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CLINICAL PRACTICE GUIDELINES

Management of Drug Overdose and Poisoning



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of Health

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This publication is meant as a general guide to the management of drug overdose and poisoning and not as an authoritative reference on the subject. Because of the dynamic nature of information on poisoning, readers are advised that decisions regarding drug therapy must be based on the independent judgement of the clinician, changing information about a drug/chemical and changing medical practices. While care has been taken to ensure the accuracy of the information presented at the time of publishing, the Ministry of Health, the authors, and the publishing editors will not be liable for any errors or omissions, or any untoward effect arising from the use or misuse of this book.

Management of Drug Overdose & Poisoning

Message

Clinical toxicology has advanced considerably in the last 10 years since the publication of the first handbook on the management of poisoning by the Ministry of Health. The pattern of poisoning has also changed as people are now exposed to other new drugs and chemicals. New antidotes and therapies have been developed for the management of such poisoning, and are now available to health professionals.

The publication of this new edition on the management of drug overdose and poisoning is most timely. The workgroup has put in great efforts to produce this comprehensive handbook, which will serve as a quick and easy reference for health professionals in the management of poisoning.

I would like to congratulate the workgroup members and all contributors for their achievement. I trust that the handbook will meet the information requirements of our healthcare workers.

Dr Chen Ai Ju
Director of Medical Services
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Preface

The first handbook on management of poisoning was published by the Ministry of Health ten years ago. The objective then was to provide a quick and reliable reference for the complex management of drug overdoses/poisoning. Since then, great strides have been made in scientific technology, medicine, agriculture and pest control which have led to the development of many new products with associated toxic effects. Therefore, it has become necessary to revise and update the information pertaining to toxicology.

This new edition of the handbook provides comprehensive advice for the management of drug overdose and poisoning. It is organised into 4 main sections, each identified by coloured tags in the right margins. Section A gives an overview of principles in the management of poisoning including the medico-legal and socio-psychiatric aspects. Section B provides information on diagnosis and treatment of overdoses of 11 classes of therapeutic agents. Section C focuses on household, industrial and metallic poisoning; and Section D is on agricultural poisoning. To make the handbook a practical and useful guide, a comprehensive index with extensive cross referencing is provided.

The revision and publishing of the handbook has been a challenging and rewarding task. We hope it will be well utilised by the health professionals. We would like to record our grateful thanks to the workgroup members for their time and contribution to the various chapters.

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S E C T I O N **A**

OVERVIEW OF MANAGEMENT

Poison Management Systems

Introduction

Poison management systems refer to the whole series of processes that begin from the time a drug or chemical is produced, to its ingestion as a poison, and all the steps required for a complete patient management. Such a system may have various components, some of which are: -

1. Formulation and manufacture.
2. Distribution and control of access.
3. Measures to ensure prophylaxis against wrongful ingestion in the home, workplace or general environment.
4. Community measures for handling one or more episodes of poisoning.
5. Poisons information.
6. Emergency patient management and after-care.
7. Toxicological analysis.
8. Education of patient and relatives.

Formulation and Manufacture

Drugs and chemicals cause toxicological effects when they gain access to the body in large concentration and when countermeasures are delayed. Examples of such adverse consequences are numerous. Sometimes modifications in formulation can decrease the tendency to toxicity, for example:

1. Banning or reducing the manufacture or sale of toxic agents such as those used in chemical warfare e.g. sarin, tabun mustard gas, phosgene and pesticides, e.g. dichloro diphenyltrichloroethane (DDT) and aldrin.
2. Modifying the formulation of a product to make it less injurious e.g. adding methionine to acetaminophen to ensure ready availability of sulphhydryl groups during toxic ingestion so as to minimise the likelihood of hepatic damage.

3. Substituting products with less toxic agents but which are at least equally effective, e.g. removing alcohol from children's cough and cold preparations decreases the likelihood of toxicity.

The manufacture of chemicals is also a potential source of poisoning on a large scale. Industrial chemical disasters such as what happened in Bhopal, India in the early hours of Dec 3, 1984, when about 45 tons of methyl isocyanate escaped from an insecticide plant is an example of how shortfalls in the manufacturing process affect lives adversely. The catastrophe resulted in 2500 deaths and 50,000 injured persons. Safety standards in chemical plants have to be a primary concern of states that allow such plants to operate within their boundaries.

Distribution and Control of Access

Safety aspects and limiting access of chemicals and drugs can be incorporated into the design of the packaging. Some methods may include: -

1. Introducing packaging that allows easy recognition of drugs and that avoids confusion, viz. avoiding the use of similar labelling and design for different drugs and ensuring that drugs look different in size, shape, texture and colour.
2. Use of child-resistant containers, blister packs and tamper-resistant containers. The increased time and effort required to gain access to the drug decreases the risk of toxic ingestion.
3. Restricting the sale of commonly abused over-the-counter medications e.g. analgesics and sedatives, or of toxic agricultural products without licensing of purchaser e.g. paraquat.

Chemicals in bulk are often transported across roads and highways. Accidents involving the transport vehicles can result in the release of large amounts of these chemicals into the environment.

In 1995, the release of a nerve gas (Sarin) in the subway network of Tokyo, Japan, with the resulting large number of casualties, again demonstrated the tremendous potential for terrorist groups to use dangerous agents of chemical warfare to further their political aims.

Prophylaxis Against Wrongful Ingestion

People will be able to recognise poisonous/toxic substances and be warned of the possible toxic potential if :-

1. Warning stickers are affixed to household and medicinal products. Such stickers may depict a skull and cross-bones, a serpent or a scowling face.
2. Dark coloured containers are used for storage of poisons not meant for oral ingestion.
3. Labels are affixed to the back of vehicles transporting hazardous substances in bulk.

Below is a list of common sense measures to be taken in the home environment: -

- a) All medicines and chemicals should be clearly labelled so that both children and adults will be fully aware of the contents.
- b) Medicines and household chemicals should be kept in safe areas in the home out of reach of children.
- c) All chemical items should be kept in their original containers. Never store toxic substances in soda bottles or cups, or any unmarked or unauthorized containers.
- d) Use child-resistant containers. Keep the caps securely shut between uses.
- e) Discard household cleaning aids or other products that are no longer used.
- f) Store toxic household and garden products in cabinets fitted with safety latches and/or locks. When in use, make sure that an adult is present. Put away the product immediately after use.
- g) Never equate medicines with candy when administering drugs to children. Do not make light of or joke to a child about taking medication.
- h) Never take medication in the dark or if you are not fully awake. If you normally wear glasses, put them on before taking the medicine(s).

- i) Work with household chemicals in well-ventilated areas. Do not mix chemicals (e.g. bleach and toilet-bowl cleaner) unless specifically directed to do so.
- j) Periodically check and discard medicines no longer in use. Flush them down the toilet.
- k) Keep poisonous plants away from children or others likely to ingest them.
- l) Educate children about the dangers of poisons in the home.

Community Measures for Handling Episodes of Poisoning

In certain countries such as the United States of America, Israel and Canada, access to Poison Control Centres has made it possible for the community to obtain advice on immediate measures required to minimise adverse effects of ingested or administered chemicals. States with poison control centres have been able to demonstrate improvements in telephone triage patterns, avoidance of excessive visits to emergency departments, and improved outcomes because of the better quality and quantity of information provided to callers.

Communities which have strong and active first-aid programs or that advocate use of activated charcoal as part of home first-aid kits also have the potential to demonstrate better outcomes.

There is a need to ensure rapid access to a community's Emergency Medical Services so that victims of major poisoning can reach a definitive and appropriate treatment centre early. Such rapid access is now available with the use of the 995 emergency telephone number for the Emergency Ambulance Service in Singapore. In addition to an easily accessible number, the community has a responsibility to ensure that the Emergency Medical Services have the necessary numbers and types of vehicles with appropriately trained personnel to reach the poisoned victim, render necessary first-aid, initiate decontamination measures where applicable and ensure the rapid evacuation of the victim to an appropriate hospital.

Communities that either manufacture chemicals, store them in large quantities or transport large amounts in vehicles will need to draw up safety guidelines and train response agencies in managing hazardous material incidents.

Poisons Information

Evaluation and assessment of any exposure to a poison require gathering of appropriate information to gauge the potential health risk to the victim. The victim himself may be able to volunteer such information, or else it may have to be obtained from close friends and relatives. Often home-members may themselves require information on what needs to be done.

Very often the evaluation has to be done over the telephone. If all persons exposed to chemicals or drugs arrived in emergency departments without prior telephone evaluation, such emergency departments would be overloaded by patients requiring no care or only simple first aid.

During the interview, the following information should be obtained: -

- a) *Who was exposed?* Age, sex and weight are important.
- b) *What substances were involved in the exposure?* As far as possible, the exact name of the product must be obtained. If this is not available, a clear description of the agent and its packaging may be useful.
- c) *How much of the potentially toxic agent was involved in the exposure?* The number of tablets or the volume of solution that the patient is thought to have been exposed to should be mentioned.
- d) *Time of exposure* is important to determine the urgency of the situation. If exposure has just occurred and symptoms have begun, then rapid activation of the Emergency Medical Services and transportation and life support can be provided.
- e) Does the victim have any *previous history of other medical problems?* This will help the doctor to determine the mode of decontamination and further management.
- f) *The condition of the victim* at the time of call will help in determining the type and rapidity of medical response that is required.
- g) *Any initial measures already taken* will need to be known and documented, e.g. if emesis has already occurred or an emetic has

already been administered, further attempts at inducing vomiting would not be warranted.

The person making the assessment must be able to determine whether the victim is in any danger, potential or immediate, from the exposure. If there is no danger, reassurance that the victim will not be likely to develop adverse reactions can be given.

If an assessment of immediate danger is made, emergency first aid and medical treatment measures can be recommended to be instituted with minimal or no delay.

An assessment of potential danger requires that the victim should be carefully evaluated or observed in an appropriately equipped observation facility, e.g. at an Emergency Department, or is admitted to the hospital to be managed as an inpatient.

For those assessed to be in no danger or in potential danger and not admitted into the hospital, follow-up calls or early review is mandatory to be assured of the continued well being of the victim.

Staff who man emergency departments and poison control or poison information centres should be trained to ask the relevant questions and make appropriate assessments.

Poisons information would be available from various sources, viz. the local family doctor, information stored in either microfiche, compact disc or poison manuals or available by a telephone call or on-line via a modem or computerised system of graded access for members of the public. The information sought is not only on the identity of the poisoning agent, if unknown, but advice on the step-by-step management of the patient.

Emergency Patient Management and After-Care

The care given to victims of poisoning is usually determined by the symptomatology produced. Generally speaking, aggressive treatment measures are not necessary if the patient is asymptomatic. Eight stages have been identified in the approach to the poisoned patient.

- a) *Emergency management.* This refers to the resuscitation and stabilisation of the patient by paying attention to attaining a conscious state, maintenance of an open airway, adequate ventilation and oxygenation and ensuring adequacy of the hemodynamic state. This may sometimes require the use of specific antidotes in the very initial stages of management.
- b) *Clinical evaluation.* This includes obtaining the history, performing a physical examination and laboratory evaluation and an assessment of major toxic signs such as coma, cardiac arrhythmias, metabolic acidosis, gastrointestinal disturbances and seizures. Completion of clinical evaluation would allow the patient to be triaged into one of three categories, viz. mild, moderate or severe. The overall management of each of these categories of patients is as described in Section A, Chapter 2 “Principles of Management of Acute Poisoning”.
- c) *Decontamination of the patient.* This can be gastrointestinal, topical or respiratory. Many methods of decontamination are available. The method used would depend on the route of poisoning and known responses of the toxic agent to the effect of the decontaminants. Whatever procedure used should be carried out aggressively so as to limit the toxic effects of the poison.
- d) *Antidotes.* Though specific antidotes are relatively uncommon, administering these should be done as early as possible not only to reverse pharmacological effects of the poison, but also to displace poisons from target organ receptor sites or to deactivate the poison by binding irreversibly to the molecule.
- e) *Enhanced elimination of absorbed poison.* This is usually resorted to when antidotes are not available. Methods of enhanced elimination include forced diuresis, alkalinisation or acidification of the urine, dialysis, haemoperfusion and hyperbaric oxygen.
- f) *Supportive therapy.* This may be all that is required in some poisoned patients. During this phase, frequent monitoring of vital signs, fluid

and electrolyte balance, cardiorespiratory support as indicated, and aggressive nursing care to preserve integrity of body systems, should all be carried out.

- g) *Observation and disposition.* Observation may be necessary to evaluate delayed effects of certain poisonings, to manage an underlying disease that has been exacerbated because of the overdose and to evaluate and treat complications. Final disposition would depend on the results of this further observation.
- h) *After-care.* Management of the poisoned victim is not only the relief of the physical effects of the toxic agent on the human body. Many victims of poisoning have lead acutely stressful lives that lead them to overdose themselves with various medicaments and chemicals. They require emotional support through all phases of emergency management and very early intervention of the medical social worker and perhaps even a psychiatrist. Follow-up by both may be required even after discharge from the hospital. Victims of accidental exposure to toxic agents have undergone an acutely stressful situation. Rather than only providing psychological support to those with overt symptoms of post-traumatic stress disorder, one has to presume that all have potential for stress disorders. Therefore stress counselling for all has to be planned for. Such counselling must continue in the post-hospital phase of management.

Toxicological Analysis

Though a toxicological laboratory can be a useful resource for managing the poisoned patient, every physician must have a good understanding of the capabilities of his own community's set up. Effective use of such a laboratory must be ensured. The ability of laboratories to make definitive diagnosis depends on the range of pharmacological reagents available. The physician intending to use the laboratory should, therefore, first obtain the appropriate specimen that the laboratory is able to analyse, know which tests to order, when the results will be available and the reliability of the assay techniques employed. One must remember that the toxicological laboratory is only an "aid" in the management of the poisoned patient. For this "aid" to be useful, timeliness of results is important to influence the clinical management of the poisoned patient. It is also important to know

that blood levels of poisoning agents do not necessarily correlate with clinical features of toxicity. Treatment of the patient and not the blood level should therefore continue to be the prime concern of physicians.

Education of Patient and Relatives

There have been too few educational programs to implement poisoning prevention on a community-wide basis. Possible programs could be in the form of community outreach seminars, poster contests, school curriculum changes, mass media and educational material distribution activities. Some such programs in Monroe County, New York led to a 66% drop in poisonings requiring emergency department treatment in area hospitals and a 71% drop in poisoning admissions. Education should be in the following areas: -

- a) Education of public about recognition of potential poisons.
- b) Education on techniques for safe storage of poisons.
- c) Teaching proper disposal of partially used products.
- d) Educating residents to be ready for a poisoning event such as by the home storage of decontaminating agents/antidotes and the use of telephone stickers with emergency telephone numbers.
- e) Teaching of appropriate first response (first aid) to the public.

Poison prevention educational programs should have the following attributes :-

- a) Focus on specific community groups, e.g. mothers attending a well woman's clinic, participants of well-child programs or factory workers before being confirmed in their appointments or orientated to their work environments.
- b) Clarity and ease of understanding by the target population.
- c) Timeliness of programs during windows of receptivity such as when a member of the target group becomes a victim of poisoning.

- d) Relevance of the program to the well being and to the health of the target group and their families.
- e) The program must provide practical information that is easy to comply with.
- f) Repetition of educational modules to reinforce the intended message and help to ingrain safety habits e.g. checking labels for toxic ingredients and using containers with child-resistant caps.
- g) The educator must be of professional standing for listeners to value his suggestions. Impersonal programs usually have a low effectiveness rate.
- h) Programs should involve learners in an active and collaborative learning experience. They should not be too short for learners to ignore or too long such that they lose their attention span.
- i) Whatever educational programs are instituted for the community should be actively supported by the physician community and by community self-help groups for greater effectiveness.

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CHAPTER 2

Principles of Management of Acute Poisoning

Introduction

The management of a patient with acute poisoning consists of:

- Emergency management
- Clinical evaluation
- History
- Physical examination
- Investigations
- Treatment
- Decontamination
- Antidotes
- Enhanced elimination of absorbed drugs
- Supportive therapy
- Observation
- Follow-up

It must be remembered that one of the most important aspects in managing such patients is “knowing what to do, and in what order to do it” (Gossel and Bricker, 1990).

In the course of managing toxicological patients, we should have the following aims:

- to assess the patient's condition and stabilize it
- to identify the poison
- to institute the appropriate treatment

Emergency Management

Resuscitation and Stabilization

On first contact with the patient, assessment of the level of consciousness is important. For an unconscious patient, careful evaluation of the Airway, Breathing and Circulation (ABC) should be followed by active measures to not only secure these, but also to reverse the unconscious state, if possible. It would also be pertinent to look for obvious associated trauma.

A - airway

A patent airway is critical in the further management of the patient. Patency may be maintained by one or more of the following, if the patient is unconscious :

- a) The head-tilt, chin-lift technique or the classical jaw thrust would be the initial method of choice. However, in the event that neck trauma is suspected, the head tilt should not be employed. The modified jaw thrust is an alternative technique that may be employed in traumatized patients.
- b) Insertion of oro-pharyngeal or naso-pharyngeal airway with regular suctioning. Prior to this the oral cavity should be inspected and any obvious foreign bodies such as food or broken dentures should be removed.
- c) Turning the patient to the recovery (three-quarters prone) position. This allows oral secretions and vomitus in the oro-pharynx to drain out of the mouth.
- d) Endotracheal or nasotracheal intubation. If performed, this should only be with a cuffed tube.
- e) Surgical cricothyrotomy

Examination of the airway is not complete without evaluating for the presence or absence of the gag reflex. Especially in the unconscious patient, the absence of the gag reflex mandates definitive measures to protect the airway, such as with a cuffed endotracheal tube before any procedures for gastrointestinal decontamination are instituted.

B - breathing

Assessment of breathing should include not just whether the patient is breathing, but also if the breathing is slow or fast. Any patient with abnormal breathing should be provided with 100% oxygen. Slowing of respiration may be a sign of narcotic overdose and assisted ventilation, either via a bag-valve mask or positive pressure ventilation, may be instituted.

C - circulation

Assessment of circulation should include heart rate, blood pressure, peripheral circulation and hydration status of the patient. To maintain the circulation:-

- Ideally, the systolic blood pressure (BP) should be kept above 90 mmHg
- Dopamine and dobutamine may be needed to maintain the BP
- IV fluids (crystalloids, colloids) may be necessary
- CVP monitoring may be necessary
- The patient may require ECG monitoring
- If in shock, the patient should be maintained in the head - down position

Other Problems

The patient may also have other problems e.g. altered mental states, seizures, etc. These will have to be dealt with urgently, but separately. These problems are addressed later in the chapter.

In addition, empirical antidote administration (naloxone, flumazenil) may prove to be necessary. In some cases of impaired consciousness, measuring the blood glucose level may be useful.

Clinical Evaluation

A clinical evaluation of the patient's condition is achieved by means of the following:

- Knowing the history
- Conducting a physical examination

In addition, appropriate investigations are very important in assessing the patient's condition, helping in decisions on management, and assessing the response to treatment.

History

The primary aims of taking the history are to:

- Confirm that poisoning has occurred
- Identify the substance or substances involved

If the patient is unconscious or unable to give any form of history, a search of the patient's personal belongings may provide clues (e.g. medicine bottles) to the type of poisoning.

The following are important to establish when taking the history:

- Poisoning-related information
 - type of drug or poison ingested
 - dosage and amount
 - time of ingestion
- Accidental or intentional poisoning
 - presence of suicide intent
- Current medical history
 - current symptoms
 - treatment received so far
- Past medical history
 - includes history of past suicide attempts
 - includes history of drug allergy
- Family history
- A brief social history

Note: this can be taken when the patient's condition is stable

The amount of detail elicited in taking the history depends on the patient's condition. Obviously, a number of aspects of the history can wait if the patient is critically ill.

In some cases, we might not be sure that poisoning has occurred, such as when:

1. The patient cannot give a history (e.g. he may be unconscious)
2. There are symptoms of other unknown toxic exposure

Suspected Cases of Poisoning

Such patients are sometimes brought to the hospital in an unconscious state and poisoning might be suspected.

The following aspects of the history are important and should be elicited from the relatives or friends who found the patient:

- Situational history
 - where the patient was found
 - the circumstances under which the patient was found
 - presence of pills, drugs or empty medicine bottles in the area
- Occupational history
 - in particular, exposure to potentially toxic substances
- Past history
 - history of chronic or terminal illness
 - depression
 - suicidal thoughts
 - substance abuse

Symptoms of Unknown Toxic Exposure

In such cases, in addition to a full medical history, the following points should be elicited:

- Chronology of complaints
- Changes in type of medication or dosage
- Occupational history

Physical Examination

In many cases, the physical examination will not reveal significant abnormalities in the initial phase. Physical signs usually manifest later when clinical toxicity develops. A full physical examination should be carried out for all patients. In addition to a quick primary survey in which the conscious state, airway, breathing and circulation are assessed as described above, a proper secondary survey is also required. This consists of a detailed head-to-toe examination. In a toxicological patient, particular attention may should be paid to the following:-

- Consciousness level
- Odour of breath on the patient
- Pupil size

- Rate and depth of respiration
- Heart rate and blood pressure
- Dryness of oral mucosa and skin
- Oral ulcers
- Evidence of drug abuse e.g. needle marks
- Evidence of suicidal intent, e.g. cuts on the wrists

The physical signs can sometimes give a clue to the type of poisoning when the patient himself does not know or is unable to give a history due to impaired consciousness. This is because certain symptoms and signs tend to appear in clusters.

Gastrointestinal Tract (GIT)

Nausea and vomiting

These are common symptoms in poisoning and are generally non-specific.

However, it must be borne in mind that nausea and vomiting need not be due to a GIT cause and can also be due to a central cause.

This may be seen in overdoses of:

- Digoxin
- Opioid analgesics
- Theophylline derivatives

Abdominal pain

The possible causes include:

- Arsenic
- Corrosive agents
- Heavy metals
- Lead
- Narcotic withdrawal
- Organophosphates

Pain and ulceration

Pain and ulceration are often caused by strong acids or alkalis, which cause tissue destruction. In some cases, the entire GIT may have been eroded and this possibility should always be borne in mind in managing such patients.

Phenol can also cause ulceration but generally, there is much less pain than expected. This is due to the destruction of nerve endings.

Increased salivation

The possible causes include:

- Arsenic
- Chlormethiazole
- Cholinesterase inhibitors
e.g. carbamates
organophosphates
- Corrosive fluids
- Mercury
- Phencyclidine

Dry mouth

This is often due to anticholinergic drugs.

Other causes include:

- Antihistamines
- Narcotics

Diarrhoea

The possible causes include:

- Arsenic
- Boric acid
- Iron
- Organophosphates

Constipation

The possible causes include:

- Lead
- Narcotics

Jaundice

This is often caused by hepatotoxic effects of drugs but as it takes several days to develop, it is rarely of diagnostic importance in the acute phase although clinical management decisions may be affected by this.

Respiratory System

Cough and breathlessness

This is often seen in patients who suffer from inhalation of poisonous or irritant gases.

Wheezes and crackles

The most common direct cause of this in a poisoned patient is bronchitis or pneumonitis from:

- Aspiration of chemicals
- Inhalation of irritant gases

Cyanosis

The possible causes include:

- Methaemoglobinaemia
- Respiratory depression due to centrally-acting drugs

It must be remembered that the cause may also be due to the obstruction of the respiratory tract.

Hyperventilation

The possible causes include:

- Carbon monoxide
- Cyanide
- Metabolic acidosis
- Salicylate overdosage
- Theophylline

Hypoventilation

The possible causes include:

- Alcohol
- Opioids
- Sedatives / hypnotics

Cardiovascular System (CVS)

Tachycardia

The possible causes include:

- Alcohol
- Amphetamines
- Anticholinergic drugs
- Cocaine
- Salicylates
- Sympathomimetic drugs
- Theophylline
- Tricyclics

Bradycardia

The possible causes include:

- Beta-blockers
- Cardiac glycosides (e.g. digoxin)
- Cholinesterase inhibitors (e.g. carbamates and organophosphates)
- Opioids
- Sedatives

Arrhythmias

The possible causes include:

- Anticholinergic drugs
- Antimalarial drugs
- Cardiac glycosides
- Chloral hydrate
- Phenothiazines
- Sympathomimetic drugs

Also, it must be remembered that antiarrhythmic agents in high doses can cause arrhythmias.

Hypotension

In almost any type of severe poisoning, hypotension can occur. As such, this is relatively non-specific as to the type of poisoning.

The more common causes of hypotension include:

- Beta-blockers
- Organophosphates
- Tricyclics

Hypertension

This is an uncommon finding in cases of acute poisoning. When it occurs it tends to be associated with an overdose of:

- Monoamine oxidase inhibitors
- Phencyclidine
- Sympathomimetic drugs

Another possible cause is opiate withdrawal.

Central Nervous System (CNS)

Ataxia

The possible causes include:

- Alcohol
- Barbiturates
- Bromides
- Hallucinogens
- Heavy metals
- Organic solvents
- Phenytoin

Coma or drowsiness

This is very common in poisoning and is usually due to CNS depression. A large number of drugs can cause this, for example:

- Alcohol or other toxic alcohols
- Anticonvulsants
- Antidepressants
- Antihistamines
- Antipsychotics
- Clonidine
- Hypnotics
- Opioid analgesics

However, coma and drowsiness seldom occur in poisoning by:

- Salicylates
- Paracetamol

Hypotonia and hyporeflexia

The possible causes include:

- Barbiturates
- Benzodiazepines
- Other hypnotics

Hypertonia and hyperreflexia

The possible causes include:

- Anticholinergic drugs
- Monoamine oxidase inhibitors
- Sympathomimetic drugs

Sometimes, muscle tone is very greatly increased and opisthotonos can be seen. In such cases, the following should be considered:

- Alpha-chloralose
- Monoamine oxidase inhibitors
- Strychnine

Convulsions or fasciculations

There are a large number of possible causes. These include:

- Alcohol
- Amphetamines
- Anticholinergic drugs
- Antihistamines
- Chlorinated hydrocarbons
- Cyanide
- Isoniazid
- Lead
- Mefenamic acid
- Methaqualone
- Monoamine oxidase inhibitors
- Opioid analgesics
- Organophosphates
- Phenothiazines

- Salicylates
- Strychnine
- Sympathomimetic drugs
- Tricyclic antidepressants

When taken in excess, anticonvulsants can also cause convulsions. Another possible cause is barbiturate withdrawal.

Dystonic reactions

Dystonic reactions involving the mouth, eyes and head may be caused by:

- Haloperidol
- Metoclopramide
- Prochlorperazine.
- Trifluoperazine

Delirium and hallucinations

The possible causes include:

- Alcohol
- Anticholinergic drugs
- LSD
- Opioid withdrawal
- Phencyclidine
- Poisonous mushrooms
- Sympathomimetics

A differential diagnosis that should be considered is delirium tremens.

Eyes

Loss of Vision

This may be partial or total. The most likely causes are:

- Methanol
- Quinine

Pupils

Small or pinpoint pupils are usually present in poisoning by:

- Cholinesterase inhibitors
- Opioid analgesics
- Phenothiazine

Dilated pupils are usually present in poisoning by:

- Amphetamines
- Anticholinergic drugs
- Antihistamines
- Barbiturates
- Cocaine
- Glutethimide
- LSD
- Methanol
- Sympathomimetics
- Tricyclics

Opiate withdrawal can also result in dilated pupils.

Nystagmus

The possible causes include:

- Barbiturates
- Phenytoin
- Sedatives
- Alcohol

Papilloedema

This is uncommon. When it is present, it is generally due to cerebral oedema secondary to prolonged hypoxia. This usually suggests that it may be a case of poisoning by:

- Carbon monoxide
- Glutethimide
- Methanol

Skin

Reddish skin

The possible causes include:

- Atropine
- Boric acid
- Carbon monoxide
- Cyanide

Moist skin

The possible causes include:

- Organophosphates
- Sympathomimetics

Dry skin

This may be caused by anticholinergic drugs.

Blisters and / or bullae

This may be seen in poisoning by:

- Barbiturates
- Carbon monoxide
- Glutethimide
- Sedatives

Needle tracks

These are often present in drug addicts e.g. heroin users.

