World Health Organization publications

Guidelines for Poison Control

This book provides authoritative guidelines for the establishment or improvement of national programmes for poison control. Addressed to policymakers and the administrators of specialized facilities, the book responds to the need for comprehensive advice on the most rationale and effective ways to manage the greatly increased number of poisoned patients seen throughout the world. Strategies for the prevention of poisoning are also described.

The guidelines draw on the practical experiences of numerous well-established poison centres in different parts of the world. Although recommended lines of action have universal relevance, the book gives particular attention to the situation in developing countries, where a basic infrastructure for the care of poisoned patients is often absent and special problems arise from the lack of adequate communications, transportation, drugs and support services. Throughout, emphasis is placed on the role and functions of a poison information centre as a crucial component of any national programme for poison control.

The book has nine chapters presented in two parts. Part one provides an overview of the policy issues surrounding decisions to introduce measures, including specialized facilities, for the prevention and management of poisoning. Arguing that a poison information centre should be available in every country, part one also describes the benefits of such centres, outlines their principal functions, and suggests various options for their logical and cost-effective operation.

Against this background, part two provides detailed technical advice on how to organize and operate the various facilities and services that make up a comprehensive system for poison control. Separate chapters describe the functions and requirements of information services, clinical services, and analytical toxicological and other laboratory services, and discuss the importance of toxico-vigilance as a strategy for prevention. Subsequent chapters explain how to deal with major emergencies involving toxic chemicals, and outline solutions to the problem, encountered in most developing countries, of obtaining essential antidotes. Part two concludes with advice on the design and content of forms for collecting, storing, and reporting data, followed by a detailed list of the main literature required in a poisons information centre.

Additional practical information is provided in a series of annexes, which describe a computer software system for the management of poisons data, reproduce several model record and reporting forms, and classify a large number of antidotes and related agents according to their proven effectiveness and urgency of availability.

WHO, Distribution and Sales, 1211 Geneva 27, Switzerland.

Guidelines for Poison Control, 1997, xii + 112 pp. (available in English; French and Spanish in preparation) ISBN 92 4 154487 2, CHF35.-/USD31.50, In developing countries: CHF24.50. Order no. 1150439.

Management of Poisoning. A Handbook for Health Care Workers. J.A. Henry & H.M. Wiseman

This handbook provides a practical guide to the emergency management of poisoning in settings, such as the rural areas of developing countries, where doctors are scarce and rapid access to health services is difficult. Addressed to health workers having little or no medical training, the handbook communicates a wealth of information about specific poisons, the signs and symptoms they cause, and the immediate actions to take in order to save lives and minimize complications. While all common causes of poisoning—from natural plant toxins to medicines and household products—are covered, particular attention is given to pesticides as one of the most frequent causes of fatal poisoning in the developing world.

To ensure accuracy and practical utility, the handbook was prepared in consultation with numerous experts and widely field-tested in training workshops prior to finalization. Throughout, illustrations, lists of do's and don'ts, extensive cross-referencing, and a simple nontechnical language are used to facilitate rapid action in emergencies. Recommended treatments are restricted to those that can be safely undertaken by nonmedical personnel with minimum equipment. Medical treatments that require hospital facilities are not included.

The handbook has two parts. The first, which helps prepare health workers to respond to emergencies, opens with basic information about the principal causes of poisoning and the preventive measures that can be taken by households, communities, workers, and their employers. Following a logical and clearly structured approach, subsequent chapters illustrate and explain the exact steps to follow in an emergency. Readers learn how to give first aid, get medical help, examine the patient**,** determine exactly what happened, and care for patients until they can be seen by a doctor. Part one concludes with a chapter on medicines and equipment, which includes a list of useful medicines and antidotes that can be given by nonmedical workers.

The second and most extensive part serves as a manual for the emergency management of some 70 specific causes of poisoning in four main groups: pesticides, chemicals and chemical products used in the home and the workplace, medicines, and plants, animals, and natural toxins. Each poison is covered according to a common format, which includes information on uses of the substance, how it causes harm, the severity of its effects, signs and symptoms of poisoning, and the exact steps to follow when poisoning occurs. The book concludes with definitions of terms and an extensive index.

