the health facilities at which treatment is provided. Antidotes for which there is a longer timeframe for use may be stocked at central or regional depots, provided there are adequate facilities for transporting them when necessary. For all categories of antidotes, a small amount sufficient to start treatment may be stocked locally, with further supplies available from a central source as required (14). In areas where certain types of poisoning are frequent or where certain chemicals are heavily used, the appropriate antidotes may be kept in ambulances that are sent out to treat cases of poisoning.

Poisoning with natural toxins may be seasonal and may be specific to certain regions (for example snakebite in rural areas during planting and harvesting seasons). When antivenoms are available, and if the cold chain can be maintained, they may be sent to health care facilities in rural areas during these seasons, so that they are readily available when required.

As antidotes might have to be transported rapidly in certain circumstances, appropriate advance arrangements should be made, for example, for use of official cars, aircraft or other means (9). Arrangements for rapid transport of patients to hospitals with appropriate facilities and antidotes may be necessary in some cases. Comprehensive instructions on interim treatment measures should be given to first-aid workers and other medical or paramedical professionals.

7.5.3 MANAGEMENT OF ANTIDOTE STOCKS

When antidotes are stocked in a hospital or a holding centre, scheduled stocktaking should be conducted regularly to ensure that both sufficient quantities of the antidote are available and the stock has not passed its expiry date. In an antidote-sharing network among local (or even national) hospitals, a product that is close to its expiry date and unlikely to be used before that date can be sent to a hospital with more frequent use.

The use of expired antidotes is usually prohibited by regulatory authorities; however, pharmaceutical manufacturers do not necessarily test for extended stability, and products may continue to be safe and effective beyond the stated expiry date (15, 16). A national regulatory authority may permit extension of the shelf-life of a product in exceptional cases, provided the storage conditions have been strictly maintained and documented and periodic quality control has been performed to check that the product quality is maintained. In some high-income countries such as the USA, procedures allow shelf-life extension for selected medicines held in strategic stockpiles (15).

The factors to be considered in deciding where antidotes should be stocked include:

- the size of the country and the area to be covered by the depot;
- the density of the population;
- the incidence of poisonings that require special therapeutic measures and/or antidotes or antivenoms;
- the social and economic activities of the region that may be associated with a high risk of poisoning;
- the distance of hospitals and health centres from the depot;
- communications (for example roads, air services) between the depot and hospitals or health centres; and
- comparison of the cost of antidotes and of the wastage due to expiry with the cost of transport in an emergency.

A logical location for a regional central depot is a poison centre or a central hospital pharmacy. The conditions in which antidotes and antivenoms are stored are important determinants of their maximum shelf-life, which should be taken into account in choosing storage depots. The economics of managing the supply of antidotes could be improved by a central, preferably computerized, record system that is regularly updated (9, 10). The need to hold contingency stocks of antidotes for responses to chemical disasters should be considered, especially in areas where large amounts of potentially hazardous chemicals are manufactured, used, transported or stored, for which regional cooperation among centres to exchange information on the availability of antidotes is highly desirable. Web-based management of antidote stocks has been tested in a number of countries, including Italy and Thailand (see boxes 8 and 9).

Box 8. Organization of antidote provision in Italy (17) ¹²

In Italy, a continuously updated national database, the Banca Dati Nazionale degli Antidoti, was established in 2004 to improve the availability of antidotes. The online database, developed and managed by the Pavia Poisons Centre, is a 24-hour service, free to hospitals registered in the national health system. The users enter and update information on their antidote stocks and must confirm responsibility for the information given. The uploaded details of the antidotes available in the registered hospital are shared with other users, permitting rapid location and retrieval of antidotes. A red, amber or green colour indicates the date of the last update. The advantages of this system are: (i) the availability of antidotes in every hospital (particularly antidotes that are less commonly used); (ii) availability of additional doses of an antidote; (iii) better understanding of, and attention to, the availability of antidotes in emergency departments and hospital services; and (iv) cost containment and resource optimization at regional and national levels.

The Pavia Poisons Centre also coordinates information about antidote supplies in high-risk industrial plants, where the antidotes are held by the occupational health services at the companies concerned and are available for urgent use in case of a chemical emergency. Training is provided for the company health personnel on management of chemical exposures.

The poison centre also has a role in managing the national antidote stockpile for chemical and radionuclear emergencies on behalf of the Italian Government. Staff at the centre provide telephone and direct support for the management of exposed patients as well as training for health personnel.

¹² C. Locatelli, Pavia Poisons Centre, personal communication, 2 January 2020

Box 9. Organization of antidote provision in Thailand (10)

In 2010, Thailand established a national antidote programme and created national and subnational stocks of antidotes and, later antivenoms. Distribution was managed and stock levels determined by demand and the urgency and cost of treatment, and health care providers were trained in clinical management and effective use of antidotes. The result of this programme was that antidotes and antivenoms became readily available and clinical management of poisoned patients improved. Better stock and distribution control has also proved to be cost-effective, with a decrease in the overall cost of antivenoms from US\$ 2.23 million to US\$ 1.2 million.

7.5.4 CHEMICALS AS ANTIDOTES

Some chemical substances with antidotal properties, such as sodium thiosulfate, sodium nitrite and Prussian blue, may not be available for use as pharmaceuticals in some countries although they are readily available from chemicals suppliers. Hospital manufacturing pharmacies could purchase these analytical grade chemicals and process them to produce formulations suitable for human administration. As ensuring the quality and purity of the chemicals is essential, pharmacopoeial commissions should consider issuing monographs on such chemicals. Ethical approval or consent from the patient or next-of-kin must be sought if a pharmaceutical preparation is not available and a non-pharmaceutical formulation is being considered.

7.6 CHALLENGES IN LOW- AND MIDDLE-INCOME COUNTRIES

In addition to the general problems of availability discussed above, low- and middle-income countries may face particular difficulties in the management of poisoning cases and in accessing and using antidotes and antivenoms. Health authorities are sometimes unable or reluctant to facilitate the importation of antidotes and antivenoms, as the procedures are often cumbersome and lengthy. Economic problems, including a shortage of convertible currency, worsen the situation.

Because of limited documentation of cases of poisoning admitted to health care facilities, data on the pattern of poisoning that would be useful for decisions on antidote procurement are often lacking. Many countries do not have poison centres to collect data on poisoning cases and to advise physicians on the management of cases and appropriate use of antidotes. They may lack equipment and resources for supportive treatment of poisoning cases, such as haemodialysis equipment or ventilators, and thus have a greater need for certain antidotes or antivenoms that can reverse toxicity quickly.

Lack of adequate communication systems and transport infrastructure in certain countries may make it impossible to transport antidotes and antivenoms sufficiently quickly in an emergency. Measures to ensure the rapid transport of antidotes and antivenoms to affected areas, or, alternatively, the transport of poisoned patients to appropriate treatment facilities are therefore of the greatest importance.

It may also be difficult to find adequate facilities for emergency storage depots; furthermore, local conditions and climate may make routine storage of antidotes and antivenoms difficult in certain areas of the country. Nevertheless, it is essential to ensure correct storage, and due account should be taken of expiry dates and the necessary conditions of temperature, light and humidity. Proper storage conditions are also essential during the transportation of antidotes and antivenoms from the point of importation to local depots and in transitional storage areas.

Greater effort should be made to find antidotes and antivenoms with longer shelf-lives and better stability under harsh conditions, particularly of temperature and humidity, for use in areas where proper storage is difficult to achieve.

7.7 THE ROLE OF POISON CENTRES

Poison centres play a key role in a national antidote programme. In general, they are in the unique position of having an overall picture of poisoning in the region or country they cover, so that they can identify the necessary antidotes for their area and analyse data to localize cases. This role is particularly important when the documentation and reporting of poisoning cases in hospitals is inadequate.

Even an effective, readily available antidote will be of minimal benefit if the attending physician cannot establish a correct diagnosis or is unaware of the availability or indications for use of the antidote. Poison centres should educate clinical personnel in the proper use of antidotes and antivenoms and, ideally, organize programmes to train clinical personnel in the diagnosis and management of poisoning (18).

As poison centres are centres of expertise in clinical toxicology, they should review and evaluate the relevant literature on the effectiveness of antidotes and provide advice to the appropriate authorities for decisions on registration and procurement. Poisons information centres should also encourage creation of a national network for the supply of antidotes, which will require close collaboration with the responsible authorities and with hospital pharmacies.

Poison centres can also participate in international exchanges of information to critically assess the efficacy and safety of antidotal agents. Such assessments should be based on data on antidote use that are collected in an internationally standardized manner to allow comparison of results. As the data that were available at the time certain antidotes were registered may have been limited, they should be updated with more recent findings. Poisons information centres should also collect data on medicinal products that are used for other indications and have been found to be useful in the treatment of poisoning.

7.8 ANTIDOTES FOR VETERINARY USE

Poisoning of animals is a serious problem in many parts of the world, and poisons information centres often receive enquiries about their treatment. The use of antidotes in veterinary medicine poses a number of problems with regard to choice, dosage, route of administration and availability. It is therefore recommended that each country make arrangements for examination of various aspects of veterinary use of antidotes by a working group with the necessary expertise, which should include poison specialists, veterinarians and registration authorities.

Some countries may allow off-label use of human drugs for animals. For example, in the USA, the Animal Medicinal Drug Clarification Act of 1994 allows veterinarians to administer or prescribe any human or veterinary drug for off-label purposes, although the liability is the responsibility of the prescribing veterinarian (19). Veterinary prescribing raises additional concerns about the medicines or antidotes used, as they may enter the food chain. Appropriate guidelines on withdrawal periods should therefore be adhered to.

As for humans, the agents involved in veterinary poisoning vary geographically. Thus, poison centres that take calls on animal poisoning should be aware of the most common poisons in their region, and antidote holding centres should ensure that adequate stocks of commonly required antidotes are available.

Additional factors discussed in this section with regard to the development, supply and use of antidotes for the treatment of human poisoning apply equally to the use of antidotes in the treatment of animal poisoning.

7.9 RECOMMENDATIONS

7.9.1 ACTION AT NATIONAL LEVEL

The primary task of national authorities is to ensure that the necessary antidotes are available according to the pattern of poisoning in the country, especially those antidotes on the WHO Model List of Essential Medicines (6, 7). Inclusion of relevant antidotes and antivenoms in the national essential medicines list or the national formulary is important to ensure that resources are allocated for their procurement and distribution and that they are therefore

available through public health services. Mechanisms should be set up to ensure rapid importation of antidotes for emergency use. Special arrangements might also be required to permit the controlled clinical use of antidotes that are still under development.

The process for approving generic antidotes could be simplified, which could reduce the price of some antidotes. Approval by a competent national regulatory authority or the WHO prequalification process can accelerate and simplify national registration and ensure use of quality-assured products. The WHO Assessment and Listing of Snake Antivenoms is a new initiative to facilitate access to antivenoms of acceptable quality, safety and efficacy (20).

National health authorities should encourage the manufacture and distribution of antidotes that are not yet available on the local market and could even provide incentives to local pharmaceutical manufacturers, hospital pharmacies and service laboratories. Exportation of these antidotes could also be encouraged. National health authorities could assist or encourage the organization of depots for antidotes and systems for the distribution of antidotal agents.

7.9.2 ACTION AT INTERNATIONAL LEVEL

Establishment of an international mechanism for the purchase, storage and distribution of certain antidotes might alleviate the problems of their availability in some countries. It is recognized, however, that this might be difficult to organize and would demand economic resources and political will. Formation of a regional cooperative group for the supply and storage of antidotes would remove many obstacles. This is an area of possible collaboration among international organizations, poison centres and toxicological associations (see Box 10).

Box 10. Pilot project to improve the availability of antidotes in the WHO South-East Asia Region (21)

A pilot project, the “Initiative for coordinated antidotes procurement in the South-East Asia Region” has been organized by the WHO Regional Office for South-East Asia for regional procurement of selected antidotes. Procurement and distribution to countries will be coordinated by the Ministry of Health, Thailand, and there will be a facility for emergency provision of antidotes at the Ramathibodi Poison Center in Bangkok.

The WHO Model List of Essential Medicines is reviewed continuously, with new antidotes added and others removed because of lack of adequate evidence of efficacy. It is hoped that the Model List will encourage national health authorities to include antidotes in their national essential medicines lists to facilitate national procurement of antidotes and antivenoms (see Annex 5).

By making resources and experience available through development assistance programmes, high-income countries could transfer knowledge and skills on the appropriate management of poisoned patients and support the establishment of storage depots for antidotes in low- and middle-income countries. This could be a two-way process, in which poisons information centres in high-income countries gain experience in the treatment of forms of poisoning that are less common in their countries, such as intentional exposure to organophosphates and snakebites.

In low- and middle-income countries with suitable hospital pharmacy facilities, some antidotes could be prepared locally, in cooperation with local poison centres, provided their quality can be assured in adequate quality control processes. Education grants and training courses for pharmaceutical staff in this area would be useful and could be encouraged through international exchange programmes for the development of human resources.

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Medical staff member at Tygerberg Poisons Information Centre, Cape Town South Africa / Credit: John Lawrence

8

POISON CENTRES: DATA COLLECTION AND DATABASES



8.1 INTRODUCTION

An essential function of a poison centre is the collection and retention of records of enquiries to the centre and of information on substances and products. The day-to-day operation of centres and the generation of reports on their activities are facilitated when these data sets are recorded in standard formats in suitable data storage software, such as a database.

Databases in poison centres are used principally to provide information on poisons (through searches for a substance or product record), to record details of cases of poisoning and subsequent follow-up where applicable, to record details of general enquiries and to report on recorded cases. These functions may be performed either in a combined database or, more commonly (for ease of use and construction) in several different databases.

This section describes data collection and databases on enquiries and on substances and products. Databases for information and advice on the management of poisoning are described in section 9.

8.2 ENQUIRY RECORDS

Poison centres document and keep records of the enquiries they receive and on specialist consultations for a number of purposes. The most important is to document the information exchanged between enquirers and the specialist in poisons information or the medical toxicologist. This is essential for medico-legal, audit and administrative purposes, but the information is also used to better understand the circumstances and effects of exposure to different substances and to update the substance database.

When cases are followed up after the initial enquiry, valuable information can be collected on the outcome of exposure, including the type and efficacy of treatment. Systematic collection of enquiry and outcome data allows the centre to:

- maintain its own clinical and other data registry;
- implement toxicovigilance activities (see section 5);
- support epidemiological and statistical studies;
- perform self-audit and continuously evaluate the quality and efficiency of its services (see section 10);
- fulfil its clinical and legal responsibilities;
- validate new techniques for patient management;
- provide data to update treatment protocols and for scientific reports; and
- contribute to knowledge on human toxicology.

Poison centres should keep systematic records of all enquiries, i.e. incoming and outgoing telephone calls, e-mails, faxes and letters, and of any personal consultations. Poisons enquiry records should distinguish between calls for general information and those for cases of suspected or confirmed poisoning. Simple data, such as the total number of enquiries received each year, can indicate the workload of the centre and justify staffing levels.

Each enquiry record should include information about the poisoning incident and the exposed individual. The enquiry records at different poisons information centres have the same basic structure, but the amount of data that should be recorded depends on the needs and resources of the centre and the scientific background of the staff providing the information service. To maximize their usefulness, the records should be as comprehensive and accurate as possible. Annex 3 describes the data elements that could be included in an enquiry record and indicates why they are important.

The details of each case can be collected on a paper record that is subsequently computerized, or they may be entered directly into a computer database. Commercial data collection systems are available, and some poison centres have local or national bespoke systems.

The enquiry record provides only a snapshot of a possibly evolving case of poisoning. Moreover, because of time constraints, it may not be possible to collect all the information on the circumstances of exposure. Establishing a mechanism for follow-up of cases provides more data on the evolution and outcome of the case. Follow-up can take various forms, such as a telephone call to the patient or the carer in the case of a child, a letter, questionnaire or link to an online questionnaire sent to the treating physician requesting additional information, or a copy of the patient's case record (if this is permitted under confidentiality laws). Follow-up requires collection of sensitive, identifiable data, such as patients' names, postcodes, dates of birth and hospital numbers, and these must be handled responsibly and stored securely. The follow-up information received by the poison centre can then be attached retrospectively to the initial enquiry record if the database has the functionality to allow this.

In countries where there are several poison centres, sharing of real-time information facilitates toxicovigilance and the identification of emerging incidents, as well as improving the provision of information for returning enquiries.

8.2.1 DATA QUALITY

The use of rules and agreed terminology within the poison centre enquiry database, whether hardcoded into the database itself or specified in a user guide and data manual for staff, will greatly improve the quality of the information recorded and its usefulness for future analysis. Predetermined coding structures prevent the use of synonyms and misspellings, which can undermine subsequent data analysis and reporting. For example, if one patient is described as having "abdominal pain" and another as having "stomach pain", a future database search for cases of exposure in which abdominal pain was reported will miss those documented as having stomach pain. This can be avoided by using one agreed term or code. Data harmonization is discussed further in section 2.

Some international coding schemes are available. One is the Medical Dictionary for Regulatory Activities (1), which was prepared to standardize documentation of adverse events associated with medicinal products and biopharmaceuticals but is also being used in some poison centre databases to classify toxic effects. The Poisoning Severity Score, developed in an international poison centre project, is used to grade the severity of poisoning in cases referred to the poisons information centre (2). Other examples of standardization protocols used more generally in medicine include the Systematized Nomenclature of Medicine (3), often used in hospitals, and the tenth and eleventh editions of the International Classification of Diseases (4, 5), both of which have a broader dictionary of terms, codes and synonyms for use in recording data. An advantage of using internationally accepted methods of recording data is that it facilitates collaborative research and sharing of data with other agencies: if the coding structures are the same, the data are more harmonized.

A number of countries, particularly those with several poison centres, have bespoke data collection forms, with classifications and coding manuals to support their data collection practices and reduce variation. Examples include France, Germany, the United Kingdom and the USA. The WHO INTOX Data Management System (6), while no longer available as a data collection system, had a data collection format, controlled terminologies and classifications that are used as the basis for poison centre databases in a number of countries, including Argentina, Australia, Brazil, Chile, South Africa, Thailand and Uruguay.

8.2.2 STORAGE OF ENQUIRY DATA

Patient details recorded in poison centre databases are confidential. Processes should be in place to ensure that the records are accurate, cannot be modified subsequently and are password-protected and securely stored. Electronic data may be stored on the poison centre's own server or on a hospital or commercial server. The latter may be a cloud-based system, in which data are saved and consulted on the Internet. Whichever system is used, it must have the necessary safeguards for data access and back-up procedures.

Use of poison centre data should comply with the legislative requirements of the country concerned and the requirements of the appropriate ethical review body.

8.2.3 ANNUAL REPORTS

Poison centres are encouraged to prepare annual reports of their activities. Such reports provide an overview of the poisoning data collected and information on the workload, staffing and activities of the centre during that year. The information can include the call volume, call types, substances involved in cases of poisoning, a summary of the circumstances in which the poisoning occurred, the demographic distribution of cases, severity of poisoning and trends. The description of activities may include publications, training courses and research. Other information may include discussions on clinical governance, challenges faced and new directions. The annual report is a valuable resource for the poison centre in discussions with funders and also indicates the pattern of poisoning in the country. An example of the content of an annual report is provided in Annex 6. Most poison centres produce their annual report in their own format. In countries with several poison centres, use of a harmonized format facilitates comparison and pooling of data.

8.3 SUBSTANCE INFORMATION

To answer enquiries, poison centres must have readily available information on the toxicological and other properties of the wide range of substances and agents, including chemicals, pharmaceuticals, plants, animals and fungi, to which people may be exposed. The substance information records should include the following information:

- identity of the substance
- routes of exposure
- doses at which toxicity occurs
- mechanism of toxicity
- pharmacokinetics or toxicokinetics data
- toxic effects on organ systems and bodily functions
- clinical features that may arise
- recommendations for the types and frequency of bedside and laboratory monitoring
- recommended treatment.

Substance information records may be researched and compiled by the poison centre, or the centre may subscribe to an online database such as AfriTox, POISINDEX, TOXBASE or TOXINZ. These databases are described in section 9.

Variations in nomenclature, classification systems and coding systems for substances and agents present a challenge for the standardization of data collection and reporting of exposures both nationally and internationally. A few internationally adopted classifications exist for specific types of substances, such as the Anatomical Therapeutic Chemical classification for pharmaceuticals (7, 8). Poison centres are encouraged to develop standardized coding systems for the nomenclature and classification of substances or agents and to refer to systems used globally.

8.4 PRODUCT INFORMATION

Product information records are an important category of substance records. Poison centres require information about the composition of products, their form (for example, powder, aerosol, emulsion), the size of containers and the type of packaging. The information provided should be sufficiently detailed to allow identification of a product and evaluation of its toxicity.

Creation of a product database may be challenging for a number of reasons.

- Manufacturers are usually concerned about protecting commercially sensitive information on product formulations and may be reluctant to provide this information.
- The cost to the manufacturer or supplier of providing the poison centre with regularly updated information may be a disincentive.
- Product names can be difficult to determine accurately, as a manufacturer may have a suite of products with similar names but different formulations.
- Product information may be provided in different formats, and receiving, processing, storing and updating this information can require significant resources on the part of the poison centre.