Others**Retention of urine**

This is common in cases of poisoning by anticholinergic drugs.

Tinnitus and deafness

This is common in cases of salicylate poisoning. It is present in almost every patient whose plasma salicylate concentration exceeds 300 mg / L.

Hypothermia

The possible causes include:

- Alcohol
- Barbiturates
- Sedatives

Hyperthermia

The possible causes include:

- Monoamine oxidase inhibitors
- Salicylates
- Sympathomimetic drugs
- Anticholinergic drugs
- Neuroleptic malignant syndrome in antipsychotic drugs

Clinical Toxidromes

Certain drugs or classes of drugs are known to cause a cluster of signs and symptoms which may sometimes be fairly typical for that drug or class of drugs. Some of the more common ones are as follows:

Anticholinergics

The characteristics of anticholinergic poisoning are best remembered by way of the following well-known mnemonic:

- Hot as a hare (hyperpyrexia)
- Red as a beet (cutaneous vasodilatation)
- Dry as a bone (decreased salivation)
- Blind as a bat (cycloplegia and mydriasis)
- Mad as a hatter (delirium and hallucinations)

In addition, the patients may have the following problems:

- Decreased GI motility
- Tachycardia
- Urinary retention

Caustic substance ingestion

This tends to be characterised by:

- Dysphagia
- Acute abdomen
- Chest pain
- Respiratory distress

Cholinergics

Poisoning by cholinergics tends to be characterised by:

- CNS signs and symptoms
- Agitation
- Coma
- Confusion
- Muscle fasciculations
- Seizures
- Weakness
- GIT signs and symptoms
- Defaecation
- Emesis

- Gastric cramping
- Salivation
- Lacrimation
- Odour of garlic
- Profuse sweating
- Urination

Cyclic antidepressants

Poisoning by cyclic antidepressants tends to be characterised by:

- CNS stimulation with delirium
- Coma
- Hypotension
- Seizures
- Tachyarrhythmia

Toxicity usually occurs 1 - 3 hours after ingestion.

Opioids

Poisoning by opioids tends to be characterised by:

- Coma
- Pinpoint pupils
- Respiratory depression

Organophosphates

Poisoning by organophosphates tends to be characterised by:

- Muscarinic effects
 - abdominal cramps
 - bradycardia
 - bronchoconstriction
 - bronchorrhoea
 - defecation
 - heart block
 - lacrimation
 - nausea and vomiting
 - salivation
 - sweating
 - urination

- Nicotinic effects
 - breathlessness
 - fasciculation
 - muscle fatigue
 - pallor
 - paralysis
 - tachycardia
 - tremor
 - twitching
 - weakness
- CNS effects
 - anxiety
 - ataxia
 - coma
 - confusion
 - convulsions
 - headache
 - slurred speech

Phenothiazines

Poisoning by phenothiazines tends to be characterised by:

- Coma
- Convulsions
- Extrapyrarnidal reactions
- Hypothermia
- Lethargy
- Miosis
- Postural hypotension

Salicylates

Poisoning by salicylates tends to be characterised by:

- Fever
- Lethargy
- Tachypnoea
- Tinnitus
- Vomiting
- Coma (rarely)

Sedatives / Hypnotics

Poisoning by sedatives and hypnotics tends to be characterised by:

- Coma
- Confusion
- Hypotension
- Hypothermia
- Respiratory depression
- Variable pupillary changes
- Vesicles or bullae

Sympathomimetics

Poisoning by sympathomimetics tends to be characterised by:

- Anxiety or delirium
- Hyperpyrexia
- Hypertension
- Mydriasis
- Tachycardia

Theophylline

Poisoning by theophylline tends to be characterised by:

- CNS signs and symptoms
 - agitation
 - anxiety
 - seizures
 - tremor
- CVS signs and symptoms
 - hypotension
 - tachyarrhythmias
- GIT signs and symptoms
 - diarrhoea
 - nausea and vomiting

The following are likely to be found on investigation:

- Hypokalaemia
- Acidosis

Investigations

There are many possible investigations in a case of poisoning. Each investigation ordered should be selected because it contributes to the management of the patient. Investigations should not be ordered as part of a mindless routine.

A number of investigations that can be carried out in cases of poisoning have been sub-divided into several groups and are listed below:

Identification of agent

One or more of the following samples may be sent for toxicology:

- Blood
- Urine
- Gastric aspirate

Emergency toxicology screen

This should be done if necessary and is discussed in a separate chapter.

Other tests for initial management

This is a broad group and may encompass a number of different investigations. However, it should be borne in mind that the following investigations can be done quickly in most hospital laboratories:

- Serum digoxin level
- Serum paracetamol level
- Serum phenytoin level
- Serum salicylate level
- Serum theophylline level

They should therefore be ordered without hesitation if indicated.

Effects of agent

A number of different investigations may be necessary for evaluating the effects of a poison. Some examples of these are:

- Full blood count (FBC)
- Urea and electrolytes (U/E)
- Liver function test (LFT)
e.g. hepatotoxic drugs
- Prothrombin time / partial thromboplastin time (PT / PTT)
e.g. hepatotoxic drugs
- Group and cross-match (GXM) for fresh frozen plasma (FFP)
e.g. anticoagulants

- Arterial blood gas (ABG)
e.g. sedative poisoning, salicylates, toxic alcohols
- Urine full examination and microscopic examination (UFEME)
- Electrocardiogram (ECG)
- Chest X-ray (CXR)
e.g. inhalation of poisonous gas
paraquat poisoning
- Blood urea nitrogen (BUN)
e.g. antibiotics
paracetamol
- Creatine phosphokinase (CPK)
e.g. autonomic drugs
- Magnesium, calcium and phosphate levels
- Methaemoglobin
e.g. dapsone
- Serum cholinesterase levels
e.g. anticholinesterases
- Electroencephalography (EEG)
e.g. some centrally-acting drugs
- Serum osmolality for toxic alcohols

Reminder: these tests should not be done as a matter of routine but should be done only if there is a specific indication for them

ECG Changes

A number of drugs can cause ECG changes. Some of the more well-known ones are:

ECG Changes	Drugs
bradycardia and AV block	alpha adrenergic agonists beta blockers calcium channel blockers carbamates clonidine cyclic antidepressants digitalis glycosides disopyramide encainide flecainide lithium opiates organophosphates physostigmine procainamide quinidine
prolongation of the QRS complex	cyclic antidepressants digitalis glycosides diphenhydramine disopyramide encainide flecainide procainamide propranolol quinidine thioridazine
prolongation of the QT interval / torsade de pointes	amiodarone arsenic organophosphates thallium
tachycardia	anticholinergic agents sympathomimetic agents
ventricular tachycardia & ventricular fibrillation	amphetamines chloral hydrate cocaine cyclic antidepressants digitalis glycosides phenothiazines sympathomimetic agents theophylline

Treatment

The principles of managing a case of poisoning are as follows:

- Emergency management
- Decontamination
- Antidotes
- Enhanced elimination

Treatment generally consists of:

- Supportive therapy
- Keeping the patient under observation

Nursing Care

The main nursing care instructions include:

- Complete rest in bed (CRIB)
- Rest in bed (RIB) if patient is relatively well
- Conscious level chart
- Hourly parameters
- Input / output (I/O) chart
- Suicide precautions

Other Considerations

Any poisoning must be made a police case in Singapore and if it has not been reported yet, should be done once the time can be spared to attend to it.

Any suspected poison should be left in its original container and any vomitus should be collected and placed in a clean jar as it may be useful for identification of the poison.

Common Problems in Poisoning and Their Treatment

Problem	Treatment
acid-base, fluid and electrolyte disturbances	These occur frequently in cases of poisoning. They should be corrected as appropriate.
arrhythmias	<p>These may occur in cases of poisoning by a number of drugs. e.g.</p> <ul style="list-style-type: none">beta-blockerscardiac glycosideschloral hydratetheophyllinetricyclic antidepressants <p>ECG monitoring in such patients is very important. The treatment can be difficult as there is a risk of drug interaction if an antiarrhythmic agent is administered. As such, any antiarrhythmic agent administered should be carefully selected and should only be used in cases of persistent and life-threatening arrhythmia. In serious ventricular tachyarrhythmias, the drug of choice is lignocaine. Its short half-life makes it easy to adjust the dosage as appropriate. In torsade de pointes, the use of magnesium sulphate can be considered.</p>
cerebral oedema	The treatment involves correcting any hypoxia, hypercapnia or hypotension. The patient may also be given mannitol and dexamethasone.
convulsions	Short isolated convulsions generally require no treatment. In recurrent and protracted convulsions IV diazepam should be considered. However, it must be borne in mind that this may potentiate any respiratory depressant effects of the poison. In very severe cases, intubation and ventilation may

	be necessary, along with the administration of anticonvulsants.
hypotension	The minimum acceptable systolic BP is 80mmHg in young adults and 90 for patients above 40 years of age. However, these values are arbitrary and more reliance should be placed on the clinical assessment, e.g. the patient's mental state, skin temperature, hourly urine output and other factors. Treatment is best monitored by a central venous pressure (CVP) line and involves IV fluids and, if severe enough, dopamine and / or dobutamine.
hypothermia	The patient should be kept warm and cold IV fluids should be avoided.
pulmonary oedema	There are a number of different causes for this. Generally, the treatment involves stopping IV fluids, starting diuretics and giving the patient oxygen.
severe pain	Particularly in the case of poisoning with corrosive agents, the pain may be very severe. In such cases, morphine can be considered. However, it is inadvisable to use morphine in cases of CNS and respiratory depression.
urine retention	This tends to occur in cases of poisoning with tricyclic antidepressants and anticholinergic agents. Such patients should be catheterised.

Specific Substances and Problems and their Antidotes and Treatments

Substance and / or Problem Associated With It	Antidote / Treatment
anaphylaxis	adrenaline
anticholinergic drugs	physostigmine
anticoagulants	vitamin K, clotting factors, fresh frozen plasma
antimony	dimercaprol
arrhythmias due to cardiac drugs / toxins	lignocaine
arsenic (except arsine)	dimercaprol, penicillamine
benzodiazepines	flumazenil
beta blockers	isoprenaline
bismuth	dimercaprol
calcium antagonist overdose	calcium
carbarnates	atropine
chromium	dimercaprol
copper	dimercaprol, penicillamine
cyanide	sodium nitrite, sodium thiosulphate, dicobalt edetate
digoxin	digoxin-binding antibodies
drug-induced bradycardia e.g. digitalis, beta-blockers	atropine
ethylene glycol	ethanol, folic acid
extrapyramidal effects of drugs	diphenhydramine
gold	dimercaprol
heparin	protamine
hydrofluoric acid	calcium
hydrogen sulfide	sodium nitrite
hyperkalaemia	calcium
hypertension due to drug-induced vasoconstriction	nifedipine
hypocalcaemia due to fluorides, oxalates and citrates	calcium
hypoglycaemic agents	glucagon
hypotension due to drugs with a cardio-depressive effect	adrenaline
iron	desferrioxamine
lead (except alkyl lead compounds)	dimercaprol, EDTA, penicillamine
malignant hyperthermia	dantrolene
mercury (except monoalkyl mercury)	dimercaprol, penicillamine
metabolic acidosis	sodium bicarbonate
methaemoglobinaemia	methylene blue
methanol	ethanol, folic acid
methotrexate	calcium leucovorin (folic acid)
nickel	dimercaprol
opioid analgesics	naloxone
organophosphates	atropine, pralidoxime
paracetamol	N-acetylcysteine
propranolol	aminophylline, glucagon
sympathomimetics	beta-blockers
thallium	prussian blue
tungsten	dimercaprol
zinc	dimercaprol

The exact dosages and methods of administration are described in the individual sections detailing the drugs. Toxic antidotes should not be administered unless positive identification of the poison has been made.

Follow-up

Generally, such a patient would be followed-up by the following:

- Physician
- Psychiatrist
- Surgeon, in some cases
- Ophthalmologist, in cases of eye injuries
- Any other appropriate specialist

Once the patient is stable, a referral to the following is often made:

- Psychiatrist
- Medical social worker
- Surgeon, if indicated

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CHAPTER 3

Decontamination After Poisoning

Introduction

The method of decontamination after an episode of poisoning depends on the route of administration of the poison - gastrointestinal, topical or respiratory.

Gastrointestinal Decontamination

This is used for poisons which have been ingested. Decontamination can be achieved by one or more of the following methods:

- Dilution
- Emesis
- Gastric lavage
- Catharsis
- Intestinal lavage
- Whole bowel irrigation
- Gastrostomy
- Oral adsorbents

Dilution

Water is the best diluent. Generally, 100 - 200 ml is administered to children and 200 - 400 ml to adults.

Household products e.g. cleaning agents, can be well managed with dilution.

Dilution with water is useful as:

- Water helps to reduce the gastric irritation induced by the poison
- The added bulk allows ipecac-induced emesis to be more effective

Precautions

Excessive fluid may distend the stomach wall. This may cause premature emptying of the stomach contents into the duodenum making it more difficult to remove the poison as well as enhancing the absorption of the poison.

Contraindications

Dilution should not be used under the following circumstances:

- When the poison ingested is in the solid form e.g. capsules, tablets; this is because dilution will tend to promote dissolution and absorption of the poison
- Unconscious patients
- Patients without a gag reflex

Milk

Milk can also be used as a diluent. It is most often used for ingestion of caustic or irritant substances. However, it should not be used for phosphorus. It must be noted that milk may delay the onset of Ipecac emesis and reduce the efficacy of activated charcoal.

Emesis

For many years, emesis has been widely used for treating patients suffering from poisoning. It is generally more useful if there is sufficient bulk, particularly fluids, in the stomach. As such, dilution with water prior to inducing emesis can increase the efficacy of this technique.

Indications

Emesis is indicated under the following circumstances:

- A potentially toxic dose was ingested
- It is likely that much of the substance is still in the stomach
- Large undissolved tablets or capsules are present (reason: these are generally too large for removal by gastric lavage)
- The ingested substances are not well adsorbed by activated charcoal e.g. enteric-coated or sustained release tablets

Contraindications

The contra-indications for emesis are:

- Convulsions
- Corrosive substances
- Impaired consciousness / no gag reflex

- Petroleum distillates
- Severe cardiovascular disease
- Emphysema
- Under 6 months of age
- A poison that causes:
 - a rapid decrease in level of consciousness
 - seizures
 - cardiovascular collapse
 - neuromuscular paralysis

Note: ingestion of petroleum distillates is not an absolute contraindication to the use of emesis, although it is generally advised that emesis should be avoided in such cases; under certain circumstances, it may be necessary to remove the substance despite the risk; in such cases, steps should be taken to minimise the risk of aspiration.

Methods of Inducing Emesis

Emesis can be induced by a number of different methods. Many are outdated and/or unsafe. Two currently in use are:

- Pharyngeal stimulation
 - this is used mainly as a first aid measure and is of limited effectiveness
- Ipecacuanha (Ipecac) syrup
 - this is the method of choice
 - it causes emesis through stimulation of chemoreceptors in the CNS

Procedure - Inducing Emesis with Ipecac syrup

The recommended doses are:

- 6 months to 1 year - 10 ml
- 1 year to 12 years - 15 ml
- Above 12 years - 30 ml

If emesis does not occur, gastric lavage should be considered.

Poisoning By Antiemetic Agents

In such cases, emetics can be given and will usually work. However, if the emetic fails, no further doses should be administered due to the risk of toxicity.

Side Effects of Ipecac

Although Ipecac is generally safe and well tolerated, some patients do suffer from adverse effects. These include:

- Protracted vomiting
- Diarrhoea
- Excessive sweating
- Fever
- Lethargy

Avoid using fluid extract of Ipecac.

Gastric lavage

This is most effective in cases when ingestion of the poison was less than 1 hour before commencing treatment, although a larger time frame is allowed for slow-release formulations or drugs which slow gastric emptying.

Indications

The indications for gastric lavage are as follows:

- A potentially toxic dose was ingested
- The substance was ingested less than 60 minutes (a longer time is allowable for anticholinergic agents, salicylates, tricyclic antidepressants)
- To remove corrosive liquids ingested acutely
(Note: this is not a universally accepted indication)

Contraindications

The contraindications to the use of gastric lavage are as follows:

- Convulsions
- Petroleum distillates
- Strong acid or alkali (this contraindication is not universally accepted)
- Unconscious patients unless airway is protected

Note: Gastric lavage may potentially increase absorption of toxins by quickening the gastric emptying time and increasing absorption from the small intestines.

Procedure

1. In patients with impaired consciousness, it will be necessary to protect the airway with a cuffed endotracheal tube. If the patient is conscious, he or she should be given a glass of water to drink prior to passing the tube.
2. Place the patient in the left lateral position to permit pooling of gastric contents and to reduce the risk of aspiration. His head should be lower than the rest of his body to reduce the chances of accidental aspiration.
3. Use the largest diameter orogastric lavage tube. A size 32 to 36 French Ewald tube is ideal.
4. Once inserted, check the position of the tube to ensure that it is in the stomach and not the trachea. The position must be confirmed prior to commencing lavage. This can be done by the following manoeuvres:
 - a) placing the outer end in a glass of water. Active bubbling on expiration suggests that the tube is in the trachea. In such a case, the tube should be removed and another attempt made to insert it.
 - b) testing aspirate with litmus paper to detect acid
 - c) listening for gurgle sound over epigastrium on pumping air.
5. Administer 100 - 300 ml of lavage fluid via the tube (in children, administer 50 - 100 ml). Then, manually agitate the stomach. After that, withdraw the fluid.
6. Repeat this until the lavage return is clear. Generally, anywhere from 5 to 20 L are required to thoroughly cleanse the stomach.
7. Remember to save the aspirate for toxicology screening.
8. After completion of the lavage, activated charcoal may be administered via the orogastric lavage tube.

Note: it must be borne in mind that even though the procedure is carried out until the aspirated fluid is clear, there may still be particles or clumps of solids remaining in the stomach.

Potential Complications

Complications that could arise from gastric lavage are:

- Aspiration pneumonia
- Bleeding
- Cardiac arrest
- Gagging and vomiting
- Perforation
- Psychological trauma
- Vasovagal effects
- Laryngospasm
- Fluid and electrolyte disturbances

Catharsis

This can be used to remove unabsorbed poisons or poisons that have entered the intestines. They can also be used to quicken the passage of the charcoal-toxin complex. However, there is some controversy about the efficacy of these methods of elimination.

Although cathartics have been used in poisons management, there is no proven record of their efficacy in clinical practice. In theory, the advantage of using catharsis as the sole method of gastro-intestinal decontamination is that the increased gastro-intestinal transit speed will decrease the time available for absorption of the poison.

However, recently, cathartics have been used to neutralise the constipating effect of activated charcoal. This allows more of the charcoal to be administered and come into contact with the poison.

Contraindications to Catharsis

The contra-indications to catharsis are:

- Abdominal trauma
- Corrosives
- Electrolyte imbalances
- Ileus or intestinal obstruction
- Impaired renal function
- Pre-existing diarrhoea
- Volume-depleted states

Cathartics containing magnesium should not be administered to:

- Patients with renal disease
- Patients exposed to nephrotoxins
- Patients in whom myoglobinuria or haemoglobinuria is present or likely

Cathartics containing sodium should not be administered to patients with congestive cardiac failure.

Precautions

The following precautions should be borne in mind when using cathartics:

- Catharsis should not be used for trivial ingestion in children
- Phospho-soda preparations should not be used in children
- Repetitive doses of magnesium containing cathartics should be minimised
- In children, sorbitol or sorbitol-based charcoal should be used with care and a close watch should be kept on fluid and electrolyte status
- Oil-based catharsis should not be used because of the risks of aspiration and enhanced toxin absorption

Procedure for Catharsis

1. Give the patient 250 mg / kg body weight of magnesium sulphate.

Note: the maximum is 25 g

Alternatives are magnesium citrate, magnesium sulphate, sodium sulphate and sorbitol.

2. The cathartic effect should follow within 30 - 60 minutes.
3. Keep a close watch on the fluid and electrolyte balance.

Intestinal Lavage

Like catharsis, the main use of this procedure is in the removal of the poison from the intestine.

This is carried out by instilling 100 - 250 ml portions of mannitol into the small intestine by means of an intestinal suction tube. The mannitol is then removed by gentle continuous suction.

Whole Bowel Irrigation

This procedure is similar to colonic washout in bowel preparation. It involves inducing diarrhoea by mechanically flushing the bowel contents through the GIT. This is achieved by using large volumes of isotonic non-absorbable solutions. No significant fluid shifts are expected to occur with this technique. It is especially useful in overdoses with enteric coated tablets and sustained release formulations.

Although this method is not used very commonly, it is expected that its use will increase, especially in combination with multiple dose activated charcoal (MDAC).

Whole bowel irrigation is carried out by giving the patient 2 L of polyethylene glycol orally.

Gastroscopic Removal

This is done only when large quantities of capsules or tablets are ingested and a mass of drug is formed in the stomach, such that it cannot be removed by gastric lavage or emesis.

Gastroscopic removal of drug concretions or bezoars are advised in such patients.

Oral Adsorbents

These are used to decrease the absorption of the poison into the system. One of the more commonly used oral adsorbents is activated charcoal. In recent years, this has been used increasingly in the initial management of poisoned patients.

Oral adsorbents are generally used in the following situations:

- When both emesis and lavage are contraindicated
- After completion of emesis or lavage
- In multiple doses as part of GIT dialysis

Activated charcoal is inadvisable under the following conditions:

- Ileus or intestinal obstruction
- Corrosive agent ingestion
(charcoal obscures the view during endoscopy)

Generally, oral adsorbents are most effective when administered within 1 hour of poisoning. However, in cases of poisoning by a sustained-release formulation or by drugs which decrease gastrointestinal motility and gastric emptying, oral adsorbents can still be fairly effective even if administered a little later.

Note: multiple dose activated charcoal (MDAC) has been found to be as efficacious as haemodialysis in several studies.

Drugs that Activated Charcoal is Effective in Adsorbing

Activated charcoal has been shown to be effective in adsorbing the following drugs:

- Acetaminophen
- Tricyclic antidepressants
- Antipyridines
- Arsenic
- Aspirin
- Atropine
- Chlorpheniramine and related antihistamines
- Chlorpromazine and related phenothiazines
- Dextro-amphetamine
- Digoxin
- Glutethimide
- Isoniazid
- Meprobamate
- Salicylates
- Morphine
- Paraquat
- Phenobarbitone and other barbiturates
- Penicillin
- Phenylpropranolamine
- Phenytoin
- Propoxyphene
- Quinidine
- Quinine

Drugs that Activated Charcoal is Not Effective in Adsorbing

Activated charcoal has not been shown to be effective in adsorbing the following:

- Acids and caustic alkalis
- Aromatic alcohols
- Boric acid
- Ethylene glycol
- Heavy metals
- Iron
- Lithium
- Malathion
- Methylcarbamate
- Methanol

Administration of Charcoal

The dosage for adults is as follows:

- First dose: 50 - 100 g
(orally or via a nasogastric tube)
- Subsequent doses: 15 - 20 g at 4 - 8 hourly intervals for up to 24 hours

The dosage for children is as follows:

- First dose: 1 g / kg body weight
(orally or via a nasogastric tube)
- Subsequent doses: 0.5 g / kg body weight at 4 - 8 hourly intervals for up to 24 hours

Note: 1) commercially available charcoal tablets are not suitable as the dosage is too low and the surface area is insufficient
2) first dose of activated charcoal is preferably with sorbitol but subsequent doses should be pure activated charcoal unless no bowel movement occurs.

Precautions

Some antidotes (e.g. methionine) are strongly bound to adsorbents like charcoal and as such, they should not be given together.

Activated charcoal should not be given together with Ipecac syrup as the active compounds in Ipecac syrup will be bound by the activated charcoal. Traditionally, it has been stated that activated charcoal should not be given within 30 minutes of administration of Ipecac syrup. However, recent research suggests that it can be given 10 minutes after the Ipecac.

Potential Adverse Effects

Activated charcoal is known to result in constipation and repeated doses may result in ileus and vomiting. If vomiting occurs, it must be borne in mind that while activated charcoal is not known to have any direct adverse effect on the lungs, it is often mixed with bacteria and gastric acid and these will cause damage to the lungs if aspirated. As such, activated charcoal is preferably given with a cathartic.

Preparations of activated charcoal that contain a cathartic have been known to induce diarrhoea in some patients.

Topical Decontamination

Procedure

Remove any clothing and other materials (e.g. jewellery, contact lenses) that may be contaminated.

Precaution: This should be done with care and the decontamination team should avoid being contaminated themselves. Team members should be wearing protective equipment - the minimum precautions include disposable hospital gowns, plastic goggles, latex gloves and a surgical mask. In cases involving concentrated acids or alkalis or dangerous chemicals, disposable waterproof and chemical-proof overalls and gloves should be used. For radioactive materials, further measures are required.

Gently dust off powdery materials with a brush. Add water to some of the dusted off material to test for any reaction prior to wetting the patient.

In cases of mustard gas poisoning, Fuller's Earth can be used for dry decontamination.

Irrigate the affected areas thoroughly with lukewarm water or saline for at least 15 minutes.

Note: In the case of caustic alkalis, irrigation should be for at least 30 minutes.

Mild soap solutions may be used to neutralise acid if necessary. They can also be used for oily or greasy contaminants. This is then followed by flushing with water.

Scrub the nails with a scrub brush or plastic nail cleaner.

Neutralising Agents

Generally, neutralising agents should not be used as there is a risk of further injury from the heat generated by the chemical reaction.

However, there are several exceptions, as listed in the following table:

Contaminant	Treatment
hydrofluoric acid	magnesium sulphate or calcium gluconate
oxalic acid	calcium gluconate
phenol	mineral oil or other types of oil
white phosphorus	copper sulphate 1% (imparts blue colour to phosphorus granules, making them easier to remove)

Eye injury from Chemical Irritants

1. Place the patient in a reclining chair. Remove contact lenses, if present.
2. Irrigate the eyes for at least 15 minutes with sterile normal saline or sterile water and taking care not to cross contaminate in uniocular injuries.
Note: use at least 1 L of fluid
3. If the substance is an acid or alkali, check the pH of the tears after irrigation. If the pH remains abnormal, continue irrigation.
4. Instill a few drops of 1% sterile fluorescein solution into the eye. If the fluorescein produces a yellow or green stain, which is indicative of corneal injury, irrigate the eyes for another 5 minutes.

Important: Chemical neutralisation should not be attempted as there is a definite risk of further damage from the chemical reaction.

5. The patient should then be sent to an ophthalmologist, preferably within 2 hours of the injury.

Respiratory Decontamination

This consists of the following:

- Removal from exposure
- Establishing an airway
- Giving of humidified oxygen
- Intubation and assisted ventilation, if required
- Administration of specific antidote, if available

The patient should be observed carefully as there is a risk that oedema will develop in the upper respiratory tract and cause respiratory obstruction. In such cases, intubation may become necessary.

The patient is also potentially at risk of late-onset non-cardiogenic pulmonary oedema.

Pregnant Patients

Unwanted pregnancy may be a cause for an intentional overdose.

Inducing emesis with Ipecac syrup is probably safe in early pregnancy but may not be advisable later, particularly in the third trimester. Generally, in such patients, gastric lavage and activated charcoal are the methods of choice.

It must also be borne in mind that some toxins are teratogenic.

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CHAPTER 4

Enhancing the Elimination of Toxic Substances from the Body

Introduction

The main methods for elimination of toxic substances from the body are:

- 1) Forced diuresis
- 2) Dialysis
- 3) Haemoperfusion
- 4) Haemofiltration
- 5) Hyperbaric oxygen
- 6) Multiple dose activated charcoal

Some of these methods, in particular, forced diuresis, were previously very popular but now they are used only when indicated. They should not be routinely used for all poisoning cases.

Indications

The use of one of these methods for the elimination of a toxic substance is indicated mainly when:

- The patient's condition is serious
- The method chosen will remove a significant amount of the poison

In addition, there are indications and contra-indications specific to each method.