WHO, Distribution and Sales, 1211 Geneva 27, Switzerland. *Management of Poisoning, A Handbook for Health Care Workers*, J.A. Henry & H.M. Wiseman, 1997, xiv + 315 pp. (available in English; French and Spanish in preparation), ISBN 92 4154481 3, CHF102.-/USD91.80, In developing countries: CHF71.40, Order no. 1150438.

Press releases from WHO

Starting materials for manufacturing of pharmaceuticals must comply with international standards

The active and inactive starting materials used in the manufacture of pharmaceutical products often change hands many times before reaching the manufacturer of a pharmaceutical product. Along the distribution and trade chain, there are many opportunities for the type and quality of material to change. As a result, chemicals required for the production of pharmaceuticals can become contaminated, resulting in unsafe pharmaceutical products with grave dangers for the patients who use them.

The most often documented example of the above happening is the incorporation of diethylene glycol (DEG) into pharmaceutical preparations. Ingestion of DEG may affect the central nervous system, liver and kidneys, and can lead to death through kidney failure. The latest large-scale, well-documented instance of this happening was in Haiti in 1996, where some one hundred children died after taking contaminated cough syrup, but similar accidents have occurred previously in many countries, resulting in a total of at least 500 unnecessary deaths during the last 10 years.

International action is consequently needed urgently to prevent such accidents in the future and the World Health Organization (WHO) convened a meeting of experts at the WHO headquarters in Geneva from 25 to 27 May 1998 to address this issue. The experts came from 15 countries and represented national drug regulatory authorities, pharmacists' associations, traders, chemical and pharmaceutical manufacturers' associations, international nongovernmental organizations, major pharmacopoeias, consumer organizations and world customs organizations. The meeting formulated several concrete recommendations.

In addressing the experts, WHO Assistant Director-General, Dr Fernando Antezana, underlined that 'the risk is not limited to diethylene glycol, similar incidents may happen at any time with other starting materials if quality assurance is not in place'.

As contamination is most likely to occur either during manufacture of the starting material itself or during its trading, transportation and distribution to the pharmaceutical manufacturer of the final drug product, the group's major recommendations addressed these areas. Manufacturing activities with starting materials for pharmaceutical products should be covered by an authorisation, from the competent health authority, requiring adherence to Good Manufacturing Practice (GMP). Governmental inspectorates should also be able to conduct inspections of manufacturing facilities at any time and place and be able to inspect containers of starting material produced.

Perhaps the major problem is in the transhipment of starting materials. Starting materials often pass through several agents or traders and can be repacked and relabelled at any stage, so that there can be an inaccurate indication of what a container holds by the time it has reached its final destination. To combat this, the group of experts insisted that a system of Good Distribution Practice be installed. Traders and agents should preferably hold an authorisation from the local government. Moreover, national inspectorates should have access to free ports, areas which are exempt from many regulations.

It was recommended that WHO itself should actively develop a list of critical excipients (inactive starting materials) and their nomenclature. This would aid manufacturers, traders, inspectorates and other officials in recognizing and checking the quality of starting materials for pharmaceutical products. Furthermore, the group recommended that each manufacturer or country should have testing facilities for analysis of starting materials and final pharmaceutical products. Where no such analysis is possible, WHO should also advise developing countries to use formulations in essential drugs with ingredients for which they have appropriate testing facilities. Whereas every party in the chain has his own responsibilities, the final responsibility remains with the manufacturer of the final product.

'We have to have safe trading in all starting materials for pharmaceutical manufacturing. There have been repeated catastrophes with diethylene glycol, and now WHO will help develop activities to prevent this happening again,' said Dr Juhana Idänääpn-Heikkilä, Director of WHO's Division of Drug Management and Policies (DMP).

WHO experts re-evaluate health risks from dioxins

Forty specialists from 15 countries met at the headquarters of the World Health Organization (WHO) in Geneva from 25 to 29 May to evaluate the risks which dioxins might cause to health. Since the Seveso incident in 1976, this group of persistent environmental chemicals has consistently grabbed the headlines, although the real effect of these substances is difficult to determine. This group of chemicals includes polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFS) and polychlorinated biphenyls (PCBs), although the most toxic dioxin of all is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). TCDD has been shown to cause dermatological problems, notably chloracne, a chronic and disfiguring skin disease.

These substances are omnipresent in the ground, river beds and air. They are involuntary by-products formed when thermal processes produce chlorine and other organic substances. They can also be produced by volcanic activity, which cannot be controlled, and by forest fires, but the principal controllable sources of dioxin production are waste incinerators.