Obtaining product information from manufacturers and suppliers is easier when there is a legal or regulatory requirement to provide it. Even then, the manufacturer may compromise in the amount of detail about product composition that it provides. To ensure receipt of up-to-date information, relations should be built and maintained with manufacturers, suppliers and trade associations, so that they understand the role of the poison centre and why the information is needed.

While the legislative requirement for disclosure of product composition differs by country, most companies provide safety data sheets giving some of the necessary information, which can be requested and may also be available on the Internet. In many countries, the structure and content of safety data sheets follow the specifications of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (9). THE GHS requires that chemicals classified as hazardous that are in a product should be listed together with their concentration ranges and hazard warnings (for example, corrosive). Other information provided on the safety data sheet includes physicochemical, toxicological and ecological data, and first aid and sometimes medical management. The latter, however, does not necessarily accord with best medical practice, and it is better for the poison centre to follow its own treatment recommendations.

In the case of pharmaceuticals, manufacturers in many jurisdictions are obliged to provide a data sheet, sometimes called a “summary of product characteristics”, which contains information on the ingredients, physical form, adverse effects, effects in overdose and reproductive hazards. Some information can also be obtained from pharmacopoeias and formularies.

At its simplest, a product database is a collection of safety data sheets and other information, arranged by manufacturer or alphabetically. In the longer term, particularly as the collection grows, it is better to store this information digitally in document management software with good search functionality. It is important to retain safety data sheets for older products in case individuals are exposed to them. The utility of a product database is increased by the addition of pre-prepared assessments by the poison centre of the toxicity and required treatment for key products, so that this information does not have to be synthesized for each enquiry.

Various approaches are used nationally and internationally to facilitate access to product data for poison centres. In the United Kingdom, the National Poisons Information Service maintains a standalone Product Data Centre to record safety data sheets found online, sent by a physician treating a poisoning case or obtained by directly contacting the manufacturer. In Australia, the National Poisons Register compiles a registry of the composition and physical characteristics of the domestic, commercial, agricultural and industrial products available in the country. The Register collaborates with companies to include comprehensive details relevant to poisons information that may be missing in some safety data sheets, including interpretation of hazard categories and substance names, and also provides treatment recommendations from the database POISINDEX.

National or regional poison centres or toxicology associations can advocate with industry trade associations and with regulators to improve the provision of product information to poison centres. In the European Union, for example, manufacturers are required to provide poison centres with specific information on hazardous products and on cosmetics through the European Chemicals Agency Poison Centres Submission Portal and the Cosmetic Products Notification Portal, respectively (10). For hazardous products, the information must be submitted in a standard format via the online submission portal. The required information includes a unique formula identifier (a 16-digit product code) that is also on the product label, allowing rapid identification by poison centres of a product's ingredients (11). The advocacy and engagement of the European Association of Poisons Centres and Clinical Toxicologists was important in achieving this information provision.

The poison centre toxicology databases mentioned above contain information mainly on nationally available products (see section 9).

8.5 CONCLUSIONS

Enquiry and substance databases are essential for the work of poison centres. While some of the necessary information can be obtained by subscription to databases specifically designed for poison centres, more locally relevant information on toxins and products is always necessary, and this must be compiled and processed by the poison centre. In addition, analysis of the cases reported to the poison centre can be used to improve the substance databases by adding information on toxic effects.

Database subscriptions and database development and maintenance require dedicated resources, both financial and staff, and this must be considered when establishing a poison centre.

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9

TOXICOLOGICAL INFORMATION SOURCES



9.1 INTRODUCTION

To fulfil their functions, poison centres must have access to a wide range of toxicological information resources. A key resource is the specialized clinical toxicology database, which includes information on patient management. Other important resources are general toxicology databases, bibliographic databases, journals, books and the grey literature, which provide research results and other data for evaluating the toxicity of a wide range of substances and for developing management protocols. These resources are described in this section.

9.2 CLINICAL TOXICOLOGY DATABASES

Toxicological and clinical databases provide information on a wide range of substances and products, including toxicokinetics, the features of toxicity after exposure by various routes and at various doses and how exposure should be managed. Many databases began as collections of information written and compiled by one or more poison centres for their own use and have evolved into electronic databases available online, often for subscription. While they were developed for use by poisons information specialists, the databases may also be available to medical practitioners as an alternative to calling a poison centre. In some countries, their use is encouraged for routine cases to reduce the number of calls to the centre (1). They cannot, however, substitute for a poison centre, where specialists in poisons information are trained to interpret the information provided in such databases and can apply it appropriately to specific cases. Specialists in poisons information also have broad experience of poisoning enquiries and may be more alert to potential sources of error, such as a small difference in the name of a product, drug or chemical, and may identify unusual or severe symptoms that might not be recognized by a health professional who sees only the occasional poisoning case. Enquiries about cases that may not be entirely straightforward, therefore, should be addressed to a poison centre.

More specialized databases provide information on exposure in pregnancy and possible teratological effects.

A number of other toxicological resources are available online that include information on patient management. Not all are necessarily of good quality, and the user should consider the source of the information carefully before relying on it. Members of the public who do not have training or special knowledge in clinical toxicology should be particularly cautious about using online databases. One poison centre in the USA, however, has designed an online database for use by the general public (2).

9.2.1 WHAT TO LOOK FOR IN A CLINICAL TOXICOLOGY DATABASE

A clinical toxicology database should provide expert, peer-reviewed, evidence-based information on the toxicity and features of, and the clinical management after, exposure to pharmaceuticals, chemicals (environmental, agricultural and industrial), plants, animal toxins and household and industrial products. The information should be in line with the best current medical practices to promote the provision of optimal patient care.

When considering use of a clinical toxicology database, it should be examined to ensure that the content is produced and reviewed by appropriately trained clinical toxicology professionals, who may include experienced specialists in poisons information but should also include medical toxicologists. The database entries should be based on systematic searches of published literature and an evaluation of case-based experience. Database entries should be reviewed and updated regularly.

Some of the clinical toxicology and teratology information databases offer comprehensive information but are not freely available, while others offer free access but may provide limited information (for example, literature citations or summaries) or standard safety data sheet information only. Prospective users should therefore decide what they require from such a database. Trial access can be useful for databases that are password protected and/or that charge for access.

Brief information is provided below about a number of databases that provide advice on clinical management. This summary is for information only and does not imply endorsement by WHO or that WHO guarantees the quality or accuracy of the information they contain. The references are listed in Annex 2, with links for additional information.

9.2.2 OPEN ACCESS DATABASE THAT PROVIDES SOME CLINICAL INFORMATION

PubChem is an open access chemistry database provided by the National Institutes of Health in the USA. It is a compilation of information about chemicals from hundreds of data sources. The information includes chemical structures, identifiers, chemical and physical properties, biological activities and data on health, safety and toxicity, including first aid. One of the data sources for PubChem is the Hazardous Substances Data Bank compiled by the US National Library of Medicine. For chemicals with an entry in this Data Bank, information is also provided about emergency medical management.

9.2.3 RESTRICTED (USER REGISTRATION REQUIRED) ACCESS CLINICAL TOXICOLOGY DATABASES

A few clinical toxicology information databases are designed for poison centres and can be accessed only by registered users. Access may be granted free of charge, or there may be an annual subscription fee. Users of subscription databases in low-income countries may be able to negotiate free or reduced-cost access.

AfriTox is produced by the Poisons Information Centre at Red Cross Children's Hospital, Cape Town, South Africa. An online version is available for use in settings with a good Internet connection, and the offline version can be used where Internet connections are less reliable. This database can be used only by registered health care professionals, and access is limited to subscribers. There is a subscription charge, but there are special arrangements for African poison centres. AfriTox contains information on an extensive range of substances but focuses on local medicines and commercial products, local plants, bites and stings. The following information is provided for each agent:

- name of the toxicant (and manufacturer when applicable)
- use
- generic product composition
- specific product composition
- toxicology
- symptoms
- treatment

AfriTox MinTox is a publicly accessible database, which helps users to identify substances with little toxicity. It does not provide medical advice.

The **POISINDEX** system identifies the ingredients of over 400 000 commercial products (mainly in Canada and the USA) and provides information on a wide range of chemicals, drugs, toxic plants and animals. Each entry is linked to one of 1780 detailed management protocols, structured as follows:

- Overview
- Substances included/synonyms
- Clinical effects
- Laboratory/monitoring
- Abstracts
- Treatment
- Level of toxicity
- Kinetics
- Pharmacology/Toxicology
- Animal toxicology
- References
- Author information

POISINDEX also provides links to additional databases, including Hazardtext for incidents such as spills, leaks, fires or explosions involving hazardous materials; and Meditext to assist in evaluating and treating acute exposure to industrial chemicals, reporting potential adverse health effects and treating exposure to chemical release.

POISINDEX is produced by IBM Micromedex with Watson and is widely used around the world, including in all Australian poisons information centres and all poison centres certified by the American Association of Poison Control Centers. An application for use on mobile telephones is also available, although the information is limited to pharmaceutical entries. A subscription is required, and there are various pricing structures.

TOXBASE is the product of the National Poison Information Service in the United Kingdom. The content is produced by specialists in poisons information and reviewed by a network of consultant medical toxicologists working in clinical toxicology treatment units across the country. TOXBASE is directly available to health care professionals for use at points of care. Although TOXBASE was developed for use in the United Kingdom, it is also used in other countries, including a number of low-income countries, by special arrangement.

TOXBASE provides advice on the features and management of exposure to tens of thousands of products and substances, each entry linking to one of over 1580 detailed management protocols. TOXBASE is available online and offline via the TOXBASE application (App) for smartphones. The App is updated in synchronization with TOXBASE online. The standard format for each substance entry is as follows:

- Patient referral criteria
- Type of product
- Ingredients
- Toxicity
- Features
- Management
- Additional information: fully referenced

TOXBASE requires a subscription, but access is available free of charge to United Kingdom National Health Service health care providers. Discounted access may be available for lower-income countries.

TOXINZ was created by the National Poisons Centre of New Zealand and is now published by EBSCO Health. TOXINZ provides information and treatment guidelines on over 200 000 chemicals, chemical products, pharmaceuticals, plants and hazardous animals. Each entry is linked to one of over 6500 treatment protocols. TOXINZ is fully referenced, with direct links to PubMed abstracts. For each agent, the following information is provided:

- Description
- Signs and symptoms
- Intervention criteria
- Toxicity
- Treatment

While TOXINZ was developed for use in New Zealand, it is also used in some other countries. Access is by paid subscription; however, discounted access may be available for low-income countries (for example, via Hinari, see subsection 9.4.1).

9.2.4 TERATOLOGY POISONS INFORMATION DATABASES

The toxicological databases described above may include some information on the reproductive and fetal toxicity of chemicals and pharmaceuticals. Teratology information databases provide such information in more detail. This information is important because many pregnant women require treatment for a medical condition that occurs or persists during pregnancy, and some drugs are known to increase the rates of structural congenital malformations and other adverse pregnancy or developmental outcomes. Prescribers and the women themselves must be able to balance the risks of continuing a treatment during pregnancy against stopping the treatment and risking recurrence or worsening of a medical condition. Both situations could present a risk to the fetus.

Teratology information databases are compiled by groups conducting research specifically on the effects of pharmaceuticals and, in some cases, chemicals on pregnancy outcomes. The databases provide evidence-based evaluations to support a risk assessment of exposure to chemicals and/or the use of medicines and vaccines during pregnancy. Some databases are limited to providing support for decisions about appropriate choices of medicines and vaccines for use in pregnancy, especially when their safety is uncertain. A few open-access sources and examples are given below.

AUSTRALIA

The Therapeutic Goods Administration publishes the Prescribing Medicines in Pregnancy database on an open-access website (3). The database provides information to health professionals planning the medical management of pregnant patients or patients intending to become pregnant.

The Royal Hospital for Women in Randwick, New South Wales, hosts a website that provides factsheets on exposures in pregnancy and breastfeeding (4).

EUROPE

The European Network of Teratology Information Services hosts a website that directs users to teratology information summaries (5). The contact details of teratology information specialists in the user's geographical location are also available on this site. Although the Network is labelled as European, it has member centres based in Australia, Japan and South America.

The four teratology information databases listed on this website (in January 2020) are:

- In France, the Reference Centre on Teratogenic Agents (Centre de Référence sur les Agents Tératogènes) provides information on the risks of drugs, vaccines, radiation and addiction during pregnancy and breastfeeding, in French only (6).
- In Germany, Embryotox offers up-to-date scientific information on over 400 medicines (7), available only in German. Applications for smartphones are available.
- The Netherlands Pharmacovigilance Centre Lareb provides information in English and Dutch (8).
- The United Kingdom Teratology Information Service, which provides two open-access databases with summary entries on over 350 drug and chemical exposures in pregnancy (9). One of the databases, called “Best Use of Medicines in Pregnancy” or “BUMPS” is written specifically for the general public and provides factsheets on all common drugs and some chemicals, written in plain English (10). More detailed, fully referenced monographs on drug and chemical exposure during pregnancy are available for registered United Kingdom health care professionals via TOXBASE.

NORTH AMERICA

The Organization of Teratology Information Specialists hosts the MotherToBaby website, which provides expert information about exposures during pregnancy and breastfeeding (11) in English and Spanish.

9.3 GENERAL TOXICOLOGY RESOURCES

In addition to the clinical toxicology databases mentioned above, other resources are available online or through smartphone applications, which provide access to a wide range of compiled information on chemicals, pharmaceuticals and other substances. Some are commercial databases that require a subscription, and some are resources provided by national or international bodies free of charge. A selection of relevant resources is listed in Annex 2.

A number of international organizations publish toxicological evaluations of high-priority chemicals:

- Food and Agriculture Organization of the United Nations (FAO)
- International Agency for Research on Cancer
- International Labour Organization
- United Nations Environment Programme (UNEP)
- World Health Organization (WHO)
- Organisation for Economic Co-operation and Development (OECD)
- European Chemicals Agency
- European Food Standards Agency (EFSA)

Assessment reports and other publications are available free of charge from the organizations’ websites and from electronic portals. Some key publications are described below.

The Environmental Health Criteria series (12) and the Concise International Chemical Assessment Documents (13), published by WHO, provide evaluations of chemicals, including information on their effects on human health and the environment, hazards and dose–response of exposure and information about environmental levels and environmental fate.

WHO also publishes the *Guidelines for drinking-water quality*, which include chemical factsheets and supporting background documents (14). WHO and FAO jointly publish toxicological assessments of food additives, contaminants and pesticides that may be found as residues in food. These assessments include information on acceptable daily intakes (15).

Monographs from the International Agency for Research on Cancer on the identification of carcinogenic hazards to humans include reliable, up-to-date information on a large number of chemicals (16).

The secretariats of the Rotterdam and Stockholm Conventions (FAO and UNEP) publish compilations of toxicological information on industrial chemicals and pesticides that are being considered for listing under the conventions. This information is provided on the convention secretariat websites.

OECD publishes Screening Information Datasets on selected high-production-volume chemicals, which include reviews of toxicity data. OECD also provides a portal for accessing information from intergovernmental sources, the eChemPortal.

9.4 BOOKS, JOURNALS AND BIBLIOGRAPHIC DATABASES

Each poison centre should have at its disposal documentation relevant to the country or region, written when possible in the local language(s). The main literature required includes:

- indexes, guides and listings of medicines and of agricultural and other chemical products on the local market and the national pharmacopoeia and medicines formulary;
- books or other publications on animal and plant toxins in the region;
- standard textbooks of medicine (general and paediatric), chemistry, pharmacology and analytical toxicology;
- current awareness bulletins;
- journals of medicine and toxicology; and
- trade and telephone directories (also found online).

A list of suggested reference books in various languages is given in Annex 2.

9.4.1 JOURNALS

A list of some of the numerous periodicals that deal with toxicology or closely related areas is given in Annex 2. In some countries, the national toxicology association may also publish a journal.

It is recommended that a poison centre have access to other medical journals that may contain reports of relevance to the work of the centre, notably those dealing with emergency medicine, epidemiology, intensive care, occupational medicine, pharmacology and adverse drug reactions, clinical medicine, paediatrics, public health and psychiatry. Journals and newsletters published by agencies dealing with accident prevention or associations that undertake research in this area may also be useful, as may journals devoted to more general industrial, chemical and environmental topics. Many journals are available online. Some are free of charge, while others require a subscription; the latter are usually available at teaching hospitals and in university libraries.

The cost of journal subscriptions and textbooks may be a barrier to access for poison centres in low-resource settings. The Hinari programme, set up by WHO with major publishers, enables low- and middle-income countries to access a large number of biomedical and health journals, including a number of toxicological journals, free of charge or at low cost (17). Hinari is one of five programmes available through Research4Life, which also provides access to databases of legal, agricultural, environmental, and research and development information (18).

9.4.2 BIBLIOGRAPHIC DATABASES

Current awareness publications, abstracts and bibliographical indexes are useful for updating information. WHO produces the Global Index Medicus, which provides universal access to biomedical and public health literature produced by and within low- and middle-income countries (19). The material is collated and aggregated by the WHO Global Library Group on a central search platform, allowing retrieval of bibliographical and full-text information.

Other key sources include Medline/PubMed (US National Library of Medicine), Toxline (US National Library of Medicine), ProQuest Dialog, Current Contents Connect (Web of Science Group) and Excerpta Medica. Some of these are free of charge, while others require a subscription; the latter are usually available through university libraries.

9.5 OTHER ELECTRONIC RESOURCES

A number of open-source tools can be used by poison centre libraries to manage collections of papers and other publications. These include dSpace (20), LibLime Koha (21) Greenstone Digital Library Software (22).

Although a great deal of biomedical information is now available online, access may be limited in low-resource settings owing to poor Internet connectivity. The eGranary Digital Library (23) provides an offline collection of 32 million Internet resources. This digital library comes in two forms: servers that connect to wired or wireless local area networks and can serve thousands of patrons and standalone USB drives that connect to a single computer. Both have a built-in proxy and search engine that emulates the Internet experience. Both include built-in tools for subscribers to upload local materials.

9.6 CONCLUSIONS

Information resources of various kinds are essential for the successful operation of a poison centre. As information is increasingly becoming digitalized, poison centres are moving towards electronic resources. These may be stored on hard drives at the poison centre or its host institution or stored in cloud servers. Electronic resources offer the advantage of rapid searching and compact storage; however, their utility is limited if up-to-date computing resources are not available or if access to the Internet is unreliable. Hence, paper-based resources still have their uses, especially for poison centres in low-resource settings.

While many databases, books and journals are costly, free or low-cost access for academic and health institutions is often available for low- and middle-income countries.

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10 POISON CENTRE STAFF TRAINING AND QUALITY ASSURANCE



10.1 INTRODUCTION

A good-quality, authoritative poisons information service requires both well-trained staff and good physical resources. Without well-trained staff, good resources are wasted, and without good resources, well-trained staff will be found lacking. Procedures should be in place for continuous quality assurance to ensure that standards remain optimal and that users of the service remain highly satisfied.

This section addresses training of specialists in poisons information to provide a telephone information service and training of medical toxicologists attached to a poisons information centre or a clinical toxicology unit. Information on training analytical staff in laboratories is given in section 4. This section gives an overview of the content and methods for training in these two specialties. This section also discusses methods for continuous assessment of the quality of work and of the abilities of poisons information staff. The section is intended as a guide; poison centres should decide on the training methods most appropriate for their circumstances.

10.2 TRAINING OF POISONS INFORMATION STAFF

Poison information staff may have a variety of backgrounds, skill sets and education. For example, staff may have a background in science (for example, pharmacology, biochemistry, pharmacy, toxicology, veterinary science) or may be physicians or qualified nurses. None of these fields provides the necessary education and training for the unique work of a specialist in poisons information who answers telephone enquiries about poisoning, and a bespoke training course is required.

To ensure that all staff are trained to the same level, a detailed programme for training new staff should be developed by each poisons information centre according to local circumstances and user needs. The duration of training may depend on the skills available in the centre; however, a period of about 3 months is typical.

The aims of the training programme are to ensure that new poisons information specialists are:

- aware of their role and obligations as part of the poison centre team;
- confident in the operational procedures of the poison centre;
- competent to handle telephone enquiries about poisoning;
- able to find the information necessary to answer an enquiry;
- able to recognize when to refer an enquiry to a senior colleague if it exceeds their competence;
- knowledgeable about the toxicology of the most common types of poisoning in enquiries to the poison centre; and
- knowledgeable about the basic principles of management of a poisoned patient.

A thorough training programme consisting of presentations (usually covering both common poisoning agents and less commonly encountered agents), clinical scenarios, directed reading and, most importantly, time to gain the important skills of telephone communication and triage, is essential. Training methods are discussed in more detail in the WHO poison centre training manual (1).

Once the training period is completed, trainees' skills and competence should be tested before they are allowed to answer telephone enquiries unsupervised.