Forced Diuresis

In the past, forced diuresis was commonly used in many patients and for most forms of poisoning. However, it has been shown that the clinical course of most poisonings is not affected by forced diuresis. In addition, the procedure carries with it the dangers of volume overload and electrolyte disturbances.

Theoretical Basis

Forced diuresis is based on the principle that for drugs that are excreted by the kidneys, the amount excreted can be increased by increasing the urine output.

This is, however, useful only for drugs that are excreted either unchanged or as active metabolites. Generally, this method is not useful for drugs that are metabolised by the liver and then excreted as inactive metabolites.

Most drugs are partially reabsorbed in the renal tubules. This will reduce the amount of drug excreted despite any increase in urine output. However, this reabsorption primarily affects un-ionised, lipid-soluble molecules. By increasing the concentration of the drug that is in the ionised form, reduced re-absorption can be brought about. This will result in increased excretion.

An increase in the concentration of the ionised drug can be achieved by manipulating the urine pH. Acidic drugs tend to remain ionised when in alkaline urine and basic drugs tend to remain ionised when in acidic urine.

A number of drugs have large volumes of distribution and the amount that can be eliminated by forced diuresis is somewhat limited.

Indications

The indications for forced diuresis are:

- The substance or its active metabolites are excreted in the urine
- There is a high plasma concentration of the substance
- There is a high probability that supportive therapy alone will be insufficient

Contraindications

The contraindications for forced diuresis are:

- Impaired renal function
- Cardiac disease, in particular, cardiac failure
- Shock
- Hypotension despite administration of IV fluids

Care should also be taken when attempting forced diuresis in:

- Elderly patients
- Poisoning by cardiotoxic agents
- Poisoning by nephrotoxic agents

All unconscious patients undergoing forced diuresis should be catheterised. Urine flow rate should be at least 6 - 8 ml / minute.

Potential Complications

The complications that may result from forced diuresis include:

- Electrolyte and acid-base disturbances
- Hypokalaemia
- Hypocalcaemia
- Hypomagnesaemia
- Cerebral oedema
- Pulmonary oedema
- Water intoxication

Types of Forced Diuresis

There are two forms of forced diuresis:

- Forced diuresis without manipulation of urinary pH
- Forced diuresis with manipulation of urinary pH

Forced diuresis with manipulation of the urinary pH is further sub-divided into:

- Forced alkaline diuresis
- Forced acid diuresis

Forced Diuresis Without Manipulation of Urinary pH

Drugs that can be removed by simple forced diuresis include the following:

- Alcohol
- Amphetamines
- Aniline
- Barbiturates (long-acting)
- Bromide
- Ethylene glycol
- Isoniazid
- Lithium
- Methanol
- Penicillin
- Phencyclidine
- Quinine
- Salicylates
- Strychnine
- Sulphonamides

Reminder: The use of forced diuresis must be carefully controlled and it is not a procedure that should be done routinely in patients as it carries risks that have been discussed previously.

Procedure

The procedure involves a cycle of 1.5 L of fluid every 3 hours, consisting of:

- 500 ml of normal saline
- 500 ml of 5% dextrose + 20 ml of 7.45% potassium chloride
- 500 ml of normal saline

IV furosemide 20 mg is given at the end of each cycle.

Monitoring

The following should be monitored when attempting forced diuresis:

- Plasma electrolyte levels
- Patient's input and output
- Patient's condition and vital signs

Forced Alkaline Diuresis

While this method is theoretically useful for a number of weakly acidic drugs, in practice it is used primarily for salicylates and sometimes, phenobarbitone, barbitone, phenoxyacetate herbicides and tricyclic antidepressants.

Indications

The indications for forced alkaline diuresis are those for forced diuresis in general, as listed above. In addition, the plasma level of the drug should be:

- Phenobarbitone plasma level > 10 mg / dL
- Barbitone plasma level > 10 mg / dL
- Salicylate plasma level > 50 mg / dL

Respiratory alkalosis is not a contraindication to forced alkaline diuresis as there is a significant base deficit still.

Preliminary Investigations

Before commencing forced alkaline diuresis, the following investigations should be carried out:

- Baseline electrolyte levels
- Blood sugar level
- Plasma drug level
- Arterial pH
- Urinary pH

It is also important to have the following in place:

- CVP line
- Urinary catheter

Procedure

The following are given in 3-hour cycles, with 500 ml being administered each hour, in the following order:

- 500 ml of 5% dextrose + 8.4% sodium bicarbonate solution (sodium bicarbonate solution: 1 - 2 ml / kg body weight)
- 500 ml of 5% dextrose + 30 ml of 7.45% potassium chloride
- 500 ml of normal saline

IV frusemide 20mg should be given at the end of each cycle.

If the urine flow at 1 hour is less than 3 ml / minute (180 ml / hour), diuresis should be discontinued.

The urine pH should be monitored and maintained at a level above 8.0. This can be done by adjusting the rate of the bicarbonate infusion.

In addition, serum pH and electrolytes should be monitored closely.

Forced Acid Diuresis

Forced acid diuresis is rarely done in practice. It must be emphasised that this is a dangerous procedure. As such, it should only be used in situations where the clinical effects of the overdose cannot be managed by other means.

Possible Indications

The possible indications for forced acid diuresis include:

- Quinine poisoning
- Phencyclidine poisoning

Forced acid diuresis can also be considered in the following cases, although they are not definite indications for the procedure:

- Amphetamine poisoning
- Fenfluramine poisoning

Contraindications

The contra-indications are those for forced diuresis in general.

Procedure

The baseline information required is similar to that for forced alkaline diuresis.

Each cycle of forced acid diuresis is run over 3 hours and consists of the following:

- 500 ml 5% dextrose + 1.5 g ammonium chloride
- 500 ml 5% dextrose + 20 ml 7.45% potassium chloride
- 500 ml normal saline + 1 g ascorbic acid

IV frusemide 20mg is given at the end of each cycle

Important: Serum pH and bicarbonate, as well as urinary pH, must be monitored. The serum bicarbonate should be maintained above 18 mg/dl and the urinary pH below 5.0.

Serum electrolyte levels and the patient's input and output should also be monitored

Dialysis

There are three forms of dialysis:

- Haemodialysis
- Peritoneal dialysis
- Charcoal haemoperfusion
- Haemofiltration
- GIT dialysis with multi-dose charcoal

It must be noted that haemodialysis and peritoneal dialysis are not routinely carried out in poisoned patients. Instead, they should be used as adjuncts to management in severe cases.

Haemodialysis

This is useful for drugs which fulfill the following conditions:

- Low molecular weight and size (<500 daltons)
- Freely soluble in body water
- Slowly metabolised and inactivated so that dialysis will contribute to its elimination
- Limited protein binding

As such, it has been shown to be useful in cases of poisoning by:

- Sedatives and hypnotics
e.g. long, intermediate and short acting barbiturates
glutethimide
ethchlorvynol
- Analgesics
e.g. acetaminophen
salicylates
- Alcohols
e.g. ethanol
ethylene glycol
methanol
isopropyl alcohol
- Metals
e.g. lithium
- Others
e.g. theophylline
tricyclic antidepressants

Indications

The indications for haemodialysis are:

- Severe clinical intoxication with unstable vital signs or metabolic disturbances which have failed to show significant improvement despite aggressive supportive therapy
- Concurrent renal and/or hepatic failure i.e. failure of the organ system responsible for the excretion of the drug; this can be induced by the drug itself or by underlying disease

- Metabolites equal or greater in toxicity e.g. ethylene glycol, which is converted to oxalic acid
- Significant underlying disease that would add significantly to the morbidity and mortality of prolonged coma e.g. lung disease

Contraindications

The following are contra-indications to haemodialysis:

- Hypotension
- Shock

Procedure

Suitable anticoagulation measures should first be taken. A catheter is usually placed in the inferior vena cava (via the femoral vein).

Through this, blood is passed through the dialyser before being returned to the venous circulation, either through the second lumen (if a double-lumen catheter was used) or through a separate catheter.

Sometimes, haemoaccess may be obtained via another large vein or the arterial circulation.

Complications

The potential complications of haemodialysis are:

- Air embolism
- Bleeding or thrombosis at the haemoaccess site
- Bleeding due to systemic anticoagulation with heparin
- Hypotension
- Increased elimination of therapeutic agents
- Nosocomial infection

Peritoneal Dialysis

Important: Peritoneal dialysis is seldom used now.

The main drawback of this procedure is that it takes a long time to carry out. Also, the efficiency of the procedure is generally only about 1/6 that of haemodialysis.

Previously, peritoneal dialysis had been shown to be of use in poisoning by:

- Ethylene glycol
- Lithium
- Methanol
- Phenobarbitone
- Salicylates
- Sodium chlorate

GIT Dialysis With Multi-Dose Activated Charcoal (MDAC)

In this procedure, activated charcoal is administered to the patient.

Multiple doses of activated charcoal are believed to enhance elimination of certain drugs. The mechanism of action is thought to be interruption of the enterohepatic circulation and a gastro-intestinal dialysis effect.

Dosages

The dosage for adults is as follows:

- First dose: 50 - 100 g
(orally or via a nasogastric tube)
- Subsequent doses: 15 - 20 g at 4 - 8 hourly
intervals for up to 24 hours

The dosage for children is as follows:

- First dose: 1 g / kg body weight
(orally or via a nasogastric tube)
- Subsequent doses: 0.5 g / kg body weight at 4 - 8 hourly
intervals for up to 24 hours

Note: 1st dose of activated charcoal is to be given with sorbitol and subsequent doses should be pure activated charcoal unless no bowel movement occurs.

Haemoperfusion

This is a process by which blood is passed through a column containing activated charcoal, activated carbon or ion-exchange resins, resulting in adsorption of the poison.

It is a very useful procedure but is also very expensive.

This procedure is most useful for drugs which fulfil the following criteria:

- Lipid-soluble
- Poorly dialysable

- Protein-bound
- Relatively long half-life
- Low volume of distribution (1 - 8 L/kg)

As such, it has been shown to be effective in removing:

- Analgesics
e.g. acetaminophen
salicylates
- Antidepressants
e.g. amitriptyline
desipramine
- Barbiturates
- Non-barbiturate sedatives
e.g. chloral hydrate
chlorpromazine
diazepam
ethchlorvynol
glutethimide
meprobamate
methaqualone
methylprylon
promazine
- Cardiovascular drugs
e.g. digoxin
procainamide
- Others
e.g. carbon tetrachloride
methotrexate
organochlorine insecticides
some organophosphates
paraquat
polychlorinated biphenyls

Indications

Haemoperfusion should not be carried out unless at least 3 of the following criteria are present:

- Severe clinical intoxication
 - e.g. grade 4 coma
 - hypotension
 - hypothermia
 - hypoventilation (in patients who have ingested hypnotic drugs)
- Progressive clinical deterioration despite good supportive management
- No evidence of improvement despite full resuscitative measures
- Prolonged coma with complications
 - e.g. pneumonia
- High plasma levels of the drugs as shown in the table below

Plasma Drug Concentration for Effective Haemoperfusion (mg / L)	
Phenobarbitone	> 100
Barbitone	> 100
Other barbiturates	> 50
Ethchlorvynol	> 150
Glutethimide	> 40
Meprobamate	> 100
Methaqualone	> 40
Salicylates	> 1000
Theophylline	> 60
Trichloroethanol derivatives	> 50

Procedure

Suitable anticoagulation measures should first be taken. A catheter is usually placed in the inferior vena cava (via the femoral vein). Through this, blood is passed through the dialyser before being returned to the venous circulation, either through the second lumen (if a double-lumen catheter was used) or through a separate catheter.

Alternatively, haemoaccess may be obtained via another large vein or the arterial circulation.

Complications

The complications of haemoperfusion are similar to those of haemodialysis but, in addition, the following complications may also occur:

- Charcoal microembolisation
- Leukopenia
- Thrombocytopenia

However, some of these complications have been largely eliminated by the use of newer haemoperfusion cartridges.

Haemofiltration

This technique uses a haemofilter that contains thousands of hollow-fibre filters made of polysulfone or polyamide. Blood is passed through these fibres and, in the process, substances with molecular weights of less than 10,000 daltons are removed. The cellular components and larger molecules are then returned to the circulation via a venous line. Lost electrolytes must be replaced intravenously.

Haemoaccess is usually obtained via a catheter placed in a peripheral artery or vein.

Haemofiltration is able to remove compounds not removable by haemodialysis. Although it is not used very widely at present, it is potentially very useful in the management of poisoning.

Hyperbaric Oxygen

This is used primarily for patients poisoned by gases that interfere with oxygen carriage.

It has been found to be of use in poisoning by:

- Carbon monoxide
- Cyanide
- Hydrogen sulphide

Procedure

The patient breathes in 100% oxygen intermittently while the pressure of the treatment chamber is increased to a point higher than sea level pressure i.e. greater than 1 atmosphere absolute (atm abs).

Currently, the accepted opinion is that the pressure should be 1.4 atm abs or higher. Some studies have also been carried out with oxygen at 2 - 5 atm for at least 2 - 3 hours.

Note: breathing 100% oxygen or exposing isolated parts of the body to 100% oxygen does not constitute hyperbaric oxygen therapy

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CHAPTER 5

Medico-Legal Aspects of Poisoning

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Poisoning, whether accidental, suicidal or homicidal, is an unnatural event. When death occurs due to poisoning, such death must be reported to the Coroner through the police. Sometimes death may not occur immediately after poisoning but as long as the death can be linked to the poisoning episode, a report must be made to the Coroner. If the suspected poison is found, this must be sent to the Toxicology Laboratory of the Department of Scientific Services in the Institute of Science and Forensic Medicine. Stomach washouts and other biological samples are to be sent to the same laboratory for analysis. In sending stomach washouts, it is essential to send the first aspirates as these would contain the poison, and not the subsequent gallons of fluid.

There are three Acts concerning poisoning that the medical practitioner should be aware of. They are:

1. The Poisons Act,
2. The Misuse of Drugs Act,
3. The Factories Act.

The Poisons Act

This Act regulates the importation, possession, manufacture, compounding, storage, transport and sale of poisons. Medical practitioners are reminded to keep proper records of the medicine they prescribe or dispense to their patients, which should be labelled with the date the medicine was supplied, serial number or mark, the ingredients or name of the medicine, name and address of the person to whom the prescription was given. (Please refer to the Act)

The Misuse of Drugs Act

This Act requires medical practitioners, dentists, pharmacists, veterinary surgeons and other persons dealing in controlled drugs to keep records and make returns. Medical practitioners are required to furnish to the authority particulars of the person he attended to whom he considers, or has reasonable ground to suspect, to be addicted to controlled drugs. He is also prohibited from administering, supplying and authorising the administration and supply to persons addicted to controlled drugs, and to prescribe to them these drugs.

The Factories Act

Under the Sixth Schedule of this Act, notifiable industrial diseases include the following:

- Aniline poisoning
- Anthrax
- Arsenic poisoning
- Asbestosis
- Barotrauma
- Beryllium poisoning
- Byssinosis
- Cadmium poisoning
- Carbon bisulphide poisoning
- Chrome ulceration
- Chronic benzene poisoning
- Compressed air illness
- Epitheliomatous ulceration (due to tar, pitch, bitumen, mineral oil and paraffin or any compound product or residue of any such substance)
- Industrial dermatitis
- Lead poisoning
- Liver angiosarcoma
- Manganese poisoning
- Mercurial poisoning
- Mesothelioma
- Noise-induced deafness
- Occupational asthma
- Phosphorus poisoning
- Silicosis
- Toxic anaemia
- Toxic hepatitis

CHAPTER 6

Socio-Psychiatric Aspects of Poisons Management

Introduction

The socio-psychiatric aspects of poisons management are complex and depends on whether it was an act of attempted suicide or not.

If it is not an attempted suicide, it may be accidental poisoning, in which case all that may be required is a medical follow-up, and a short-term psychiatric follow-up to ensure that the patient does not develop any psychological problems from the episode.

However, if it is an act of poisoning by another party, it is likely to become a legal matter. Medically, it can be managed in a manner similar to any other poisoning case and it is unlikely that a great deal of psychiatric follow-up treatment will be required. However, there are definite medico-legal issues involved and this must be borne in mind, particularly with regard to documentation and case notes.

If it is a case of attempted suicide, then the psychiatric aspect of the patient's follow-up takes on a new dimension of importance.

Suicide And Deliberate Self-Harm

There is a difference between patients who have actually attempted suicide and failed in the attempt and those who have engaged in parasuicide, or non-fatal deliberate self-harm. The management of the patient depends very much on which category the patient falls into. The suicide risk of the former category of patients is much higher.

The vast majority of patients do not actually have a suicide intent and thus, they come under the category of 'deliberate self-harm'. In general, the management of such patients is complex and they are often evaluated by both the psychiatrist and the medical social worker.

Besides a psychiatric history, a social history must be taken as it is not uncommon for social problems to contribute greatly to the patient's current condition.

In terms of the psychiatric aspect of the patient's problems, depressive symptoms are almost always present. Sometimes, a strong element of anxiety may be present as well. A distinct proportion of suicide patients may exhibit a personality disorder but generally, only a small percentage has evidence of a severe psychiatric illness.

Cause

In many patients, deliberate self-harm has been precipitated by some specific event in their lives which has upset them greatly. Sometimes, this may be a single event that is the culmination of a chain of events, like "the straw that broke the camel's back".

The intention of many such patients, subconsciously sometimes, is often to draw attention to their plight. Even for those who seek to escape from their problems once and for all, often the suicide intention is often a transient one.

Assessment

It is not always easy to assess such patients as some can be very uncommunicative and even hostile. However, it must be attempted.

It must be ascertained whether the patient falls under the category of a failed suicide or of deliberate self-harm as the suicide risk of patients in the former category is very much higher.

Characteristics Which Suggest a Case Of Failed Suicide

The following characteristics suggest that a patient is not a case of deliberate self-harm (DSH) but is actually a case of failed suicide:

- Massive overdose, which can be fatal
 - often DSH patients take much smaller doses
- Deep extensive lacerations
 - DSH patients who cut themselves usually have small, shallow cuts
- Use of firearms
 - DSH patients seldom use firearms

- Precautions to avoid discovery or to succeed
 - e.g. locking the door, waiting till no one is at home
 - DSH patients usually make sure that others can find and save them
 - some DSH patients also announce their intent beforehand
- Social problems
 - e.g. bereavement, marital problems, employment problems
- Medical problems, particularly terminal illnesses
- Psychiatric problems
 - e.g. depression, schizophrenia
- Alcoholism
- Drug addiction

It has also been found that there are more male patients than female patients cases of failed suicides while the reverse is true in cases of DSH.

If any of the above risk factors are present, added precautions will be necessary as there is a definite likelihood of the patient making a second attempt.

Management

The initial management of such patients focuses primarily on the medical problems caused by the poisoning. However, precautions must be taken to ensure that the patient does not have the means to make a second attempt at suicide.

Once the immediate problems have been settled, psychiatric management of the patient can commence.

Generally, depression must be treated. Any other underlying medical or psychiatric problems should also be dealt with. In addition, the medical social worker may be able to assist the patient in dealing with some of the social problems.

The psychiatric management of the patient is a very specialised area and is best carried out by personnel trained for the task.

The options available for psychiatric management of the patient include the following:

- Electro-convulsive therapy (ECT) for the acute phase of severe depression
- Antidepressants
- Appropriate medication for any psychiatric or medical problems (some medical problems can cause psychosis and other psychiatric problems)
- Psychotherapy and cognitive therapy
- Crisis intervention
- Stress management

Follow-Up

The follow-up of the patient is important as a significant number of patients, both failed suicides as well as DSH cases, do repeat either a suicide attempt or DSH. As such, it is important that such patients are properly followed-up and managed in order to minimise this risk.

References

1. Haddad, LM and Winchester, JF (eds). *Clinical Management Of Poisoning And Drug Overdose. 2nd Edition. WB Saunders Company. 1990.*
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CHAPTER 7

The Toxicology Laboratory

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Toxicology Laboratory
Institute of Science and Forensic Medicine

Readers are advised to note that the information provided is current at time of printing. They should check with the Toxicology Laboratory directly for the latest information. The telephone number is 229-0740.

Scope of Services

The Toxicology Laboratory of the Institute of Science and Forensic Medicine is the only laboratory in Singapore which provides a comprehensive range of services in clinical toxicology. These services are open to all hospitals.

Purpose for Conducting Clinical Toxicology

Clinical toxicology is conducted primarily for the following medico-legal purposes:

- (i) To confirm an overdose situation including overdose by ethanol or methanol.
- (ii) To exclude common drugs and poisons in specimens pertaining to potential organ donors.
- (iii) To help confirm drugged-and-robbed, drugged-and-raped and other cases of drug-assisted criminal intent.
- (iv) To ascertain whether or not blood ethanol level exceeds the legal limit of 80 milligrams of ethanol per 100 ml of blood in road traffic accident and suspected drunken driving cases.

Making Use of the Services

When to submit specimens

Specimens are to be submitted to the laboratory during office hours. The office hours are as follows:

Weekdays:	8.00 a.m. to 4.30 p.m.
Saturdays:	8.00 a.m. to 12.30 p.m.
Sundays and Public Holidays:	Closed

How to submit specimens

The Toxicology Laboratory is located on the third floor of 11 Outram Road, Singapore 169078. A pass must first be obtained from the administration office on the first floor. Entry to the laboratory is made through a security door temporarily unlocked by the toxicology personnel. Documentation must be properly completed and signed. Registration is then made at the administration office.

Submission Requirements

- Disposable containers and tubes with leak-proof screw caps should be used.
- The following requirements on clinical specimens should be noted:

<u>Specimen</u>	<u>Volume Needed</u>
Gastric aspirate	at least 50 ml (plain)
Blood for drugs screening	10 ml (citrate, oxalate or heparin)
Blood for alcohol determinations	5 ml (citrate, oxalate or heparin).

Note: Alcohol must not be used for swabbing the area to be punctured or for sterilising the hypodermic needle

Blood for carboxyhaemoglobin	5 ml (citrate)
Urine	at least 20 ml (plain)

- Specimens must be legibly labelled and sealed.

- Specimens must be submitted with a request form. The following information should be given in the form:
 - (i) The particulars of the patient.
 - (ii) Signs, symptoms and condition of the patient.
 - (iii) The nature of toxic agent(s) suspected.
 - (iv) The name (in block letters) and signature of the person requesting the analysis.
 - (v) Any other information which may help the analyst identifying the toxic agent(s).
 - (vi) Any alteration of the entries on the form should be initiated by the person requesting the analysis.

Any non-compliance of the above may lead to the rejection of the specimen(s).

Toxic Agents Screened For

Blood Specimens

Blood specimens could be screened for the following panels of drugs and poisons.

PANEL ONE	:	Carboxyhaemoglobin
PANEL TWO	:	Cyanide
PANEL THREE	:	Chloroxylenol
PANEL FOUR	:	Salicylates
PANEL FIVE	:	<u>Alcohols and Other Volatiles</u> acetone ethanol isopropanol methanol

- PANEL SIX : Alcohols and Other Volatiles
acetone
benzene
ethanol
isopropanol
methanol
paraldehyde
toluene
xylenes
- PANEL SEVEN : Anaesthetics
propofol
- Antiepileptics
carbamazepine
ethosuximide
phenobarbitone
phenytoin
primidone
thiopentone
valproic acid
- PANEL EIGHT : Analgesics
diclofenac
diflunisal
flufenamic acid
flurbiprofen
ibuprofen
indomethacin
ketoprofen
mefenamic acid
meclofenamic acid
naproxen
paracetamol
phenylbutazone
piroxicam
propyphenazone
salicylic acid
sulindac

Antibacterials

fluconazole
griseofulvin
metronidazole
sulfapyridine
sulfadiazine
sulphamethoxazole
trimethoprim

Anticoagulants

coumarin
coumachlor
warfarin

Antidiabetics

chlorpropamide
gliclazide
tolazamide
tolbutamide

Antiepileptics

carbamazepine
ethosuximide
phenytoin
primidone

Barbiturates

amylobarbitone
phenobarbitone
quinalbarbitone

Diuretics

chlorthalidone
diazoxide
frusemide

Muscle relaxants

chlormezanone
chlorzoxazone
methocarbamol

Others

theophylline
8-chlorotheophylline

PANEL NINE : Benzodiazepines
alprazolam
bromazepam
chlordiazepoxide
clobazam
clonazepam
diazepam
estazolam
flunitrazepam
flurazepam
lorazepam
midazolam
nimetazepam
nitrazepam
nordiazepam
triazolam

PANEL TEN : Amphetamines and Other Anorexic Agents
amphetamine
ethylamphetamine
fenfluramine
MDMA
methamphetamine
phentermine

Antihistamines

brompheniramine
buclizine
chlorpheniramine
cinnarizine

cyclizine
diphenhydramine
doxylamine
hydroxyzine
promethazine
triprolidine

Antimalarials

chloroquine
pyrimethamine
quinine

Benzodiazepines

alprazolam
bromazepam
chlordiazepoxide
clobazam
diazepam
estazolam
flunitrazepam
flurazepam
midazolam
nimetazepam
nitrazepam
nordiazepam

Cardiac and Antihypertensive Drugs

diltiazem
lignocaine
propranolol
quinidine
verapamil

Narcotics

codeine
methadone
pentazocine
phenazocine
pethidine

methorphan
propoxyphene
tramadol

Phenothiazines
chlorpromazine
prochlorperazine
thioridazine
trifluoperazine

Antidepressants
amitriptyline
clomipramine
clozapine
dothiepin
fluoxetine
fluvoxamine
imipramine
melitracen
moclobemide
mianserin
sertraline
trimipramine

Others
metoclopramide
ticlopidine
zolpidem

PANEL ELEVEN : morphine

Gastric Aspirate Specimens

Gastric aspirate specimens could be screened for the following panels of drugs and poisons:

PANEL ONE : Heavy metals: arsenic, selenium, mercury and antimony (Reinch Test).

PANEL TWO : Cyanide.

PANEL THREE : Chloroxylenol.

- PANEL FOUR : Salicylates.
- PANEL FIVE : Alcohols and Other Volatiles
acetone
chloroform
ethanol
isopropanol
methanol
- PANEL SIX : Alcohols and Other Volatiles
acetone
chloroform
ethanol
isopropanol
methanol
benzene
paraldehyde
toluene
xylenes
- PANEL SEVEN : Common organophosphorus and
carbamate insecticides
- PANEL EIGHT : Paraquat and diquat
- PANEL NINE : Alkaloids
atropine
strychnine
yohimbine
- Amphetamines and Other Anorexic Agents
amphetamine
ethylamphetamine
fenfluramine
MDMA
methamphetamine
phentermine

Analgesics

diclofenac
diflunisal
flufenamic acid
flurbiprofen
ibuprofen
indomethacin
ketoprofen
mefenamic acid
meclofenamic acid
naproxen
paracetamol
phenylbutazone
piroxicam
propyphenazone
salicylic acid
sulindac

Antibacterials

fluconazole
griseofulvin
metronidazole
sulfapyridine
sulfamethoxazole
trimethoprim

Anticoagulants

coumarin
coumachlor
warfarin

Antidiabetics

chlorpropamide
gliclazide
tolazamide
tolbutamide

Antiepileptics

carbamazepine
ethosuximide
phenytoin
primidone

Antihistamines

brompheniramine
buclizine
chlorpheniramine
cinnarizine
cyclizine
diphenhydramine
doxylamine
hydroxyzine
promethazine
triprolidine

Antimalarials

chloroquine
pyrimethamine
quinine

Barbiturates

amylobarbitone
phenobarbitone
quinalbarbitone

Benzodiazepines

alprazolam
bromazepam
clobazam
chlordiazepoxide
diazepam
estazolam
flunitrazepam
flurazepam
midazolam
nimetazepam
nitrazepam
nordiazepam

Cardiac and Antihypertensive Drugs

diltiazem
lignocaine
propranolol
quinidine
verapamil

Diuretics

chlorthalidone
diazoxide
frusemide

Muscle Relaxants

chlormezanone
chlorzoxazone
methocarbamol

Narcotics

codeine
methadone
pentazocine
phenazocine
pethidine
methorphan
propoxyphene
tramadol

Phenothiazines

chlorpromazine
prochlorperazine
thioridazine
trifluoperazine

Antidepressants

amitriptyline
clomipramine
clozapine
dothiepin
fluoxetine
fluvoxamine
imipramine
melitracen
mianserin
moclobomide
sertraline
trimipramine

Others

metoclopramide

ticlopidine

zolpidem

theophylline

8 - chlorotheophylline

Urine Specimens

Urine specimens are normally screened for the presence of opiates. They could also be screened for the presence of drugs and poisons listed in Panels 3 to 10 of Blood Specimens and Panels 1 and 8 of Gastric Aspirates by the methods listed below:

Sensitivity, Specificity, Quantitation and Reporting

Our users are to take note of the following:

- (i) As far as practicable, the blood level of a drug or poison detected will be quantified (gas chromatography and liquid chromatography).
- (ii) The methods employed are sufficiently sensitive to detect most of the drugs listed under Blood Specimens at therapeutic levels in the blood. Confirmation is usually carried out using gas chromatography / mass spectrometry.
- (iii) The screening methods employed are sufficiently specific such that no confirmation would be carried out in the therapeutic drug monitoring (TDM) cases.
- (iv) A screening or confirmation procedure may take up to three hours to perform. The procedure may include among other things, calibration, the verification with standards and sample pre-treatment.
- (v) In emergency toxicology, the confirmed analytical outcome which is usually reached in 3-4 hours after receiving the specimens, would then be passed on verbally to the client requesting the work. A written report would then follow later. In non-emergency cases, the final written report on the confirmed analytical outcome may take a few days.