In recent years, the WHO European Centre for Environmental and Health (WHOECEH) has been coordinating a comprehensive programme, in collaboration with the International Programme on Chemical Safety (IPCS) on PCDDS, PCDFs and PCBS, to evaluate the possible health risk, as well as methods of prevention and control of environmental exposure of the general population to these chemicals.

During a previous meeting on dioxins, held at Bilthoven, in the Netherlands, in 1990, WHO experts established a tolerable daily intake of 10 pg/kg body weight for TCDD, said to be the most toxic dioxin. (One picogram, pg, equals a millionth of a millionth of a gram).

Since then, new epidemiological data has emerged, notably concerning dioxins' effects on neurological development and the endocrine system, and WHO thus convened the consultation which has just taken place in Geneva to re-evaluate the tolerable daily dose of dioxins to which a human can be exposed. After ample debate, the specialists agreed on a new tolerable daily intake range of 1–4 pg/kg body weight. The experts, however, recognized that subtle effects may already occur in the general population in developed countries at current background levels of 2–6 pg/kg body weight. They therefore recommended that every effort should be made to reduce exposure to the lowest possible level.

The background documents for the experts' meeting discussed carcinogenic and noncarcinogenic effects of dioxins on humans and animals, the risks for young children, transmission mechanisms, general exposure to dioxins and the compounds of the same nature, as well as current means of evaluating these risks in different countries.

'Recent exposure data show that measures introduced to control dioxin release in a number of countries have resulted in a substantial reduction in intake of these compounds in the past few years', emphasized Dr Maged Younes, Chief of the Assessment of Risk and Methodology unit in the WHO Programme for the Promotion of Chemical Safety. 'This is evidenced by a marked decrease in dioxin levels in human milk, as found in an exposure study conducted by the WHO European Centre for Environment and Health, with the highest rates of decrease being observed in areas which had the highest initial concentrations.'

Tenth WHO Model List Of Essential Drugs

A World Health Assembly Report of 1975 recognized the urgent problems of lack of essential drugs in many countries, and provided the impetus for the first WHO Model List of Essential Drugs, published in 1977. Since that time, the concept of essential drugs has been widely applied. It has provided a regional basis not only for drug procurement at national level but also for establishing drug requirements at various levels within the health care system.

Essential drugs are those that satisfy the health care needs of the majority of the population and should therefore be available at all times in adequate amounts and in the appropriate dosage forms. This definition remains as valid today as it was 20 years ago.

The choice of such drugs depends on many factors, such as the pattern of prevalent diseases; treatment facilities; training and experience of the available health care personnel; financial resources; as well as genetic, demographic and environmental factors.

Since 1975, there have been nine reports in total, each one updating and improving the list and providing guidelines on selection and use. Because of differing views on the definition of an essential drug in terms of what is meant by the 'health care needs of the majority', the list has been gradually expanded since its introduction and has evolved with changing health needs and therapeutic options.

Over the 20 years, 166 new drugs have been added while 68 drugs have been deleted, resulting in an overall increase from the original 208 to 306 drugs after the last Expert Committee meeting, which took place in December 1997.

Each selected drug must be available in a form in which adequate quality can be assured and its stability under the anticipated conditions of storage and use must be verified.

Where two or more drugs appear to be similar in the above respect, the choice between them should be

made on the basis of a careful evaluation of their relative efficacy, safety, quality, price and availability.

The WHO List of Essential Drugs is a model, to guide countries and health services in developing their own national and local lists. Such lists should be evidence based, considering prevalent diseases, treatment facilities, training and experience of health personnel, financial resources, genetic factors and demographic factors.

The concept of essential drugs has been disseminated and promoted extensively at the country level by WHO's Action Programme on Essential Drugs, as well as by disease control programmes in WHO, international and nongovernmental organizations throughout the world and bilateral agencies.

Over the last 20 years the WHO Model List has proven to be an invaluable tool for saving lives and improving health through more rational use of drugs, wider access to drugs, and improved drug quality.

In the preparation of the Tenth WHO Model List of Essential Drugs which was recently published in *WHO Drug Information*, Vol. 12, No. 1, priorities were to 'fine tune' the list in the light of the latest evidence, to correct any major omissions and to address drug treatment issues for some of the major health priorities today, including the problem of antibiotic resistance, asthma and diabetes.