In addition to basic training of new staff, all staff should have continuous training and professional development to ensure that their knowledge of poisoning and the treatment of poisoned patients is up to date with current practice. Such training could take the form of in-house case discussions and journal clubs, meetings with other poison centres, attendance at international meetings and other forms of continuing professional development as identified by the poison centre.

10.2.1 AREAS TO BE COVERED IN TRAINING

The training programme for new poisons information staff should encompass the following:

- local policies and procedures
- principles of clinical toxicology
- assessment of a poisoned patient
- knowledge about different agents
- information sources
- provision of telephone advice and communication skills
- documentation
- assessment.

These topics are described briefly below. Most of the subjects listed in subsection 10.4.1 for medical toxicologists are also relevant to the training of specialists in poisons information, although the subjects may be covered in less depth.

LOCAL POLICIES AND PROCEDURES

New staff and trainees should, as part of their induction, be made aware of local policies and procedures, such as operating procedures, how the centre handles enquiries from specific groups (for example, from the police, public, media, legal teams) and the usual working practices that the new trainee will be expected to follow. This training will also cover procedures for referring enquiries to more senior colleagues (including clinicians) or external experts or escalating enquiries that may have wider implications, such as on chemical incidents and deliberate release of toxic substances.

New trainees must know what is expected of them in their role and that in-house policies or standard operating procedures are in place to enable them to deal calmly and methodically with any expected or unexpected situation.

PRINCIPLES OF CLINICAL TOXICOLOGY

The principles of clinical toxicology should be introduced during the training period. Some staff, depending on their background, may already have a basic understanding of human physiology and pharmacology. Otherwise, this will be developed during the training period.

In addition to these basic requirements, the trainee should understand, and be familiar with routes of exposure, mechanisms of toxicity, recognition of common toxidromes and the principles of general management of poisoning, including decontamination, symptomatic and supportive care, antidotes and methods for enhancing elimination.

ASSESSING THE POISONED PATIENT

The depth of training included in these sessions may vary from centre to centre, but trainees should understand “normal” physiological parameters and how different poisons may affect them, particularly in relation to potential “red flags” (for example, symptoms of severe toxicity) that should alert them to refer a case to a senior colleague or clinician. Basic understanding of electrocardiography and typical electrocardiographic abnormalities seen in cases of poisoning with cardiotoxic agents would be useful. Similarly, interpretation of blood gas results, how different poisons affect them, and the common investigations used in the management of poisoned patients should be covered.

SUBJECT KNOWLEDGE

Acquiring a good understanding of the toxicity and management of the most common types of poisoning that the poison centre deals with is one of the most important parts of training. According to the pattern of poisoning in the country or region, selected pharmaceuticals, chemicals, chemical products and biological toxins should be covered in detail in teaching sessions led by senior staff members. Training should also cover toxic substances known to cause serious harm but which may be less commonly encountered.

In addition to the teaching sessions, relevant directed reading should be given, such as recent literature or book chapters. Shortly after each teaching session, clinical scenarios or mock calls involving the poisons covered should be organized, both to give the trainee an example of the types of calls they will be dealing with and to identify any gaps in knowledge, which can be rectified with additional training.

INFORMATION SOURCES

A poison centre should have access to many sources of information (see also section 9). These can include internally produced documents on the management of poisoning, product information files, scientific journals (electronic and hard copy), internal and external databases, relevant toxicology handbooks and external consultants for specific cases such as snake envenoming. The trainee should become familiar with the available sources used at their poison centre and should also be able to identify those sources that are best for specific enquiries.

If the poisons information centre produces its own documents on the management of poisoning, the trainee should become familiar with how they are produced, particularly if part of their role will be to assist in their production.

The trainee should be able to find specific information and management recommendations relevant to a particular case in a timely manner. While databases and books may describe the entire management of a case, the poisons information specialist must develop the particular skill to understand what information the caller requires and tailor the information accordingly.

As the primary data sources in a poisons information centre are usually electronic, the trainee should be familiar with the back-up arrangements in case of power outage or unavailability of the Internet.

TELEPHONE SERVICE AND COMMUNICATION SKILLS

Each poisons information centre must establish its own policy for how enquiries should be handled and also identify target user groups. For instance, some poisons information centres take calls only from medical professionals, while others also take calls from members of the public.

A standard internal operating procedure may be in place for dealing with situations that occur frequently, such as:

- answering and giving priority to calls;
- dealing with requests for antidotes and requests for laboratory services;
- managing calls from people who are suicidal or have attempted suicide;
- handling common therapeutic errors, such as double doses of medication;
- identification of plant material;
- dealing with queries from the police and media; and
- general questions from the public about toxic and lethal doses.

The trainee should listen in to calls taken by senior staff, ideally through a dual headset so that the trainee can hear both sides of the conversation. If a computer work station is available nearby, the trainee could also try to find information in “real time” during an enquiry, which will give them additional practice.

Training in telephone communication skills is extremely important. These include questioning the caller and taking an accurate history, having good listening skills, showing empathy and checking that they have correctly understood the information provided. The trainee should also learn how to deal with angry, aggressive or upset people and how to end a call. Such training is usually provided internally, but some poison centres may use external training courses run by telephone communication specialists. Telephone communication skills are particularly important in taking calls from members of the public, which might require some additional training in counselling or conflict resolution.

The most efficient, practical way of training new staff for the telephone service is experiential learning under supervision. A suggested strategy involves a step-by-step process, in which the trainee takes increasing responsibility for answering and documenting poisons information enquiries. The objectives are to:

- ensure that the trainee is familiar with the typical telephone dialogue between callers and poisons information staff;
- allow trainees to build their skills in telephone triage and the principles of risk assessment; and
- familiarize trainees with the centre’s enquiry record form, how to complete it and the documentation standards required for all enquiries.

The trainee should understand the limitations of telephone conversations, such as mishearing letters, words or numbers and be able to identify common mistakes, such as confusion of agent names, and should double-check their spelling.

As trainees gain experience by answering “mock” calls, they should have the opportunity to take real calls, under the supervision of a senior member of staff, who listens in, gives prompts when necessary and gives feedback. Before answering the caller, trainees will discuss their findings with the senior staff member, and once the staff member is satisfied, the trainee can relay the information to the caller.

Once trainees have successfully completed training and demonstrated competence, they can begin to take full responsibility for answering enquiries. Some centres may consider that a short probationary period of supervised calls is appropriate.

DOCUMENTATION

Poisoning cases must be accurately, consistently documented. This is often a requirement for medico-legal reasons and is also important for epidemiological research, toxicovigilance, collection of follow-up data and compiling statistics. Each centre has its own method for recording enquiries, usually in a computer database. Enquiries may be logged live, as the call is taking place, or initially recorded on paper and the information entered into a database at a later stage, ideally soon after the enquiry is complete.

Trainees should be shown how to complete the enquiry record accurately, ensuring that the document is clear, scientifically accurate and completed in a timely manner. Training should include an explanation of the reasons for entering particular information and the importance of an accurate, complete record of each case.

10.2.2 ASSESSMENT AND EXAMINATION

After completion of the training programme, the poisons information centre should have some form of assessment of trainees' skill before they answer calls unsupervised. This is important for clinical governance. The competence of trainees can be assessed by:

- a formal examination;
- a detailed checklist that indicates a minimum level of competence in each training objective; or
- by setting a threshold number of calls or of calls about specific poisons that the trainee has to answer while under supervision.

The training period may be regarded as a probation for the new member of staff until they are certified as competent by the assessment method selected. Once trainees are established as competent, they will be able to participate in the staff rota and answer telephone enquiries unsupervised.

10.3 TRAINING OF MEDICAL TOXICOLOGISTS

Medical toxicologists are physicians with this medical specialization (in some countries) or with specialist knowledge and experience in managing poisoned patients. Their skills will be used in the diagnosis, investigation, and management of individuals poisoned by a variety of agents, including medicines, drugs of abuse, natural toxins and chemicals, with exposure occurring intentionally, accidentally, occupationally or environmentally.

Senior specialists with a special interest in clinical toxicology may be hospital physicians accredited in clinical or medical toxicology, general internal medicine, acute medicine, emergency medicine, intensive care medicine, clinical pharmacology and therapeutics or other relevant specialities. Hospital medical toxicologists may provide telephone advice to colleagues managing suspected poisoning, provide clinical expertise to poisons information centres and be involved in training and research in poisoning. In addition, medical toxicologists may work in public health and may specialize in response to chemical incidents affecting large populations.

As discussed in section 3, the availability of training courses and training placements for medical toxicologists varies widely, and regulations with regard to accreditation and training options differ from country to country. A typical course is described below.

10.3.1 AREAS TO BE COVERED IN TRAINING FOR MEDICAL TOXICOLOGISTS

Before accreditation as a medical toxicologist, a physician must undergo training, through a fellowship or placement in a hospital or a clinical toxicology unit in which clinical toxicology expertise is available. Training should be both didactic and practical, including in particular clinical experience in the diagnosis and treatment of poisoned patients. Didactic training may be given in a classroom or by distance learning. A complete programme for training in medical toxicology should cover the topics listed below.

PART I

1. General principles of medical toxicology

Type and circumstances of poisoning:

- acuity of poisoning (acute, subacute, chronic)
- type of poisoning: deliberate (suicidal, criminal, dependence, abortion) or unintentional (home, workplace, environmental)
- poisoning epidemics
- groups at risk (children, older people, pregnant women, specific occupations)
- adverse drug reactions

Basic principles of toxicology and toxinology:

- toxicodynamics (mechanisms of toxic action)
- toxicokinetics (metabolism)
- experimental data and evaluation
- toxicity testing
- routes of exposure
- carcinogenesis
- teratogenesis
- genetic toxicology

Clinical diagnosis:

- clinical aspects
- toxic syndromes
- differential diagnosis
- role of analytical services

General principles of treatment of poisoning:

- first aid and decontamination
- resuscitation and stabilization
- prevention of absorption
- enhancement of elimination
- symptomatic and supportive treatment
- antidotal and antivenom therapy

Organizations and groups with a role in poison control programmes:

- poison control centres
- governmental and regulatory authorities
- universities
- experimental toxicologists
- other research groups concerned with assessment of human toxicity

2. Human toxicology of specific substances: Systematic study of the most common and important causes of, and substances involved in, human poisoning:

- medical products
- industrial products
- pesticides and other agricultural products
- household products
- poisonous plants and fungi
- poisonous and venomous animals
- environmental pollutants
- food poisoning

For each substance, the following should be considered: main use, physical and chemical properties, kinetics, metabolism, mode of toxic action, toxicity data, laboratory data (for example, toxic levels), pathology, symptomatology, diagnosis, treatment, carcinogenicity, teratogenicity, legal aspects, prevention, particular aspects of acute and chronic toxicity, long-term effects.

PART II

- Human toxicology: extended study, including coverage of less commonly encountered substances
- Prediction of toxicity
- Statistics and epidemiology: for evaluating acute and chronic toxicity of specific substances
- Critical evaluation of literature sources
- Medico-legal aspects
- Research: an appreciation of the methods used in experimental toxicology, toxicovigilance and epidemiology
- Other areas of toxicology: for example, ecotoxicology, occupational toxicology, immunotoxicology, genotoxicity, nanotoxicology, toxinology, forensic toxicology.

TOXICOKINETICS

Trainees in medical toxicology should understand the principles of toxicokinetics and be knowledgeable about the potential effects of absorption by different routes (for example, oral, parenteral, dermal). They should learn basic kinetics modelling and kinetics in overdose and disease states. This section of training should also cover pathways of drug or chemical elimination and modification of absorption (for example, oral activated charcoal) or elimination (for example, haemodialysis, chelation therapy).

TOXIDROMES

Training should cover the toxidromes encountered in poisoning (for example, anticholinergic, cholinergic, opioid, sympathomimetic and sedative–hypnotic), how to recognize a specific toxidrome, the potential drug or chemical causes and how to treat them.

ADVERSE DRUG REACTIONS

While adverse effects after therapeutic use of medications are not strictly poisoning, it is likely that a medical toxicologist will treat patients with such reactions. Therefore, knowledge of the mechanisms of

adverse reactions and assessment of causality should ideally be covered in the curriculum. As some medical toxicologists may be involved in regional or national pharmacovigilance monitoring, knowledge of mechanisms for reporting adverse drug reactions may also be useful.

EPIDEMIOLOGY OF POISONING

The trainee should be familiar with the epidemiology of poisoning, including the prevalence, age- and gender-related risk, geographical variation and any relevant environmental factors. The most commonly occurring toxic substances according to the poisoning pattern in the country or region should be identified, and selected pharmaceuticals, chemicals, chemical products and biological toxins should be the subject of detailed teaching sessions.

MECHANISMS OF TOXICITY OF IMPORTANT AGENTS

Pharmaceuticals: Training should include detailed sessions on antidepressants, antipsychotics, anticonvulsants, antidiabetic drugs, antihistamines, antihypertensives, chloroquine, digoxin, iron, lithium, non-steroidal anti-inflammatory agents, opioids, paracetamol, quinine, salicylates, sedatives and hypnotics, theophylline and warfarin. Other medicines may be added or substituted according to the local epidemiology.

Complementary and alternative medicines: Training should cover Ayurvedic, Chinese and other traditional medicines, homeopathy and herbal medicines., depending on local practices.

Substances of abuse: Training should usually cover stimulants (including amphetamines and related drugs), cannabis, cocaine, γ -hydroxybutyrate (GHB), lysergic acid diethylamide (LSD), opioids, new psychoactive substances (such as synthetic cannabinoids, cathinone derivatives), solvents, volatile nitrites and commonly used herbal substances of abuse, depending on the region.

Chemicals: Training should cover chemicals such as acetone, ammonia, toxic alcohols, carbon monoxide, chlorine, corrosives, cyanide, household products, insecticides (for example, organophosphates), rodenticides, herbicides, hydrofluoric acid, hydrogen sulfide and volatile substances. Depending on the risk, training may also include chemical warfare agents (for example, blister and nerve agents) and toxic industrial chemicals. The choice of chemicals to be covered in greater depth will depend on the local epidemiology of poisoning.

Toxic metals and metalloids: Training should cover lead, arsenic, copper, mercury and thallium. Cadmium and chromium may be important in countries where they are used industrially. In regions with heavy industry and occupational exposure to toxic metals, training may also cover environmental and occupational monitoring.

Natural toxins: Natural toxins (particularly from snakes, spiders and scorpions) are a significant public health concern in many regions, and knowledge of local venomous species and current treatment is essential. Training should cover the local species of snakes and other venomous animals and current guidelines for the treatment of snakebite and stings. Training in poisonous plant and fungal species should also be covered, including both major plant and fungi toxins and commonly occurring local species.

Mixed intoxications: Information is often lacking about this complex area. Understanding interactions and how other agents can increase the effects of poisons and providing advice on clinical management require the best possible clinical and toxicological knowledge.

Radiation: Training may also cover the management of patients exposed to radioactive substances. In some countries, enquiries about radiation may be handled by other specialists.

ELIMINATION AND REDUCED ABSORPTION OF POISONS

The trainee should be taught gastric decontamination methods, including use of activated charcoal, whole bowel irrigation and appropriate use of gastric lavage, on the basis of the latest evidence of the effectiveness

of these measures. The evidence is reviewed periodically as a joint activity by the European Association of Poisons Centres and Clinical Toxicologists and the American Academy of Clinical Toxicology in published position statements.

Trainees should also be familiar with methods for increasing elimination, including extracorporeal methods such as haemodialysis, urinary alkalization, multiple-dose activated charcoal and endoscopic decontamination. Training should include identification of the substances for which such methods are effective and the indications for their use.

ANTIDOTES

Trainees should understand the general mechanism of action of the antidotes and antivenoms commonly used in the treatment of poisoning. They should understand the indications for use and also avoiding indiscriminate use of antidotes that may not be required, the limitations of their use, dosing and any dosage alteration required because of a patient's age or underlying medical condition.

KNOWLEDGE AND TREATMENT OF PSYCHIATRIC CONDITIONS

Trainees should be aware of how psychiatric conditions may influence the incidence and type of poisoning. They should also be aware of any potential implications for treatment of the patient. Trainees should be fully conversant with any legislation regarding consent and treatment of patients who may be regarded as lacking capacity.

10.3.2 OTHER TRAINING ACTIVITIES

Trainees should not only study and gain clinical experience in the management of poisoning but also write a dissertation and participate in teaching activities. Trainees can gain experience in other work in the poison centre and in related disciplines, for example by spending time in:

- a poisons information centre (including training in preparing documents, collecting information, replying to enquiries, recording case data and following up cases);
- a clinical toxicology unit, emergency department or intensive care unit in which poisoned patients are treated (if the poison centre is not already based there); and
- a toxicological laboratory, to gain practical understanding of sampling and analytical methods and of medical interpretation of the results of analyses.

They should also use opportunities to attend or participate in seminars, courses, lectures, conferences, congresses and meetings within and outside the centre and to be active in national and international clinical toxicology associations.

10.3.3 EXAMINATION OR ASSESSMENT

After completion of a medical toxicology training programme, participants should undergo some form of assessment to test their knowledge, skills and approach. The form will depend on the national requirements for certifying specializations.

Competence may be assessed by:

- completion of a logbook or portfolio that demonstrates a minimum level of competence in each training objective;
- peers;
- submission of course work during training; or
- a formal summative assessment, for example, a formal examination.

Once trainees have successfully completed training and passed any required assessment, they may be eligible for accreditation as a medical toxicologist, in countries in which this is a recognized specialty.

10.3.4 CONTINUING PROFESSIONAL DEVELOPMENT

Although the basic professional training of clinical staff is supplemented by experience obtained in their work, the rapid development of toxicology makes continuing education and updating of knowledge a professional and ethical responsibility. The means include reading scientific literature, participating in local, regional and national seminars, meetings and workshops and participating in training courses of several days or weeks. Continued updating of expertise can also be stimulated, for example, by making participation in scientific meetings a condition of certification. In the USA, where professional certification is controlled by boards such as the American Board of Emergency Medicine, evidence of active interest in new developments is necessary to maintain expert status in toxicology. This system not only encourages continuing education but also contributes to career advancement by raising professional status.

10.4 TRAINING RESOURCES

Training resources are posted periodically on the websites of clinical toxicology associations such as the European Association of Poisons Centres and Clinical Toxicologists (2), the American Academy of Clinical Toxicology (3), the American College of Medical Toxicology (4) and the Middle East & North Africa Clinical Toxicology Association (5). Most courses are available online. Some course materials are available free of charge, while other courses require payment. An open-access curriculum project called WikiTox provides a repository of toxicology teaching materials (6).

10.5 QUALITY ASSURANCE AND CONTROL

In order to ensure that a poisons information centre operates effectively and provides the best possible service to users, it should use procedures for quality assurance and control. Quality assurance comprises procedures for the recruitment, training and appraisal of staff, written operating procedures for the main activities of the centre and ensuring the availability of the necessary equipment and information resources, a plan for service continuity in the event of, for example, a power failure or loss of Internet access and procedures to check user satisfaction with the service. Quality control mechanisms include routine audits.

The essential requirements in terms of staffing, IT and telecommunications equipment and information resources are described in earlier sections. Some quality management activities are described below.

10.5.1 OPERATING PROCEDURES

Operating procedures consist of step-by-step instructions issued by organizations, which describe complex routine operations in detail to ensure that staff perform the tasks to a specified, measurable standard. Operating procedures for handling enquiries and situations not only ensure that all staff do so the same way but also guide less experienced staff and can build confidence.

The poison centre should determine the objectives of its service and identify which actions require detailed operating procedures. The actions may include answering poisons enquiries, dealing with enquiries from the media, checking enquiries, following up enquiries and referring complex enquiries to internal (for example, medical toxicologist) and external (for example, botanists, toxinologists) specialists. Annex 7 gives an example of an operating procedure for answering poisons information enquiries.

10.5.2 STAFF APPRAISALS

Routine measurable assessment of staff performance is an important component of a quality assurance system to ensure that employees are working to their optimum ability. The most common mechanism is an annual meeting for staff appraisal. The formality of the procedure depends on local requirements and practice. The appraisal usually includes reviewing the work performed over the year in relation to the staff member's objectives for that year. A common approach to setting objectives is ensuring that they are specific, measurable, achievable, relevant and time-bound (SMART). Staff objectives should allow the poison centre to achieve its goals. Staff appraisals may also indicate staff development and training requirements.

Regular one-to-one meetings throughout the year are another means of monitoring staff performance, in addition to formal yearly appraisals. They ensure that any problems are identified and addressed at an early stage, helping staff to achieve their objectives by the end of the year.

10.5.3 AUDITING AND CALL CHECKING

Auditing the handling of poisons information calls can ensure that enquiries are answered and documented to a high standard. Auditing may consist of checking the documentation of a call or listening to a call recording. In some poison centres, each electronic or paper call record is reviewed by a colleague shortly after the call is completed to check compliance with documentation standards, such as fully completed database fields and accurate, correct spelling and coding, and to check that the correct information was given in response to the enquiry. Depending on the number of calls handled and the staffing level, the policy may be to check every call record, a set proportion (for example, one in five) or only those for which the poisoning was of a specific severity. It might be good practice to check initially all the records made by new staff.