Requesting For Emergency Toxicology

What is Emergency Toxicology?

Emergency toxicology is toxicology carried out on an urgent basis. As cases requiring emergency toxicology literally jump queue and disrupt normal workflow, emergency work is to be requested only when absolutely necessary. The following categories of cases qualify for emergency toxicology:

- (i) Life-threatening cases with a strong overdose suspicion.
- (ii) Life-threatening cases with no apparent underlying causes.
- (iii) Potential organ donors.
- (iv) Cases whose treatment depends on or is likely to be altered by the analytical outcome.

Even when requests for emergency toxicology are justified, our clients are asked to bear in mind the following:

- (i) Physiological support (airway, breathing and circulation) forms the basis of overdose management.
- (ii) Emergency treatment usually depends on the symptoms observed without having to await the analytical outcome.
- (iii) The analytical results are more relevant for later management of the patient.

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CHAPTER 8

Antidotes & Therapeutic Drugs

Acetylcysteine (@ N-Acetylcysteine, NAC)

Indications	- Paracetamol overdose
Dosage	- IV - to be given in glucose 5% w/v intravenous infusion, initially 150 mg / kg in 200 ml over 15 minutes, followed by 50 mg / kg in 500 ml over 4 hours, then 100 mg / kg in 1000 ml over 16 hours
Method of Use / Administration	- IV infusion
Contraindications	- Known hypersensitivity to the drug
Adverse Reactions	- Rash, pruritus, nausea, vomiting, wheezing, angioedema, tachycardia, bronchospasm, hypertension, flushing and hypotension, especially with IV administration
Drug Interactions	- Not known

Note:

- 1) This antidote is most efficacious within 8 hours of ingestion and should be given as soon as possible. Re-assess when serum concentration result is available.*
- 2) Late administration of NAC has been found to be beneficial. Therefore, NAC is still recommended in patients who are already in liver failure.*

In case of overdose:

Minimum Toxic Dose	- Not known
Maximum Tolerated Dose	- 5 g/day for 3 months

- | | |
|-----------------------------|---|
| Sign & Symptoms of Toxicity | - Anaphylactoid reactions - urticaria, hypotension
- Nausea, vomiting |
| Management of Toxicity | - Aimed at reversing anaphylactoid reactions and controlling nausea & vomiting
- Supportive treatment such as airway support, maintaining vital signs and reversal of bronchospasms, may be required
- Emesis, gastric lavage and/or activated charcoal may be applied if the overdose is detected soon after ingestion |

Atropine

- | | |
|--------------------------------|--|
| Indications | - Organophosphate / Carbamate insecticide poisoning
- Drug-induced atrioventricular conduction impairment (e.g. digitalis, beta-blockers, organophosphates, carbamates, physostigmine) |
| Dosage | <u>Organophosphate / Carbamate poisoning</u>
- 2 - 5 mg, intravenously
- Children - 0.05 mg / kg IV
- Dose repeated every 10-15 minutes until atropinisation is achieved

<u>Drug-induced bradycardia.</u>
- 0.5 - 1 mg, intravenously
- Children - 0.01 -0.05 mg / kg up to a maximum dose of 0.5 mg IV
- Dose repeated as necessary, up to a maximum of 3 mg in adults (additional doses not expected to be effective) |
| Method of Use / Administration | - Administer by IV injection
- Treatment aimed at achieving satisfactory relief of clinical symptoms |
| Contraindications | - Close-angle glaucoma |

- Hypertension, tachyarrhythmias, congestive heart failure, coronary artery disease
 - Obstructive uropathy
 - Myasthenia gravis
- Adverse Reactions
- Dry mouth, blurred vision, cycloplegia, mydriasis, urinary retention, tachycardia, (aggravation of) angina, constipation
 - Paradoxical bradycardia
- Drug Interactions
- Increased atropinisation when used concurrently with pralidoxime
 - Additive effects with other antimuscarinics and antihistamines
 - Delayed gastric motility reduces drug absorption from the GI tract

In case of overdose:

(see also "Atropine" in section B)

- Minimum & Maximum Doses
- Variable & unpredictable. Judgement on toxicity should be based on clinical signs & symptoms, rather than on quantitative values
- Sign & Symptoms of Toxicity
- CNS effects - delirium, hallucinations, coma, seizures
 - disordered body temperature levels, hyperthermia/hypothermia
 - mydriasis, peripheral vasodilation, dry mouth, urinary retention, dilated pupils, diminished bowel signs
 - CVS effects - tachycardia, hypertension, arrhythmias, shock, cardiorespiratory arrest

Bicarbonate, Sodium

- Indications
- Severe metabolic acidosis due to lactic acidosis or poisoning by methanol, ethylene glycol, salicylates
 - Urinary alkalinisation for enhanced renal elimination of salicylates, phenobarbital, myoglobin (in cases of rhabdomyolysis)

-
- Cardiotoxicity due to Type Ia / Ic antiarrhythmic drugs or cyclic antidepressants
 - Gastric lavage medium for excessive iron ingestion
- Dosage
- Metabolic Acidosis
- 0.5 - 1.0 mEq/kg, intravenously.
 - Repeat the dose until serum pH is adjusted to at least 7.2. For salicylates, methanol or ethylene glycol, raise the pH to 7.4-7.5
- Urinary Alkalinisation
- 100 mEq in 1L of 5% dextrose solution, intravenously
- Antiarrhythmic / Antidepressant Drug Poisoning
- 0.5 - 1.0 mEq/kg, intravenously. Repeat the dose until cardiotoxic symptoms are controlled and serum pH is brought to 7.45-7.5.
- Gastric Lavage
- 4-5 mL/kg
- Method of Use / Administration
- Metabolic Acidosis
- Administer as a bolus dose, by IV injection.
- Urinary Alkalinisation
- Administer as IV infusion.
 - Infuse at 2-3 mL/kg/hour. Adjust to maintain urine pH at 6-7.
- Antiarrhythmic / Antidepressant Drug Poisoning
- Administer as bolus dose, by IV injection.
- Gastric Lavage
- Make up a 1-2% solution of sodium bicarbonate in saline.
- Contraindications
- Metabolic / respiratory alkalosis
 - Hypernatraemia
 - Pulmonary oedema

- Adverse Reactions - Excessive alkalaemia; hypocalcaemic tetany, paradoxical intracellular acidosis, hypokalaemia, impaired oxygen release from haemoglobin.
- Hyponatraemia, hyperosmolality.
 - Aggravation of congestive heart failure and/or pulmonary oedema.
- Drug Interactions - May cause inactivation or precipitation of other parenteral drugs in an admixture.

In case of overdose:

- Minimum Toxic Dose - Death from hyponatraemia is a frequent occurrence when serum sodium rises above 185 mEq/L.
- Topical application of sodium bicarbonate to denuded perineum resulted in toxicity in a 7-week-old infant.
- Maximum Tolerated Dose - Not known.
- Large amounts are needed to cause hyponatraemia.
- Sign & Symptoms of Toxicity - Metabolic abnormalities - alkalosis, hyponatraemia, hypokalaemia, hypochloraemia, and hypocalcaemia
- Initial symptoms of alkalosis or hyponatraemia - nausea, vomiting, dizziness, weakness, irritability, and mental changes/confusion
 - Hypotension, tachycardia; hypertension may occur
 - Severe toxicity - progressive obtundation, coma, seizures
 - Chronic toxicity within 4 - 10 days after ingestion of large amounts
 - Apnoea, cyanosis, pulmonary oedema, transient albuminuria and elevations in BUN - secondary to alkalosis
- Management of Toxicity - The major aspect of treatment is correction of fluid, electrolyte, and acid-base imbalances. When chloride and potassium deficits are corrected, the kidney will naturally eliminate bicarbonate in persons with normal renal function.

- Treatment for symptoms after oral/parenteral exposure
- Treat seizures
- Hypotension - administer IV fluids and place in Trendelenburg position; if unresponsive to these measures, administer dopamine (2 to 5 mcg/kg/min) or norepinephrine (0.1 to 0.2 mcg/kg/min) and titrate as needed to desired response.
- Chloride and potassium deficit - administer D5W and 0.45 to 0.9% sodium chloride with potassium chloride 40 mEq/L, at a rate (usually 2/3 of daily maintenance) calculated to normalise sodium no sooner than 24 to 36 hours.
- Alkalosis - using acetazolamide, may selectively correct alkalosis by promoting bicarbonate excretion; CANNOT be used if serum potassium is < 3.5 mEq/L. (Dose : 250-500 mg PO or IV every 6 to 12 hours).
- Severe alkalaemia - administer ammonium chloride in normal saline, administered over 12 to 24 hours. Alternatively, dilute hydrochloric acid (0.1N) through a central line may be given at 10 mEq/hour).
- Dialysis - using high chloride, low acetate dialysates to remove bicarbonate and replace chloride deficit when other measures fail or in cases of renal insufficiency.

Calcium

Indications

- Symptomatic hypocalcaemia due to intoxication by fluoride, oxalate, phosphate or intravenous anticoagulant citrate salts
- Corrosive effects of topical hydrofluoric acid exposure
- Black widow spider envenomation with muscle cramping/rigidity
- Hypotension due to calcium antagonist overdose
- Severe hyperkalaemia with cardiotoxic manifestations

Dosage

Oral Ingestion of Fluoride / Oxalate Salts

- 2 - 3 g of calcium-containing antacid, orally.

Dermal Exposure to Hydrofluoric Acid

Topical : Topical gel - 1 g of calcium gluconate / chloride in 30 g of water-soluble base (K-Y Jelly or "Surgilube")

Subcutaneous : Calcium gluconate 10%, 0.5-1 ml/ cm² of affected skin area. (not chloride salt)
Repeat 2-3 times at 1-2 hour intervals.

Intra-arterial : Infuse 20ml calcium gluconate 10% in 250ml Dextrose 5% saline over 3-4 hours via radial or brachial artery proximal to injury.

Symptomatic Hypocalcaemia, Hyperkalaemia, Black Widow Spider Envenomation or Calcium Antagonist Poisoning

Adult; 10 - 20 ml of calcium gluconate 10%
OR

intravenously : 5 - 10 ml of calcium chloride 10%.

Children; 0.2 - 0.3 ml/kg calcium gluconate 10%
OR

intravenously : 0.1 -0.2 ml/kg calcium chloride 10%

Repeat as needed to control symptoms.

Method of Use / Administration

Oral Ingestion of Fluoride / Oxalate Salts

- Use the suspension or tablet (to be chewed first) dosage forms.

Dermal Exposure to Hydrofluoric Acid

Topical : Apply liberally over the affected areas.
For finger burns, cover with a loose-fitting latex glove.

Subcutaneous : Inject using a 27-gauge or finer needle

Symptomatic Hypocalcaemia, Hyperkalaemia, Black Widow Spider Envenomation or Calcium Antagonist Poisoning

Administer by slow IV injection.

- | | |
|-------------------|--|
| Contraindications | <ul style="list-style-type: none"> - Hypercalcaemia - Digitalis therapy; may result in digitalis intoxication and aggravate digitalis-induced ventricular tachyarrhythmias |
| Adverse Reactions | <ul style="list-style-type: none"> - Tissue irritation (especially with calcium chloride); extravasation may cause localised cellulitis or tissue necrosis. - Hypercalcaemia, especially in patients with diminished renal function - Hypotension, bradycardia, syncope and cardiac arrhythmias; caused by rapid intravenous administration. - Use of oral calcium salts may cause constipation. |
| Drug Interactions | <ul style="list-style-type: none"> - Potentiates inotropic and arrhythmogenic effects of digitalis. - May cause inactivation / precipitation of other parenteral drugs in an admixture e.g. carbonates, phosphates, sulphates, some antibiotics. |

In case of overdose:

- | | |
|--------------------|--|
| Minimum Toxic Dose | <ul style="list-style-type: none"> - Particular risk in patients with predisposing factors, e.g. renal failure. |
|--------------------|--|

Maximum Tolerated Dose	- Not known.
Sign & Symptoms of Toxicity	- Anaphylactoid reactions - urticaria, hypotension - Nausea, vomiting
Management of Toxicity	- Aimed at reversing anaphylactoid reactions and controlling nausea & vomiting. - Supporting treatment such as airway support, maintaining vital signs and reversal of bronchospasms, may be required. - Emesis, gastric lavage and/or activated charcoal may be applied if the overdose is detected soon after ingestion.

Charcoal, Activated

Indications	- Ingestion of drug overdose or poisons - High serum levels of drugs & toxins with long half-lives; useful in cases where rapid elimination would be beneficial
Dosage	<u>Initial dose</u> - (amount of ingested drug / toxin unknown) 1 g/kg body weight. - (amount of ingested drug / toxin known) 10 times the amount of ingested toxin by weight, in divided doses if necessary. <u>Repeat dose</u> - 15-20 g, every 4-8 hours.
Method of Use / Administration	- Administer orally or through a nasogastric tube. - First dose of activated charcoal is preferably given together with sorbitol as a cathartic. Subsequent doses should be pure activated charcoal, and the cathartic is given only when no bowel movement occurs.

Note: a cathartic should NOT be given with every dose. In young children, usually only one dose of cathartic is needed.

- Contraindications
- Gastrointestinal obstruction
 - Ingestion of strong acids or alkalis (charcoal makes endoscopic evaluation more difficult)
- Adverse Reactions
- Constipation; diarrhoea, dehydration and hypernatraemia due to the concurrent use of cathartics.
 - Distention of the stomach; risk of aspiration.
 - Intestinal bezoar / particulate concretion with obstruction.
- Drug Interactions
- Reduces, prevents and/or delays absorption of orally administered drugs, including antidotes.
 - The adsorptivity of charcoal is reduced by concurrent ingestion of dairy / milk products and syrups.

In case of overdose:

This substance is not believed to cause any adverse effects if an overdose is ingested.

Note : Activated charcoal is available commercially in 2 forms : those formulated in sorbitol (cathartic) and plain. Do not administer another cathartic when using sorbitol type.

See also pg 48 & 63.

Dantrolene

- Indications
- Malignant hyperthermia (due to reaction to anaesthetic agents)
 - May be useful in hyperthermia and rhabdomyolysis caused by drug-induced muscular hyperactivity

Dosage

IV
1 - 2 mg/kg, repeated as necessary every 5 - 10 minutes.
Maximum total dose of 10 mg/kg.

Oral
1 - 2 mg/kg, up to a maximum of 100 mg per dose,
4 times a day for 2 or 3 days.

Method of Use / Administration	<p><u>IV</u> Administer by rapid injection. Observe & repeat as needed.</p> <p><u>Oral</u> Use only for prophylaxis i.e. recurrence of hyperthermia.</p>
Contraindications	- Use with caution in patients with muscular impairment and/ or respiratory impairment.
Adverse Reactions	<ul style="list-style-type: none"> - Muscle weakness, aggravating respiratory depression - Drowsiness, diarrhoea - Hypersensitivity hepatitis (with chronic therapy)
Drug Interactions	<ul style="list-style-type: none"> - Additive effects to CNS depressants. - Preparation contains mannitol (3 g in a 20 mg vial)

In case of overdose:

Minimum Toxic Dose	- Fatal poisonings are rare, and lethal doses are not established.
Maximum Tolerated Dose	- Dosage in excess of 400mg daily is not recommended.
Sign & Symptoms of Toxicity	<ul style="list-style-type: none"> - CNS effects - depression (ranging from mild drowsiness to coma), stimulation (euphoria, confusion, hallucination), headache, dystonic reactions, muscular incoordination - Horizontal and vertical nystagmus, mydriasis, blurred vision - Mild tachycardia, hypotension - Respiratory depression (in patients with major CNS depression) - Hepatotoxicity reported (idiosyncratic reaction to therapeutic dose)
Management of Toxicity	- gastric decontamination if overdose is oral.

Desferrioxamine (@ Deferoxamine)

Indications	- Iron intoxication, with serum levels $>450 \mu\text{g/dL}$.
Dosage	- 15 mg/kg/h intravenously. Up to a maximum dose of 6 g per day
Method of Use / Administration	- Administer by IV infusion until serum iron level drops to $<350 \mu\text{g/dL}$ or until resolution of clinical symptoms.
Contraindications	- Known sensitivity to desferrioxamine - Use in pregnancy only with cases of serious intoxication - Use with caution in patients with renal impairment
Adverse Reactions	- Hypotension, anaphylactoid reaction (from rapid IV administration). - Pain, sterile abscess, induration at injection site, with IM injection
Drug Interactions	- None known

In case of overdose:

Minimum Toxic Dose	- The minimum lethal dose has not been established. - Chronic administration of 50 to 235 mg/kg per day.
Maximum Tolerated Dose	- Do not give $>80\text{mg/kg}$ in 24 hours.
Sign & Symptoms Toxicity	- Acute administration - hypotension, pulmonary of toxicity (seen after 24 hours when high doses $>15 \text{mg/kg/hour}$ are given), anaphylaxis with erythema, pruritus, and hypotension - Chronic administration - ocular/auditory toxicity, bone dysplasia and growth retardation in children, Yersinia gastroenteritis, sepsis and mucormycosis

- Management of Toxicity
- Aimed at managing symptoms, e.g hypotension, anaphalaxis.
 - For hypotension due to rapid IV administration, slow or discontinue infusion and administer vasopressor therapy if there is an inadequate blood pressure response.
 - In cases of ocular/auditory toxicity or Yersinosis, discontinue drug therapy of desferrioxamine.

Diazepam

- Indications
- Anxiety or agitation due to intoxication by sympathomimetic or hallucinogenic drugs.
 - Acute seizure activity or status epilepticus due to convulsant drug overdose or idiopathic epilepsy.
 - Excessive muscle rigidity or contractions, caused by black widow envenomation or strychnine poisoning.
 - Cardiotoxicity due to chloroquine overdose (possibly useful).
 - Alcohol or sedative-hypnotic withdrawal

Dosage

Anxiety / Agitation

- 0.1 - 0.2 mg/kg, intravenous. Repeat as needed every 1-4 hours.

Convulsions

0.1 - 0.2 mg/kg intravenous, every 10-15 minutes to a total dose of :

- adults, 30 mg intravenous.
- older children, 10 mg intravenous.
- young children, 5 mg intravenous.

Muscle Relaxation

- 0.1 - 0.2 mg/kg, intravenous. Repeat as needed every 1-4 hours.

Chloroquine Intoxication

- 1 mg/kg, intravenous.

Alcohol Withdrawal

- Initial 5-10mg, intravenous. May be repeated with 5mg every 10 minutes.
- Method of Use / Administration
- Administer by slow intravenous injection; do not use intramuscular route.
 - Rectal administration (5 mg) can be used to control status epilepticus in young children.
 - Patients on high-doses of diazepam (eg. 1 mg/kg for cardiotoxicity) are likely to experience apnoea; they should be intubated and have their ventilation controlled.
- Contraindications
- Known sensitivity to benzodiazepines.
- Adverse Reactions
- Respiratory arrest due to rapid and/or high-dose IV administration.
 - Cardiorespiratory depression caused by the diluent.
- Drug Interactions
- Potentiates other CNS depressant drugs.
 - Causes false-negative reaction for some urine glucose test strips.
 - Response reduced by flumazenil

In case of overdose:

(see “Benzodiazepines” in Section B)

Digoxin-Specific Antibodies (@ Digoxin-Binding Antibodies)

- Indications
- Life-threatening arrhythmias and/or hyperkalaemia due to poisoning by digoxin and other cardiac glycosides.
- Dosage
- 80 mg of digoxin-specific Fab (Digitalis Antidote BM) for each 1 mg of digoxin. (see table and calculation of load from serum concentration at steady state)

- Method of Use / Administration - Administer as IV infusion, over a period 30 minutes.
- Contraindications - Exercise caution in patients with known hypersensitivity to ovine (sheep) products, and those previously treated with these antibodies.
- Adverse Reactions - Hypersensitivity and 'serum sickness'.
- Re-intoxication, due to complex degradation in patients with impaired renal clearance.
- Exacerbation of cardiac conditions in patients currently on digoxin, e.g. heart failure, atrial fibrillation.
- Drug Interactions - Cross-reaction with other cardiac glycosides e.g. digitoxin, ouabain; possible other glycosides in oleander, strophanthus, Lily of the Nile.
- The digoxin-Fab complex reacts with antibodies used in quantitative immunoassay techniques.

Approximate Dosing of Digoxin-Specific Antibodies (Digitalis Antidote BM) for Known Amount of Ingested Digoxin

Dose Ingested (mg of digoxin)	Approximate Dose Absorbed (mg of digoxin)	Recommended Dose (mg of antidote)
2.5	2	160
6.25	5	400
12.5	10	800
18.75	15	1500
25	20	1600
37.5	30	2400

Approximate Body Digoxin Load based on Serum Digoxin Concentration

$$\text{Body digoxin load (mg)} = 0.001 \times [\text{Serum conc. (ng/mL)} \times 5.6 \times \text{body weight (kg)}]$$

In case of overdose:

Minimum Toxic Dose	- Not known.
Maximum Tolerated Dose	- Not known.
Sign & Symptoms of Toxicity	<ul style="list-style-type: none"> - Hypokalaemia, due to reactivation of ATPase - Indirect effects (due to neutralisation of digoxin) - congestive heart failure and low cardiac output states, exacerbated by withdrawal of the inotropic effects of digitalis - Atrial fibrillation and rapid ventricular response, due to the withdrawal of the effects of digitalis on the AV node
Management of Toxicity	- Supportive and symptomatic treatment.

Dimercaprol (@ BAL)

Indications	<ul style="list-style-type: none"> - Arsenic poisoning (except arsine) - Mercury poisoning (except monoalkyl mercury) - Lead poisoning (except alkyl lead compounds), in conjunction with edetate and penicillamine - Gold poisoning - Poisoning due to bismuth, chromium, copper, nickel, tungsten or zinc
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Dosage	<p><u>Arsenic, mercury and gold poisoning.</u></p> <ul style="list-style-type: none">- 3 mg/kg every 4 hours for 2 days, then every 12 hours for 7-10 days (or until recovery). <p><u>Lead (in conjunction with calcium EDTA therapy)</u></p> <ul style="list-style-type: none">- With acute encephalopathy, 4-5 mg/kg every 4 hours for 5 days- Without encephalopathy, 3 mg/kg every 4 hours for 5 days. May discontinue if blood lead < 50 mcg/dL after 3 days.
Method of Use / Administration	<ul style="list-style-type: none">- Deep IM injection.
Contraindications	<ul style="list-style-type: none">- Heavy metal poisoning due to iron, cadmium, selenium or uranium- Poisoning due to thallium, tellurium or vanadium- G6PD-deficiency (use only in life-threatening situations)- Hepatic impairment (except in arsenic-induced jaundice)- Renal impairment (use with extreme caution)- Pregnancy (use only in life-threatening situations)
Adverse Reactions	<ul style="list-style-type: none">- Local pain at injection site; sterile abscess formation.- Hypertension with/without tachycardia. Dose-related; use with caution in hypertensive patients.- Nephrotoxicity; alkalinise urine to protect renal function and prevent dissociation of metal-complex.- Nausea, vomiting, headache, lacrimation, rhinorrhea, salivation, urticaria, myalgias, paraesthesia, dysuria, fever, CNS depression and seizures.
Drug Interactions	<ul style="list-style-type: none">- Forms toxic complexes with iron, cadmium, selenium and uranium.- Reacts with gold compounds in preparations for rheumatoid arthritis- Interferes with iodine accumulation in the thyroid.

In case of overdose:

Minimum Toxic Dose	- Not known.
Maximum Tolerated Dose	- Not known.
Sign & Symptoms of Toxicity	- Tachycardia - Hypertension - Persistent hyperpyrexia, especially in children - Haemolysis, especially in patients with G6PD deficiency
Management of Toxicity	- CNS depression, seizures - Aimed at managing symptoms, e.g. hypertension, anaphylaxis. - For urticaria, diphenhydramine may be effective.

Diphenhydramine

Indications	- Pruritus caused by plant toxins or insect bites/stings - Prophylaxis against hypersensitivity reactions when administering horse serum-derived products; esp. for patients with previous history of hypersensitivity reactions and/or positive skin test - Drug-induced extrapyramidal effects; dystonia
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Dosage	<u>Pruritus</u>
	- Adults; 25-50 mg, oral. Repeat as needed after 6-8 hours. (max: 300 mg / day) - Children; 5 mg/kg/day in divided doses, oral.

<u>Prophylaxis</u>
- Adults; 50 mg, intravenous. - Children; 0.5-1 mg/kg, intravenous.

Extrapyramidal Side Effects

Initial dose : adults, 50 mg, intravenous.
children, 0.5-1 mg/kg,
intravenous.

Maintenance dose : adults, 25-50 mg, oral.
children, 0.5-1 mg/kg, oral.

Repeat the dose every 4-6 hours, for up to 2 days.

Method of Use / Administration	- For pre-treatment prophylaxis, administer (preferably) about 15-20 minutes before using the serum product.
Contraindications	- Close-angle glaucoma - Prostatic hypertrophy with obstructive uropathy - Concurrent therapy with monoamine-oxidase inhibitor
Adverse Reactions	- Sedation, drowsiness, ataxia. - Paradoxical excitation (in young children). - Flushing, tachycardia, blurred vision, delirium, toxic psychosis, urinary retention, respiratory depression.
Drug Interactions	- Added sedative effect with other sedating or anticholinergic drugs.

In case of overdose:

(see "Diphenhydramine" in Section B)

Dopamine

Indications	- Hypotension due to venodilation or reduced cardiac contractility - Shock due to low peripheral arterial resistance
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Dosage	<u>Low Dose - for Inotropic Effects</u> - Begin with 1 mcg/kg/min, intravenously. - Increase to 5-10 mcg/kg/min as needed.
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High Dose - for Vasopressor Effects

- 10 - 20 mcg/kg/min, intravenously.
Increase as needed.
 - Warning: Doses > 50 mcg/kg/min may result in severe peripheral vasoconstriction and gangrene.
- Method of Use / Administration
- Administer as an IV infusion.
 - Ensure a free-flowing infusion. Avoid extravasation.
- Contraindications
- Hypertension
 - Hypersensitivity to sulphite preservatives
 - Use with extreme caution in patients on general anaesthetics or poisoned by aromatic / halogenated hydrocarbon solvents
 - High-dose infusion should be used cautiously in patients with ergot intoxication, or those with occluded peripheral arteries
- Adverse Reactions
- Severe hypertension, resulting in myocardial necrosis or infarction, intracranial haemorrhage, pulmonary oedema.
 - Ventricular arrhythmias.
 - Tissue necrosis; due to extravasation at site of injection, gangrene due to aggravation of peripheral tissue ischemia.
- Drug Interactions
- Increased arrhythmogenic effect with aromatic and halogenated hydrocarbon solvents, including general anaesthetics.
 - Adrenergic effects antagonised by alpha-blocking and beta- blocking agents; dopaminergic effects antagonised by dopamine antagonists.
 - Enhanced vasopressor effects with cocaine, cyclic antidepressants and monoamine oxidase inhibitors.