One important advance in the new Model List is the addition of a new drug, triclabendazole, for the treatment of liver and lung flukes. This illustrates the way the List can be used to highlight a therapeutic need and speed up availability of new drug treatment.

AIDS treatment was also addressed and zidovudine (AZT) has now been introduced into the WHO Model List of Essential Drugs for the specific treatment of HIV-infected pregnant women in order to reduce mother-to-child transmission and to protect the new-born baby.

A further note on triple therapy in HIV/AIDS was also included to the effect that it was a new therapy beyond the budgets of most National Drug Programmes and must be decided at country or institutional level. However, several drugs were added for the treatment of opportunistic infections.

The WHO Model List of Essential Drugs is considered to be as an informational and educational tool for professionals and consumers. Since concern about health care costs is now a priority even in developed countries, the Model List is of greater importance than ever as an aid to developing treatment guidelines, national formularies, consumer drug information, and other measures to improve drug use.

The List also serves as the basis for WHO model drug information, a new model formulary, and basic drug quality tests.

The List should be seen in the context of national drug policies that address not only drug use, but also procurement and supply strategies, drug financing, drug donations, and research priorities.

Major gaps in research on antibiotic resistance need filling

Fluoroquinolones are important members of the quinolone group of antibiotics which are licensed to treat diseases in humans and animals. However, their use in livestock animals can contribute to increased resistance in food-borne bacteria (such as *Campylobacter* and *Salmonella*) which may infect humans. Fluoroquinolones are important for the treatment of invasive *Salmonella* and *Campylobacter* infections in humans and an increase in the resistance in these bacteria is therefore of concern.

'To date, there has been little documented impact on human health of fluoroquinolone use in livestock, but there is concern over the potential human health consequences if resistance were to increase and spread. Further research and data gathering are thus essential,' said Dr David Heymann, Director of the World Health Organization's (WHO) Division of Emerging and other Communicable Diseases Surveillance and Control (EMC).

Consequently, the WHO convened a meeting on the medical impact of quinolone use in food animals at WHO headquarters in Geneva from 2 to 5 June. The meeting, in which over 60 experts from both the human and animal health fields participated, agreed that that major emphases of future research should include: determining the full extent of quinolone usage outside human medicine; improving epidemiological evidence on how resistance in both animals and humans develops, persists and spreads between animal species and humans; developing surveillance techniques specifically designed to capture the above data; determining the mechanisms and levels of resistance in important zoonotic pathogens to quinolones and how important these resistance levels are in terms of human health risk; developing strategies for prudent use in animals to maximize therapeutic benefit while minimizing development of resistance; developing alternatives, such as vaccines, to the use of antimicrobials for animal disease prevention.

Following the introduction of fluoroquinolones in several countries, *Salmonella* with reduced susceptibility to fluoroquinolones have emerged in food animals; resistant *Campylobacter* have also emerged. Although no human cases have been documented, the experts expressed concern that there could be treatment failures in humans infected with *Salmonella* with reduced susceptibility. The experts also noted that, with the use of fluoroquinolones in humans, human pathogens have

begun to develop resistant strains and there are now several circumstances in which resistance has limited the therapeutic use of this class of antibiotic for important diseases such as for gonorrhoea and typhoid.

While fluoroquinolones are not used as growth promoters, they are currently used for treatment of animal disease in many countries of the world and, in some regions, they are also used for disease prevention in animals. However, the data available so far on their usage are scarce and are often the proprietary information of the drugs' manufacturers. Consequently, correlations between quinolone usage and the emergence of resistance are hard to make. WHO and the meeting's participants welcomed the initiative by COMISA (the World Federation of the Animal Health Industry) at the 2–5 June meeting that provided sales and volume data for the major fluoroquinolones in more than 30 countries.

The experts, from 18 countries, requested that WHO, in conjunction with the Food and Agriculture Organization of the United Nations (FAO) and the Office International des Epizooties (OIE—the World Organization for Animal Health), work together to gather data, standardise testing methods and develop a code of practice for the prudent use of antimicrobials in food animals. WHO should also, the participants agreed, ensure that public health safeguards are given prominence in such a code of practice.

All WHO Press Releases, Fact Sheets and Features as well as other information on these subjects can be obtained on Internet on the WHO Home Page. URL: http://www.who.int/