In a poison centre where calls are recorded electronically and resources allow, the manager or a senior staff member can listen to the recordings of a number of calls with the poisons information specialist. The handling of the call can be assessed against clearly defined criteria and any problems discussed. The assessment criteria may include the accuracy with which information was recorded, whether an appropriate history was taken, the manner in which the poisons information specialist spoke to the caller and whether the correct information was provided. Such routine auditing of calls in the presence of the poisons information specialist will indicate any improvements that may be required in call handling or identify whether further training is required. The frequency and the number of calls that are audited is at the discretion of the poison centre. Assessment of staff every 3–6 months may be sufficient, providing that calls are also checked or peer-reviewed daily. Annex 8 is an example of a call auditing form.

10.5.4 USER SATISFACTION SURVEY

Another component of quality assurance is use of feedback from users of the service to establish users' requirements and expectations of service performance and to identify areas for improvement. Feedback can be obtained by sending a standardized questionnaire to a random sample of enquirers periodically throughout the year. The questionnaire could take the form of an online survey or an e-mailed or posted questionnaire, depending on local circumstances. Each poison centre should decide what percentage of their call volume to sample; for a centre with a high call volume, a 5% sample may be sufficient.

Suggested topics for the survey include the reason for contact, ease of contact, quality of information supplied and staff attitude. Respondents are often asked to score their satisfaction or dissatisfaction. There should be an area for free text at the end of the questionnaire, in which the user can make any comments about the service that they consider relevant. Annex 9 is an example of a quality assurance form.

The results should be collated, reported and used to make any improvements that may be required.

10.6 CONCLUSIONS

The reputation of a poison centre depends on the quality of the service that it offers. This, in turn, is determined to a large degree by having competent, experienced, well-trained staff. The centre should also have a mechanism for monitoring the quality of the service, so that any corrective action can be taken quickly. Training and quality assurance both require resources, which should be considered when planning a poison centre.

10.7 FURTHER READING

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1657920	414264	58742	221233	1
1215720	5498216	3322144	3221	
326225	32154316	32366987	21258	
32255021	1245755	121554	32186664	
1245755	2154756	323150	232312	
2154756	320659	221550	12789452	
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221233	32659			
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11 POTENTIAL SOURCES OF FUNDING FOR POISON CENTRE ACTIVITIES



11.1 INTRODUCTION

Poison centres must have adequate, reliable funding to provide high-quality poisons information advice and to maintain high standards for clinical and other services. In the past, poison centres were often funded by national governments; however, many now depend on an often unique combination of funding sources. A broad funding base provides greater security for the poison centre, protecting it from funding shortfalls, although identification and negotiation with several funding streams can require substantial work and administration.

This section addresses the various sources from which a poison centre may obtain funding, although some of the sources may not be suitable or available to all poison centres. Information is provided on the rationale for seeking funding from each source, the advantages and disadvantages and, when relevant, additional infrastructure that a poison centre might require to ensure that each funding source is viable.

The operating costs of poison centres vary substantially (1). They are determined by factors that include the number and professional categories of the staff employed and their salary scales, rental costs, database subscriptions, activities and equipment maintenance and renewal costs. A clear understanding of costs will indicate funding requirements and areas in which costs might be saved.

Regardless of the source of funding, there must be no conflict of interest for the poison centre. Hence, any contracts or funding agreements must be justified and transparent, with a clear statement protecting the poison centre's impartiality and independence. If this is not done, claims of bias could damage the credibility and the reputation of the centre.

11.2 GOVERNMENT HEALTH AGENCY OR DEPARTMENT FUNDING

RATIONALE

Poison centres are an important part of a country's health care system, as they help improve the clinical management and outcomes of poisoning, reduce health care expenditure and protect public health. They can also conduct toxicovigilance, contribute to the national capacity to deal with chemical threats and help meet the requirements of the IHR (see section 1). The value of these activities and outcomes to the health care system and to public health is a strong argument for poison centres to receive funding or support from relevant government health agencies or departments.

ADVANTAGES

The advantages of funding a poison centre from a government health budget (national, regional or state) are listed below.

- The poison centre is established as an integral component of the health care system.
- The poison centre is given authority and recognition, thereby facilitating interactions within the health care system (for example, obtaining follow-up information on patients), with official authorities and with manufacturers and trade associations.
- It can facilitate collaboration with other government agencies or departments (for example, those responsible for chemicals, health education and public health).
- It may provide access to official resources such as closed health networks and restricted information (for example, reports of illegal drug use, analyses of threats of the deliberate release of chemicals).
- The poison centre is more likely to be integrated into long-term government health strategies and international collaboration.
- It provides some financial stability, so that the poison centre can plan more strategically and devote more resources to toxicological activities rather than securing funding, and the staff have greater job security, thereby improving retention and development of staff expertise.

DISADVANTAGES

The disadvantages include the following points.

- Funding depends on the overall health budget and may be cut if government and/or health care priorities change.
- Budgets are usually fixed and might be inflexible for any change in the poison centre's needs during a financial year.
- Strict conditions on how the funding can be spent may be applied.
- Limitations may be imposed on the activities of the poison centre (for example, public communications may be subject to official approval).

ADDITIONAL INFRASTRUCTURE NEEDS

It is unlikely that a poison centre will require substantial additional infrastructure, other than that described in earlier sections. It must, however, maintain a high standard of service provision, in terms of both service availability (for example, operating reliably 24 hours a day, 7 days a week) and service quality (ensuring good clinical governance and a high standard of information and advice). Ideally, a poison centre should provide some public education or outreach (for example, leaflets, materials for schools) in order to contribute to the prevention of poisoning and protecting public health and also to further justify receiving government funding.

USEFUL ADVICE

The economic and public health benefits of a poison centre (described in section 1) to the health care system are not always well recognized in government departments or by other official bodies. Poison centres must therefore continually demonstrate their value to those responsible for providing funding and more widely within government. One means is the production and distribution of high-quality publications, such as an annual report and data on epidemiological trends in poisoning. When possible, a poison centre should seek additional funding from other sources to ensure greater financial stability and flexibility in how it uses its funding.

11.3 HOST INSTITUTION SUPPORT

RATIONALE

Support from a host institution (for example, hospital, university) is often provided in kind, including physical infrastructure (for example, computers, office space, telecommunications), access to host institution facilities (for example, laboratories, libraries) and access to administrative and support services. The hosting of a poison centre by an institution can be mutually beneficial. In particular, the presence of a well-regarded poison centre can enhance the reputation of the host institution, and the poison centre may be able to make important contributions to its activities (for example, by collaborating in research or providing specialist training). In-kind support may be a substantial benefit to a poison centre and should not be undervalued.

ADVANTAGES

- It can substantially reduce a poison centre's administrative and financial overheads.
- Hospitals and universities may provide access to a wide range of relevant information (such as databases, journals, libraries) and other resources (for example, laboratories) of benefit to a poison centre.
- There may be opportunities for networking and collaborative work (for example, research) with the host institution.
- In some host institutions (for example, hospitals), poison centre staff may have opportunities to increase their experience and skills (for example, by observing ward rounds or attending training courses).

DISADVANTAGES

Although the benefits to a poison centre usually outweigh any potential disadvantages, the latter can include the following.

- In-kind support may depend on the overall financial position of the host institution, and, if it changes, internal charges may be introduced or increased.
- The host institution may expect the poison centre to adhere to its policies and procedures, which may not be conducive to maintaining the impartial and independent status of the poison centre.

ADDITIONAL INFRASTRUCTURAL NEEDS

Substantial additional infrastructural needs are unlikely to be necessary.

USEFUL ADVICE

For maintenance of in-kind support, the host organization must see continuing benefit of hosting the poison centre. Therefore, the poison centre must maintain a high quality of service and be proactive in demonstrating its value to the host institution. Additionally, the poison centre director and senior staff should establish and maintain good professional networks and relationships within the host institution. Other activities of benefit to a host institution may include the provision of regular training (for example, on toxicological issues), ensuring that the host institution is acknowledged or credited on all publications and publicity and providing the host institution with free access to poison centre services.

11.4 CHARGING FOR POISON CENTRE ADVICE AND SERVICES

RATIONALE

Charging for access to certain clinical advice and services might allow a poison centre to generate income to fund its activities. Services that could be charged for include antidote provision, clinical toxicological consultations, poisons information advice and toxicological analytical services. Charging models can include subscription (for example, an annual fee), fee per service use (for example, per poisons information enquiry or toxicological analysis) and internal cross-charging (for example, the emergency department of a hospital pays a fee to access the poison centre in the same hospital).

The charging model could be to provide services free of charge to some users (for example, state health care organizations, the general public) and to charge other service users (for example, private health care providers), or it could charge only for specialist services (for example, veterinary poisons information advice (Box 11)). Poison centres may make a profit by charging for one service (for example, toxicological analyses), which they can then use to fund the provision of other services (for example, poisons information advice) without charge.

ADVANTAGES

Charges for access to poison centre services can provide a steady income (2). Furthermore, contractual relationships can encourage regular communication and feedback between poison centres and service users, leading to better, more efficient use of the poison centre.

DISADVANTAGES

Charging for poisons information and advice may be a disincentive for making an enquiry (3), which could result in a delay in the appropriate treatment and poorer outcomes. It could also result in a lower call volume (4), reduce the scope of toxicovigilance activities and limit data collection and analysis of the epidemiology of poisoning in the population.

ADDITIONAL INFRASTRUCTURAL NEEDS

The poison centre should have a good business administration system to negotiate and maintain contracts and to differentiate contracted users from non-contracted users, who may be charged per service.

USEFUL ADVICE

Establishing good working relationships with the relevant staff of contracting organizations, such as health insurers, is essential. It is also important to provide regular feedback to the organization (including to senior management) on service use to maintain awareness of the services offered by the poison centre and their value. The provision of additional services (for example, free continuing professional development training, poisoning prevention materials) can add value to a contracting organization and can increase the likelihood that the organization will continue to contract with the poison centre. If a charge is levied for poisons information and advice, subscriptions (for example, annually) are easier to administer and may have less impact on call volume than charging per enquiry (4).

Box 11. Providing a veterinary poisons information service

Rationale

Animals, especially companion animals, are prone to poisoning, and members of the public and veterinarians may need advice on management. As veterinary services are usually fee-based, a poison centre can reasonably charge a fee for advice on poisons, thereby generating additional income.

Advantages

- Provision of veterinary poisons information can increase the toxicological skills of poison centre staff.
- Opportunities to provide continuing professional development services to veterinary staff could generate further income.
- Other services offered by a poison centre (for example, analysis of biological samples, providing antidotes) may be adaptable to veterinary cases.

Disadvantages

A veterinary poisons information service involves additional administration, operating systems and training. Furthermore, such a service may be viable only in societies in which people are willing to pay for advice on animal care.

Additional infrastructural needs

A separate telephone line for veterinary calls is essential, and specialist staff, such as veterinarians, might have to be recruited to deal with complex or severe cases. In addition, the poison centre must have good business administration, operating and data collection systems.

Useful advice

Endorsement of a veterinary poisons information service by a national veterinary association will attract service users.

11.5 CHARGING FOR ACCESS TO CLINICAL TOXICOLOGY INFORMATION

RATIONALE

Some poison centres have set up clinical toxicology databases (see section 9) containing information on chemicals, household products, pharmaceuticals, plants and other substances of toxicological concern and advice on how to manage exposure. Some poison centres have also developed innovative technological tools, such as applications for smartphones (5). A poison centre with its own clinical toxicology information resources can provide access to other poison centres and health care institutions on a subscription basis, thereby generating income. The subscription charge may be discounted or waived case by case, depending on the country's economic status.

ADVANTAGES

The availability of clinical toxicology information resources can facilitate access by clinicians and other users to information on substances of toxicological concern and obviate the need to telephone a poison centre, particularly at times of high service use. Furthermore, technological tools, such as applications for smartphones, can allow

mobile health care personnel, for example, paramedics, and those where Internet connectivity is poor to access toxicological advice remotely. The income generated from subscriptions can be used to fund maintenance and development of the database, as well as operation of the poison centre.

DISADVANTAGES

To develop IT resources, a poison centre must have access to the relevant IT expertise. If this is not available in-house, it may be expensive to sub-contract it to another organization. Careful project management is required to ensure that the IT system meets the needs of the poison centre and other potential users.

ADDITIONAL INFRASTRUCTURAL NEEDS

A well-developed, authoritative, fully referenced database of toxicological monographs is essential for such a database, and a work programme should be established to review and update database entries continually. Sufficient IT infrastructure and support are also required to host, maintain and develop the database, as is a good business administration system to manage requests for access and for charging users.

USEFUL ADVICE

Consideration should be given to whether the initial investment for an information database is likely to be recovered by charging for access and how long it will take to recover the initial investment. This should be weighed against the potential public health benefit, and the decision to develop a toxicological database might not be purely economic. An international group of reviewers could be formed to ensure the quality and reliability of the database and/or provide advice to a steering group overseeing database development.

11.6 HEALTH CARE INSURANCE PROVIDERS

RATIONALE

In many countries, health care is financed through private insurance schemes, which pay the health care provider or reimburse the patient for treatment and investigations. Poison centres prevent unnecessary attendance at health care facilities and, when consulted, reduce the length of stay of patients in health care facilities (6–9). Poison centres thus help to reduce claims to and payments made by health care insurance providers. It is therefore in their interests to support poison centres.

ADVANTAGES

As health care costs tend to be high, a relatively small contribution to a poison centre by a health care insurance provider could, in principle, yield financial savings for the provider while also being a source of useful additional funding for the poison centre.

DISADVANTAGES

In practice, it may be difficult to demonstrate the benefit of a poison centre to an individual health care insurance provider and to negotiate funding if the poison centre provides services without charge. Additionally, the administrative burden of negotiating contracts with and reporting to each health care insurance provider should be considered.

ADDITIONAL INFRASTRUCTURAL NEEDS

Substantial additional infrastructure is unlikely to be required.

USEFUL ADVICE

The more a poison centre can show the cost–benefit for an individual health care insurance provider, the easier it will be for the provider to appreciate the direct value to their company. In return for funding, however, a health care insurance provider might wish to have input into or representation on the management of the poison centre (10).

11.7 PROVISION OF SERVICES TO GOVERNMENT AGENCIES

RATIONALE

Data collected by a poison centre are often not available elsewhere. These include the numbers, severity and circumstances of exposure to certain substances, which may be of particular value to government agencies for understanding the risks posed by these substances and in formulating policy. Hence, government agencies (for example, with responsibility for regulation of chemicals, pesticides or pharmaceuticals) might be prepared to contribute to funding a poison centre, particularly if this gives them access to data relevant to their area of responsibility. Alternatively, government agencies might be willing to pay for reports on specific issues.

ADVANTAGES

The provision of data to government agencies can help to protect public health. In addition, positive relations with government agencies can foster government support for the poison centre.

DISADVANTAGES

If data and reports have been provided to government agencies without charge in the past, it may be difficult to start demanding payment. The collection of data that are not usually collected by the poison centre and writing bespoke reports can be time-consuming.

ADDITIONAL INFRASTRUCTURAL NEEDS

Substantial additional infrastructure is unlikely to be required.

USEFUL ADVICE

When providing information to government agencies, poison centres must make clear what kinds of information they can provide and establish the basis on which the information is being provided (for example, is a government agency paying for the service, or is it provided free of charge in recognition of government funding?).

11.8 PROVISION OF SPECIALIST EDUCATION AND TRAINING

RATIONALE

Poison centre staff are uniquely experienced and qualified to teach and train others in clinical toxicology. Furthermore, health care and other professionals are often obliged to participate in continuing professional development. The provision of fee-based specialist training is therefore a means of generating additional income. Funding for such activities may also be provided by the ministry of education, channelled through universities.

ADVANTAGES

Besides the generation of additional income, other benefits accrue to a poison centre in running specialist education or training courses.

- Training courses help raise the profile and enhance the reputation of a poison centre.
- Networking with course attendees may lead to further collaborative opportunities (for example, providing additional training, research collaborations).
- Regular specialist training can improve the skill and knowledge of the workforce, leading to wider benefits for health care and public health.

DISADVANTAGES

The resources and time required to develop training materials and run a training course may be considerable. Therefore, all the costs (such as materials, promotion of courses, staff time, travel, venue hire) and ensuring that course materials are regularly updated must be considered when charging for a course.

ADDITIONAL INFRASTRUCTURAL NEEDS

A suitable training venue and equipment (for example, laptops, projectors) should be identified. If a course is conducted at the poison centre or host institution, training rooms and equipment may be available at no or reduced cost.

USEFUL ADVICE

Training courses should be suitably advertised and promoted, usually several months before they start. Formal accreditation of the course by a professional body will improve enrolment.

11.9 PROVISION OF SERVICES TO COMMERCIAL COMPANIES

RATIONALE

Poison centre staff are trained to collect and evaluate information on commercial products, assess their toxicological risks, answer queries about exposures and provide advice on the management of and response to chemical incidents. Moreover, most poison centres conduct surveillance to identify trends in exposure to chemicals and products. These activities provide unique expertise, and poison centres can provide a range of services that may be valuable to companies that manufacture and/or supply consumer products, pharmaceuticals and other chemical agents (for example, pesticides). The services can include:

- registering product data;
- providing toxicological assessments for products (for example, writing or checking safety data sheets, product labels);
- providing consumer health advice at a dedicated telephone number;
- monitoring product enquires to the poison centre; and
- providing advice on chemical incidents.

A company may choose to contract services from a poison centre in order to fulfil regulatory requirements (for example, producing safety data sheets), in the interests of good product stewardship (for example, monitoring enquiries associated with a product) or if the company lacks specific expertise (for example, in chemical incident risk assessment and management). The poison centre can charge a commercial company for the provision of such services and thereby generate income.

ADVANTAGES

The provision of services to commercial companies has a number of advantages, as listed below.

- The poison centre can gain access to product information (for example, through product registration schemes, writing safety data sheets) that better enables the poison centre to provide advice about patients exposed to those products.
- As data (for example, enquiry data) and expertise (for example, to write a safety data sheet) are already available within a poison centre, providing services to a commercial company is unlikely to require substantial additional infrastructure or training of staff.
- Some work (for example, generating product enquiry reports, providing advice on chemical incidents) may not require substantial additional effort by a poison centre.

DISADVANTAGES

While providing services to commercial organizations may be a valuable source of income to a poison centre, there may be disadvantages.

- A conflict of interests may arise if a poison centre receives funding from a commercial organization, and the centre may not be perceived as impartial or independent by other users.
- Companies will expect a high standard of service, which could place pressure on core services for example, answering poison enquiries.
- Issues of liability could arise if a poison centre makes a mistake (for example, in a safety data sheet or in assessing risks associated with a chemical incident).
- The provision of some services (such as product registration) may require substantial additional work, particularly if there is a large volume of data to be managed.

ADDITIONAL INFRASTRUCTURAL NEEDS

Additional infrastructural needs will depend on the services provided. They could include:

- sufficient, suitable bespoke data management and storage systems (for example, for product registration);
- sufficient staff capacity to undertake the work in addition to maintaining core services;
- suitable model business agreements for establishing a contract with a commercial organization;
- sufficiently detailed enquiry information in order to monitor enquiries about a specific brand or product; and
- means to promote the services of a poison centre to relevant commercial companies.

USEFUL ADVICE

When a contractual relation is established with a commercial company, the contract must not (and must not be perceived to) affect the impartiality and independence of the poison centre, and any contract must include clear statements to that effect. The poison centre must also ensure that the commercial company has realistic expectations of the services and data it will receive (for example, level of product detail, nondisclosure of patient-identifiable information). The poison centre should charge a sum that is sufficient to cover actual costs and generate income in excess of expenses.

11.10 PROVISION OF CODE-BREAK SERVICES FOR CLINICAL TRIALS

RATIONALE

The proper conduct of blinded clinical trials requires that there be emergency 24-hour access to code-break services for participating patients. A poison centre can act as the responsible holding centre for code-break envelopes and decoding lists for a trial and, if requested by an authorized person, can un-blind them for a particular patient or the whole trial. In the case of a serious adverse reaction or overdose, the poison centre may also be able to advise on treatment.

ADVANTAGES

A reliable code-break service is essential for blinded clinical trials, valuable to a pharmaceutical company and usually involves only modest additional day-to-day work for a poison centre. Providing such a service will also give the poison centre access to information on the trial drug, so that it is in a better position to provide advice on the drug in the event of an adverse reaction or overdose.

DISADVANTAGES

The poison centre may have to demonstrate compliance with relevant regulatory guidelines and standards for clinical trials, and companies may wish to inspect the poison centre to ensure that a satisfactory quality of service is provided. Such quality assurance activities carry an administrative overhead and can be time-consuming. Furthermore, coding systems may vary from trial to trial, necessitating additional training of poison centre staff.