In case of overdose:

(see “Dopamine” in Section B)

Edetate, Calcium Disodium (@ EDTA, Calcium)

Indications	<ul style="list-style-type: none">- Acute or chronic lead poisoning; administer concomitantly with dimercaprol in cases of encephalopathy- Heavy metal poisoning by manganese, zinc, chromium, nickel or heavy radioisotopes (Ineffective with arsenic, gold or mercury)
Dosage	<p><u>Lead poisoning (blood lead level > 100 mcg/dL; encephalopathy)</u></p> <ul style="list-style-type: none">- Up to 40mg/kg twice daily, (Avoid rapid IV infusion) IV infusion or deep IM injection, for 5 days. <p><u>Lead poisoning (blood lead level 50 - 100 mcg/dL)</u></p> <ul style="list-style-type: none">- 20 mg/kg/day, IV infusion or deep IM injection, for 5 days. <p><u>Other metal poisonings</u></p> <ul style="list-style-type: none">- 10 mg/kg/day, IV infusion, for 3 days. Maximum 1 g/day.
Method of Use / Administration	<p><u>Lead poisoning</u></p> <ul style="list-style-type: none">- IM injection: Administer the total daily dose in 2 - 3 divided doses.- IV slow infusion: Administer in saline or 5% dextrose solution with a concentration of 2 - 4 mg/mL.- Reevaluate blood lead levels after 5 days; continue treatment if lead mobilisation test is positive. <p><u>Other metal poisonings</u></p> <ul style="list-style-type: none">- Administer as slow IV infusion, over 5 hours.
Contraindications	<ul style="list-style-type: none">- Use with extreme caution in patients with renal dysfunction- Use with caution in pregnant women

- Adverse Reactions
- Nephrotoxicity e.g. proteinuria, haematuria, acute tubular necrosis.
 - Intracranial hypertension with use of rapid intravenous infusion.
 - Nausea, vomiting, myalgia, arthralgia, chills, fever, hypotension.
 - Local pain at IM injection site, thrombophlebitis with IV infusion.
 - Zinc depletion, hypercalcaemia
- Drug Interactions
- None known. - IV infusions may be incompatible with 10% dextrose, amphotericin, hydralazine

Note - EDTA Calcium is NOT edetate disodium

In case of overdose:

- Minimum Toxic Dose
- Not known.
- Maximum Tolerated Dose
- Not known.
- Sign & Symptoms of Toxicity
- Renal tubular injury - dose related
 - Chelation of other metals in the body, depletion of the body's iron and zinc stores
- Management of Toxicity
- Gastrointestinal decontamination. Whole bowel irrigation may be considered.

Edetate, Dicobalt

- Indications
- Acute cyanide poisoning (for confirmed cases only, where patient is in danger of losing consciousness).
- Dosage
- 300 mg, intravenously.
 - Repeat the dose after 5 minutes if the response is inadequate.
 - A maximum of 3 doses in total.

- Method of Use / Administration
- Administer by slow IV injection, over a period of no less than one minute (can be slower if patient's condition is less serious).
 - Each dose to be followed immediately with 50 mL of glucose 50% solution, IV.
 - can be used with other standard cyanide antidotes
- Contraindications
- None known.
- Adverse Reactions
- Hypotension, hypertension, tachycardia, vomiting, cardiac irregularities, severe anaphylactoid reactions, seizures
- Drug Interactions
- None known.

In case of overdose:

- Minimum Toxic Dose
- Not known.
- Maximum Tolerated Dose
- Not known.
- Sign & Symptoms of Toxicity
- Severe hypertension/hypotension, cardiac ischaemia, arrhythmias, tachycardia
 - Severe anaphylactoid reactions; periorbital / facial / neck oedema, airway obstruction / compromise
 - Nausea, vomiting, rashes, chest pains, diaphoresis, nervousness, tremulousness, GI haemorrhage, seizures
 - Increased plasma catecholamine levels
 - Metabolic acidosis
- Management of Toxicity
- Symptomatic and supportive treatment.

Epinephrine (@ Adrenaline)

- Indications
- Anaphylaxis and/or anaphylactoid reactions
 - Hypotension due to overdose of cardiac-depressant drugs & beta-blockers
- Dosage
- Severe anaphylaxis
- IV injection: 0.5 - 1 mg (5 - 10 ml of 1:10,000 solution), repeat every 5 - 10 minutes if needed.
 - IV infusion: 1 - 4 mcg/min.
 - Intratracheal: 0.5 mg, (5 ml of a 1:10,000 solution) repeat every 5 - 10 minutes if needed.
- Mild/moderate allergic reactions
- 0.3 - 0.5 mg (0.3 - 0.5 ml of 1:1,000 solution), by subcutaneous or intramuscular injection.
 - Repeat after 10 - 15 minutes if needed.
- Hypotension
- Infuse at 1 mcg/min; titrate upwards if necessary, every 5 minutes.
- Method of Use / Administration
- IV bolus
- Administer using a 1:10,000 solution.
- IV infusion
- Ensure a free-flowing infusion. Avoid extravasation.
- SC or IM
- Use a 1:1,000 solution.
- Intratracheal
- By endotracheal tube, using a 1:10,000 solution.
- Contraindications
- Ventricular fibrillation
 - Hypovolemia
 - Hypertension
 - Hypersensitivity to sulphite preservatives
 - Use with extreme caution in patients on general anaesthetics or poisoned by aromatic / halogenated hydrocarbon solvents

- Use cautiously in patients with digitalis or ergot intoxication, or those with occlusive vascular diseases (esp. peripheral arteries)
- Adverse Reactions
- Anxiety, restlessness, tremors, headache.
 - Severe hypertension, resulting in myocardial necrosis or infarction, intracranial haemorrhage, pulmonary oedema.
 - Ventricular arrhythmias.
 - Tissue necrosis; due to extravasation at site of injection, gangrene due to aggravation of peripheral tissue ischaemia.
- Drug Interactions
- Increased arrhythmogenic effect with aromatic and halogenated hydrocarbon solvents, including general anaesthetics.
 - Paradoxical hypertension with non-selective beta-blockers.
 - Enhanced stimulant effects with cocaine and cyclic antidepressants.
 - Enhanced vasopressor effects with monoamine oxidase inhibitors.

In case of overdose:

(see "Epinephrine" in Section B)

Ethanol (@ Ethyl Alcohol)

- Indications
- Methanol poisoning; with confirmed ingestion, metabolic acidosis or serum methanol concentration > 20 mg/dL
 - Ethylene glycol poisoning; with confirmed ingestion, metabolic acidosis or serum ethylene glycol concentration > 20 mg/dL
- Dosage
- Loading dose 750 mg/kg, maintenance dose 100 - 150 mg/kg/h.
 - Adjust maintenance dose upwards for chronic alcoholics and during haemodialysis

- Method of Use / Administration
- Parenteral preparation 10 % v/v ethanol in 5 % dextrose
 - Oral preparation 50 % or less solution
 - Administer by oral or intravenous routes over 30 minutes; similar dose for both. Obtain serum ethanol level after loading dose and at intervals thereafter; maintain concentration of 100 mg/dL.
- Contraindications
- Patients currently or recently (< 2 weeks) on disulfiram therapy
 - Patients on other drugs with CNS depressant effects
 - Head trauma or altered mental state
- Adverse Reactions
- Causes nausea, vomiting and (possibly) gastritis when given orally.
 - Inebriation, sedation and hypoglycaemia. Vasodilation, may result in postural hypotension. Local phlebitis at site of injection.
- Drug Interactions
- Potentiates effect of other drugs with CNS depressant properties.

In case of overdose:

(see “Ethanol” in Section B)

Flumazenil

- Indications
- Rapid reversal of coma induced by benzodiazepine overdose
 - Post-operative reversal of benzodiazepine sedation
- Dosage
- Benzodiazepine overdose
- 0.2 mg, IV. Repeat after 30 seconds if desired response not obtained at 0.3 mg IV. Additional doses of 0.5 mg IV can be given at 1 minute intervals up to a total cumulative dose of 3 mg.
- Reversal of benzodiazepine anaesthesia
- 0.2 - 1 mg, IV.

- Method of Use / Administration - Administer at a rate of no more than 0.5 mg/min. Titrate dosage until desired response is achieved. Monitor for at least 5-6 hours, to prevent relapse.
- Contraindications - Known hypersensitivity to the drug
- Known history of withdrawal reactions to benzodiazepines/alcohol
- Known seizure disorder
- Increased intracranial pressure
- Physical dependence on benzodiazepines
- Adverse Reactions - Anxiety, agitation, headache, dizziness, nausea, vomiting, tremors and facial flushing. May cause acute withdrawal state, including hyperexcitability, tachycardia and seizures.
- Drug Interactions - None known.

In case of overdose:

- Minimum Toxic Dose - Not known.
- Maximum Tolerated Dose - Not known.
- Sign & Symptoms of Toxicity - Seizures, in cases of patients with benzodiazepine dependence
- Management of Toxicity - Aimed at management of symptoms. Overstimulation may be treated by slow IV diazepam or midazolam.

Folic Acid

- Indications - Adjunctive treatment for methanol and ethylene glycol poisoning.
- Dosage - Adults; 50 mg intravenously.
- Children; 1 mg/kg, intravenously.
- Repeat the dose every 4 hours until symptoms are resolved, up to a maximum of 6 doses.
- Method of Use / Administration - Administer by IV injection.
- Contraindications - None known.
- Adverse Reactions - Allergic reactions following intravenous administration (rare).
- Drug Interactions - None known.

In case of overdose:

- Minimum Toxic Dose - Not known.
- Maximum Tolerated Dose - Not known.
- Sign & Symptoms of Toxicity - Most water-soluble vitamins produce no acute toxic symptoms.
- Management of Toxicity - Discontinue or reduce intake.

Glucagon

Indications	<ul style="list-style-type: none"> - Hypotension, bradycardia, and conduction impairment due to beta-blocker intoxication - Persistent hypoglycaemia due to overdose of long-acting oral hypoglycaemic drugs or insulin (although IV dextrose is preferred)
Dosage	<p><u>Beta-blocker overdose</u></p> <ul style="list-style-type: none"> - Adults; loading dose 5-10 mg IV bolus, then IV infusion 1-5 mg/h - Children; loading dose 0.15 mg/kg IV bolus, then IV infusion 0.05-0.1 mg/kg/h - If dose of glucagon is greater than 2 mg, sterile water should be used for reconstitution. <p><u>Hypoglycaemia</u></p> <ul style="list-style-type: none"> - Adults, 0.5 - 1 mg ; children, 0.025 mg/kg. - Repeat 1-2 times as necessary, after 20 minutes. (if adequate response not obtained, may use IV dextrose concomitantly)
Method of Use / Administration	<p><u>Beta-blocker overdose</u></p> <ul style="list-style-type: none"> - Administer loading dose by intravenous injection, maintain with intravenous infusion. <p><u>Hypoglycaemia</u></p> <ul style="list-style-type: none"> - Administer by subcutaneous, intramuscular or intravenous injection.
Contraindications	<ul style="list-style-type: none"> - Phaeochromocytoma
Adverse Reactions	<ul style="list-style-type: none"> - Hyperglycaemia. - Nausea, vomiting. - Hypersensitivity reactions (rare).
Drug Interactions	<ul style="list-style-type: none"> - Epinephrine potentiates hyperglycaemic and cardiovascular effects.

In case of overdose:

Minimum Toxic Dose	<ul style="list-style-type: none"> - Not known.
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Maximum Tolerated Dose	- Not known.
Sign & Symptoms of Toxicity	- Nausea, vomiting - Hyperglycaemia, hypokalaemia (secondary to hyperglycaemia)
Management of Toxicity	- Supportive treatment and measures to prevent aspiration due to vomiting.

Glucose (@ Dextrose)

Indications	- Hypoglycaemia - Empirical therapy for patients with stupor, coma or seizures who may have unsuspected hypoglycaemia
Dosage	<u>Empirical Therapy for Coma</u> - Adult; IV 50 - 100 mL of 50% dextrose - Child; IV 2 - 4 mL of 25% dextrose <u>Persistent Hypoglycaemia (e.g. from oral hypoglycaemic - induced hypoglycaemia)</u> - Same as above but may require repeated IV boluses of 50% and 25% (for children) dextrose and infusions of 5 - 10% dextrose, titrated as needed. - May need to consider use of IV diazoxide 0.1 - 2mg/kg/hr, if dextrose infusions do not maintain satisfactory glucose levels. Start with the lower infusion rate initially. Minimise hypotension by keeping patient supine. Duration of infusion is 22 - 60 hrs. Alternatively, oral dose of 200 mg every 4hr.
Method of Use/ Administration	<u>Empirical Therapy</u> - Administer through a secure IV line. - Administer 50% dextrose at a rate of 3 mL/min or 6mL/min with 25% solution.

*Note : 1) Do NOT use 50% dextrose solution for children.
2) In cases of alcoholics and/or malnourished patients, thiamine should be given concomitantly to avoid acute Wernicke-Korsakoff syndrome.*

- Contraindications - May aggravate recent ischaemic brain injury.
- Adverse Reactions - Hyperglycaemia, hyperosmolarity.
- Local phlebitis and cellulitis due to extravasation at injection site.
- Drug Interactions - None known.

In case of overdose:

This substance is not believed to cause any adverse effects if an overdose is ingested.

Ipecac Syrup (@ Syrup Of Ipecacuanha)

- Indications - Early, initial management of oral poisoning (immediately)
- In cases where activated charcoal and gastric lavage are unavailable or not possible
- Dosage - Adults & children over 12 years old : 30 mL
- Children 1 - 12 years old : 15 mL
- Children 6 - 12 months : 5 - 10 mL (use with caution).
- Method of Use / Administration - Administer dose orally, followed by 50 - 100 mL of water. Repeat dose if emesis does not occur after 30 minutes. If second dose fails, consider alternative procedures eg. gastric lavage.
- Contraindications - Comatose
- Ingestion of caustic or corrosive substances, hydrocarbon distillate
- Ingestion of drugs likely to cause sudden onset of seizures or coma, e.g. antidepressants, strychnine, camphor, nicotine, cocaine, amphetamines, isoniazid
- Severe hypertension

- Adverse Reactions
- Persistent GI upset, Mallory-Weiss tear or haemorrhagic gastritis.
 - Drowsiness and diarrhoea, especially in children.
 - Cardiomyopathy and arrhythmias arising from chronic overuse.
- Drug Interactions
- Potentiates nausea and vomiting effects of other gastric irritant drugs
 - Adsorbed by activated charcoal.

In case of overdose:

- Minimum Toxic Dose
- 10 mL of syrup. Fatalities have occurred with 16 mg.
- Maximum Tolerated Dose
- Repeated doses of 60 mL of syrup taken by adults resulted in few serious consequences.
- Sign & Symptoms of Toxicity
- Vomiting within 15-30 minutes of administration
 - Lethargy, diarrhoea, protracted emesis
 - Neuromuscular / Cardiac toxicity in cases of chronic ingestion
- Management of Toxicity
- Supportive treatment of respiratory & cardiovascular functions.
 - Monitor the patient's fluid and electrolyte status closely.
 - Minimise external stimuli.
 - Activated charcoal may be given.
 - Control convulsions with diazepam.

Note: Please see Gastric Decontamination for more information (pg 41)

Leucovorin Calcium (@ Folinic Acid, Citrovorum Factor)

- Indications
- Folic acid antagonists poisoning (eg. methotrexate, trimethoprim, pyrimethamine)
 - Methanol poisoning, as alternative to folic acid

- Dosage
- Methotrexate (MTX) Poisoning
- For a known dose of methotrexate, give an amount of intravenous leucovorin equal to or slightly more than the methotrexate.
 - For a large but unknown dose of methotrexate, start with a loading dose of IV infusion of 75 mg and maintain with IM 12 mg every 6 hours for 4 doses.

Leucovorin dose based on MTX serum levels:

MTX Conc $\times 10^6$ M	Hours Post-MTX Infusion	Dose of Leucovorin
0.1-1	24	10-15 mg/m ² Q6H for 12 doses
1-5	24	50 mg/m ² Q6H until $<1 \times 10^{-7}$ M
5-10	24	100 mg/m ² Q6H until $<1 \times 10^{-7}$ M

Other Folic Acid Antagonists

- 5-15 mg/day IM, IV or oral for 5-7 days.

Methanol Poisoning

- 1 mg/kg (up to a maximum of 70 mg) intravenously, every 4 hours for 2 doses. Follow with similar doses orally, every 4 - 6 hours until symptoms of intoxication are resolved.

Method of Use / Administration

Methotrexate Poisoning

- Administer by IV injection. Do not administer orally.
- When the methotrexate dose is not known, use serum methotrexate levels as a guide to therapy.

Methanol Poisoning

- Whenever possible, use folic acid instead.

Note: for MTX poisoning, leucovorin is most effective if given within the first hour and may be ineffective if not given within 4 hours post-exposure.

- Contraindications - None known.
- Adverse Reactions - Allergic reactions
- Hypercalcaemia
- Drug Interactions - Antagonises the antifolate effects of methotrexate.

Note: Folic acid is NOT an effective alternative to leucovorin in MTX poisoning

Lignocaine (@ Lidocaine)

- Indications - Ventricular arrhythmias arising from poisoning by cardioactive drugs or toxins (e.g. digoxin, stimulants, theophylline).
- Dosage - Loading dose 1 mg/kg, intravenous.
- Maintenance dose 20 - 50 mcg/kg/min, intravenous.
- Titrate to maintain serum concentration at 1-5 mg/L.
- If there is significant ectopy after the initial dose, a further bolus dose of 0.5 mg/kg can be given.
- Repeat as necessary at 10-minute intervals, but no more than 3 mg / kg total dose.
- Dosage should be halved in patients with congestive heart failure or liver disease.
- Method of Use / Administration - Administer the loading dose as a bolus IV injection over 2 minutes
- Administer the maintenance dose as an IV infusion.

- Contraindications
- Nodal or ventricular rhythms in the presence of atrioventricular or intraventricular block
 - Hypersensitivity to lignocaine or other amide-type anaesthetics
- Adverse Reactions
- Dizziness, confusion, agitation and seizures.
 - Conduction defects, bradycardia, hypotension
- Drug Interactions
- Chronic use of cimetidine and/or propranolol decreases the hepatic clearance of lignocaine.
 - Additive effect with other local anaesthetics.

In case of overdose:

(see "Lignocaine" in Section B)

Methylene Blue

- Indications
- Drug-induced methaemoglobinaemia, with signs & symptoms or with methaemoglobin level > 25 - 30 %
- Dosage
- 1 - 2 mg/kg, intravenously. May be repeated in 30 - 60 minutes.
- Method of Use / Administration
- Administer by slow IV injection (1% solution), over several minutes.
- Contraindications
- G6PD-deficiency
 - Severe renal failure
 - Known hypersensitivity to methylene blue
 - Methaemoglobin reductase deficiency
- Adverse Reactions
- Gastrointestinal upset, headache and dizziness.
 - Methaemoglobinaemia or haemolysis, with large doses > 7 mg/kg.
 - Anaemia, with long-term use.
 - Local tissue necrosis due to extravasation.
- Drug Interactions
- None known, but do not mix IV preparations with other drugs.

In case of overdose:

Minimum Toxic Dose	- 4 mg/kg in adults. May be lower in children.
Maximum Tolerated Dose	- 26 g orally, taken over a period of several weeks, did not produce any toxic symptoms.
Sign & Symptoms Toxicity	- Nausea, abdominal pains, chest pains, headaches, of profuse sweating, mental confusion, painful micturation - Methaemoglobinaemia
Management / Antidotes	- Support respiratory and cardiovascular functions; oxygen, hyperbaric oxygenation, exchange transfusion.

Metoclopramide

Indications	- Persistent and severe nausea and vomiting
Dosage	<u>Low Dose</u> - Adults; 10-20 mg, intramuscular or intravenously. - Children; 0.1 mg/kg, intramuscular or intravenously.
	<u>High Dose</u> - 1-2 mg/kg, intravenous infusion - Repeat if necessary after 2 - 3 hours. Maximum of 10 mg/kg/24 hours
Method of Use / Administration	<u>Low Dose</u> - Administer by slow IV or IM injection.
	<u>High Dose</u> - Administer as IV infusion using 50ml dextrose or saline solution. Infuse over a period of 15 minutes. - A pre-treatment dose of diphenhydramine 50 mg (or children 1 mg/kg) may be given to reduce extrapyramidal effects.

- Contraindications
- Pheochromocytoma
 - Obstruction or perforation of the gastro-intestinal tract
 - Known sensitivity to the drug and sulphite preservatives; cross-sensitivity to procainamide
- Adverse Reactions
- Sedation, restlessness, fatigue, diarrhoea.
 - Extrapyramidal effects, especially with high-dose therapy.
 - Increased frequency and severity of seizures in those with pre-existing condition.
- Drug Interactions
- Increased sedative effect with other CNS depressants.
 - Increased extrapyramidal effects with other dopamine antagonists.
 - Hypotensive reaction when given together with some anaesthetics.
 - Enhanced gastric absorption of drugs by promoting gastric emptying

In case of overdose:

(see “Metoclopramide” in Section B)

Midazolam

- Indications
- Acute anxiety or agitation due to psychosis, hallucinogen/stimulant intoxication, or metabolic encephalopathy
 - Status epilepticus, where intravenous access cannot be established for use of other antiepileptics.
- Dosage
- Agitation or Excessive Muscle Hyperactivity
- 0.05 - 0.1 mg/kg IV, or 0.1mg/kg IM.
- Repeat as needed every 30-60 minutes.**
- Status Epilepticus (with no IV access)
- 0.1 - 0.2 mg/kg IM.
- Repeat if necessary after 5-10 minutes.**
- Method of Use / Administration
- IV or IM; administer by slow injection.

- Contraindications - Known sensitivity to benzodiazepines.
- Use with caution in patients with compromised respiratory status.
- Adverse Reactions - Respiratory arrest; especially when administered rapidly.
- Drug Interactions - Additive effect with other CNS depressants.

In case of overdose:

(see “Benzodiazepines” in Section B)

Morphine

- Indications - Severe pain caused due to envenomation by black widow spiders or rattlesnakes, or other bites and stings
- Pain due to corrosive injury to the eyes, skin or GI tract
- Pulmonary oedema due to congestive heart failure (do NOT use in cases of non-cardiogenic pulmonary oedema)
- Dosage Adult:
- Initial dose
- 5-10 mg intravenous OR
- 10-15 mg intramuscular / subcutaneous.
- Maintenance dose
- 5-20 mg intravenous / intramuscular.
- Children:
- 0.1 - 0.2 mg/kg, intravenous / intramuscular.
- Titrate and repeat doses every 4 hours to maintain analgesia.
- Method of Use / Administration - Administer by injection, as a bolus dose.
- Avoid oral and rectal route - low and erratic bioavailability
- Contraindications - Known hypersensitivity to morphine

- Respiratory and/or CNS depression
- Adverse Reactions
 - Respiratory arrest; prolonged depression, especially in patients with chronic renal or hepatic impairment.
 - Hypotension.
 - Nausea, vomiting, constipation.
 - Bradycardia, wheezing, flushing, pruritus, urticaria and other histamine-like effects.
- Drug Interactions
 - Additive depressant effects with other drugs affecting the CNS.
 - Physical incompatibility with other drugs in parenteral solutions.

In case of overdose:

(see also “Morphine” in Section B)

Naloxone

- Indications
 - Reversal of acute opioid intoxication, manifested by CNS and respiratory depression
 - Empirical therapy for stupor or coma suspected to be drug-induced
- Dosage
 - Injection
 - 0.8 - 2 mg, repeated every 2 to 3 minutes, up to 10 mg.
 - Infusion
 - 0.4 - 0.8 mg/h, titrated to clinical effect.
- Method of Use / Administration
 - Injection
 - Administer intravenously.
 - Infusion
 - Treatment may need to be repeated for long-acting opioids;.
 - Infuse in 5 % dextrose solution. Titrate accordingly.
- Contraindications
 - Known hypersensitivity to the drug.

- Adverse Reactions - Acute withdrawal syndrome in opiate-dependence. Pulmonary oedema and/or ventricular fibrillation. Agitation, hypertension and ventricular irritability, when used with other stimulant drugs.
- Drug Interactions - Antagonises analgesic effects of opioids.

In case of overdose:

- Minimum Toxic Dose - Low potential for toxicity.
- Acute dose of 0.3 mg/kg may have some CNS effects.
- Maximum Tolerated Dose - Relatively safe when given as successive divided doses, over a period of time.
- Total doses of up to 2.5 mg/kg have been used therapeutically.
- Total doses of up to 20 mg have been used in children
- Sign & Symptoms of Toxicity The following are rarely seen:
- Memory impairment
- Dysphagia
- Increased respiration, pulmonary oedema, laryngospasms
- Elevated blood pressure
- Management of Toxicity - Supportive treatment of respiratory and cardiovascular functions.
- Do NOT readminister opioid agonists to counter effects of naloxone.

Nitrite, Sodium

- Indications - Cyanide poisoning
- Hydrogen sulfide poisoning
- Dosage - 300mg, intravenously. Additional half-dose to be given if no methaemoglobinaemia detected after 30 minutes.
- Paediatric dosing as listed in the table below.

**Paediatric Dosing of Sodium Nitrite based on Haemoglobin Concentration
(Maximum : 300mg/dose)**

Haemoglobin Conc. (g/dL)	Initial Dose (mg/kg body weight)
7	5.8
8	6.6
9	7.5
10	8.3
11	9.1
12	10.0
13	10.8
14	11.6

Method of Use / Administration - Administer over a period of at least 5 minutes.

Contraindications - Profound hypotension
- Significant pre-existing methaemoglobinaemia
- Concurrent carbon monoxide poisoning (relative contraindication)

Adverse Reactions - Headache, facial flushing, dizziness, nausea, vomiting, tachycardia, sweating.
- Rapid administration may result in hypotension.
- Excessive methaemoglobinaemia.

Drug Interactions - Vasodilators will exacerbate hypotensive effect.
- Methylene blue reverses medically-induced methaemoglobinaemia.

In case of overdose:

Minimum Toxic Dose - Estimated lethal dose in adults is 2.6 g.

Maximum Tolerated Dose - Ingestion of about 700 mg resulted in severe methaemoglobinaemia, but recovered after treatment with methylene blue.

Sign & Symptoms of Toxicity	<ul style="list-style-type: none">- Uncontrolled vasodilation and/or methaemoglobinemia- Cardiovascular collapse, coma, convulsions, and death
Management of Toxicity	<ul style="list-style-type: none">- Immediate life support measures to control hypotension, seizures and methaemoglobinemia-induced anoxia.- Administer fluids / volume-expanders to correct hypotension- Prevent further absorption of the drug.

Norepinephrine (@ Noradrenaline)

Indications	<ul style="list-style-type: none">- Shock due to venodilation or low systemic vascular resistance.
Dosage	<p><u>Starting dose:</u> Adults; 4-8 mcg/min, intravenously. Children ; 0.1 mcg/kg/min, intravenously.</p> <p>Increase as needed every 5 - 10 minutes.</p>
Method of Use / Administration	<ul style="list-style-type: none">- Administer as IV infusion in 5% dextrose or dextrose-saline.- Recommended conc. 4 mcg/mL.- Ensure a free-flowing infusion. Avoid extravasation.- (Note : Norepinephrine is rapidly oxidised in air; keep it in the unopened ampoule until immediately before dilution.)
Contraindications	<ul style="list-style-type: none">- Hypovolaemia- Hypertension- Hypersensitivity to sulphite preservatives- Use with extreme caution in patients on general anaesthetics or poisoned by aromatic / halogenated hydrocarbon solvents- Use cautiously in patients with ergot intoxication, or those with occlusive vascular diseases (esp. peripheral arteries)

- Adverse Reactions
- Severe hypertension, resulting in myocardial necrosis or infarction, intracranial haemorrhage, pulmonary oedema.
 - Tissue necrosis; due to extravasation at site of injection, gangrene due to aggravation of peripheral tissue ischaemia.
 - Anticholinergic drugs may enhance the hypertensive response.
- Drug Interactions
- Increased arrhythmogenic effect with aromatic and halogenated hydrocarbon solvents, including general anaesthetics.
 - Antagonised by alpha-blocking and beta-blocking agents.
 - Enhanced vasopressor effects with cocaine, cyclic antidepressants and monoamine oxidase inhibitors.

In case of overdose:

(see “Norepinephrine” in Section B)

Penicillamine

- Indications
- Lead poisoning (used alone or as adjunctive therapy)
 - Mercury, copper, arsenic poisoning (after initial treatment with dimercaprol)
- Dosage
- 250 - 500 mg given 4 times a day, orally.
- Method of Use / Administration
- Administer on an empty stomach (at least 1 hour before meals) and at bedtime. Duration of treatment is indicated by urine / blood concentration of toxic metal.
- Contraindications
- History of penicillin hypersensitivity
 - Concomitant administration of other haematopoietic-depressants
 - Severe renal insufficiency
- Adverse Reactions
- Hypersensitivity reaction e.g. rash, pruritus, haematuria, drug fever.

- Leukopenia, thrombocytopenia, haemolytic anaemia, agranulocytosis.
 - Hepatitis and/or pancreatitis
 - Anorexia, nausea, vomiting, epigastric pain, taste impairment.
- Drug Interactions
- Potentiation of other haematopoietic-depressant drugs e.g gold salts, immunosuppressants, antimalarials, phenylbutazone.
 - Increased requirement of pyridoxine.

In case of overdose:

- Minimum Toxic Dose
- Not known.
- Maximum Tolerated Dose
- Not known.
- Sign & Symptoms of Toxicity
- Mild - fever, CNS depression, anorexia, nausea, abdominal pains, myalgia
 - Serious - nephrotic syndrome, hypersensitivity reactions, transient blood dyscrasias, aplastic anaemia, neutrophilic agranulocytosis, neutropenia, thrombocytopenia, rashes, autoimmune responses
- Management of Toxicity
- Initial step is to discontinue penicillamine.
 - Other treatment are supportive and symptomatic.

Phenytoin

- Indications
- Tonic-clonic seizure or status epilepticus caused by drugs or poison
 - Cardiac arrhythmias associated with digitalis intoxication; may be used to treat arrhythmias due to overdose of cyclic antidepressants
- Dosage
- Loading dose: 15-20 mg/kg, intravenously.
 - Maintenance dose: 5 mg/kg/day, orally.

Method of Use / Administration	<u>IV</u> <ul style="list-style-type: none">- Administer as a slow IV injection, at a rate not exceeding 50 mg/ min (or 1 mg/kg/min for children). <u>Oral</u> <ul style="list-style-type: none">- Administer as a single oral dose in adults but in 2 divided doses in children.- Monitor serum level of phenytoin (<20 mg / L) during the course of treatment.
Contraindications	<ul style="list-style-type: none">- Known sensitivity to phenytoin and other hydantoin compounds.
Adverse Reactions	<ul style="list-style-type: none">- Drowsiness, ataxia, nystagmus, nausea.- Hypotension, atrioventricular block, cardiovascular collapse due to rapid intravenous administration.- Tissue necrosis and sloughing due to extravasation.
Drug Interactions	<ul style="list-style-type: none">- None known (for acute emergency use).

In case of overdose:

(see "Phenytoin" in Section B)

Physostigmine

Indications	<ul style="list-style-type: none">- Severe anticholinergic syndrome (agitated delirium, urinary retention, severe sinus tachycardia, hyperthermia with absent sweating) due to overdose or poisoning. Its overall utility is limited as most patients with anticholinergic poisoning can be managed supportively.
Dosage	<ul style="list-style-type: none">- Adult; 0.5 - 2 mg, intravenously.- Children; 0.02 mg/kg, intravenously. <p>Repeat as needed every 20 - 30 minutes.</p>
Method of Use / Administration	<ul style="list-style-type: none">- Administer as slow IV push.- Monitor closely for signs of excessive muscarinic stimulation; atropine should be kept at hand for reversal of overstimulation.
Contraindications	<ul style="list-style-type: none">- Poisoning by cyclic antidepressants- Concurrent use of depolarising neuro-muscular blocking agents (eg. succinylcholine)

- Adverse Reactions
- Bradycardia, heart block, asystole.
 - Seizures (especially with rapid administration).
 - Nausea, vomiting, diarrhoea.
 - Bronchorrhoea, bronchospasms.
 - Fasciculations, muscle weakness.
- Drug Interactions
- Potentiates depolarising neuro-muscular blocking agents.
 - May have additive depressant effect on cardiac conduction when used with cyclic antidepressants.

In case of overdose:

(see “Physostigmine” in Section B)

Pralidoxime (@ 2-PAM, Pyridine Aldoxime)

- Indications
- Organophosphate poisoning, usually insecticides
- Dosage
- 1 - 2 g (children 25 - 50 mg / kg), intravenously.
 - Repeat dose in 1 hour if muscle weakness is not relieved.
 - Repeat dose every 4 to 12 hours as needed, to control nicotinic symptoms, especially for long-acting organophosphates. Max. dose 12 g/24 hours
- Method of Use / Administration
- Bolus
- Administer over 5 - 10 minutes at a rate not exceeding 200 mg/min.
 - (4 mg / kg / min in children)
- Infusion
- Give in 100 mL of normal saline, over 15 - 30 minutes.
 - Maintain therapy with careful observation of clinical response
- Contraindications
- Patients with myasthenia gravis
 - Use with caution in patients with renal impairment
- Adverse Reactions
- Nausea, headache, dizziness, diplopia, hyperventilation.
 - Rapid administration may result in tachycardia,

laryngospasm, muscle rigidity and transient neuromuscular blockade.

Drug Interactions - Enhanced atropinisation when used with atropine and related drugs.

In case of overdose:

Minimum Toxic Dose - Not known.

Maximum Tolerated Dose - Not known.

Sign & Symptoms of Toxicity - Neuromuscular blockade
- Visual disturbances
- Asystole
- CVS effects - transient hypertension, ECG changes

Management of Toxicity - Supportive treatment, only for critical symptoms.

Protamine

Indications - Reversal of anticoagulation due to overdose of heparin.

Dosage - For heparin by IV bolus dose : see table below
- For heparin by constant infusion : 25 - 50 mg
- For heparin by SC : 1 - 1.5 mg/100 units of heparin

Approximate Dosing for Overdose of Heparin Administered by Intravenous Bolus Injection

Time Lapsed Since Heparin Administration	Amount of Protamine (per 100 units of heparin)
0 minutes	1.0 - 1.5 mg
30 - 60 minutes	0.5 - 0.75 mg
2 hours or more	0.25 - 0.375 mg

- Method of Use / Administration - Administer by slow, IV injection, not exceeding 50 mg in 10 minutes.
- Contraindications - Known sensitivity to protamine
- Neonates, for formulations reconstituted with benzyl alcohol
- Adverse Reactions - Hypotension, bradycardia, anaphylactoid reactions.
- Rebound effect due to heparin (within 8 hours of giving protamine).
- Drug Interactions - Inhibits anticoagulants effects of heparin.

In case of overdose:

- Minimum Toxic Dose - Not known.
- Maximum Tolerated Dose - Not known.
- Sign & Symptoms of Toxicity - Hypersensitivity or anaphylactoid reactions - anaphylaxis, flushing, hypotension, bradycardia, syncope, ventricular fibrillation, asystole, bronchospasm, apnoea, dyspnoea, pulmonary oedema, urticaria
- Management of Toxicity - Supportive and symptomatic treatment.

Thiamine (Vitamin B₁)

- Indications - To prevent Wernicke-Korsakoff syndrome in alcoholic or malnourished patients
- As adjunct in patients with ethylene glycol poisoning (possibly enhance the detoxification of glyoxylic acid)

Dosage By injection:
Adult: 100mg Child: 50 mg

- Method of use/
Administration - Slow IV (over 5 minutes) or IM. Repeat every 6 hours if necessary
- Contraindications - Known hypersensitivity to the drug
- Adverse Reactions - Anaphylactoid reactions, vasodilation, hypotension, weakness
- Drug Interaction - May enhance the effect of neuromuscular blockers.

In case of overdose:

- Minimum toxic
Dose - Not known
- Maximum tolerated
Dose - Not known
- Signs & Symptoms
of toxicity - Anaphylactoid reactions
- Management
of toxicity - Treat shock arising from anaphylaxis

Thiosulphate, Sodium

- Indications - Cyanide poisoning (given alone or with nitrites)
- Suspected cyanide poisoning
e.g. smoke inhalation victims
- Dosage - 12.5g, intravenously (children 400 mg / kg, up to a maximum of 12.5 g). May be repeated with half the dose in 30 - 60 minutes, as needed.
- Method of Use /
Administration - Administer 50 mL of a 25% solution at a rate of 2.5 - 5 ml / min.
- Contraindications - None known.

Adverse Reactions - May produce burning sensation during infusion.

Drug Interactions - None known.

In case of overdose:

Minimum Toxic Dose - Ingestion of 12 g resulted in violent catharsis.
- IV dose of over 0.2 g/kg has been known to cause toxicity.

Maximum Tolerated Dose - Not known.

Sign & Symptoms of Toxicity - Gastrointestinal disturbances e.g. diarrhoea
- Transient hypotension and ECG changes, with rapid IV infusion

Management of Toxicity - Gastric decontamination, for oral exposure.
- Treatment of hypotension

Vitamin K₁ (@ Phytomenadione)

Indications - Anticoagulant overdose
- Vitamin K deficiency
- Hypoprothrombinaemia due to salicylate poisoning

Dosage Oral
- Adults, 10 - 25 mg. Children, 5 - 10 mg.
- May be repeated in 12- 24 hours.

SC
- Adults, 5 - 10 mg. Children, 1 - 5 mg.
- May be repeated in 6 - 8 hours.

IV
- Adults, 10 - 50 mg. Children, 5 - 20 mg.
- May be repeated every 4 hours, as necessary.

Method of Use / Administration	<u>Oral and SC</u> <ul style="list-style-type: none">- Administer and repeat, as necessary. Therapy may be required for weeks or months. Maintain patient under observation, especially in cases involving long-acting anticoagulants. Change to oral therapy as soon as possible. <u>IV</u> <ul style="list-style-type: none">- Administer in preservative-free, dextrose or saline solution.- To be given slowly, at a rate < 1 mg/min.- Use only when haemorrhage is present or imminent.
Contraindications	<ul style="list-style-type: none">- Known hypersensitivity to menadione and its derivatives
Adverse Reactions	<ul style="list-style-type: none">- Anaphylactic reaction, with IV administration.- Pain and/or haematomas, with IM injections.- Blood coagulation and associated complications in patients already on anticoagulant therapy.
Drug Interactions	<ul style="list-style-type: none">- Antagonises coumarin, inandione and their derivatives.

In case of overdose:

Minimum Toxic Dose	<ul style="list-style-type: none">- Not known.
Maximum Tolerated Dose	<ul style="list-style-type: none">- In normal adults, doses of up to 1,000 mg of phytomenadione have resulted in no signs of toxicity.
Sign & Symptoms of Toxicity	<ul style="list-style-type: none">- Flushing, cyanosis, dizziness, hypotension, bronchoconstriction- Acute cardiovascular collapse, related to rapid rates of IV infusion (greater than 1 mg/min)
Management of Toxicity	<ul style="list-style-type: none">- Support respiratory and cardiovascular function.- Monitor liver and renal function in patients with signs or symptoms after massive parenteral overdose.

References

1. *Prescriber's J* (1993) 33: 45-50
2. *Drug Safety* (1992) 7: 170-177
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S E C T I O N **B**

MEDICINAL POISONING

CHAPTER 1

Antihistamines

Antihistamines (H_1 antagonists) are common in OTCs and prescription medicine for motion sickness, allergy, coughs and colds. They are also used as sleep aids.

Antihistamines and Their Usual Contents in Dosage Forms

- Azatadine (1 mg), brompheniramine (2-12 mg), buclizine (25 mg), carbinoxamine (1-24 mg), chlorpheniramine (2-4 mg), clemastine (1 mg), cyclizine (50 mg), cyproheptadine (4 mg), dexbrompheniramine (6mg), dexchlorpheniramine (2 mg), dimenhydrinate (50-100mg) diphenhydramine (7.5-14 mg), hydroxyzine (10-25 mg), mebhydrolin (50 mg), meclozine (12.5mg), mebhydrolin (50 mg), oxatomide (30 mg), pheniramine (50-75 mg), trimепразине (2.5 mg), triprolidine (1.25-2.5 mg), promethazine (5-25 mg)
- Non-sedating: acrivastine (8 mg), astemizole (10 mg), cetirizine (10 mg), loratadine (5-10 mg), terfenadine (60 mg)

Table 1. Preparations containing promethazine

Product	Promethazine and Other Contents
Avomine	promethazine theoclate
Delix	promethazine, pholcodine, phenylpropanolamine
Dhasedyl	promethazine, codeine, ephedrine
Dhasilix	promethazine, pholcodine, phenylpropanolamine
Hosedyl	promethazine, codeine, ephedrine
Macodrine	promethazine, codeine, ephedrine
Metaryl	promethazine
Panquil	promethazine, paracetamol
Phenergan	promethazine
Phensedex	promethazine, ipecacuanha, guaiacosulphonate
Phensedyl	promethazine, codeine
Procodyl	promethazine, codeine, ephedrine
Promedyl	promethazine, codeine, ephedrine
Promegan	promethazine
Promethazine DHA	promethazine,
Sedilix	promethazine, codeine, ephedrine
Tixylix	promethazine, pholcodine
Unisedyl Forte	promethazine, codeine, ephedrine
Xepagan	promethazine

Table 2. Preparations containing non-sedating antihistamines

Product	Non-Sedating Antihistamine
Clarityne	loratadine
Hismanal	astemizole
Histafen	terfenadine
Semprex	acrivastine
Tamagon	terfenadine
Teldane	terfenadine
Terfedine	terfenadine
Zyrtec	cetirizine

Table 3. Preparations containing other common antihistamines

Product	Antihistamine and Other Contents
Actidil	triprolidine
Actifed compound — DM — Expectorant	triprolidine, pseudoephedrine, codeine + dextromethorphan + guaphenesin
Alleryl	chlpheniramine
Antamine	chlpheniramine
Atlandryl — CP	diphenhydramine, chloroform, menthol, alcohol 5% + codeine
Avil/retard	pheniramine
Benadryl — CD — DMP	diphenhydramine, menthol, alcohol 1%, ammonium chloride + codeine + dextromethorphan, phenylephrine
Bisolvon compositum	diphenhydramine, bromhexine, ephedrine, codeine, papaverine, noscapine
Buclizine	buclizine
Celestamine	dexchlorpheniramine, betamethasone
Chlonaryl	clemastine
Chloramin/LA	chlorpheniramine
Chlormine	chlorpheniramine
Chlorpyrimine	chlorpheniramine
Chlor-Trimeton	chlorpheniramine
Clodyl	chlorpheniramine, codeine, ephedrine
Coricidin — D	chlorpheniramine, aspirin, caffeine + phenylephrine
Co Tylenol	carbinoxamine, paracetamol, phenylephrine
Dextromin	dexchlorpheniramine
Dhaflu	chlorpheniramine, paracetamol, caffeine, phenylpropanolamine
Dibendyl	diphenhydramine, ammonium chloride
Diligan	meclizine, hydroxyzine, nicotinic acid
Dimetapp	brompheniramine, phenylephrine, phenylpropanolamine
Diphendryl — CP	diphenhydramine, ammonium chloride, menthol, sodium citrate + codeine
Dristan	chlorpheniramine, phenylephrine, acetaminophen

Table 3. (Con't)

Product	Antihistamine and Other Contents
Drixoral	dexbrompheniramine, d-isoephedrine
Ephedrex — N	chlorpheniramine, ephedrine, codeine + noscapine
Fedac — compound	triprolidine, pseudoephedrine + codeine
Hismine	chlorpheniramine
Histodryl	diphenhydramine, ammonium chloride, menthol, sodium citrate
Homoclomin	homochlorcyclizine
Hova expectorant	diphenhydramine, ammonium chloride,
Longifene	bucizine
Lotussin	diphenhydramine, dextromethorphan, ephedrine, guaifenesin
Neo-meton	brompheniramine
Paramine	chlorpheniramine, paracetamol, phenylpropanolamine
Periactin	cyproheptadine
Petina	cyproheptadine
Phenexpect — CD	diphenhydramine, ammonium chloride + codeine
Pilian	cyproheptadine
Piriton	chlorpheniramine
Polaramine — expectorant	dexchlorpheniramine, + pseudoephedrine, guaifenesin
Polyfed	triprolidine, pseudoephedrine
Rhiniramine	dexchlorpheniramine
Temaril	trimeprazine
Tempro	chlorpheniramine, paracetamol, phenylpropanolamine
Tinset	oxatomide
Triprodine — CPD	triprolidine, pseudoephedrine + codeine
Unirhinol/forte	chlorpheniramine, paracetamol, phenylpropanolamine
Unitifed — compound	triprolidine, pseudoephedrine + codeine
Vallergan	trimeprazine
XSP-Bena	diphenhydramine, ammonium chloride, Sodium citrate
Zadine	azatadine

Toxicity

Occurrence: more common in children

Peculiarity: similar to anticholinergic poisoning, CNS stimulation or depression, and membrane-depressing effect on the heart, especially:

- diphenhydramine
- promethazine
- non-sedating antihistamines

Fatal dose: diphenhydramine 20-40 mg/kg (oral)

Toxicity:

- occurs after ingestion of 3-5 times usual daily doses
- promethazine: usual dosage is not more than 100 mg per day
- children are more sensitive than adults

Half-life

- | | |
|--------------------------|---------|
| • chlorpheniramine | 12-15 h |
| • diphenhydramine | 4-8 h |
| • promethazine | 5-14 h |
| • astemizole/metabolites | 19 days |
| • terfenadine | 16-23 h |

Clinical features

- Drowsiness, anticholinergic effects, CNS stimulation or depression, hypertension, arrhythmias, seizures, nystagmus, hallucinations, acute dystonic reactions
- Toxicity in children: mainly CNS stimulation; may resemble atropine poisoning (dilated pupils, flushed face, dry mouth, fever, ataxia); symptoms occur within 30 min - 2 h after ingestion; death may occur within 18 h
- Non-sedating antihistamines (especially astemizole and terfenadine): cardiotoxicity (ventricular arrhythmias, torsade de pointes), convulsions

Management of Toxicity

- Maintain airway, treat coma, seizures, arrhythmias, hyperthermia if they occur; monitor patient for at least 6-8 h after ingestion
- Perform gastric lavage for large ingestions. Do NOT induce emesis (risk of abrupt onset of seizures and coma).
- Administer activated charcoal and cathartic .
- Treat arrhythmias with lignocaine.
- Treat seizures with diazepam or midazolam .
- Treat dystonia with diazepam .
- Treat hypertension with nitroprusside or diazoxide .
- Reverse severe anticholinergic CNS effects with physostigmine. (Use cautiously, some authors do not recommend physostigmine because antihistamine overdose carries a greater risk for seizures. Supportive management is preferred. See pg 133)

Antidotes: no specific antidotes

Laboratory tests: FBC, electrolytes, glucose, arterial blood gases, ECG. Blood drug concentrations are not useful for guiding therapy.

References

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2. Krenzelok EP, Anderson GM, Mirick M : Massive diphenhydramine overdose resulting in death. *Ann Emerg Med* 11: 212, 1982.

CHAPTER 2

Anti-Infective Agents

2.1 Anthelmintics

Anthelmintics are used to treat helminth or worm infestations. Toxicity is uncommon. Table 1 shows the most commonly used anthelmintics and their dosages.

Table 1. Anthelmintics

Anthelmintic	Common Trade Names	Usual Dosage
albendazole	Alzental, Zentel	400 mg
diethylcarbamazine	Hetrazan	2-13 mg/kg
ivermectin	Mectizan	150 µg / kg
levamisole	Ketrax	150-300 mg
mebendazole	Vermox,	100mg
piperazine	Antepar, Baili worm syrup, Camin syrup, Vermizine	2-4 g
praziquantel	Biltricide	20-50 mg/kg
pyrantel	Quantrel	5-20 mg/kg

Toxicity

Occurrence: accidental overdose in the home

Frequency: cases of poisoning by these drugs are few

Peculiarity: adverse effects are diverse and may be mistaken for progression or complications of the disease. Some may be cumulative and fatal if unrecognised. Many side effects are caused by the large antigenic mass of dying worms released into the blood stream.

Clinical Features

- diethylcarbamazine: anorexia, vomiting, headache, weakness, arthralgias
- mebendazole/albendazole: poorly absorbed from GI, may cause abdominal pain and diarrhoea
- levamisole: confusion, insomnia, weakness, pruritus, headache, rash.
- piperazine: vomiting, abdominal pain, rash fever, weakness, diarrhoea, cerebellar ataxia, visual disturbances and seizures in doses above 1 g/kg

Management of Toxicity

- Treatment is symptomatic and supportive
- Perform gastric lavage for large and recent ingestions or induce emesis. Emesis is not recommended if drug has a potential for CNS depression or seizures e.g. piperazine, mebendazole, levamisole.
- Administer activated charcoal and cathartic
- Treat seizures with diazepam
- In piperazine overdose, administer antihistamine for allergic reactions

Antidotes: no specific antidotes

Laboratory tests: Liver function tests. Blood drug concentrations are not very useful. Renal function tests, FBC.

2.2 Antibacterial Drugs

There are many classes of antibiotics for the treatment of various infections. These are listed in pages 162-168.

Toxicity

Occurrence: Uncommon

Peculiarity: Toxic effects are different and vary according to the antibiotic. Acute oral overdose usually causes nausea, vomiting and diarrhoea. Accidental overdoses via intravenous injections are more likely to cause toxicity. In general, harmful effects have resulted from allergic reactions or inadvertent intravenous overdose. Serious toxicity from a single acute ingestion is rare.

Management of Toxicity

- Supportive treatment; maintain airway and assist ventilation.
- Treat anaphylaxis, coma, seizures, hypotension, and haemolysis if they occur.
- Replace fluid losses due to gastroenteritis
- Gastric decontamination: Administer activated charcoal and cathartic. Gut emptying may not be necessary for small ingestions if activated charcoal is given promptly.
- Maintain adequate urine flow as many antibiotics are excreted unchanged. Haemodialysis is indicated only for patients with renal insufficiency and those with very high plasma drug concentrations.
- Charcoal haemoperfusion effectively removes chloramphenicol. Indicated in patients with excessive overdose and metabolic acidosis.
- Repeat doses of activated charcoal for dapsone which undergoes enterohepatic recirculation.

Antidotes:

- Trimethoprim poisoning: administer leucovorin (folinic acid)
Folic acid is not effective. See pg 121.
- Dapsone poisoning: Administer methylene blue if
methaemoglobinaemia occurs. See pg 123.

Laboratory tests:

- Serum drug concentrations are useful for predicting toxic effects
of antibiotics especially for aminoglycosides, chloramphenicol,
vancomycin.
- FBC, electrolytes, glucose, BUN, creatinine, liver function tests,
urinalysis, methaemoglobin (for dapsone).

2.3 Antifungal Drugs

Table 2 shows the common toxic features of the antifungals.

Table 2. Antifungal drugs

Antifungal (usual content)	Common Trade Names	Toxic Clinical Features
Amphotericin B (50 mg/10 mL inj)	Amphocil, Fungizone	headache, nausea, vomiting, hypotension, arrhythmias, nephrotoxicity, hypokalaemia, hepatitis, thrombocytopenia, leucopenia, acidosis
Fluconazole (50-200 mg cap; 2mg/mL inj)	Diflucan	headache, nausea, vomiting, diarrhoea, vertigo, abdominal pain, hepatotoxicity, hyperkalaemia, rashes, thrombocytopenia, seizures
Griseofulvin (125-500 mg tab)	Fulcin, Grifulvil, Grisovin, Grivin, Krisovin, Medofulvin	nausea, vomiting, vertigo, urticaria, porphyria, mental confusion, leucopenia
Itraconazole (100 mg cap)	Sporanox	nausea, epigastric pain, headache, oedema, hypokalaemia
Ketoconazole (200 mg cap)	Nizoral	nausea, vomiting, abdominal pain, dizziness, anaphylaxis, hepatotoxicity, adrenal suppression, peripheral neuropathy
Miconazole (10 mg/ml inj)	Daktarin IV	nausea, vomiting, drowsiness, thrombocytosis, pruritus, hyponatraemia, arrhythmia, respiratory arrest, seizures
Nystatin (500,000 u tab)	Mycostatin	poorly absorbed, toxicity is low, minor GI symptoms

Toxicity:

Clinical data on overdose with these agents are rare.

Management of Toxicity

- Supportive treatment, treat anaphylaxis, cardiac arrhythmias hypotension and electrolyte imbalance if they occur.
- Perform gastric lavage for large ingestions or induce emesis where necessary
- Administer activated charcoal and cathartic.
- Treat seizures with diazepam.

Antidote: no specific antidotes

Laboratory tests: FBC, electrolytes, liver and renal function

2.4 Antimalarial Drugs

Chloroquine and other aminoquinolines are used in the prophylaxis and treatment of malarial and other parasitic diseases.

Table 3. Antimalarial drugs

Antimalarial Drug (usual content/ tab)	Common Trade Names	Toxic Clinical Features
Chloroquine (150-250 mg)	Avloclor, Malarex, Nivaquine	vomiting, diarrhoea, blurring of vision, hyperexcitability, seizures, hypotension, arrhythmias, methaemoglobinaemia, shock, coma, hypokalaemia, cardiac arrest, death may occur after 1-2 hr
Hydroxychloroquine (200 mg)	Plaquenil	
Primaquine (7.5 mg)	Primaquine	
Mefloquine (250 mg)	Lariam, Mephaquin	anorexia, vomiting, diarrhoea, dizziness, hypotension, psychosis, convulsion, coma.
Pyrimethamine (12.5-25 mg)	Daraprim	anorexia, vomiting, CNS stimulation, seizures, megaloblastic anaemia, leukopenia, thrombocytopenia, tachycardia, glossitis, crystalluria
+ Sulfadoxine (500mg)	Fansidar	
+ Dapsone (100mg)	Maloprim	
Quinine (120-300 mg, 300 mg/mL inj)	Quinine sulphate or dihydrochloride	tinnitus, diarrhoea, vomiting, visual disturbances, dizziness, blindness, headache, fever, arrhythmias, confusion, seizures, respiratory depression and circulatory collapse

Toxicity

The following plasma quinine levels have been associated with:

For quinine, >10 mg/L ——— visual impairment
 > 16 mg/L ——— cardiotoxicity
 > 20 mg/L ——— blindness

Fatal oral dose: 30-50mg chloroquine base/kg

Management of Toxicity

- Supportive treatment. Maintain respiration and circulatory function, treat seizures, cardiac arrhythmias, hypotension, shock, hypokalaemia, methaemoglobinaemia, megaloblastic anaemia and crystalluria if they occur
- Gastric decontamination. Gastric lavage should only be performed after intubation. Do not induce emesis because of risk of rapid onset of coma or seizures
- Administer activated charcoal and/or cathartic
- Administration of IV sodium bicarbonate may decrease cardiotoxicity of quinine. IV diazepam may ameliorate cardiotoxicity of chloroquine. See pg 101.
- Give phenytoin to control arrhythmias (increases AV conduction velocity) in quinine overdose. Do not use Type 1a and 1c antiarrhythmic drugs (e.g. procainamide, disopyramide, flecainide) as they can worsen cardiotoxicity. Phenytoin or lidocaine may be used to control ventricular dysrhythmias in mefloquine overdose.
- Treat seizures with diazepam.
- If haemolysis occurs, prevent haem deposition in kidney tubules by alkaline diuresis. Massive haemolysis may require a blood transfusion.
- Haemodialysis and peritoneal dialysis are of little use.

Antidotes: To correct abnormal blood cell counts in pyrimethamine overdose, administer leucovorin. See pg 121.