ADDITIONAL INFRASTRUCTURAL NEEDS

Emergency code-break services must be absolutely reliable and available 24 hours a day, requiring a robust staff rota. Contracting companies may have specific requirements for accreditation (for example, good clinical practice), quality control and standard operating procedures for responding to code-break requests. Secure, lockable storage that is accessible 24 hours a day is required for code-break documents.

USEFUL ADVICE

Hospital medical and pharmacy staff are often in regular contact with pharmaceutical companies and may therefore be able to promote a poison centre's code-break service. Use of standard contracts and operating procedures can reduce the burden of administration and training.

11.11 PROVISION OF MEDICO-LEGAL EXPERTISE

RATIONALE

In criminal and litigation court cases, toxicological expertise may be required to determine whether a victim or claimant suffered harm as a result of a toxicological cause. Senior staff (for example, medical toxicologists) at a poison centre may be asked to prepare reports or provide evidence in court in such cases, and other poison centre staff might be asked to assist in preparations for legal proceedings. A premium rate can usually be charged for this work.

ADVANTAGES

The involvement of experienced poison centre staff ensures that the legal system has access to appropriate expertise.

DISADVANTAGES

Medico-legal work is time-consuming, and other staff might have to cover for those who are testifying in court. Poison centre staff might be required to give evidence against the medical professionals whom the poison centre serves (for example, in a case of alleged mismanagement of a poisoned patient), which could subsequently discourage some medical professionals from using the poison centre.

ADDITIONAL INFRASTRUCTURAL NEEDS

The staff who undertake such work must be highly competent and must understand the legal principles of liability.

USEFUL ADVICE

Training in testifying in court is useful, if available. The costs associated with medico-legal work can be considerable, and the fees charged should at least cover those costs and generate additional income for the poison centre.

11.12 CHARITABLE FUNDING

RATIONALE

Poison centres seek to help people and are therefore often eligible for charitable funding. They could approach bodies that make charitable grants or solicit individual donations (for example, by pamphlets in post boxes).

ADVANTAGES

While the core services of a poison centre may be funded, supplementary funds can be obtained from charitable sources for specific additional activities, such as poisoning prevention, or to help specific groups. Furthermore, seeking charitable donations (for example, from members of the public) may raise the profile of the poison centre more generally.

DISADVANTAGES

The amount of staff time required to secure and meet the conditions of charitable funding (for example, applying for charitable grants, reporting back on how a grant was spent and its impact, or organizing distribution of pamphlets) is not necessarily cost-effective. Furthermore, charitable donations are often erratic and cannot necessarily be relied upon as a consistent source of funding.

ADDITIONAL INFRASTRUCTURAL NEEDS

Dedicated staff with fundraising expertise might be required to develop charitable funding as a source of supplementary income and to obtain official charitable status for the poison centre. A means for individuals to make donations could be set up, for example, a “Donate” button on the poison centre’s website.

USEFUL ADVICE

Obtaining charitable funding is often more successful if it is linked to a specific activity (for example, “poisons prevention week”) or for a specific purpose (such as helping at-risk groups), rather than requesting donations for general operational costs. The possibility that a particular donation (for example, from a commercial organization) could generate a conflict of interest should also be considered.

Endnote: Section 11 is an update of a draft prepared by WHO in 2005. Contributors to the original draft are listed below, with their positions and affiliations in 2005.

Erik Andrew, Director, National Poisons Centre, Oslo, Norway

Alex Campbell, Manager, Veterinary Poisons Information Service, Guy's and St Thomas' Poisons Unit, London, England

Nick Edwards, Manager, Guy's and St Thomas' Poisons Unit, London, England

Rita Fitzpatrick, Senior Poisons Information Specialist, Guy's and St Thomas' Poisons Unit, London, England

Ed Krenzelok, Director, Pittsburgh Poisons Center, Pittsburgh (PA), United States of America (now Emeritus Professor, School of Pharmacy, University of Pittsburgh)

Monique Mathieu-Nolf, Director, Centre Antipoison et de Toxicovigilance de Lille, Lille, France

Kent Olson, Medical Director, San Francisco Division, California Poison Control System, San Francisco (CA), USA

Naima Rhalem, Manager, Centre Antipoison et de Pharmacovigilance du Maroc , Rabat, Morocco

Rachida Soulaymani Bencheikh, Director, Centre Antipoison et de Pharmacovigilance du Maroc, Rabat, Morocco

Wayne Temple, Director, National Poisons Centre, Dunedin, New Zealand

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ANNEX 1. SUMMARY OF STUDIES OF THE ECONOMIC IMPACT OF POISON CENTRES

This table summarizes a number of studies, most of which were conducted by poison centres, of their economic impact. Most of the studies were conducted in developed countries. The table includes the conclusions of a literature review by the Lewin Group on behalf of the American Association of Poison Control Centers (2); the studies included in that review are not repeated in the table, with the exception of two papers on the real-life consequences of the temporary removal of a poison centre service (3, 4). The other studies listed are studies in the USA published after the review by the Lewin Group and studies in other countries.

Study	Method	Costs measured	Measure of effectiveness or benefit	Economic results	Conclusion
Americas					
Galvão et al., 2011 (Brazil) (1)	Retrospective review of patients admitted for poisoning to a single hospital over 3 years to investigate outcomes and whether the poison centre had provided assistance.	Direct medical costs	Length of hospital stay	Patients about whom the poison centre was consulted stayed an average of 3.42 days fewer than those not discussed with the poison centre.	Consulting the poison centre can reduce the length of hospital stay and therefore hospital costs. The poison centre is underused.
Lewin Group, 2012 (USA) (2)	Literature review of published cost-benefit studies of poison centres.	Return on investment in terms of savings in direct and indirect medical and social costs	Averted use of medical services Shorter hospital stay Personal outreach Fewer days of work lost	The poison centre was estimated to save more than US\$ 1.8 billion per year in medical costs and productivity. The return on investment was US\$ 13.39 for every US\$ invested in the poison centre system.	Significant savings by federal, state and local governments and the health sector. Savings were probably an underestimate, as the value of some services, e.g. toxicovigilance, was not costed.
Phillips et al., 1998 (USA) (3)	Evaluation of actual costs of losing access to the poisons information centre.	Direct and indirect costs		The average additional cost per blocked call was US\$ 10.89 from a societal perspective and US\$ 33.14 from a health care purchaser perspective. 14% of callers with restricted access to poison centres and only 2% of callers with direct access to poison centres were treated at an inappropriate location.	Restricting direct public access to poison centres created additional costs to society, the health care sector and callers.

Study	Method	Costs measured	Measure of effectiveness or benefit	Economic results	Conclusion
King & Palmisano, 1991 (USA) (4)	Evaluation of actual costs of losing access to a poisons information centre in two districts.	Direct medical costs	Rate of self-referral to a health care facility	During 7 months when the poisons information centre was not available, the cost attributable to excess visits to health care facilities was US\$ 183 950. Projected annual cost of excess use of health care facilities was US\$ 1.4 million, which was more than three times the state funding for the poison centre.	In an attempt to reduce state expenditure of US\$ 400 000 by withdrawing funds for the poison centre, health care costs of US\$ 1.4 million were shifted to insurers, citizens and health care facilities.
Friedman et al., 2014 (USA) (5)	Retrospective analysis of inpatient cases treated in hospitals by linking a poison centre database with a hospital billing dataset; comparison with admissions for poisoning with no poison centre involvement.	Cost savings to health service	Hospital length of stay	Poison centre-assisted inpatients stayed 1.5 days less than non-assisted inpatients. After adjustment for covariates, poison centre-assisted patients stayed 0.58 days less than patients with no such assistance. Hospital charges for poison centre-assisted patients in the lower quintiles of severity were significantly higher than those for patients with no such assistance but were substantially lower for the most costly quintile of patients. Balancing the higher charges for treating patients with poison centre assistance in the lower quintiles with the savings in the highest quintile among inpatients indicated a potential cumulative saving of US\$ 2078 per 10 patients.	The most severe cases of poisoning are the main beneficiaries of poison centre involvement in treatment in terms of hospital charges.
Europe					
Descamps et al., 2019 (Belgium) (6)	Prospective survey of members of the public calling about unintentional poisoning. At follow-up, callers were asked what they would have done if there were no poisons information call centre and what they did after the call.	Direct costs to Government and to patient	Averted hospital attendance	The estimated average weighted cost per case was €57.93 with the poison centre and €330.48 without, for a cost-benefit ratio of 5.7. Total annual saving to the Government was €9 568 339. In a more conservative scenario, the cost-benefit-ratio was 2.34.	Financial savings can be made if people first call the poison centre for unintentional poisonings.

Study	Method	Costs measured	Measure of effectiveness or benefit	Economic results	Conclusion
Lavon et al., 2015 (Israel) (7)	Retrospective review of enquiries to a poisons information centre to determine the number of cases of non-toxic ingestion (silica gel) who attended hospital.	Direct medical costs	Potential averted emergency hospital visits specific to silica gel	546 enquiries about silica gel received in 2008. 10% of cases of reported exposure attended hospital. Poisons centres could save an estimated US\$ 99 383 from averted hospital visits.	Timely advice from a poisons information centre reduces hospital referrals for silica gel ingestion and reduces health care costs.
Toverund et al., 2009 (Norway) (8)	Satisfaction survey of telephone interviews with public callers and questionnaire survey of doctors and nurses.	Direct medical costs	Averted emergency department visits, hospitalizations	Running costs of the poison centre were approximately the same as the estimated additional cost to the health care system if the service did not exist.	The poison centre does not incur more cost than not having a centre. Survey included all poisonings, including low-risk ones.
Personne & Persson, 2002 (Sweden) (9)	Survey of hospital doctors and members of the public who contacted the poison centre to determine what they would have done if they could not call a poison centre.	Direct medical costs	Time saved by doctors in seeking information, in-patient days, hospital admissions, general practitioner visits	Total estimated savings for society, approximately SEK 22 million, exceeding the SEK 20 million required for running the centre.	A poison centre offers a positive return on investment.
Elamin et al., 2018 (United Kingdom) (10)	Prospective telephone survey of primary health care providers who consulted a poisons information service and online survey of TOXBASE users. Enquirers asked to choose planned course of management before and after receiving advice.	Direct medical costs	Averted emergency hospital referrals	1178 telephone enquiries and 2028 toxicological database accesses from health care professionals over 2 months were analysed. Hospital referrals were reduced by > 40% after consultation with the poison centre or database. Extrapolation of these figures to estimate that 41 000 emergency hospital visits were avoided annually by poisons information service provision.	The estimated savings from avoided emergency referrals exceeded the budget of the poison centres, demonstrating cost-effectiveness.

Study	Method	Costs measured	Measure of effectiveness or benefit	Economic results	Conclusion
Western Pacific					
Ponampalam & Loh, 2010 (Singapore) (11)	Retrospective review of poison centre records for number of patients managed at home who would otherwise have gone to hospital and number of patients managed in the emergency department who would otherwise have been admitted.	Direct medical and personal costs	Averted emergency visits and hospital admissions; lost pay	Cost savings for patients who did not require hospital admission or an emergency department visit was SG\$ 1390, and SG\$ 1170 for patients managed in the emergency department visit. Saving for the hospital was SG\$ 1477 per case.	Use of a drug and poisons information centre resulted in significant cost savings to both the health care system and individuals.
Huynh et al., 2019 (Australia) (12)	Two prospective surveys of members of the public who called about unintentional poisoning. In the first, callers were asked what they would have done if they could not call the poisons information centre. The second was a follow-up survey to determine whether the caller followed the advice to stay at home.	Direct medical costs	Averted hospital visits	In the first survey, 19% would have gone to hospital. In the second survey, there was 97.6% adherence to poison centre advice. Estimated saving to the health service was AUS\$ 10.1 million (conservative estimate) to AUS\$ 39.6 million (high costs estimate).	In the absence of a poisons information service, health care costs would be three to four times higher.
West et al., 1987 (Australia) (13)	Telephone survey of members of the public who called about low-risk poisonings to determine what they would have done if there was no access to a poison centre.	Direct medical costs	Averted family doctor consultations and emergency department visits	A call to the poison centre costs on average AUS\$ 5.33, while a face-to-face consultation costs AUS\$ 20 and a telephone consultation with a family doctor costs AUS\$ 12. Costs incurred by consulting a hospital accident and emergency department (not formally evaluated) would be substantially higher.	A poison centre is a cost-effective way of providing advice about incidents requiring only reassurance or minimal treatment that can be administered at home. The costs incurred through such service are substantially lower than that of hospital accident and emergency departments or a family doctor.

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ANNEX 2. RESOURCES ON TOXICOLOGY AND GENERAL MEDICINE

This annex lists books and journals that were identified by members of the WHO expert group that reviewed this document as useful resources for a poison centre. Listing does not imply endorsement by the World Health Organization.

In addition to the resources suggested below, it is also recommended that the centre or a readily accessible library have up-to-date textbooks on paediatrics, nephrology, hepatology, pulmonary disease, gastroenterology, cardiology, ophthalmology, gynaecology, obstetrics, dermatology and psychiatry.

MEDICAL AND GENERAL TOXICOLOGY

IN ENGLISH

Ballantyne B, Marrs T, Syversen T, editors. General and applied toxicology. 3rd edition. Chichester: John Wiley & Sons; 2009.

Bateman DN, Jefferson RD, Thomas SHL, Thompson JP, Vale JA, editors. Oxford desk reference: toxicology. Oxford: Oxford University Press; 2014.

Bingham E, Cohns B, editors. Patty's toxicology. 6th ed. Vols 1–6. Hoboken (NJ): John Wiley & Sons, Inc.; 2012.

Brent J, Burkhart K, Dargan P, Hatten B, Megarbane B, Palmer R, et al., editors. Critical care toxicology. 2nd edition. Cham: Springer International Publishing; 2017.

Dart RC, editor. The 5 minute toxicology consult. Philadelphia (PA): Lippincott Williams & Wilkins; 2000.

Fernando R. Management of poisoning. 3rd edition. Colombo: National Poisons Information Centre; 2007.

Gupta PK. Illustrated toxicology. London: Academic Press; 2018.

Klaassen CD, editor. Casarett and Doull's toxicology: the basic science of poisons. 9th edition. New York City (NY): McGraw-Hill Education; 2019.

Murray L, Little M, Pascu O, Hoggett, KA. Toxicology handbook. 3rd edition. Sydney: Churchill Livingstone; 2015.

Nelson LS, Howland MA, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS, editors. Goldfrank's toxicologic emergencies. 11th edition. New York City (NY): McGraw-Hill Education; 2019.

Olson KR, Anderson IB, Benowitz NL, Blanc PD, Clark RF, Kearney TE, et al., editors. Poisoning and drug overdose. 7th edition. New York City (NY): McGraw-Hill Education; 2017.

Pandey K, Shukla JP, Trivedi SP. Fundamentals of toxicology. 4th edition. Kolkata: New Central Book Agency Pvt Ltd; 2011.

Pillay VV. Modern medical toxicology. 4th edition. New Delhi: Jaypee Brothers Medical Publishers; 2013.

Pillay VV. Comprehensive medical toxicology. 3rd edition. Hyderabad: Paras Medical Publisher; 2018.

IN FRENCH

Baud F, Garnier R. Toxicologie clinique. 6th edition. Paris: Lavoisier; 2017.

IN GERMAN

Dekant W, Vamvakas S. Toxikologie: Eine Einführung für Chemiker, Biologen und Pharmazeuten. 2nd edition. Munich: Elsevier GmbH; 2005.

Ludewig R, Regenthal R, editors. Akute Vergiftungen und Arzneimittelüberdosierungen. 11th edition. Stuttgart: Wissenschaftliche Verlagsgesellschaft; 2015.

von Mühlendahl KE, editor. Vergiftungen im Kindesalter. 4th edition. Stuttgart: Thieme; 2003.

Mutschler E, Geisslinger G, Kroemer HK, Schäfer-Korting M. Mutschler. Arzneimittelwirkungen. 10th edition. Stuttgart: Wissenschaftliche Verlagsgesellschaft; 2013.

Zilker TR. Klinische Toxikologie für die Notfall- und Intensivmedizin. Bremen: UNI-MED-Verlag; 2008.

IN ITALIAN

Olson KR. Intossicazioni acute. Veleni, farmaci e droghe. Mailand: Springer Verlag; 2009.

IN PORTUGUESE

Andrade Filho A, Campolina D, Dias MB Toxicologia na prática clínica. 2nd edition. Belo Horizonte: Folium; 2013.

Hernández EMM, Rodríguez RMR, Torres TM. Manual de toxicología clínica: orientações para assistência e vigilância das intoxicações agudas. São Paulo: Secretaria Municipal da Saúde; 2017.

Oga S, Camargo MMA, Batistuzzo JAO. Fundamentos de toxicología. 4th edition. São Paulo: Atheneu; 2014.

IN SPANISH

Córdoba Palacio C, editor. Toxicología. 5th edición. Bogotá: Manual Moderno; 2006.

Giménez Poderós T. Guía de utilización de antidotos. Santander: Servicio de Farmacia, Hospital Universitario Marqués de Valdecilla; 2016.

Harris CR. Manual de toxicología para médicos. Barcelona: Elsevier; 2008.

Klaassen CD. Manual de toxicología clínica la ciencia básica de los tóxicos. México DF: McGraw-Hill Interamericana; 2001.

Klaassen CD. Cassarett y Doull. Fundamentos de toxicología. Madrid: McGraw-Hill Interamericana, DL; 2005.

Lazcano R. Toxicología clínica. Buenos Aires: Akadia; 2003.

Mintegi S. Manual de Intoxicaciones en pediatría. 3rd edición. Madrid: Ergon; 2012.

Morán Chorro I, Baldirá Martínez de Irujo J, Marruecos-Sant L, Nogué Xarau S. Toxicología clínica. Madrid: Difusión Jurídica y Temas de Actualidad; 2011.

Net A, Marruecos L. Intoxicaciones agudas graves. Barcelona: Ars Medica; 2006.

Nogué S. Toxicología clínica para médicos de urgencias. Barcelona: Laboratorios Menarini DL; 2009.

Repetto Jiménez M, Repetto Kuhn G. Toxicología fundamental. 4th edición. Madrid: Díaz De Santos; 2009.

Talamoni M, Crapanzano G, López Sarmiento C. Guía de diagnóstico y tratamiento en toxicología. Buenos Aires: Editorial Universitaria de Buenos Aires; 2004.

PHARMACEUTICALS

IN ENGLISH

SERIALS

American Hospital Formulary Service drug information. Bethesda (MD): American Society of Health System Pharmacists (annual publication).

Joint Formulary Committee. British National Formulary. London: British Medical Association, The Pharmaceutical Press (published twice a year).

Model list of essential medicines. 21st edition (WHO/MVP/EMP/IAU/2019.06). Geneva: World Health Organization; 2019 (<https://apps.who.int/iris/handle/10665/325771>, accessed 16 April 2020).

Paediatric Formulary Committee. BNF for children. London: The Pharmaceutical Press (annual publication).

Physicians' desk reference. Whippany (NJ): PDR Network; 2018 (published annually).

BOOKS

Aronson JK, editor. Meyler's side effects of drugs: the international encyclopedia of adverse drug reactions and interactions. 16th edition. Amsterdam: Elsevier; 2015.

Ashley C, Dunleavy A. The renal drug handbook: the ultimate prescribing guide for renal practitioners. 5th edition. Boca Raton (FL): Taylor & Francis Group; 2019.

Brayfield A, editor. Martindale: the complete drug reference, 39th edition. London: Pharmaceutical Press; 2017.

Briggs GG, Freeman RK, Towers CV, Forinash AB. Drugs in pregnancy and lactation: a reference guide to fetal and neonatal risk. 11th edition. Philadelphia (PA): Wolters Kluwer; 2017.

Brown M, Sharma P, Mir F, Bennett PN. Clinical pharmacology. 12th edition. Edinburgh: Elsevier; 2019.

Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman & Gilman's: The pharmacological basis of therapeutics. 13th edition. New York City (NY): McGraw-Hill Education; 2018.

Hale TW. Hale's medications and mother's milk. 18th edition. New York City (NY): Springer Publishing Company; 2018.

Hansten PD, Horn JR. Top 100 drug interactions: a guide to patient management. Freeland (WA): H&H Publications; 2019.

Preston CL, editor. Stockley's drug interactions. 12th edition. London: Pharmaceutical Press; 2019.

Schaefer C, Peters PWJ, Miller RK, editors. Drugs during pregnancy and lactation. 3rd edition. London: Academic Press; 2014.

IN GERMAN

Linse I, Wulff B, von Harnack GA, Janssen F (Begr.). Pädiatrische Dosistabellen: Dosierung kinderärztlich verordneter Arzneimittel. 15th edition. Stuttgart Wissenschaftliche Verlagsgesellschaft; 2018.

IN SPANISH

Finkel R, Clark MA, Cubeddu LX. Farmacología. Barcelona: Lippincott William & Wilkins; 2009.

Rodriguez Carranza R, Vidrio H, Campos Sepúlveda AE. Guía de farmacología y terapéutica. México DF: McGraw-Hill; 2007.