Laboratory tests:

- FBC, serum electrolytes, liver function, BUN, creatinine, ECG.
- For pyrimethamine: monitor renal, hepatic and haemopoietic system for at least a month after overdose .
- For quinine: prothrombin time, acid-base status and cardiac status. Serum concentration of quinine can be measured using assay for quinidine, provided quinidine is not present.
- For primaquine, include free plasma Hb, methaemoglobin.

2.5 Antituberculous Drugs

Table 4. Antituberculous drugs

Anti-TB Drugs	Common Trade Names	Dosage	Toxic Clinical Features
Isoniazid	Isoniazid Rifater Rifinah Rimactazid	300 mg/day	metabolic acidosis, polyneuritis, hepatotoxicity, convulsions, coma
Rifampicin	Ramfin Siticox Rifater Rifinah Rimactazid	600 mg/day	red urine and tears, hepatotoxicity, thrombocytopenic purpura, haemolytic anaemia, acute renal failure,
Pyrazinamide	Pza-Ciba Rifater	<30 mg/kg	hepatotoxicity, hyperuricaemia, arthralgia
Ethambutol	Ambutol Myambutol	15 mg/kg/day	optic neuritis
Cycloserine	-	0.5-1 g /day	psychiatric disorders, convulsions, coma
Ethionamide	-	0.5-1 g /day	hepatotoxicity and GI toxicity

Toxicity

Peculiarity: One of the main toxic effects with these drugs is hepatotoxicity.

Management of Toxicity

- Supportive treatment; maintain airway and assist ventilation.
- Treat coma, seizures, acidosis, anaphylaxis, haemolysis, if they occur.
- Perform gastric lavage for large, recent ingestions.

- Administer activated charcoal and cathartic. Gut emptying may not be necessary for small ingestions if activated charcoal is given promptly.
- Haemodialysis or peritoneal dialysis may reduce levels of ethambutol in blood.
- Treat seizures with diazepam 0.1-0.2 mg/kg IV

Antidotes: Pyridoxine 5g IV for isoniazid if the amount of isoniazid is not known. If known, give an equivalent amount in grams of pyridoxine to grams of ingested isoniazid.

Laboratory tests: FBC, electrolytes, glucose, BUN, creatinine, liver function tests, arterial blood gases.

2.6. Antiviral Drugs

The table below lists some of the antiviral agents.

Table 5. Antiviral drugs

Antiviral Drugs (usual content/tab)	Common Trade Names	Toxic Clinical Features
Acyclovir (200-800 mg)	Zovirax	nausea, vomiting, tremors, hallucinations, seizures, coma, renal damage, thrombocytosis, leucopenia
Amantadine (100 mg)	Symmetrel	dilated pupil, nausea vomiting, dysrhythmias, acute psychosis, seizures, respiratory distress, coma
Famciclovir (125-250 mg)	Famvir	nausea, headache, vomiting, confusion, hallucinations
Foscarnet (24 mg/mL inj)	Foscavir	nausea, vomiting, anaemia, headache, renal damage, seizures, hypo and hypercalcaemia, hypo and hyperphosphatemia, hypokalaemia, hypomagnesaemia
Ganciclovir (250 mg tab 500 mg inj)	Cymevene	fever, rash, confusion, granulocytopenia, thrombocytopenia severe myelosuppression
Methisoprinol or Inosine pranobex (500 mg)	Imin, Isoprinosine	nausea, vomiting, hyperuricaemia, renal failure
Valaciclovir (500 mg)	Valtrex	Valaciclovir is a prodrug of acyclovir and may act similarly in overdose
Zalcitabine (0.375-0.75 mg)	Hivid	rash, fever, neuropathy
Zidovudine (100-250 mg)	Retrovir	asthenia, headache, dizziness, nausea, vomiting, myalgia, anaemia, neutropenia & bone marrow suppression (>20 g dose), seizures (>36 g dose)

Toxicity

The toxic clinical effects are listed in Table 5.

Management of Toxicity

- Supportive treatment; maintain airway and assist ventilation.
- Treat coma, seizures, psychosis, dysrhythmias, if they occur.
- Perform gastric lavage for large and recent ingestions.
- Administer activated charcoal and cathartic.
- Acidifying agents may increase excretion of amantadine
- Haemodialysis may be useful for reducing serum concentrations of acyclovir, famciclovir, ganciclovir and valaciclovir
- Treat tachyarrhythmias with beta blockers.
- Neuroleptic malignant syndrome may respond to dantrolene
- In the presence of bone marrow suppression, transfusions and protective treatment for granulocytopenia may be needed until recovery of bone marrow function.
- Do not use physostigmine.

Antidotes: no specific antidotes

Laboratory tests: FBC, serum electrolytes, BUN, creatinine, liver and renal function tests, ECG.

Table 6. Summary of Antibiotics and their Properties.

Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T^{1/2} b (h)	Toxic & Clinical Features
Aminoglycosides					Ototoxicity to vestibular and cochlear cells, nephrotoxicity, neuromuscular blockade
Amikacin	Amikin, Aemycin	15-25 mg/L	>35 mg/L	2-3	Ototoxicity and nephrotoxicity
Gentamicin	Cidomycin, Lisarin Miramycin, Servigenta, Genta, Genticin	5-10 mg/L	>12 mg/L	2-4	
Kanamycin	Kancin, Kana	15-25 mg/L	>30 mg/L	2-4	
Neomycin	Tergynan, Neosporin, Cebemyxine, Pocin G, Spersapolymyxin	1-4g/day		—	
Streptomycin	Streptocin	20-30 mg/L	>40 mg/L	2.4-2.7	
Tobramycin	Nebcin	5-10 mg/L	>10 mg/L	3	
Bacitracin	(Usually in ointments)			1.5	
Cephalosporins					Nephrotoxicity for most cephalosporins
Cefazolin	Kefzol	<6 g/day		1.9	Convulsions in patients with renal diseases
Cephalothin	Cefadin	<12 g/day		1	Interstitial nephritis, nephrotoxicity
Cephaloridine	Ceporin	1-4 g/day	6 g/day	1	

Table 6. (Cont'd)

Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T _{1/2} b (h)	Toxic & Clinical Features
Cephmandole	Kefadol	<12 g/day		1	Disulfiram-like reaction with ethanol; bleeding tendencies (-Vit K)
Cefoperazone	Cefobid	<12 g/day		2	
Moxalactam	Moxam	<12 g/day		2	
Cefmetazole	Cefmetazon	4 g/day		1.5	
Chloramphenicol	Beaphenicol, Chloroptic, Enclor, Herpidu, Kemicetine, Mindaril, Spersacet C, Spersanicol, Xepanicol	10-20 mg/L	>50 mg/L	1.6-4	Aplastic anaemia, circulatory collapse, (Gray Baby Syndrome)
Dapsone	Maloprim	<100 mg/day	>500 mg	28	Haemolysis, acidosis, confusion, hepatitis
Quinolones					Convulsions, confusion, headaches
Fluoroquinolones:					
Ciprofloxacin	Ciprobay	0.5-1.5 g/day		3-6	Convulsions, hallucinations, metabolic acidosis, intracranial hypertension
Enoxacin	—	0.4-1.2g/day		4-6	
Pefloxacin	Peflacine	0.8g/day		7-14	
Norfloxacin	Effectsal, Gyrablock, Lexinor, Urobacid	0.8-1.6g/day		4	
Ofloxacin	Inoflox, Tarivid	0.4-0.8g/day		6-7	
Nalidixic acid	Wintomylon	<4 g/day		6	
Isoniazid	—	300 mg/day	1-2 g	0.5-4	Metabolic acidosis, convulsions, hepatotoxicity

Table 6. (Cont'd)

Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T _{1/2} b (h)	Toxic & Clinical Features
Lincomycin	Lincocin	<4.8 g/day		5	Hypotension, cardiopulmonary arrest with rapid IV injection
Clindamycin	Tidact, Dalacin C	300mg - 4800mg/day		2.4	
Macrolides					
Erythromycin	EES, Eritrazon, E-Mycin, Ericin, Erocin, Erotab 250, Ery, Eryped Granules, Erysol, Eryson, Erythro, Erythrocin, Ettrocin, Servitrocin, Ermycin, Erytab-S, Etocin, Tiprocin	<4 g/ day		1.3-2.4	Cholestatic hepatitis especially with estolate
Clarithromycin	Klacid	500mg-2g /day		5-7	
Azithromycin	Zithromax	250mg-1g /day		50	
Metronidazole	Elyzol, Flagyl, Metrogyl, Metrozine, MND, Protogyl, Servizol, Stanzil	<4 g/day	5g/day	8.5	Convulsions; disulfiram-like reactions with ethanol
Nitrofurantoin	Furan	<400 mg /day		0.3-0.5	Haemolysis in G6PD-deficient patients

Table 6. (Cont'd)

Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T _{1/2} (h)	Toxic & Clinical Features
Penicillins					Hypersensitivity reactions. Anaphylaxis in 0.015-0.04% treated patients. Mortality rate is 0.002% in treated patients.
Benzylpenicillin	Crystalline penicillin	<24 megaU /day	100 megaU /day IV or CSF >5 mg /L	0.5	IV doses can cause encephalopathy, convulsions, coma, especially in patients with renal impairment.
Penicillin V	Ospen, Beapen, Asillin V	2 g/day		0.5	
Aminopenicillins:					
Amoxicillin	Amoxil, Amoxapen, Amoxicap, Aroxin, Betamox, Biomox, Clonamox, Lamoxy, Moxilen, Moxipen, Ospamox, Ranoxyl, Servamox, Synamox	<4 g/day		1.0	Acute renal failure caused by crystal deposits
Ampicillin	Ampillin, Ampexin, Ampicap-T, Ampiclox, Ampicyn, Ampilin, Ampisol, Ampitab, Cloxamix, Cloxamp, Dhacillin, Hiperbiotico, Ingacillin, Pamecil, Penbritin	<12 g/day		1.0-1.5	Acute renal failure caused by crystal deposits
Bacampicillin	Penglobe	<1.6 g/day		1.0	
Carboxypenicillins:					
Carbenicillin		<6 g/day		1	
Ticarcillin		<20 g/day		1.2	Platelet aggregation

Table 6. (Cont'd)

Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T _{1/2} (h)	Toxic & Clinical Features
<i>Isoxazolpenicillins:</i> Cloxacillin	Ampiclox, Cloxamp, Cloxacap, Cloxcin, Cloxillin, Isoxacillin, Monoclox, Orbenin, Procap-C, RosciloX	2 g/day		0.5-1	
Methicillin	Celbenin	<12 g/day		0.5-1	Interstitial nephritis, leucopenia
Nafcillin	Nafcil	< 6 g/day		0.5-1	Neutropenia
Piperacillin	Pipracil	<24 g/day		1	
<i>Ureidopenicillins:</i> Azlocillin	Securopen	<24 g/day		1	
Mezlocillin	Baypen	<24 g/day		1	
Polymyxins					
Polymyxin B	Terramycin	15,000-30,000 U/kg/day	>30,000 U/kg/day	6	Nephrotoxicity, neuromuscular blockade
Polymyxin E (Colistin)		5-15mg/kg/day		1.6-4	
Rifampicin	Ramfin, Siticox	<0.6 g/day	>5 g/day	2-5	Facial oedema, pruritus, vomiting, diarrhoea, red urine and tears
Spectinomycin	Trobicin	2-4 g/day		2.5	

Table 6. (Cont'd)

Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T _{1/2} b (h)	Toxic & Clinical Features
Tetracyclines					Increased intracranial pressure, nephrotoxicity, azotemia, acidosis, hyperphosphatemia, hepatotoxicity, photosensitivity
Tetracycline	Achromycin "V", Ibicyn, Beatacycline, Dhatriacin, Dumocycline, Latycin, Panmycin, Servitet, Talsutin, Tetra, Vemyclin, Xepacycline, Xepaphos	<2 g/day	>4 g/day, In infants: >1 g/day	6	Nephrogenic diabetes insipidus
Chlortetracycline	Aureomycin, Chlortralin	1-2 g/day		6	
Demeclocycline	Ledermycin	600mg/day		12	
Doxycycline	Bronmycin, Doxycilin, Doryx, Doxymycin-100, Medomycin, Remycin, Servidoxyne, Vibramycin, Wanmycin, Xidox, Zadorine	100-200 mg /day		15-24	
Minocycline	Minocin	200 mg/day		15	Vestibular symptoms
Oxytetracycline	Oxylim, Oxyterin, Terramycin	1-2 g/day		10	
Sulphonamides					
Sulphadiazine	Sulphadiazine	<4 g/day		8-16	Stevens-Johnson Syndrome, acute renal failure due to crystal deposition
Sulphamethoxazole	Sulphamethoxazole	3 g/day		10	

Table 6. (Cont'd)

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Antibiotic	Common Trade Names	Therapeutic Dose/Conc	Toxic Dose/Conc	T _{1/2} b (h)	Toxic & Clinical Features
Trimethoprim	Ipral, Syraprim	200-300mg /day		8-10	Blood dyscrasias
Co-trimoxazole And Other Sulphonamide-Trimethoprim Combinations	Apo-Sulfatrim, Bacin, Bactrim, Balin BS, Chemix, Chemoprim, Dhatriin, Keliprim, Rancotrim, Septrin, Sulfaprim, Suprim, Triglobe, Trimaxazole, Trizine	<1.44g/day			Stevens-Johnson Syndrome, renal failure, blood dyscrasias
Vancomycin	Vancocin CP, Vancoled	10-30 mg/L	>80 mg/L	4-6	Ototoxicity, nephrotoxicity

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CHAPTER 3

Autonomic Drugs

3.1 Adrenergic Drugs (Sympathomimetics)

This group of drugs includes:

- Those with actions on α and β adrenergic receptors and
- Those with selective actions for β_2 receptors.

A. Drugs with Actions on Both α and β Adrenergic Receptors

Many of these drugs are available OTC as nasal decongestants, cold and flu remedies.

Table 1. Drugs with actions on both α and β adrenergic receptors

Drugs	Usual Adult Dose	Usual Paed Dose	Common Trade Names
Adrenaline	0.1-1 mg	10 μ g/kg	Adrenaline Inj
Dopamine	2-50 μ g/kg/min	—	Dopamine IV, Dopmin, Intropin IV
Ephedrine	100-200 mg/day	2-3 mg/kg	Coughlax, Decofam Cough, Dhasedyl, Promedyl-B, Sedilix, Unisedyl Forte
Naphazoline	—	—	Albalon, Alergoftal, Antistin-Privin, Flucur, Naphcon-A
Oxymetazoline	—	—	Afrin, Iliadin, Oxylin
Phenylephrine	40-60 mg/day	0.5-1 mg/kg	Blephamide, Cyclomydril, Dristan, Febs, Mydfrin, Prefrin, Rhinopront
Phenylpropanolamine	100-150 mg/day	1-2 mg/kg	Allerin, Beafly, Bromanate, Coritab, Coritussal, Decolgen, Delix, Dhafly, Febricol, Panaflu/plus, Paramine, Parclorphen, Rhinopront, Sinutab, Sinuzin-D, Unirhinol

Table 1. (Cont'd)

Drugs	Usual Adult Dose	Usual Paed Dose	Common Trade Names
Pseudoephedrine	180-360 mg/day	3-5 mg/kg	Actifed, Beactafed, Clarinase, Codimal-L.A., Drixoral, Fedac, Panadol Cold and Flu, Polaramine Exp, Sudafed/Decongestant, Unitifed
Xylometazoline	6 drops of 1%/day	6 drops of 0.5%/day	Otrivin, Rynacrom Compound

Toxicity

- Phenylpropanolamine, phenylephrine and ephedrine have low therapeutic indices. Toxicity usually occurs at 2-3 times the therapeutic doses. Pseudoephedrine is slightly less toxic (toxicity occurring at 4-5 times therapeutic dose).
- Patients who are on MAO - inhibitors are very sensitive to the toxic effects of these drugs.
- The main toxic effect of these drugs is hypertension.

Clinical Features

Hypertension leading to headache, confusion, seizures, intracranial haemorrhage, atrioventricular block, myocardial infarction, coma

Management of Toxicity

- Supportive, maintain airway and assist ventilation with supplementary oxygen, if necessary
- Treat hypertension, seizures, and ventricular arrhythmias if they occur. Do NOT treat bradycardia with e.g. atropine which may abolish reflex bradycardia and worsen hypertension
- Gastric decontamination with activated charcoal and catharsis. Gastric lavage is not necessary if activated charcoal can be given promptly.

- Haemodialysis and haemoperfusion are not effective. Acidification of urine may enhance elimination of phenylpropanolamine, ephedrine, pseudoephedrine, but in patients with rhabdomyolysis this may worsen myoglobin deposition in kidneys.
- Monitor vital signs and ECG for at least 6 hours and longer if sustained-release preparations have been ingested.

Antidotes: no specific antidotes.

Phentolamine and nitroprusside are recommended vasodilators.

Do not use β_2 blockers alone without vasodilators, because paradoxical worsening of hypertension may occur.

Laboratory tests: Electrolytes, glucose, BUN, creatinine, creatine phosphokinase (CPK), ECG monitoring, CT head scan if intracranial haemorrhage is suspected. Plasma drug concentrations are not useful. Toxicology screen may show positive for amphetamine because of the presence of these drugs.

B. Drugs Acting Selectively on β_2 Receptors

This group of drugs is present in preparations for the treatment of asthma and other related respiratory disorders and premature labour. Their dosage is dependent on the dosage form.

Table 2. Drugs acting selectively on β_2 receptors

Drugs	Usual adult dose	Usual paed dose	Common Brand Names
Fenoterol (aerosol - 100 μg /puff, 200 μg /puff) (inhalation - 0.5%)	<8 puffs/day	—	Berotec
Orciprenaline, metaproterenol	oral 80mg/day	oral 30mg/day	Silomat Compositum
Procaterol	oral 50-100 μg /day	1-2 $\mu\text{g}/\text{kg}/\text{day}$	Meptin

Table 2. (Cont'd)

Drugs	Usual adult dose	Usual paed dose	Common Brand Names
Ritodrine	oral <120 mg/day	—	Yutopar
Salbutamol/ albuterol	oral 16 mg/day	oral 8 mg/day	Airomir, Apo-salvent, Clenil Compositum, Medolin, Respolin, Salbuvent, Ventide, Ventodisk, Ventolin, Volmax, Zenmolin
Salmeterol	Puff 50-200 µg/day	Puff <100 µg/day	Serevent
Terbutaline	oral 7.5-15 mg/day	oral 0.25 mg/kg/day	Anvelin, Ataline, Bricanyl, Britalin, Butylin

Toxicity

- Generally, with these drugs, a dose in excess of the total daily dose would produce toxic signs and symptoms.
- Therapeutic doses of terbutaline have been reported to produce toxic symptoms in pregnant women because of haemodynamic changes.
- Most overdoses in children result in mild toxicity.
- The main toxic effects are on the cardiovascular system.

Clinical Features

Tachycardia, hypotension, wide pulse pressure, skeletal muscle tremors, hypokalaemia (due to intracellular shift of potassium), hyperglycaemia, lactic acidosis, seizures

Management of Toxicity

- Supportive, maintain airway and assist ventilation
- Treat hypotension with β blockers e.g. propranolol. Cerebral hypoperfusion might cause changes in mental states, seizures; treatment of hypotension should alleviate these symptoms as well. When accompanied by ventricular dysrhythmias, treat sinus tachycardia with β blockers.

- Gastric decontamination with activated charcoal and catharsis. Gastric lavage is not necessary if activated charcoal can be given promptly.
- Monitor vital signs and ECG for at least 6 hours and longer if sustained-release preparations have been ingested.
- Hypokalaemia does not require treatment.
- Haemodialysis is not useful

Antidotes: β -blockers e.g. propranolol IV 0.01 - 0.03 mg/kg or esmolol IV 25 - 50 mg/kg/min. These must be used with caution in patients with history of asthma.

Laboratory tests: Electrolytes, glucose, BUN, creatinine, creatine phosphokinase (CPK, if excess muscle activity), ECG monitoring. Serum drug concentrations do not contribute to management.

3.2 Anticholinergic Drugs

3.2.1 Antiparkinsonian drugs

Table 3. Antiparkinsonian drugs

Drug	Common Brand Names	Usual Daily Doses	Toxic Features
Benzhexol or trihexyphenidyl	Anti-Spas, Apo-Trihex, Artane, B-Hex	2-10 mg	Blurred vision, dilated and unreactive pupils, dry mouth, urinary retention, tachycardia, hypertension, hyperthermia, delirium, CNS excitation
Bromocriptine	Brometine, Parilac, Parlodel, Serocryptin, Suplac.	1.25-40 mg	Nausea, vomiting, dizziness, postural hypotension, hypertension, pulmonary fibrosis, confusion, hallucinations
Levodopa +benserazide +carbidopa	Madopar Sinemet, Syndopa	75-1500 mg	Nausea, vomiting, fainting, hypertension followed by postural hypotension, sinus tachycardia, dyskinesias, hallucinations

Toxicity

- Benzhexol or trihexyphenidyl produces antimuscarinic toxic effects.
- Bromocriptine: dangers of overdose with bromocriptine are minimal with supportive care.
- Bromocriptine is used also for the treatment of neuroleptic malignant syndrome (NMS) caused by neuroleptics e.g. haloperidol, other antipsychotics and levodopa withdrawal.
- Levodopa has GI, CVS and CNS toxic effects.

Management of Toxicity

- Supportive, maintain airway and assist ventilation
- Treat hyperthermia, hypertension and tachycardia, hypotension, seizures and coma if they occur
- Gastric decontamination with activated charcoal and catharsis. Gastric lavage is not necessary if activated charcoal can be given promptly.
- Haemodialysis and other enhancement of elimination are not useful

Antidotes: Small dose of physostigmine (slow IV 0.5-2 mg) can reverse hyperthermia, delirium and tachycardia in severe benzhexol overdose. Physostigmine is rarely used except in life-threatening emergencies. It is more used as a diagnostic agent. See pg 133.

Caution: Physostigmine may cause atrioventricular block, asystole and seizures.

For dyskinesias in levodopa overdose, pyridoxine (10-15 mg IV). Pyridoxine is not effective in reversing the action of the combination levodopa/carbidopa. Deanol (metabolised to choline) up to 900 mg/day orally may help to normalise dopamine and acetylcholine balance in CNS.

Laboratory tests: Electrolytes, glucose, ECG monitoring. Serum drug concentrations do not contribute to management.

3.2.2 Antimuscarinics and Antispasmodics

Table 4. Antimuscarinics and antispasmodics

Drug	Common Brand Names	Usual Single Doses
Atropine	Dhamotil, Erlotyl, Lomotil, Remodil	0.4-1 mg
Benztropine or Benzatropine	Cogentin	1-6 mg
Clidinium	Apo-chlorax, Librax, Medocalum	2.5-5 mg
Dicyclomine or Dicycloverine	Acolic, Colimix, Infacol-C, Spascol, Veragel-DMS	10-20 mg
Flavoxate	Urispas	100-200 mg
Homatropine	Isopto-Homatropine	1-2 drops of 2% solution into eye
Hyoscine or Scopolamine	Buscopan, Colospan, Dhacopan, Fucon, Holopon, Hybrome, Hyomide, Hyospan, Scopoderm-TS, Spasmoliv	0.4-1 mg
Hyoscyamine	Levsin	0.15-0.3 mg
Propantheline	Pro-Banthine	15-30 mg
Tropicamide	Mydriacyl	1-2 drops of 1% solution into eye

Toxicity

- The range of toxicity is variable. Fatal atropine poisoning has occurred with 1-2 mg instilled into eye of a child and after 32 mg IM injection into adult.
- Antimuscarinic toxic effects are manifested by other drugs like the tricyclic antidepressants and phenothiazines.
- A trial dose of physostigmine for reversing symptoms can be used to confirm antimuscarinic drug poisoning. This is to distinguish between functional psychosis and antimuscarinic delirium.

Clinical Features

Warm dry flushed skin, dry mouth, delirium, mydriasis, hypertension, tachycardia, ileus, urinary retention, jerky movements, hyperthermia, coma, and rarely arrhythmias and seizures

Management of Toxicity

- Supportive, maintain airway and assist ventilation
- Treat hyperthermia, hypertension, tachycardia, arrhythmias, seizures and coma if they occur
- Gastric decontamination with activated charcoal and catharsis. Gastric lavage is not necessary if activated charcoal can be given promptly.
- Haemodialysis and other enhancement of elimination are not useful

Antidotes: In severe poisoning, physostigmine (slow IV 0.5-2 mg) can reverse hyperthermia, delirium and tachycardia.

Physostigmine is rarely used except in life-threatening emergencies. It is used more as a diagnostic agent. See pg 133.

Caution: *Physostigmine may cause atrioventricular block, asystole and seizures especially in patients with tricyclic antidepressant overdose.*

Bethanechol has been used to alleviate the peripheral effects.

Laboratory tests: Electrolytes, glucose, ECG monitoring. Serum drug concentrations do not contribute to management.

3.3 Cholinergic Drugs (Parasympathomimetics)

Table 5. Cholinergic drugs

Drug	Common Brand Names	Usual Doses
Bethanechol	Urecholine	Oral 10-25 mg tds-qds
Neostigmine	Prostigmine	Oral 15-180 mg/day
Physostigmine	Antilirium	IV 0.5-2mg
Pilocarpine	Isopto Carpine, Normoglaucan, Pilogel HS, PV Carpine, Spersacarpine, Timpilo	1-2 drops of 1-4% eye drops
Pyridostigmine	Mestinon	Oral 30-180 mg bd-qds

Toxicity

- The toxic effects are due to excessive cholinergic stimulation.
- Physostigmine penetrates the blood brain barrier well and is more liable to cause central cholinergic effects. Life-threatening ventricular arrhythmias have occurred. Physostigmine is considered super toxic. Oral lethal dose is 5 mg/kg.

Clinical Features

Nausea, vomiting, pinpoint pupil, sweating, bronchospasms, bradycardia, involuntary urination and defaecation, tremors, muscle twitching, seizures. Severe overdose results in severe hypotension, shock and cardiac arrest.

Management of Toxicity

- Supportive, maintain airway and assist ventilation
- Treat seizures, circulatory collapse if they occur
- Use antidote atropine 2 to 4 mg IV, repeat every 30 minutes when necessary, then PRN for 24 hours to 48 hours. Child 0.04 - 0.08 mg/kg IV (up to 4 mg) repeated every 30 -60 minutes as necessary.

- Gastric decontamination with activated charcoal and catharsis. Gastric lavage is not necessary if activated charcoal can be given promptly.
- Adrenaline to alleviate severe cardiovascular reactions and bronchospasms
- Haemodialysis and other enhancement of elimination are not useful

Antidotes: Atropine and adrenaline. See pg 90 & 112.

Laboratory tests: Serum drug concentrations do not contribute to management. Measurement of plasma and red cell cholinesterase levels after an overdose of the anticholinesterase drugs may be indicated. Although cholinesterase levels do not correlate well with clinical toxicity, reduction of 80% activity of the enzyme is associated with severe toxicity.

3.4 Skeletal Muscle Relaxants - Centrally Acting

Table 6. Skeletal Muscle Relaxants

Drug	Common Brand Names	Usual Daily Doses	Toxic Clinical Features
Baclofen	Lioresal	15-80 mg	vomiting, salivation, muscle hypotonia, drowsiness, visual accommodation disorders, coma, respiratory depression and seizures
Carisoprodol	Alaxan, Carisoma	1g	paralysis, visual disturbances, fever, excitement, hypotension, respiratory depression, seizures and coma
Chlormezanone	Beserol, Cetazone, Paranone	300-800 mg	
Chlorzoxazone	Parafon Forte	250-750 mg	

Toxicity

- Toxicity results in central nervous system effects leading to coma.
- Baclofen levels of 17 mg/L have been found 12 h after ingestion of a fatal dose.
- Lethal doses of the other drugs have not been established.