OCCUPATIONAL AND INDUSTRIAL TOXICOLOGY

IN ENGLISH

Baxter PJ, Aw TC, Cockcroft A, Durrington P, Harrington JM, editors. Hunter's disease of occupations. 10th edition. London: Hodder Arnold; 2010.

Greim H, editor. The MAK-collection for occupational health and safety. Part 1: MAK value documentations. Vols 1–27. Weinheim: Wiley VCH; 2013.

Harbison RD, Bourgeois MM, Johnson GT, editors. Hamilton & Hardy's industrial toxicology. 6th edition. Hoboken (NJ): John Wiley & Sons, Inc; 2015.

Krieger RI, editor. Haye's handbook of pesticide toxicology. 3rd edition. London: Academic Press; 2010 (2 volumes).

Lewis RJ, editor. Sax's dangerous properties of industrial materials. 12th edition. Hoboken (NJ): John Wiley & Sons, Inc; 2012.

Lewis RJ, editor. Hazardous chemicals desk reference. 6th edition. Hoboken (NJ): John Wiley & Sons, Inc.; 2008.

O'Neil MJ, editor. Merck index: an encyclopedia of chemicals, drugs and biological. 15th edition. London: The Royal Society of Chemistry; 2013.

Roberts JR, Reigart JR. Recognition and management of pesticide poisoning. 6th edition. Washington DC: Environmental Protection Agency; 2013.

Rose VE, Cohrssen B, editors. Patty's industrial hygiene. Hazard recognition. 6th edition. Hoboken (NJ): John Wiley & Sons, Inc; 2011 (4 volumes).

Turner JA, editor. The pesticide manual – a world compendium. 18th edition. Aldershot: British Crop Protection Council; 2018.

IN FRENCH

Encyclopédie medico-chirurgicale EMC. Pathologie professionnelle et environnementelle. Paris: Elsevier Masson; 2019.

IN GERMAN

Kurzweil P. Toxikologie und Gefahrstoffe: Gifte – Wirkungen – Arbeitssicherheit. Haan-Gruiten: Europa-Lehrmittel; 2013.

IN PORTUGUESE

Mendes R. Patologia do trabalho. 3rd edition. São Paulo: Atheneu; 2013.

IN SPANISH

Delgado Bueno S, Bandrés Moya F, Lucena Romero J. Tratado de medicina legal y ciencias forenses. Volumen 2: Toxicología forense. Barcelona: Bosch; 2011.

ANALYTICAL TOXICOLOGY

IN ENGLISH

Ashley K, O'Connor PF. NIOSH manual of analytical methods (NMAM). 5th edition. Cincinnati (OH): National Institute for Occupational Safety and Health; 2017.

Baselt RC. Disposition of toxic drugs and chemicals in man. 11th edition. Seal Beach (CA): Biomedical Publications; 2017.

Flanagan RJ, Braithwaite RA, Brown SS, Widdop B, de Wolff FA. Basic analytical toxicology. Geneva: World Health Organization; 1995 (<http://www.who.int/iris/handle/10665/37146>).

Flanagan RJ, Taylor AA, Watson ID, Whelpton R. Fundamentals of analytical toxicology. Chichester: John Wiley & Sons Ltd; 2007.

Külpmann WR, editor. Clinical toxicological analysis. Weinheim: Wiley-VCH; 2009 (2 volumes).

Moffat AC, Osselton MD, Widdop B, Watts J, eds. Clarke's analysis of drugs and poisons. 4th edition. London: Pharmaceutical Press; 2011 (2 volumes).

United Nations Division of Narcotic Drugs. Drug testing laboratories [website]: Recommended methods for identification and analysis of [individual and groups of drugs of abuse]. New York: United Nations; 2005–2018 (<https://www.unodc.org/unodc/en/scientists/publications-drug-testing-laboratories.html>).

IN PORTUGUESE

Moreau RLM, Siqueira MEPB. Toxicologia analítica. Rio de Janeiro: Guanabara Koogan; 2010.

NATURAL TOXINS

Books on natural toxins should be acquired according to the incidence of risks of poisoning by animals or plants in the geographical area concerned. Illustrated guides, with drawings, photographs or even specimens, are very useful for the identification of local plants and animals (for example, fungi, snakes, spiders, scorpions, insects, marine animals). The most relevant literature is that published in the country concerned; however, some books are proposed that include natural toxins distributed worldwide.

IN ENGLISH

Barceloux DG, editor. Medical toxicology of natural substances: foods, fungi, medicinal herbs, plants and venomous animals. Hoboken (NJ): John Wiley & Sons; 2008.

PLANTS

Cooper MR, Johnson AW, Dauncey EA, editors. Poisonous plants and fungi: an illustrated guide, 2nd edition. London: HM Stationery Office; 2003.

Frohne D, Pfandner HJ. Poisonous plants: a handbook for doctors, pharmacists, toxicologists, biologists and veterinarians. London: Manson Publishing Ltd; 2005.

Nelson LS, Shih RD, Balick MJ, editors. Handbook of poisonous and injurious plants, 2nd edition. New York City (NY): Springer; 2007.

VENOMOUS ANIMALS

Das I. A naturalist's guide to the snakes of southeast Asia. 2nd edition. Oxford: John Beaufoy Publishing Ltd; 2018.

Guidelines for the management of snakebites. 2nd edition. New Delhi: WHO Regional Office for South-East Asia; 2016 (<http://www.who.int/iris/handle/10665/249547>, accessed 16 April 2020).

Guidelines for the prevention and clinical management of snakebite in Africa. Brazzaville: WHO Regional Office for Africa; 2010 (<https://apps.who.int/iris/handle/10665/204458>, accessed 16 April 2020).

Mebs D. Venomous and poisonous animals: a handbook for biologists, toxicologists and toxinologists, physicians and pharmacists. Stuttgart: Medpharm GmbH Scientific Publishers; 2002.

White J. A clinician's guide to Australian venomous bites and stings: incorporating the updated CSL antivenom handbook. Parkville: CSL Ltd; 2013.

IN PORTUGUESE

Cardoso JLC, França FOS, Wen FH, Málaque CMS, Haddad Junior V. Animais peçonhentos no Brasil: Biologia clínica e terapêutica dos acidentes. São Paulo: Sarvier; 2003.

IN SPANISH

Bergillos F. Toxinología clínica: lesiones por picaduras y mordeduras de animales. Tomo I–II. Madrid: Bubok Publishing SL; 2013.

Bruno S, Mauger S. Guía de las serpientes en Europa. Barcelona: Ediciones Omega SA; 1992.

Catálogo de plantas medicinales 2007. Colección Consejo Plus. Madrid: Consejo General de Colegios Oficiales de Farmacéuticos, D.L.; 2007.

Nogué S, Simón J, Blanché C, Piqueras J. Intoxicaciones por plantas y setas. Barcelona: Laboratorios Menarini; 2009.

Pronczuk J, Laborde A, Fernández S. Plantas silvestres y de cultivo. Montevideo: Universidad de la Republica; 2007.

CHEMICAL WARFARE

IN ENGLISH

Gupta RC. Handbook of toxicology of chemical warfare agents. 2nd edition. London: Academic Press; 2015.

Marrs TC, Maynard RL, Sidell FR. Chemical warfare agents: toxicology and treatment. Chichester: John Wiley & Sons; 2007.

Practical guide for medical management of chemical warfare casualties. The Hague: Organisation for the Prohibition of Chemical Weapons; 2019

SPECIALIZED ASPECTS OF TOXICOLOGY

Publications on the toxicology of the eye, central nervous system, heart, lung, kidney, liver, and skin and on toxins and cancer, effects of drugs in pregnancy and lactation and drugs of abuse may be required for information on specific target organs or systems. Examples are given below.

IN ENGLISH

Barceloux DG. Medical toxicology of drug abuse: synthesized chemicals and psychoactive plants. Hoboken (NJ): John Wiley & Sons; 2012.

Dargan PI, Wood DM, editors. Novel psychoactive substance: classification, pharmacology and toxicology. London: Academic Press; 2013.

Dobbs MR. Clinical neurotoxicology: syndromes, substances, environments. Philadelphia (PA): Saunders; 2009.

Fowler JF, Zirwas MJ, editors. Fisher's contact dermatitis. 7th edition. Phoenix (AZ): Contact Dermatitis Institute; 2016.

Karch SB, Goldberger BA. Drug abuse handbook. 3rd edition. Boca Raton (FL): CRC Press; 2013.

IN GERMAN

Schäfer C, Spielmann H, Vetter K, Weber- Schöndorf C, editors. Arzneimittel in Schwangerschaft und Stillzeit. 8th edition. Munich: Elsevier; 2011.

IN PORTUGUESE

Dorta D J, Yonamine M, Costa JL, Martinis BS. Toxologia forense. São Paulo: Blucher; 2018.

VETERINARY TOXICOLOGY

IN ENGLISH

Anderson DE, Rings DM. Current veterinary therapy: food animal practice. 5th edition. St Louis (MI): Saunders; 2009.

Bonagura JD, Twedt DC. Kirk's current veterinary therapy XV. St Louis (MI): Saunders; 2014.

Gupta RC, editor. Veterinary toxicology: basic and clinical principles. London: Elsevier Inc.; 2018.

Plumb DC. Plumb's veterinary drug handbook. 8th edition. Stockholm: Pharmavet Inc.; 2015.

Riviere JE, Papich MG, editors. Veterinary pharmacology and therapeutics. 10th edition. Hoboken (NJ): John Wiley & Sons, Inc.; 2018.

Sprayberry KA, Robinson NE. Robinson's current therapy in equine medicine. 7th edition. St Louis (MI): Saunders; 2014.

IN GERMAN

Löscher W, Richter A, editors. Lehrbuch der Pharmakologie und Toxikologie für die Veterinärmedizin Toxikologie für Veterinärmediziner. 4th edition. Stuttgart: Enke; 2016.

IN PORTUGUESE

Spinosa HS, Górnica SL, Palermo-Neto J. Toxicologia aplicada à medicina veterinária. São Paulo: Manole; 2008.

CHILDREN'S ENVIRONMENTAL HEALTH

Etzel R, Balk SJ, editors. Pediatric environmental health. 4th edition. Ithaca (IL): American Academy of Pediatrics Council on Environmental Health; 2019.

Pronczuk-Garbino J, editor. Children's health and the environment – a global perspective. Geneva: World Health Organization; 2005 (<https://apps.who.int/iris/handle/10665/43162>, accessed 16 April 2020).

Childhood lead poisoning. Geneva: World Health Organization; 2010 (<https://apps.who.int/iris/handle/10665/136571>, accessed 16 April 2020).

Persistent organic pollutants: impact on children's health. Geneva: World Health Organization; 2010 (<https://apps.who.int/iris/handle/10665/44525>, accessed 16 April 2020).

Training modules covering a wide range of environmental hazards [website]. Geneva: World Health Organization (https://www.who.int/ceh/capacity/training_modules/en/, accessed 16 April 2020).

ECOTOXICOLOGY AND ENVIRONMENTAL TOXICOLOGY

Books on ecotoxicology and environmental toxicology are useful because poison centres are frequently involved in, or consulted about, the management and assessment of environmental problems and their effects on health.

IN ENGLISH

Ayres JG, Harrison RM, Nichols GL, Maynard RL, editors. Environmental medicine. London: Hodder Arnold; 2010.

Mudu P, Terracini B, Martuzzi M, editors. Human health in areas with industrial contamination. Copenhagen: WHO Regional Office for Europe; 2014 (<https://apps.who.int/iris/handle/10665/144490>, accessed 16 April 2020).

Air quality guidelines for Europe. 2nd edition. Copenhagen: WHO Regional Office for Europe; 2001 (<https://apps.who.int/iris/handle/10665/107335>, accessed 1 December 2019).

Guidelines for drinking-water quality. 4th edition incorporating the first addendum. Geneva: World Health Organization; 2017 (<https://apps.who.int/iris/handle/10665/254637>, accessed 16 April 2020).

IN SPANISH

de la Peña de Torres E, Gómez Campoy E. Toxicología ambiental: seguridad química. Murcia: Asociación Española de Toxicología; 2004.

Valverde Villarreal JL, Pérez De-Gregorio Capella JJ. Manual de toxicología medioambiental forense. Madrid: Centro de Estudio Ramón Areces, DL; 2001.

Moreno Grau D. Toxicología ambiental: evaluación de riesgo para la salud humana. Madrid: McGraw Hill, DL; 2003.

JOURNALS

Access to journals that cover toxicological topics is also important. Some well-established journals are listed below.

IN ENGLISH

- American Journal of Industrial Medicine. Published by Wiley, Hoboken (NJ), USA.
- Annals of Work Exposures and Health. Published by Oxford University Press, Oxford, United Kingdom.
- Archives of Environmental Contamination and Toxicology. Published by Springer US, New York City (NY), USA.
- Archives of Environmental & Occupational Health. Published by Taylor and Francis Inc., Philadelphia, USA.
- Archives of Toxicology. Published by Springer, Berlin, Germany.
- Biochemical Pharmacology. Published by Elsevier, Amsterdam, Netherlands.
- Occupational and Environmental Medicine. Published by The British Medical Journal, London, England.
- Clinical Toxicology. Published by Taylor and Francis Group, Abingdon-on-Thames, United Kingdom.
- Drug Safety (formerly Medical Toxicology). Published by ADIS International Springer Nature, New York City (NY), USA.

- Environmental Health Perspectives. Published by the Department of Health and Human Services, National Institute of Environmental Health Sciences, Research Triangle Park (NC), USA.
- Human and Experimental Toxicology. Published by Sage Publications, Thousand Oaks (CA), USA.
- Journal of the Indian Society of Toxicology. Published by the Indian Society of Toxicology, Pondicherry, India.
- Journal of Occupational and Environmental Hygiene. Published by Taylor and Francis Group, Abingdon-on-Thames, United Kingdom.
- Journal of Medical Toxicology. Published by Springer, Berlin, Germany.
- Neurotoxicology. Published by Elsevier, Amsterdam, Netherlands.
- Scandinavian Journal of Work, Environment and Health. Published by the Nordic Association of Occupational Safety and Health, Helsinki, Finland.
- Toxicology. Published by Elsevier, Amsterdam, Netherlands.
- Toxicology and Applied Pharmacology. Published by Academic Press, San Diego (CA), USA.
- Toxicology Letters. Published by Elsevier, Amsterdam, Netherlands.
- Toxicon. Published by Elsevier, Amsterdam, Netherlands.

IN FRENCH

- Archives des maladies professionnelles de médecine du travail et de sécurité sociale. Published by Elsevier, Paris, France.
- Bulletin d'information toxicologique. Published by l'Institut national de santé publique du Québec et le Centre antipoison du Québec, Quebec, Canada.
- Thérapie. Published by Elsevier, Paris, France.

IN ITALIAN

- La Medicina del lavoro. Published by Mattioli1885 srl, Fidenza, Italy.
- Giornale Italiano di Medicina del Lavoro ed Ergonomia. Published by ICS Maugeri, Pavia, Italy.

IN PORTUGUESE

- Revista brasileira de toxicologia. São Paulo, Brazil. Replaced by Applied Research in Toxicology.

IN SPANISH

- Acta Toxicologica Argentina. Published by Portal of Scientific and Technical Publications, Buenos Aires, Argentina.
- Revista de Toxicología. Published by Asociación Española de Toxicología, Valencia, Spain.
- Revista de Salud Ambiental. Published by Madrid Sociedad Española de Sanidad Ambiental, Madrid, Spain.

Table A2.1 lists online resources on toxicology and general medicine.

Table A2.1. Online resources on toxicology and general medicine¹³

Many of these resources are available free-of-charge or at low cost.

Name	URL	Type of information available	Cost
AfriTox	https://www.afritox.co.za	Poisons information database to guide the diagnosis and management of poisoning, with a focus on southern Africa. Information is in English only.	Requires registration for full access. Subscription charged to hospitals and others. Special arrangements for access by African poison centres.
Agency for Toxic Substances and Disease Registry (ATSDR)	http://www.atsdr.cdc.gov/	Under the US Department of Health and Human Services; publishes monographs reviewing the toxicology of a range of chemicals. Information is mainly in English, however, some summaries are provided in other languages.	Free, without registration.
Canadian Centre for Occupational Health and Safety (CCOHS)	https://www.ccohs.ca/products/&page=1	Several databases, including the Registry of Toxic Effects of Chemical Substances (RTECS) and Hazardous Substances Data Bank (see below) as well as in-house data. Many of the databases are in English only, however, some information is also available in French.	Free for some resources; full access requires a paid subscription.
Chemical Abstracts Service (CAS)	https://www.cas.org/	Authoritative source for chemical names, structures and substances, which is updated daily. Also provides numerous references with further chemical information. Information is available in English, Chinese, Japanese, Portuguese and Spanish.	Free, without registration.
Consumer Product Information Database	https://www.whatsinproducts.com/pages/index/1	Database of over 21 000 consumer products available in North America. Provides information about the ingredients of products and their health effects. Information is in English only.	Free, without registration.

¹³ Adapted from Annex 1 of *Improving the availability of poison centre services in East Africa*. Geneva; World Health Organization; 2015 (https://www.who.int/ipcs/poisons/centre/study_afro/en/).

Name	URL	Type of information available	Cost
eChemPortal	https://www.echemportal.org/echemportal/	Open access to information on chemicals from numerous organizations globally. Information includes physical and chemical properties, ecotoxicity, environmental fate and behaviour and toxicity. The portal allows simultaneous searching in several collections of chemical hazard and risk information. Most of the information is in English, however, there may be information on specific chemicals in other languages such as French.	Free, without registration.
European Chemicals Agency	http://echa.europa.eu/information-on-chemicals	The central agency that implements the European Union's chemicals legislation to protect people and the environment from the hazards of chemicals. Publicly accessible database on over 245 000 chemicals. Much of the information on chemicals is in English. Other information is available in the official languages of the EU.	Free, registration required.
European Food Safety Authority (EFSA)	https://efsa.onlinelibrary.wiley.com/journal/18314732 https://data.europa.eu/euodp/en/data/dataset/openfoodtox-efsa-chemical-hazards-database	The EFSA Journal is an open-access, English-language scientific journal that publishes the scientific output of the European Food Safety Authority, including toxicological evaluations and risk assessments of chemicals in food and feed. The EFSA Chemical Hazards Database, OpenFoodTox, provides open-source data for substance characterization, links to the relevant EFSA output, background regulations and summaries of critical toxicological end-points. Summary data sheets for each substance can be downloaded in PDF or Excel format. Information is in English.	Free, without registration.
Hazardous Substances Data Bank	https://pubchem.ncbi.nlm.nih.gov/ Information on finding the data bank in PubChem: https://www.nlm.nih.gov/toxnet/Accessing_HSDB_Content_from_PubChem.html	Comprehensive, peer-reviewed toxicology data on about 5000 chemicals. Included in the US National Library of Medicine PubChem collection. Information is in English only.	Free, without registration.

Name	URL	Type of information available	Cost
INCHEM	http://www.inchem.org	Peer-reviewed information on commonly used chemicals that may also occur as contaminants in the environment and food. Consolidates information from several intergovernmental organizations.	Free, without registration.
Integrated Risk Information System (IRIS)	https://www.epa.gov/iris	US Environmental Protection Agency programme that identifies and characterizes the health hazards of chemicals in the environment. Information is in English only.	Free, without registration.
International Chemical Safety Cards (ICSCs)	http://www.ilo.org/dyn/icsc/showcard.home	Data sheets that provide essential safety and health information on chemicals in a clear, concise way. Available in numerous languages.	Free, without registration.
National Center for Biotechnology Information (NCBI) Bookshelf	http://www.ncbi.nlm.nih.gov/books	Collection of texts on general medical subjects, with access to some toxicological material. Information is in English only.	Free, without registration.
Pan American Health Organization collection on Toxicology	https://www.paho.org/hq/index.php?option=com_content&view=article&id=7395:toxicologia&Itemid=39622&lang=en https://www.paho.org/hq/index.php?option=com_content&view=article&id=7395:toxicologia&Itemid=39622&lang=es	Collection of documents and training materials in English and Spanish on selected chemicals such as lead, mercury and pesticides.	Free, without registration.
POISINDEX	https://www.ibm.com/downloads/cas/5VLP4LGW	Poisons information database widely used in Europe, the USA and elsewhere. Data on products weighted to developed world markets. Information is in English only.	Price on application. May be discounted for low-income countries.
PubChem	https://pubchem.ncbi.nlm.nih.gov/	US National Library of Medicine integrated collection of information on chemicals from numerous databases, including those of international organizations and US regulatory agencies. Information is in English only.	Free, without registration

Name	URL	Type of information available	Cost
Public Health England Chemical hazards compendium	https://www.gov.uk/government/collections/chemical-hazards-compendium	Collection of documents on selected chemicals. Three types of information are provided on each chemical: general information, a toxicological overview and incident management, with information such as physicochemical properties, health effects and decontamination.	Free, without registration.
Répertoire toxicologique	https://www.csst.qc.ca/prevention/reptox/pages/repertoire-toxicologique.aspx	Provides information on chemical or biological products used in the workplace. Most of the information is in French, however, some summaries may be in English.	Free, without registration.
Rotterdam Convention Decision Guidance Documents	http://www.pic.int/TheConvention/Chemicals/DecisionGuidanceDocuments/tabid/2413/language/en-US/Default.aspx	Documents summarizing physico-chemical properties and environmental and health impacts of chemicals listed or being considered for listing under the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. Information is typically available in English, French and Spanish. Some information is also available in Arabic, Chinese and Russian.	Free, without registration.
TOXBASE	www.toxbase.org iOS and Android app version available for subset of data	United Kingdom clinical toxicology database, intended for use by poison centres and health professionals. Information is in English only.	Price on application. May be discounted for low-income countries.
ToxED	http://www.toxed-ip.com/ToxEdSolutions.aspx?epm=2_1	Electronic clinical toxicology reference for quick access to concise, comprehensive information at points of care for diagnosis and treatment of poisoning, drug overdoses and exposure to chemicals and hazardous waste. Information is in English only.	Price on application.
TOXINZ	http://www.toxinz.com	New Zealand poisons information database of about 200 000 chemicals (drugs, pesticides, household products and natural toxins). Information is in English only.	Price on application. May be discounted for low-income countries. Available free of charge or at low cost through Hinari (https://www.who.int/hinari/en/).

Name	URL	Type of information available	Cost
ToxToolBox	http://toxtoolbox.com	Database of clinical summaries, formulas and management guidelines for toxic exposures. Information is in English only.	Free, without registration.
Centers for Disease Control and Prevention emergency preparedness and response	https://emergency.cdc.gov/chemical/	Collection of information on chemical emergencies, including the deliberate release of chemicals. Information is mainly in English, however, some summaries are provided in other languages.	Free, without registration.
Environmental Protection Agency Comptox Chemicals Dashboard	https://www.epa.gov/chemical-research/comptox-chemicals-dashboard	Provides access to information on chemistry, toxicity and exposure for over 875 000 chemicals. Information is in English only.	Free, without registration.
WikiTox	http://www.wikitox.org/doku.php?id=wikitox:wikitox_home	Open-access curriculum project to improve the treatment of people who are poisoned. Information is in English only.	Free, without registration.
Wireless Information System for Emergency Responders (WISER)	https://webwiser.nlm.nih.gov/getHomeData.do?jsessionid=E B1106312C2618D4804DE10 DE8654252 Also available as a smartphone App	US National Library of Medicine. Provides information on hazardous substances for emergency responders, including physical characteristics, human health effects and containment advice. Can be used to find symptoms. Information is in English only.	Free, without registration
General resources			
Free Open Access Medication (FOAM / FOAMed)	https://litfl.com/foam-free-open-access-medical-education/	Search platform for a collection of open-access medical education resources. Created to complement published educational material such as textbooks and journal articles. Information is in English only.	Free, without registration.
FOAMed FOAMtox	http://www.emdocs.net/category/foamtox/	Free Open Access Medication (FOAMed) and information on toxicology (FOAMTox). Information is in English only.	

ANNEX 3. INFORMATION TO BE DOCUMENTED IN AN ENQUIRY RECORD

This annex lists the typical data fields in an enquiry record, provides an explanation for each data item and suggests whether data items should be recorded with free text or controlled text. This information is usually held on a computerized database, and use of controlled text greatly facilitates data analysis and helps to avoid data being missed because a term was misspelt or because a different, synonymous term was used.

For most of the data fields in which use of controlled text is suggested, “authority lists” and definitions are available, which were prepared by WHO with international working groups to ensure harmonized data collection by different poison centres. The lists are available at: <https://www.who.int/ipcs/poisons/harmonization/en/>.

Field	Suggested type of information	Purpose
Communication		
Identification number	Controlled text	Each record should have a unique identification number, which is usually a sequential number and may include the year, e.g. 2019/00001, 2019/00002. The poison centre decides the format. When cases are entered directly into a computerized database, the system usually assigns the number automatically.
Date and time of call	Controlled text	The date and time of each enquiry should be logged on the record. When cases are entered directly into a computerized database during the enquiry, the system can be set up to do this automatically.
Name of poisons information scientist	Free text or locally generated list	The identity of the person who dealt with the enquiry and completed the enquiry record must be documented for medico-legal and audit reasons and if information must be checked. In computerized databases, the identity may be filled in automatically according to the log-in.
Title, name, telephone number of the caller	Free text	Documentation of the name and telephone number of the person who is contacting the centre will enable further contact with the person if necessary, e.g. to obtain follow-up information. The enquirer's telephone number is very important and should be one of the first items noted, in case the telephone connection is lost. If an individual is calling from within an organization, the caller's extension, direct line or mobile telephone number should be taken rather than the organization's main (central) number.
Category of caller	Controlled text	The type of caller making the enquiry, e.g. a health or other professional, a member of the public or a member of the patient's family provides background information about the caller so that advice can be tailored appropriately. Analysis of this information can help to characterize the user population of the poison centre.

Field	Suggested type of information	Purpose
Location of the caller	Controlled text	The type of location from which the caller is contacting the centre, e.g. ambulance, home, hospital or other health care facility, provides a guide to the facilities that are likely to be available to treat the patient and, therefore, the kind of information and advice that is relevant. In complex cases, with many calls from different departments, information on location may be helpful for tracking the patient and locating the caller if it is necessary to contact them again. Analysis of this information provides data on the types of organization served by the poison centre.
Name of hospital, clinic or other organization (including telephone number)	Free text or locally generated list	Ideally, the organization name can be selected from a controlled list, at least for regular sources of enquiries such as hospitals, as this avoids any spelling errors.
Reason for enquiry	Controlled text	The reason for the enquiry may be a case of actual or suspected poisoning, an incident or a request for specific information (e.g. for prevention, information). Analysis of this information indicates the kinds of demands made of the centre and therefore the resources it requires.
Method of communication	Controlled text	Communications may be either incoming (telephone call to the centre) or outgoing (contact with the enquirer) and involve various media (e.g. telephone, videoconference, e-mail, letters, personal contact). As most enquiries are incoming telephone calls, a computerized database may set this as the default entry. Each poison centre will decide whether to log the communication medium and outgoing communications in a single database; some may prefer to log only incoming telephone enquiries.
Circumstances of exposure	Controlled text or combination of controlled and free text	Information on whether the exposure was accidental, intentional or occurred through misuse can indicate the probable severity of the exposure (e.g. a child who accidentally swallows bleach is unlikely to ingest as much as an adult who deliberately swallows bleach). This information is also useful for toxicovigilance and prevention and may be of interest for regulatory risk assessment.
Location of exposure	Controlled text	Where an exposure occurs is of interest because it extends the information about how the exposure occurred. Examples of locations include the home, workplace, enclosed public space, open public space. This information is helpful for toxicovigilance, prevention and risk assessment. Several exposures at the same type of location may indicate that a chemical release has occurred.
Number of patients	Numerical value	If an incident involves several patients, it is important to document the number to indicate the scale of the incident. This number can also be used to check if there are individual enquiry records for all the patients.
Referral	Free text or locally generated list	If a consultant or other specialist attached to the poison centre advised on the patient's management, this should be documented for medico-legal and audit reasons and if information must be checked.

Field	Suggested type of information	Purpose
Agent		
Agent name as given by caller	Free text	The name(s) of the agent(s) provided by the enquirer should be documented, even if it is not the correct name. This may be important for medico-legal reasons and is useful for toxicovigilance.
Agent name	Free text or locally generated list	The name(s) of the agent(s) involved in the exposure and the main toxic ingredient(s) should be documented. Some callers may provide an incomplete name, e.g. "Harpic toilet cleaner" or "snake", while the specialist in poisons information has made a judgement about the probable identity of the agent, e.g. "Harpic descaler and toilet cleaner" or "adder". Some poison centres document both the name given by the caller and the name identified by the specialist in poisons information for medico-legal purposes. When enquiries are documented in a computerized system, an internally generated controlled list of agent names should be used rather than free text to avoid misspellings and chemical synonyms (e.g. aspirin and aspirin; isopropyl alcohol and isopropanol) and facilitates analysis of the database. This information is also important for toxicovigilance. A detailed classification of agents facilitates database searching.
Agent category	Free text or classification	The type of agent is classified, e.g. as insecticide, window cleaner, lipstick. Although the information may be entered as free text, use of a classification scheme will facilitate database searching. The scheme should be hierarchical so that the database can be searched for general or more specific categories, e.g.: P1. Pesticide P1.1. Organochlorine P1.1.1. Aldrin P1.1.1.2. Dieldrin P1.2. Organophosphate
Amount	Numerical value, with units	The amount of the agent to which the patient was exposed is required for clinical risk assessment at the time of the call and is also important for subsequent evaluation of exposures to the agent. Even if the amount is expressed in vague terms, e.g. "a few tablets" or "a sip", or is unknown, this should be recorded.
Type of exposure	Controlled text	Whether the exposure was acute, chronic or acute on chronic

Field**Suggested type of information** **Purpose**

Duration of exposure

Numerical value,
with units

The time over which the exposure occurred is relevant for certain kinds of poisoning, such as a staggered overdose (e.g. high doses of an analgesic taken over several days) or inhalation of carbon monoxide for several hours.

Time since exposure

Numerical value,
with units

The time that has elapsed between the patient's exposure to the agent and the enquiry to the poison centre is important information for clinical risk assessment, e.g. whether enough time has elapsed for the agent to have started exerting toxicity. If so and if the patient is asymptomatic, the exposure may have been to a dose that is unlikely to be toxic.

Route of exposure

Controlled text

All routes of exposure to the agent should be recorded, the most common being ingestion, inhalation, dermal contact and ocular. The route of exposure is important for judging the risk of poisoning, as it influences the rate of absorption of the agent and the parts of the body that may be harmed.

Patient

Name

Free text

The poison centre should decide its policy for documenting patients' names. This may be determined by national policy on patient confidentiality. The patient's name is important for obtaining follow-up information on the outcome of poisoning. It is also essential for longer studies; e.g. in the case of occupational exposure to chemicals, workers may be followed up several years after the enquiry to the centre. An alternative to the patient's name is the patient's hospital identification number.

Date of birth

Free text

The date of birth is useful because many health care organizations use it as an additional means of identifying patients. The date of birth may be the sole means of distinguishing between two patients with the same name.

Weight

Numerical value,
with units

This information allows calculation of the body burden of a toxic agent and may also be necessary to calculate the dose of antidote or other drug therapy.

Height

Numerical value,
with units

This information is required for calculating body surface area, which is used in determining dosage for infants.

Address and telephone number

Free text

The poison centre should decide its policy for documenting patients' addresses. This information can facilitate the follow-up of a case when the patient leaves hospital and may be useful for toxicovigilance and prevention, as it may indicate that a particular poisoning problem is confined to a certain locality (e.g. lead poisoning in children living in an area where used lead-acid batteries are recycled informally). A telephone number at which the patient can be contacted enables follow-up calls to determine the outcome of the poisoning incident, particularly if the patient has been advised to stay home rather than go to hospital.

Field	Suggested type of information	Purpose
Gender	Controlled text	Gender is important for identifying the patient and for epidemiological purposes. The enquirer may not know the patient's gender initially, referring only to "a baby", "a worker", "a worker" or "a victim".
Age	Numerical value, with units	The age of the patient provides useful epidemiological information about poisoning and information for toxicovigilance and prevention.
Age category	Controlled text	If the enquirer does not know the age of the patient, he or she can usually indicate the age group, e.g. infant, adolescent or adult.
Occupation	Controlled text	The patient's occupation has obvious relevance for workplace exposure. If the agent is unknown, knowledge of the occupation may indicate agents to which the patient may have been exposed.
Pregnancy and trimester	Controlled text	If a female patient is of reproductive age, it is important to consider whether she might be pregnant, as the fetus could also be at risk. The fact of a patient being pregnant and the trimester of pregnancy may affect the risk assessment and decisions about management. Moreover, documentation of exposures occurring in pregnancy is valuable for determining the possible harmful effects on the fetus of exposure to chemicals and drugs. The patient may be documented as possibly pregnant, i.e. not confirmed with a pregnancy test.
Lactation	Controlled text	In cases of poisoning in lactating mothers, certain agents are secreted into breast milk, and appropriate advice may be needed.
Clinical features	Controlled text, multi-select	Clinical features should be documented with controlled text to avoid the use of synonyms to describe the same symptom or sign (e.g. miosis and constricted pupils) and to facilitate subsequent data analysis. An internationally agreed list used for reporting adverse drug reactions that can also be used for poisoning is MedDRA. ¹⁴
Relevant medical history	Free text	This information may be used in the risk assessment, e.g. if a patient is particularly frail or has a medical condition that changes the susceptibility to the exposure.
Risk assessment of poisoning	Controlled text	The specialist in poisons information assesses the details of exposure provided by the caller to determine the probability that the patient was poisoned as a result of exposure to an agent. Important factors to be considered include: dose, duration, route of exposure, intrinsic toxicity or hazard of the agent and physical condition of the patient before exposure.

¹⁴ <https://www.meddra.org/how-to-use/basics/hierarchy>

Field	Suggested type of information	Purpose
Investigations prior/recommended	Free text or controlled text, multi-select	The results of investigations conducted before the call are important for the clinical risk assessment. The record should also document the investigations that the caller has been advised to conduct for medico-legal and audit reasons.
Treatment prior/recommended/given	Free text or controlled text, multi-select	The treatment that has already been given will influence recommendations for further treatment. The recommended treatments are documented, with the source used to provide the advice, e.g. the toxicology database, for medico-legal and audit reasons. If there is a follow-up call, treatment given subsequently should be documented, to complete the record and possibly for auditing.
Disposition advice	Controlled text	The caller is given advice about whether the patient should stay home, be referred to a medical practitioner or be sent to hospital.
Severity: initial	Controlled text	The initial assessment of the severity of the poisoning, e.g. based on the Poisoning Severity Score, with the assessment of final severity and outcome, provides an overview of the clinical course of the poisoning incident. Training in use of the Score is included in the WHO poison centre training manual. ¹⁵
Severity: final	Controlled text	A poison centre may record the maximum severity of poisoning separately, on the basis of the most serious signs and symptoms seen during the clinical course. This also may be based on the Poisoning Severity Score. This information is entered retrospectively. The information in this field, with the initial severity grading and the outcome, provides an overview of the clinical course of the poisoning incident.
Outcome	Controlled text	The outcome of the case (e.g. full recovery, sequelae, death) is documented to assess the case and treatment, for audit and to identify any resource or training that might be required; e.g. the finding that many patients are dying after an opioid overdoses even though there is an effective antidote may indicate an inadequate supply of antidote or that the antidote is not being used appropriately.
Type of animal	Controlled text	If the poison centre deals with enquiries about animals, the type of animal must be documented. This may particularly important in agricultural areas where poisoning of cattle, poultry, fish or other animals might affect the local economy or nutrition. The data may also be valuable for subsequent studies or surveys. The species might not be known after, e.g. a chemical disaster in which a large area was contaminated.

¹⁵ <https://apps.who.int/iris/handle/10665/329503>

ANNEX 4. EXAMPLES OF TOXICOVIGILANCE SYSTEMS

A number of countries and regions have established structured toxicovigilance systems.

BRAZIL

The Brazilian National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária) is the regulatory authority responsible for the approval, registration and supervision of food and manufactured products such as cosmetics, tobacco, pesticides, pharmaceuticals and medical devices and also for supervision of health services and controls in ports, airports and borders (1). It is a financially and administratively independent body linked to the Ministry of Health as part of the Unified Health System and coordinates the National Health Surveillance System (Sistema Nacional de Vigilância Sanitária). The Surveillance Agency sends alerts to health professionals when there is an issue of product safety.

All health units that see cases are required to send information to the national Information System for Notifiable Diseases (Sistema de Informação de Agravos de Notificação), a mandatory notification system for poisonings caused by toxic chemicals, pesticides and heavy metals and others, as well as accidents related to venomous animals (2, 3).

The Brazilian Network of Poison Centres currently comprises 30 centres situated in most states of the country. Most of the centres in the network enter data from their enquiries into a single database, DATATOX, which is maintained by the Brazilian association of poison centres, Associação Brasileira de Centros de Informação e Assistência Toxicológica (4). The database supports professionals in Brazilian poison centres and enables clinical and epidemiological studies and national assessment of the impact of toxic agents on the health of the population. The National Health Surveillance Agency consults the database for information on exposures to specific products and pesticides.

CANADA¹⁶

The Canadian Surveillance System for Poison Information is in the second year of a 4-year implementation plan (2018–2022). It is a pan-Canadian toxicovigilance system that will aggregate, analyse and interpret data from the five poison centres to provide near real-time surveillance and national statistics on poisonings, chemical intoxications and adverse drug reactions. It is hosted by the Canadian Network for Public Health Intelligence, a secure scientific informatics and biosurveillance platform owned and operated by the Public Health Agency of Canada. The Surveillance System is steered by a committee comprising representatives from the poison centres and provincial and federal governments. Health Canada is providing resources to every poison centre in Canada to improve data quality and comparability, training and surveillance. Health Canada is also sending an epidemiologist to each centre to support surveillance activities and to act as a liaison to toxicovigilance partners.

In 2015, a virtual Canadian poison control community of practice was established on the Network for Public Health Intelligence, which was renamed Toxicovigilance Canada in 2018 to reflect the numbers and diversity of its membership, which was over 350 members in 2019. This network facilitates multidisciplinary and jurisdictional collaboration among poison centres, public health, health security, regulatory, nongovernmental organizations and academic partners, as it includes collaborators from clinical toxicology and forensic laboratories, public safety, law enforcement, border services and their international counterparts.

¹⁶ R. Wootton, Chemical Emergency Preparedness & Response Unit, Health Canada, personal communication, November 2019

While the components of Toxicovigilance Canada are in various stages of development, information exchange, trust and collaboration for poisoning prevention, treatment and harm reduction have increased. The organization promotes a comprehensive approach to risk assessment and the management of toxic exposure events of public health concern by providing a trusted environment for:

- timely detection, validation and notification of signals and trends from Canadian poison centres on toxic exposure events of public health concern through the Surveillance System;
- detection by means of laboratory analysis, data-sharing and information exchange on analytical methods and mutual aid among clinical toxicology and forensic laboratories through the Toxicology Laboratory Response Network;
- notification and alerting through an early warning system and support with expertise in the Toxicovigilance Canada network;
- access to a geographically searchable Canadian Antidote Registry to support clinical treatment and antidote planning and stockpiling; and
- better public awareness of safety signals and guidance through collaboration in the Public Outreach and Communications Working Group.

EUROPEAN UNION

The European Union has a number of rapid alert systems for different categories of product. One is the Rapid Alert System for Chemical incidents (5), which is managed by the European Commission to facilitate information-sharing among European Union poison centres and national public health authorities on unusual cases of poisoning, mass intoxications and chemical incidents. The Rapid Alert System uses standard terminology for clinical effects to facilitate identification of similar cases and analyses system records daily. Exchange of information among different organizations and countries improves early detection of trends and possible cross-border incidents. An event that could develop into a serious cross-border threat to health, as defined under Decision 1082/2013/EU, is alerted to the Early Warning Response System by the designated national focal point, analogous to alerting to a public health emergency of international concern as defined in the International Health Regulations (2005).

The Scientific Committee on Health, Environmental and Emerging Risks network of experts can rapidly assess the risks of newly identified health and environmental exposures to consumer safety or public health (6) as requested by the European Commission. These may include serious or cross-border health threats involving chemical events.

Another rapid alerting system, Safety Gate, is available for dangerous non-food consumer products (7). It excludes food, pharmaceuticals and medical devices, which have their own alerting systems. Safety Gate facilitates rapid exchange of information among the national authorities of 31 countries and the European Commission on dangerous products on the market, including chemical hazards and others, such as the risk that children's products will cause choking.

The Rapid Alert System for Food and Feed, created in 1979, allows information to be shared efficiently between food and feed authorities in member states for a rapid, coordinated response to a health threat, for example, contaminated food or feed product (8). Information exchanged through this system can result in products being recalled from the market.

FRANCE

Since 1 January 2016, the Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (Agency for Food, Environmental and Occupational Health and Safety) has been responsible for coordinating the national toxicovigilance scheme and the toxicovigilance activities of the French poison centres (9). The centres

provide a 24-hour service for poisons information to both the general public and health professionals and conduct toxicovigilance in conjunction with regional health agencies. Each poisons information enquiry is documented in a standardized way as a medical file, and the files are supplemented with the data required for toxicovigilance, including assessment of the clinical severity of cases and causality (i.e. the strength of the causal link between exposure and observed health problems) and precise documentation of the agents involved and the exposure context. The categories of information recorded include patient details, the enquirer, exposure, the substance(s) involved, clinical toxicity observed, treatment provided and medical outcome. Periodically, studies are carried out on substances of interest, for example, dimethyl fumarate (10).

UNITED KINGDOM

Since April 2004, the National Poisons Information Service (NPIS) has conducted a pesticide surveillance study of cases that required a health care consultation. Data on exposures are collected by monitoring access to the NPIS online clinical toxicology database TOXBASE and by monitoring telephone enquiries to the four NPIS units (Birmingham, Cardiff, Edinburgh and Newcastle). Currently, 1563 TOXBASE entries for pesticides and biocides are being tracked. The data from these studies indicate that poison centres can usefully monitor exposure to pesticides, resulting in improved health care in the country (11).

In a broader surveillance programme also carried out with TOXBASE, 142 chemicals are flagged as of special interest, 26 of which are highly toxic, used in chemical warfare and/or were previously released deliberately. The NPIS units are alerted automatically by e-mail whenever a TOXBASE user accesses one of these chemicals, which serves as an early warning of a potential environmental, industrial or terrorist event involving these chemicals (12).

Since 2006, all national clinical data have been logged in a specially designed database, the United Kingdom Poisons Information Database. Data are uploaded onto a central server that is accessible to all NPIS units for surveillance and toxicovigilance to determine patterns or trends in enquiries.

UNITED STATES OF AMERICA

A network of 55 poison centres provides information and advice 24 hours a day to the general public and health professionals. Each centre documents its enquiries in a standardized format to collect demographic, exposure, health management and outcome data on each case. The data are downloaded in near real-time to a centralized database, the National Poison Data System (13). This database, previously known as the Toxic Exposure Surveillance System, is maintained by the American Association of Poison Control Centers and holds data on more than 66 million calls since 2001. The Centers for Disease Control and Prevention use this database to:

- improve public health surveillance for chemical, radiological and biological exposures and illnesses;
- identify early markers of chemical, radiological and biological events in order to provide a rapid, appropriate public health response; and
- increase situational awareness of specific exposures or illnesses during a suspected or known event (14, 15).

The National Poison Data System conducts three algorithm-based automated surveillance activities (14). In the first, call volumes are monitored hourly and are compared with reference values for previous years, to detect any increase. Secondly, the number of reported incidences of 131 clinical features is monitored and compared with reference values for previous years. Thirdly, case-based surveillance is conducted for exposure to 11 case definitions associated with substances of interest. When an anomaly is detected, medical toxicologists and epidemiologists at the American Association of Poison Control Centers and the Centers for Disease Control review the case to determine the risk to public health. If an incident of public health significance is identified, the teams send an alert to local and government public health departments to ensure a prompt public health response.

In 2010, the Centers for Disease Control and the American Association of Poison Control Centers created a poison centre public health community of practice to increase collaboration among federal, state and local health agencies and departments and poison centres by sharing best practices and facilitating networking among members. This community of practice now has over 250 members and has been integral to fostering a multidisciplinary approach to public health surveillance.

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ANNEX 5. ANTIDOTES AND OTHER AGENTS USED IN THE MANAGEMENT OF POISONING LISTED IN THE WHO MODEL LIST OF ESSENTIAL MEDICINES

The antidotes in Table A5.1 are those included in the WHO Model List of Essential Medicines (1) and should be available in hospitals in which poisoning cases are treated. Other antidotes that may also be used in the management of poisoning are not on the WHO List; however, their absence does not necessarily imply lack of efficacy but reflects the procedures and criteria used for selecting medicines evaluated for inclusion on the Model List.

Some national organizations and professional groups have developed their own recommendations for antidote and antivenom stocks in hospitals, which may also be consulted. A decision on which antidotes and antivenoms should be available depends on the local epidemiology of poisoning and the availability of these medicines.

Some antidotes should be administered very quickly, ideally within 30–60 min of poisoning, and should therefore be kept in the emergency department or be otherwise readily accessible. Table A5.1 shows the antidotes listed in the WHO Model List, with an indication of the time within which they should be available.

Table A5.1. Antidotes listed in the WHO Model List of Essential Medicines, 21st List, 2019

Antidote	Main poisoning indication	Timeframe within which needed (2–4)
Activated charcoal (powder)	Decontamination of the gastrointestinal tract	< 1 h
Acetylcysteine	Paracetamol	< 2 h Treatment should be initiated within 8 h of ingestion of an acute overdose
Antivenom immunoglobulin	Snakebite: exact type to be defined according to local snake population	< 1 h For some snake envenomings, later administration may also be effective (5)
Atropine	Organophosphates and carbamates, nerve agents	Immediate
Calcium gluconate	Fluorides, hydrofluoric acid, oxalates, calcium channel blockers	Immediate
Deferoxamine	Iron	< 1 h
Dimercaprola	Lead (used with sodium calcium edetate), mercury, arsenic	< 2 h
Fomepizole (4-methylpyrazole) ^a	Methanol, ethylene glycol	< 1 h
Methylthioninium chloride (methylene blue)	Methaemoglobinaemia	Immediate
Naloxone	Opioids	Immediate
Potassium ferric hexacyanoferrate (Prussian blue)	Thallium	< 2 h

Antidote	Main poisoning indication	Timeframe within which needed (2–4)
Sodium calcium edetate ^a	Lead	< 2 h
Sodium nitrite	Cyanide	Immediate
Sodium thiosulfate	Cyanide	Immediate
Succimer ^a	Lead, mercury, arsenic	< 2 h

^a On the complementary list, Essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities and/or specialist medical care and/or specialist training are needed. Medicines may also be listed as complementary on the basis of consistently higher costs or less attractive cost-effectiveness in various settings.

A number of medicines on the List have other uses but can also be used in the management of poisoning, either as antidotes or to treat the manifestations of poisoning (Table A5.2).

Table A5.2. Medicines on the WHO Model List of Essential Medicines, 21st List 2019, for other indications but also used in the management of poisoning

Drug	Main poisoning indication or pathological condition (2)
Antipsychotic agents e.g. chlorpromazine, haloperidol	Psychotic states with severe agitation
β-blockers (β1 and β2, preferably short-acting) e.g. atenolol, bisoprolol, metoprolol	β adrenergic agonists, hypertension
Diazepam	Organophosphates, chloroquine; convulsions, excitation, anxiety, muscular hypertonia, etc
Dopamine	Myocardial depression, vascular relaxation
Epinephrine (adrenaline)	Anaphylactic shock, cardiac arrest
Ethanol (alternative to fomepizole)	Methanol, ethylene glycol
Furosemide	Fluid retention, left ventricular failure
Glucagon	β-blockers
Glucose	Hypoglycaemia
Heparin	Hypercoagulability states
Magnesium sulfate	Cardiac arrhythmias
Mannitol	Cerebral oedema, fluid retention
Midazolam	Convulsions, delirium, muscular hypertonia
Neostigmine	Neurotoxic snakebite (5), anticholinergic agents
Oxygen	Cyanide, carbon monoxide, hydrogen sulfide
Penicillamine	Lead, copper (Wilson disease)
Phytomenadione (vitamin K1)	Coumarin derivatives
Protamine sulfate	Heparin
Pyridoxine	Isoniazid
Salbutamol	Bronchoconstriction

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ANNEX 6. SUGGESTED CONTENT OF A POISON CENTRE ANNUAL REPORT

PERIOD COVERED BY THE REPORT: FROM/...../... TO/...../....

1. THE POISON CENTRE

Name of centre:

Address: City: Country:

Telephone: Fax: E-Mail: URL:

Geographical area (officially) covered by Centre:

Population served (officially) by Centre (*number*):

Hours of operation: hours/day, from : to : ; days/week

User profile:

General public

Medical professionals

Main role(s) of centre: Poisons information service

Analytical services

Patient care

Training

Other, please describe:

Staff:

Technical/Medical director/Responsible director (*of centre only*):

Administrative director (*of centre only*):

Professional(s): (*number*) (*indicate whether full-time or part-time*)

Physicians:

Pharmacists:

Nurses:

Scientists

Laboratory staff:

Other:

Administrative staff: (*number*)

General service staff: (*number*)

External experts/advisers (*number*)

Fields of expertise (for example, toxinology, mycology, botany).....

Date centre established: /..... /..... (date dd/mm/yy when service started operating)

Location of centre:

(for example, ministry, hospital, medical school, university, other)

Administrative affiliation:

(for example, Ministry of Health, university hospital, private sector, other)

2. STATISTICAL DATA ON ENQUIRIES

- a. Number of incoming, outgoing and other communications and personal contacts during the reporting period (communications include those by telephone, post, personal contact and other; post includes letter, fax, e-mail and also specific questionnaires and surveys; personal contact includes consultations)
- b. Number of enquiries related to cases, chemical incidents and requests for information (i.e. no exposure or patient involved)
- c. Number of enquiries per main category of enquirer
- d. Number of enquiries by main location of enquirer
- e. Number of enquiries per agent use or type
- f. Number of enquiries by month
- g. Number of enquiries by hour of the day (yearly average)
- h. Comments

3. STATISTICAL DATA ON INCIDENTS REPORTED¹⁷

- a. Total number of incidents with and without exposed people
- b. Number of incidents involving one or more exposed people
- c. Number of incidents by circumstance
- d. Number of incidents per agent type or use
- e. Comments

4. STATISTICAL DATA ON CASES¹⁸

- a. Total number of patients about whom enquiries were received:
 - Human
 - Animal
- b. Number of cases by circumstance and agent by type or use
- c. Number of cases, circumstances of exposure, age groups and gender of patients
- d. Number of cases involving pregnant patients, circumstance of exposure and agent type or use
- e. Number of cases by age group and agent type or use
- f. Number of cases by final severity grading

¹⁷ An event leading to or potentially leading to exposure. An incident may involve several victims (e.g. contamination of a product, fire, spill, volcanic eruption, algal bloom).

¹⁸ Data on humans or animals exposed to or poisoned by an agent.

- g. Number of cases by final outcome
- h. Number of cases by age group, gender and circumstance of exposure when outcome is death
- i. Number of cases by agent type or use, gender and circumstance of exposure when outcome is death
- j. Comments (for example, summary of main observations, trends, problems in relation to each main category of agent and to specific agents, cases of unusual symptomatology, other observations)

5. DATA FROM ANALYTICAL AND OTHER LABORATORY INVESTIGATIONS (WHEN PROVIDED BY THE CENTRE)

- a. Type and number of analytical equipment operational in the laboratory
- b. Total number of laboratory investigations undertaken on:
 - i. patients for whom the poison centre advised on or provided treatment
 - ii. other patients (for whom the poison centre was not involved in management)
- c. Main agents investigated, in decreasing order of frequency for (b.i. and b.ii.)
- d. Other investigations by the laboratory (provide numbers, if possible), for example:
 - analysis of water for chemical contaminants
 - analysis of food for chemical contaminants
 - identification of controlled or abused drugs (drug seizures)
 - urine screening of drug abusers
 - forensic toxicology
 - occupational toxicology
 - environmental toxicology
 - therapeutic drug monitoring
 - others (please specify)
- e. Comments (for example, availability of supplies and reagents)

6. DATA ON FACILITIES FOR MANAGEMENT OF PATIENTS (WHEN PROVIDED BY THE CENTRE)

- a. Number of beds for poisoned patients (for example, in the centre itself, emergency department, intensive care unit, medical ward, other)
- b. Outpatient clinic: number of consultations per year
- c. Access to specialized treatment (for example, haemodialysis, transplantation unit)
- d. Access to specialized diagnostic facilities (for example, magnetic resonance imaging)
- e. Comments

7. ANTIDOTES AND ANTIVENOMS AVAILABLE AT THE CENTRE

- a. List of antidotes and antivenoms available
- b. Number and names of antidotes and antivenoms used and distributed during the year
- c. Comments (for example, new formulations and developments)

8. PREVENTIVE ACTIVITIES

- a. Community prevention activities, including materials prepared (for example, mass media activities, public education campaigns, other)
- b. Partners in prevention activities (for example, ministries, hospitals, community groups, nongovernmental organizations, other)
- c. Toxicovigilance:
 - Number of investigations of toxic situations for which an alert might be required
 - Number of alerts called
 - Number of reports to authorities
 - Materials prepared
 - Other actions taken
- d. Results or outcome of preventive activities
- e. Comments

9. ADVISORY ROLES TO GOVERNMENTAL AND OTHER BODIES

Description of activities undertaken, for example, advice on registration of pesticides, safety measures, regulatory activities, other.

10. TRAINING AND EDUCATION OF PROFESSIONALS

- a. Training courses organized by the centre (title, objectives, place, dates, type of audience, sponsorship, other)
- b. Training activities organized by others in which members of the centre took an active part (title, objectives, place, dates, type of audience, sponsorship, other)
- c. Curricular studies organized by the centre:
 - Undergraduate level
 - Postgraduate level
- d. Comments

11. RESEARCH ACTIVITIES OF THE CENTRE

(For each area: title, objectives, partners, duration, source of funding specifically for research, other)

- a. Clinical
- b. Analytical
- c. Epidemiological
- d. Other
- e. Comments

12. PUBLICATIONS

- a. Publications, reports, brochures issued by the centre (title, brief summary, reference)
- b. Publications written by staff of the centre ((for example, case reports, articles, monographs, theses, books; provide title, brief summary and reference for each)
- c. Comments

13. NATIONAL AND INTERNATIONAL MEETINGS AND COOPERATIVE ACTIVITIES OF CENTRE

- a. Organized by the centre:
 - National meetings, congresses, workshops (title, place, dates, summary of meeting if available, number of members of the centre involved)
 - Organization of international meetings, congresses, workshops (title, place, dates, summary of meeting if available, number of members of the centre involved)
- b. Participation of the centre in:
 - National meetings, congresses, workshops (title, place, dates, summary of meeting if available, number of members of the centre involved)
 - International meetings, congresses, workshops (title, place, dates, summary of meeting if available, number of members of the centre involved)
- c. Cooperative projects or activities with other partners (title, brief description, partners, duration)
- d. Support to other poison centres (brief description of activities, which centres supported, dates, staff of the centre involved)
- e. Training provided for other poison centres (brief description, place, dates)
- f. Regional activities (brief description of activities in chronological order)
- g. Twinning arrangements established (name of poison centre)
- h. Comments

14. BUDGET FOR THE PERIOD OR YEAR OF THE REPORT

- a. Overall annual budget
- b. Staff costs
- c. Operating costs
- d. Overall increase or decrease on previous year's budget
- e. Fund allocations for specific new activities (for example, activity, duration, amount)

15. MAIN REQUIREMENTS OF THE CENTRE

This section briefly presents the main requirements of the poison centre for which technical, financial or other support or interaction with other poison centres would be useful or other requirements.

ANNEX 7. EXAMPLE OF AN OPERATING PROCEDURE FOR ANSWERING POISONS INFORMATION ENQUIRIES

An example of a standard operating procedure that could be used in a poisons information centre is given below. It should be adapted to the operations of the poison centre concerned.

INTRODUCTION AND PURPOSE

The purpose of the procedure is to guide the staff who answer the poisons information helpline of the centre and provide information on poisoning. Calls may be received from health care professionals (for example, doctors, nurses, staff nurses, pharmacists, paramedics) and the general public.

THE RESPONSE CAN BE DIVIDED INTO THREE STEPS:

1. Taking the enquirer's details and the reason for the call
2. Careful review of resources to formulate a response
3. Responding to the caller

1. TAKING THE ENQUIRER'S DETAILS AND THE REASON FOR THE CALL

- All callers should be treated with courtesy and respect.
- Answer the call by identifying yourself and the poisons information centre.
- Ask the caller to identify him- or herself and determine whether he or she is a medical professional or a member of the general public. Often, callers, especially the general public, describe the problem before identifying themselves. The caller's given and family name should be recorded.
- All callers should provide a contact number, especially if they are health care professionals. Occasionally, members of the public are reluctant to provide a contact number; the responder should explain that the telephone number would be used only if the call is cut off or if there might be a need to contact the caller again, for example to provide them with additional information.
- Record information as prompted by the call record sheet for the poisons database:
 - caller demographics: who, from where and contact number
 - patient demographics: age and gender; weight when applicable
 - substance involved (for example, drug, chemical)
 - the circumstances, exposure route, exposure duration, location of poisoning (for example, home, at work) and time since exposure
 - presenting symptoms and signs in sufficient detail and the poisoning severity score (1)
- Ask the caller to hold the line while you find the information necessary to provide advice on the exposure or poisoning.

- Information on the ingredients of products that is not found in any of the databases in use can often be found on the Internet.
- If the call does not fall within the remit of those answered by the poisons information centre, refer the caller to the most appropriate service; i.e. pharmacy enquiries should be referred to the on-call pharmacist at the enquiring hospital. Such calls include those about:
 - adverse reactions to therapeutic dosages of medications
 - drug interactions
 - dosages of drugs to administer to non-poisoned patients
- If the enquiry would be more appropriately answered by another organization, for example, a rabies hotline, give the telephone number to the caller.

All calls to the poisons information centre must be logged onto the poison information database.

- This should be done in real time, i.e. at the time the call is taken or as soon as possible afterwards. If calls are to be logged later, make a note of the time of the start and end of the call so that the times recorded in the database are accurate.
- Calls should be entered by the on-duty specialist in poisons information and signed off by 12:00 after the duty period.

2. USE APPROPRIATE RESOURCES, FOR EXAMPLE: [ADAPT FOR LOCAL USE WITH THE NAMES OF THE DATABASES TO BE USED]

- Poison centre clinical toxicology database(s) *[list]*
- National medicines formulary
- Toxinology database (for example, <http://www.toxinology.com/>)
- Teratology enquiries: use designated resources
- Appropriate toxicology books
- If the exposure was to a product that is not listed on any of the systems in use, for example, traditional medicine or unknown household product, only general advice can be offered.

3. RESPOND TO THE CALLER

- All the information provided to the caller should be adapted to the requirements of the case and the person calling (for example, physician, nurse or general public).
- Detailed clinical information should not be provided to the general public, although some information may be given about symptoms that would indicate poisoning. First-aid information may be given, for example, to rinse exposed skin. If the exposure is unlikely to result in harm, the caller can be told that there is minimal risk and to manage the case at home but to seek further advice if the situation changes. If there is a risk of poisoning, the caller should be referred to a doctor or hospital and advised whether an ambulance is indicated.
- Patients outside hospital may require only advice on referral to a health care facility.
- For callers who are medical personnel, determine the patient's risk of toxicity, and inform the caller of possible signs and symptoms.

- Inform the caller of the time frame for toxicity to manifest, including any delayed effects.
- Provide advice on clinical investigations, laboratory analyses required, specific drug assays and criteria for the use of antidotes, if appropriate.
- Make sure the caller has understood the information you have provided.
- A summary of the advice given (including advice sought from a consultant medical toxicologist) should be recorded in the appropriate section on the call record sheet or database.
- Information is usually given by telephone; however, it may be necessary to e-mail the relevant information to the caller, including a warning that the information should not be archived as it is updated regularly.

Enquiries requiring referral to a clinician

If a specialist in poisons information is uncertain about what advice to give a caller after having consulted the appropriate resources and other colleagues or considers that the enquiry is outside their area of expertise or if the caller asks specifically to speak to a medical toxicologist, a referral should be made.

In this case:

- Ask the caller to wait while you discuss the case, or
- inform the caller that you will contact the consultant medical toxicologist and report back.

Contact:

Endorsed:

Updated: XX/XXXX

Date of next planned review: XX/XXXX

REFERENCE

1. Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J. Poisoning severity score: grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36(3):205–13. doi:10.3109/15563659809028940.

ANNEX 8. EXAMPLE OF A FORM FOR ASSESSING HANDLING OF CALLS BY A SPECIALIST IN POISONS INFORMATION

An example of an assessment record that can be used to evaluate the performance of a specialist in poisons information is given below. It should be adapted to the operations of the poison centre concerned.

Staff member Call reference
 Date call taken Date of assessment

	Adequately covered	Not adequately covered	Comments
Ascertained reason for call			
Obtained sufficient information to answer the call			
Conducted risk assessment			
Gave treatment management plan			
Offered specialist referral (when applicable)			
Used appropriate language for the caller's level of understanding (member of public, health care professional)			
Ensured that the caller received sufficient information that they fully understood			

Comments on areas done well:

Comments on areas for improvement:

ANNEX 9. EXAMPLE OF A USER SATISFACTION QUESTIONNAIRE

An example of a questionnaire that can be used by a poison centre to obtain feedback from users is given below. A survey could be conducted with a paper form or online. The form should be adapted to the operations of the poison centre concerned.

[Enquirer's name]

[Department]

[Address]

Date and time of enquiry: [day]/[month]/[year]

Reference number:

Summary of enquiry:

FOR THE FOLLOWING QUESTIONS, PLEASE SCORE FROM 1 TO 5, WHERE 1 IS NOT SATISFIED AND 5 IS VERY SATISFIED.

1. My call was answered promptly.
2. The person I spoke to was helpful and had a good telephone manner.
3. I was satisfied with the advice I received.
4. The amount of information I received was sufficient.
5. I felt confident in the accuracy of the information received.
6. The information was given to me in a timely manner.
7. I would use the poisons information centre in the future.

The following area is left blank for free text. If you have any comments or suggestions about the service or the information received, please enter them below.



Environment, Climate Change and Health (ECH)

World Health Organization

20 Avenue Appia

CH-1211 Geneva 27

Switzerland

ipcsmail@who.int