Management of Toxicity

- Supportive, maintain airway and assist ventilation
- Treat hypotension, seizures and coma if they occur.
- Gastric decontamination: Administer activated charcoal and cathartic. Emesis is not recommended because of the risk of CNS and respiratory depression.
- Careful monitoring of fluid and electrolytes and urinary output
- Diuresis: not known to be useful in enhancing excretion of drug

Antidotes: no known antidotes

Laboratory tests: Serum electrolytes, renal function, creatine phosphokinase (CPK), EEG and ECG monitoring

3.5 Smooth Muscle Relaxants

Table 7. Aminophylline, theophylline and choline theophylline (oxtriphylline)

Product	Content
Aminophylline DBL	aminophylline inj 25 mg/mL
Aminophyllinum	aminophylline tab 100mg, retard tab 350 mg
Asmapax	theophylline tab 65 mg
Choledyl	oxtriphylline tab 100 mg, 200 mg
Neophylline	aminophylline tab 100 mg
Nuelin	theophylline tab 125 mg, sustained-release (SR) tab 125 mg, 250 mg, syrup 80mg/15ml
Retafyllin CR	theophylline controlled-release tab 200 mg, 300 mg
Somophylline-CRT	theophylline controlled-release tab 100 mg, 250 mg
Tedral	theophylline 65 mg, 120 mg, sustained-action (SA) tab 198 mg
Theo-24	theophylline controlled-release tab 100 mg, 200 mg, 300 mg
Theo-Dur	theophylline sustained-release tab 200 mg, 300 mg
Theolin	theophylline 100mg, sustained-release (SR) tab 250 mg
Theovent LA	theophylline controlled-release tab 125 mg, 250 mg

Toxicity

- Therapeutic concentration range of theophylline is 10-20 mg/L. Toxic effects include ventricular arrhythmias and convulsions, which may occur suddenly. Seizures may be refractory to standard anticonvulsants.
- In acute overdose, severe symptoms may occur at serum concentrations of 60 mg/L but are most common at levels >100mg/L.
- Sustained-release preparations can result in delayed and prolonged toxicity up to 50 hours after administration.
- Overdose with sustained-release preparations seems to cause more severe toxicity.

Clinical Features

Anorexia, nausea, vomiting, insomnia, hyperreflexia, hypokalaemia, sinus tachycardia, ventricular tachycardia arrhythmias and fibrillation, hypotension, seizures, respiratory arrest and coma.

Management of Toxicity

- Supportive, maintain airway and assist ventilation
- Treat hypotension, arrhythmias, seizures and coma if they occur.
- Gastric decontamination: Tablets have been recovered in gastric lavage, 6 h post ingestion. Administer activated charcoal and cathartic. Remove rectally administered aminophylline by enema. Emesis is not recommended because of potential seizures and cardiac instability.
- Monitor serial serum theophylline until it reaches 20 mg/L
- Monitor ECG, fluid and electrolytes especially potassium
- Haemoperfusion if serum theophylline concentrations exceed 40-60 mg/L or when severe symptoms are present. Haemodialysis is not as effective as haemoperfusion but is a useful alternative.

Antidotes: no known antidotes

Laboratory tests: Serum electrolytes especially potassium. Hypokalaemia may occur and is common after overdoses. Serum theophylline concentration. Levels should be followed for a longer period in overdose involving controlled-release preparations. Other tests include blood urea, glucose, BUN, creatinine, hepatic function tests and ECG monitoring.

3.6 Sympatholytic Drugs

3.6.1 Alpha-adrenoceptor antagonists

Phentolamine (Regitine 5 mg/mL inj)
Phenoxybenzamine (Dibenyline 10 mg cap, 50 mg/mL inj)
Prazosin (Minipress 1 mg tab)
Doxazosin (Cardura 1 mg tab)
Terazosin (Hytrin 2 mg, 5 mg, 10 mg tab)

Toxicity

Postural hypotension and tachycardia are most common.

Clinical Features

Vomiting, postural hypotension, tachycardia, cardiac arrhythmias, flushing, mydriasis with phentolamine, and miosis with phenoxybenzamine, dizziness, CNS stimulation and seizures may occur.

Management of Toxicity

- Supportive, maintain airway and assist ventilation.
- Treat hypotension, arrhythmias and seizures if they occur.
- Gastric decontamination: Administer activated charcoal and cathartic. Emesis is not recommended because of the potential for cardiac instability and seizures.
- If ventricular arrhythmias are present, avoid sympathomimetics like adrenaline.

Antidotes: no known antidotes

Laboratory tests: ECG, electrolytes, urinalysis

3.6.2 Ergot derivatives

The ergot derivatives were the first alpha-adrenoceptor antagonists discovered. It is now generally accepted that they are partial agonists and antagonists at dopamine, serotonin and alpha-adrenergic receptors. They also cause direct stimulation of the smooth muscles of blood vessels and uterus. Now they are used in the treatment of migraine, for its uterine contracting properties in obstetrics and in combination e.g. hydergine in treatment of dementia.

Ergotamine (Cafergot, Migril)

Dihydroergotamine (Dihydergot, Ditamin)

Ergometrine (Syntometrine)

Methysergide (Deseril) — not available in Singapore

Dihydroergocornine + dihydroergocristine + dihydroergocryptine (Hydergine, Deapril-ST)

Toxicity

- Main toxic effects are caused by vasoconstriction and spasms.
- Therapeutic dose may be fatal in patients with underlying cardiovascular or predisposing conditions.
- Acute toxicity: Toxicity has been noted following 0.5 mg ergotamine (IM, IV, or SC). A 14-month old child died after acute ingestion of 12 mg ergotamine.
- Chronic toxicity: Daily dose of >10 mg of ergotamine is associated with toxicity.

Clinical Features

Nausea, vomiting, hypertension, hypotension, coronary ischaemia, myocardial, abdominal, bowel, and renal infarctions, cyanosis, peripheral ischaemia leading to paraesthesias, pain and gangrene, psychosis seizures and coma.

Chronic use of methysergide occasionally causes retroperitoneal fibrosis.

Management of Toxicity

- Supportive, maintain airway and assist ventilation. Important to treat vasoconstriction promptly
- Treat hypotension, seizures and coma if they occur.
- Treat vasoconstriction and hypertension. Nitroprusside is useful to reverse peripheral ischaemia and hypertension. Other drugs useful for treatment are phentolamine and nifedipine. Anticoagulant (heparin) is required to prevent thrombosis.
- Treat coronary spasms with nitroglycerin and nifedipine.
- Gastric decontamination: Administer activated charcoal and cathartic. Emesis is not recommended because of the potential for CNS depression.
- Abdominal cramps may be treated with oral atropine.
- Haemodialysis and haemoperfusion are not effective.

Antidotes: The use of nitroprusside, nifedipine, phentolamine, heparin, nitroglycerin and other related drugs are effective.

Laboratory tests: FBC, electrolytes, BUN, creatinine, ECG. Arteriography of affected site.

3.7 Sumatriptan

Sumatriptan (Imigran 50 & 100 mg tab; 6 mg/0.5 mL inj, 20 mg/dose nasal spray)

Sumatriptan is a relatively new drug with agonistic action on serotonin 5HT_{1D} receptors. It is effective for the treatment of migraine.

Toxicity

Little data on sumatriptan overdose. Serious cardiovascular effects including myocardial infarction, coronary vasospasms have occurred with therapeutic doses.

Clinical Features

Nausea, vomiting, flushing and burning sensation, hypertension, myocardial infarction, ventricular arrhythmias, coronary vasospasm, dizziness, vertigo

Management of Toxicity

- Supportive, maintain airway and assist ventilation.
- Treat hypertension, arrhythmias and seizures if they occur.
- For ventricular tachycardia/PVCs, lignocaine, procainamide, propranolol, phenytoin, disopyramide and overdrive transvenous pacing may be used. Atropine may be used when severe bradycardia is present and PVCs are thought to represent an escape complex
- Administer activated charcoal and cathartic. Emesis is most effective if initiated within 30 - 60 min.
- Gastric lavage may be performed for large and recent ingestions.

Antidotes: no known antidotes

Laboratory tests: FBC, electrolytes, urinalysis. ECG monitoring in patients with myocardial ischaemic symptoms.

References

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CHAPTER 4

Cardiovascular Drugs

4.1 Anticoagulants

Anticoagulants are used medically to inhibit the clotting mechanism. Warfarin and a number of chemicals (superwarfarin) with similar, but much longer, action, including the coumarins and indanedione, are also used as rodenticides. Single doses of these compounds are not dangerous. Fatalities have been recorded following repeated daily doses.

Table 1. Anticoagulant products

Product	Content
Calciparine	Heparin Ca (Inj 5,000 iu/0.2 mL)
Hepsal	Heparin Na in NaCl solution (Inj 50 iu/5mL)
Multiparin	Heparin (Inj 5,000 & 25,000 iu/5 mL)
Uniparin	Heparin Na (Inj 5000 iu/0.2 mL)
Coumadin	Crystalline Warfarin Na (Tab 1, 2 & 5 mg)
Marevan	Warfarin Na (Tab 1, 3 & 5 mg)
Orfarin	Warfarin Na (Tab 3 & 5 mg)
Dindevan	Phenindione (Tab 10, 25 & 50 mg)

Toxicity

The toxic dose is variable. Chronic ingestion generally produces more toxicity than a simple acute episode of accidental ingestion.

Occurrence: In suicidal cases when there is deliberate overdose of the oral anticoagulant medication. In accidental exposure to rodenticide that contains an anticoagulant (common among young children), overdosage of heparin due to patient self-administration is rare as it is available only parenterally, most problems with the use of heparin are iatrogenic in nature.

Clinical Features

Haemoptysis, nosebleeds, haematuria, bloody stools, haemorrhages in organs, widespread bruising, and bleeding in joint spaces.

Management of Toxicity

- In overdoses of anticoagulant, withdraw the medicine. It is usually prudent to admit patient to the hospital for close observation of abnormal bleeding. Conduct physical examination with a check of the urine and stool for blood at 12- to 24-hour intervals. The PT and CBC are repeated daily until the PT is normal again.
- In oral ingestions, administer activated charcoal. Gastric emptying should be avoided in those who are already anticoagulated or bleeding.
- For patient with a significantly elevated PT (more than 2 times control) but with no evidence of active abnormal bleeding, administer vitamin K₁.
- Give transfusions of fresh blood or plasma if haemorrhage is severe (PT three or more times control).
- Care must be taken not to precipitate further haemorrhages. Absolute bed rest must be maintained

- Antidotes:**
- For heparin overdosage, give protamine sulphate, 1% slowly intravenously (not exceeding 50 mg in 10 min). See pg 135.
 - For overdosage of coumarin anticoagulants, give Vitamin K₁, 0.1 mg/kg parenterally (for patient with no abnormal bleeding, 5-10 mg subcutaneously once daily for 2-3 days; for patient with active bleeding, 5 - 10 mg IV very slowly every 12-24 hours (rarely used); dosage for children is 1 -5 mg. Fresh frozen plasma and packed red blood cells is also given during active bleeding as it gives immediate control since vitamin K will require 24 hours to be effective.
 - Repeated doses may be required. Intramuscular injections are best avoided because of the risk of haematoma formation.

Laboratory Tests: FBC, Prothrombin Time (PT), activated partial thromboplastin time (APTT), FBC and PT will be sufficient for warfarin poisoning; FBC and PT on presentation serve as baseline studies; the PT should not be abnormal for 1-3 days; abnormal PT on presentation suggests chronic use or exposure; prothrombin concentration is lowered after coumarin and phenindione overdosage; clotting time prolonged after heparin; urinalysis; white blood count decreased after phenindione; haemoglobin levels.

4.2 Antihypertensive Agents

4.2.1 Beta-Blockers

Table 2. Beta-blockers

Products	Contents
Sectral	Acebutolol 100, 200, 400 mg tab
Tenormin	Atenolol 25, 50, 100 mg tab
Kerlone	Betaxolol 20 mg tab
Trandate	Labetalol 100, 200 mg tab, 5 mg/ml inj
Betaloc	Metoprolol 50, 100 mg tab, 1 mg/ml inj
Corgard	Nadolol 40, 80 mg tab
Trasicor	Oxprenolol 20, 40, 80, 160 mg tab
Visken	Pindolol 5, 15 mg tab
Inderal	Propranolol 10, 40, 80 mg tab
Sotacor	Sotalol 80, 160 mg tab, 10 mg/ml inj
Betim	Timolol 10 mg tab

Toxicity

The response to beta-blocker overdose is highly variable and depends on underlying medical disease or other medication. Susceptible patients may have severe or even fatal reactions to therapeutic doses. There are no clear guidelines, but ingestion of only 2-3 times the therapeutic dose should be considered potentially life threatening in all patients. This is listed in Table 8.

Clinical Features

Dizziness, profound bradycardia with reduced unrecordable blood pressure, bad dreams, respiratory depression, convulsions, coma, bronchospasm, catatonia, delirium, hyperkalaemia and hypoglycaemia.

Management of Toxicity

- Maintain airway, breathing and circulation.
- Treat coma, seizures, hypotension, hyperkalaemia if they occur.
- Perform gastric lavage for large ingestions.
- Administer activated charcoal and cathartic.
- Charcoal haemoperfusion and dialysis may be indicated for toxicity due to atenolol, nadolol and acebutolol.
- Treat bradycardia with atropine, dopamine, dobutamine, epinephrine or norepinephrine.

- Treat hypotension with IV fluids.
- Glucagon is useful for treating bradycardia and hypotension.
- Treat bronchospasm with IV aminophylline or beta-2 aerosol.
- If hypoglycaemia is present, use an infusion of glucose and possibly glucagon

Antidotes: The antidotes to counteract cardiac effects of beta-blockade include atropine, catecholamines and glucagon. See pg 90, 117.

Laboratory Tests: ECG, cardiac monitoring, blood levels of electrolytes and glucose, renal and liver function tests, FBC, arterial blood gas.

4.2.2 ACE Inhibitors

Captopril	Lisinopril
Cilazapril	Monopril
Enalapril	Perindopril
Fosinopril	Quinapril

Table 3. Preparations Containing ACE Inhibitors

ACE Inhibitors	Common Trade Names	Usual Dosage Content
Captopril	Apo-Capto, Capoten, Capozide (+Hydrochlorothiazide), Dexacap, Tensoprel	12.5, 25, 50mg
Enalapril	Korandil 10, Renitec, Co-Renitec	2.5, 5, 10, 20mg
Lisinopril	Lisoril, Prinivil, Zestril, Prinzide (+hydrochlorothiazide), Zestoretic (+hydrochlorothiazide)	5, 10, 20mg

Toxicity

Toxic levels in humans have not been established for ACE inhibitors. The few reports of acute overdose with these drugs suggest that toxicity is mild.

Clinical Features

Diarrhoea, dry mouth, cough, fever, pruritus, angioedema, hyperkalaemia, arthralgia, prolonged hypotension, anaemia and renal failure.

Management of Toxicity

- Maintain airway, breathing and circulation
- Perform gastric lavage for large and recent ingestions
- Administer activated charcoal and cathartic
- Haemodialysis may be useful
- Treat hypotension
- Close monitoring of vital signs recommended for 24-36 hours after significant overdose of captopril and longer in cases of enalapril and lisinopril

Antidotes: no specific antidotes.

Laboratory Tests: Routine laboratory tests are usually normal; evaluate renal function (which may be transiently impaired secondary to hypotension); ECG (usually no specific changes) and electrolytes (hyperkalaemia may occur in patients with renal failure), blood glucose.

4.2.3 Calcium-Channel Blockers

Diltiazem Nifedipine Nifedipine Verapamil

Toxicity

The toxic/therapeutic ratio is relatively small, and serious toxicity may occur with therapeutic doses. Any doses greater than the usual therapeutic dose should be considered potentially life-threatening.

Verapamil

Toxic concentration : 90µg/mL

Clinical Features

CVS: Sinus bradycardia, arrest, prolonged and AV conduction, myocardial depression has resulted in hypotension, congestive heart failure or frank cardiogenic shock.

Others: Nausea, vomiting, dizziness, lethargy, coma, hyperglycaemia, metabolic acidosis and convulsion.

Management of Toxicity

- Maintain airway, breathing and circulation.
- Perform gastric lavage.
- Administer activated charcoal and cathartic.
- For large ingestions of a sustained - release preparation, consider whole bowel irrigation in addition to repeated doses of charcoal. Continue charcoal administration for 48 - 72 hours.
- Treat hypotension with IV calcium chloride. Patient who does not respond requires treatment with additional agents such as dopamine, epinephrine, norepinephrine.
- IV atropine may be used to reverse bradycardia.
- Treat seizure with diazepam.

Antidotes:

The antidotes to counteract the cardiac effects of calcium channel blockade include :

- Dopamine and catecholamines - hypotension. See pg 107.
- Atropine - Bradyarrhythmias. See pg 90.
- Glucagon - Heart block and myocardial depression. See pg 117.
- Calcium - reverses the depression of cardiac contractility. Administer calcium chloride 10% or calcium gluconate 10% to increase serum calcium by 3 -4 mg/dL to a maximum of 13 mg/dL. See pg 94.

Laboratory Tests: Serum electrolytes, arterial blood gases, ECG, FBC, BUN, creatinine.

4.2.4 Miscellaneous

Other classes of antihypertensives are :

- **Alpha-Adrenoceptor Antagonists**
Prazosin
- **Centrally Acting Sympatholytics**
Clonidine, methyldopa
- **Ganglion Blocking Agents**
Reserpine, guanethidine
- **Vasodilators**
Hydralazine, diazoxide, sodium nitroprusside

Table 4. Miscellaneous antihypertensives

Product	Content
Nipride	Sodium Nitroprusside (50 mg)
Atodel	Prazosin (1 & 2 mg)
Minipress	Prazosin (1, 2 & 5 mg)
Mizosin	Prazosin (1 & 2 mg)
Pratsiol	Prazosin (1, 2 & 5 mg)
Apresoline	Hydralazine (10 & 50 mg)
Zinepress	Hydralazine (50 mg)
Aldomet	Methyldopa (125 & 250 mg)
Amathyl	Methyldopa (125 & 250 mg)
Dopatab	Methyldopa (250 mg)
Dopegy	Methyldopa (250 & 500 mg)
Hydopa	Methyldopa (125 & 250 mg)
Scandopa	Methyldopa (250 mg)
Servidopa	Methyldopa (250 mg)
Catapres	Clonidine (0.15 mg)

Diazoxide

Clinical Features

Sodium and water retention, hyperglycaemia, myocardial and cerebral ischaemia, rash, hyperuricemia, arrhythmias, convulsions, shock and mental depression.

Toxicity

Blood level approx. 10 mcg/mL

Management of Toxicity

- Rapid IV fluid resuscitation and place in a Trendelenburg position. If patient is unresponsive, administer dopamine.
- Administer activated charcoal and cathartic.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Treat hypotension.
- Give insulin for hyperglycaemia.
- Restore fluid and electrolyte balance; catheterise patient to observe adequacy of urine output.

Laboratory tests: FBC, electrolytes, blood glucose, BUN, creatinine, ECG

Clonidine

Clinical Features

Hypotension, transient hypertension, weakness, vomiting, diminished reflexes, deep sedation or coma, seizures and respiratory depression.

Management of Toxicity

- Perform gastric lavage for large and recent ingestions; emesis may be contraindicated because of rapid onset of CNS depression leading to an unprotected airway
- Administer activated charcoal and cathartic
- Treat hypotension
- Treat transient hypertension with sodium nitroprusside should it become severe or symptomatic
- Treat bradycardia with atropine
- Treat seizures
- Administer naloxone for CNS and respiratory depression

Laboratory tests : Same as for diazoxide

Antidotes: Naloxone for respiratory or CNS depression; tolazoline for hypotension and bradycardia unresponsive to conventional therapy. The

cardiovascular response to tolazoline is not always predictable & can be associated with toxic effects such as marked hypertension and cardiac arrhythmias.

Laboratory tests: Electrolytes, arterial blood pressure and ECG

Methyldopa

Clinical Features

Nausea, vomiting, acute hypotension, dizziness, excessive sedation, bradycardia and diarrhoea.

Toxicity

Toxic oral dose : > 2g

Management of Toxicity

- Administer activated charcoal and cathartic.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Haemodialysis is useful.
- Rapid IV fluid resuscitation. In addition, place in a Trendelenburg position. If patient is unresponsive, administer dopamine or noradrenaline.

Laboratory tests : Same as for diazoxide

Hydralazine

Clinical Features

Headache, severe hypertension, coronary insufficiency and anuria.

Management of Toxicity

- Administer activated charcoal and cathartic.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Treat hypotension with IV fluids and place in a Trendelenburg position. If patient is unresponsive, administer dopamine or noradrenaline.

Laboratory tests : Same as for diazoxide

Prazosin

Clinical Features

Dizziness, headache, drowsiness, gastrointestinal disturbances, tachycardia, dyspnoea, paraesthesias, rash, dysuria and sweating.

Management of Toxicity

- Administer charcoal and cathartic.
- Gastric lavage is not necessary if activated charcoal can be given promptly.
- Treat shock with plasma volume expanders and vasopressor.
- Prazosin is not dialysable.

Laboratory Tests: Same as for diazoxide

Reserpine

Clinical Features

Drowsiness, diarrhoea, angina pain, extrasystoles, oedema, congestive heart failure, bradycardia, tremors, muscular stiffness and severe hypotension.

Management of Toxicity

- Perform gastric lavage for large and recent ingestions.
- Administer charcoal and cathartic.
- Treat hypotension.
- Observe patient closely for at least 72 hours.

Laboratory Tests: Epinephrine and norepinephrine urine levels may be elevated 1 to 2 days subsequent to acute ingestion.

Sodium Nitroprusside

Clinical Features

Disorientation, giddiness, vertigo, confusion, anxiety, low blood pressure, muscular spasm, convulsions and death.

Management of Toxicity

- Maintain airway; administer oxygen if necessary
- Treat hypotension and seizures if necessary
- If cyanide poisoning is suspected, administer IV sodium nitrite 3% 10mL at 2.5-5mL/min followed by IV sodium thiosulphate 25%, 50mL over 10 minutes.
- If necessary, repeat injections of sodium nitrite and sodium thiosulphate at half the initial recommended doses.
- If kidney function is normal, oral or intravenous fluids 2-4L daily.
- Peritoneal dialysis or haemodialysis is useful.

Note: sodium nitrite can aggravate hypotension

Laboratory tests: Monitor renal function, electrolytes, arterial blood pressure and ECG

4.3 Cardiac Drugs

4.3.1 Digitalis Glycosides

The two most commonly used digitalis glycosides are digoxin and digitoxin. Digitalis has been described as having the smallest therapeutic/toxic ratio of any commonly used drug.

Brand Names

Digoxin Lanoxin (Tab 62.5 & 250 µg, Inj 500 µg/mL & 500 µg/2mL, Paed Elixir 50 µg/mL)

Toxicity

Digoxin

Toxic concentration : > 3 ng/mL, > 15 ng/mL indicate a serious prognosis
Single lethal dose : 10-20 mg

Digitoxin

Toxic concentration : > 30 ng/mL
Single lethal dose: 20-50X usual daily maintenance dose (30-500 mg daily)
has been reported but this varies considerably and is not well established.

Occurrence: Most problems with the use of digitalis glycosides are iatrogenic in nature. Digitalis intoxication has most often resulted from slowly accumulating serum levels in patients with progressive impairment of its elimination. Occasionally, overdoses occur as a result of accidental (in paediatric population) or purposeful ingestions.

Clinical Features

Signs and symptoms depend on the chronicity of the intoxication

CNS	Headache, delirium, confusion and disorientation, amnesia, aphasia, delusions, personality changes, hallucinations, generalised muscle weakness, and neuralgic pains in the extremities
GI	nausea and vomiting, diarrhoea
Ophthalmologic	blurred vision, loss of visual acuity, aberrant colour vision, photophobia, diplopia
CVS	slow or irregular pulse, fall of blood pressure, and death, usually from ventricular fibrillation
Electrolyte Disorders	hyperkalaemia, metabolic acidosis

In infants, cardiac arrhythmias are the most common manifestation of toxicity, and in children, severe central nervous system depression sometimes occurs. Elderly patients are likely to have bizarre mental symptoms.

Management of Toxicity

- Establish and maintain vital functions.
- All patients require cardiac monitoring and a reliable intravenous line.
- Induce emesis and perform lavage in patients presenting shortly after large ingestions. Atropine should be available at the bedside. Lavage should be used in the comatose or seizing patient, with airway control via endotracheal intubation.
- Administer charcoal and cathartic.
- Steroid-binding resins such as cholestyramine and colestipol (as an alternative to charcoal) has been reported to be of value in digoxin overdosage.
- For life-threatening tachyarrhythmias or bradyarrhythmias, as well as hyperkalaemia due to digitalis toxicity, use Fab fragments of digoxin-specific antibodies.
- Conventional therapy can also be used for the treatment of arrhythmias and hyperkalaemia due to digitalis toxicity :
 - a. Treat hyperkalaemia (>6.0 mmol/L) by giving glucose (25 g intravenously) and soluble insulin (10 units intravenously)
 - b. Ventricular tachyarrhythmias are treated with either phenytoin or lignocaine.
 - c. Atropine may be useful for the management of bradycardia due to enhanced vagal tone. It can be particularly effective early in the course of the toxicity.
 - d. Propranolol may be useful for the treatment of supraventricular and ventricular tachyarrhythmias, but it should be avoided in the presence of conduction abnormalities. Its use is contraindicated in the bradycardic patients.
- Cardioversion should be avoided when possible after digitalis toxicity because of the possibility of inducing fatal arrhythmias. With the failure of all other measures with life-threatening arrhythmias, cardioconversion can be attempted at low energy levels. In general, digitalis antibodies should be given prior to the use of cardioversion unless the patient is sustaining a life-threatening arrhythmia.
- Pacemakers may rarely be used to override tachyarrhythmias and for symptomatic or refractory bradycardia. External pacers may be effective for bradyarrhythmias, but cannot override a supraventricular tachycardia. As with electrical cardioversion, pacemakers should be employed with caution because of the lower threshold for ventricular fibrillation in digitoxicity.

- IV magnesium sulphate has been recommended in the treatment of digitalis-induced rhythm disturbances.
- Haemodialysis, peritoneal dialysis and charcoal haemoperfusion are not recommended for the treatment of digitalis toxicity.

Antidotes: Fab fragments are antidotal and the treatment of choice for significant digitalis toxicity (eg, severe hyperkalaemia, symptomatic arrhythmias not responsive to drugs described above). See pg 102.

Laboratory Tests: Serum digitalis levels, ECG, serum electrolytes, calcium and magnesium, and a chest roentgenogram (to evaluate the patient's cardiac status), arterial blood gases.

4.3.2 Antiarrhythmic Drugs

All the agents have the potential for major adverse effects. The tachydysrhythmias represent a major concern, whereas the bradydysrhythmias may be readily treated with atropine, isoprenaline, or cardiac pacing. They have been classified into 5 groups based on the electrophysiologic properties of the drugs (Vaughan-Williams Classification).

Table 4. Antiarrhythmic drugs

- **Class Ia Agents**
Quinidine, procainamide, disopyramide
- **Class Ib Agents**
Lignocaine, phenytoin, tocainide HCl, mexiletine
- **Class Ic Agents**
Flecainide, encainide, propafenone
- **Class II Agents**
Beta-blockers are discussed in section 4.2.1
- **Class III Agents**
Amiodarone, bretylium, sotalol
- **Class IV Agents**
Calcium channel blockers (include verapamil but not the nifedipine group) are discussed in section 4.2.3
- **Class V Agents**
Digoxin is discussed in section 4.3.1

Toxicity

In general, these drugs have a narrow therapeutic index. However, single massive overdose of amiodarone produces little toxicity due to its large volume of distribution. See pg 216 for toxic features.

Management of Toxicity

Class Ia Agent Intoxication

- Establish and maintain vital functions.
- Perform gastric lavage for large ingestions. Emesis not recommended because of the risk of significant arrhythmias, seizures and coma in overdose.
- Activated charcoal initially and in repeated doses is recommended so long as bowel sounds are present.
- Treat hypotension. The use of vasopressors should be considered if there is failure to respond to positioning and fluids. Intraaortic balloon pump should be considered as a last resort.
- Sodium bicarbonate may be used to reverse the cardiac - depressant effects. See pg 92.
- Correct underlying electrolyte abnormalities (hypomagnesaemia, hypokalaemia, hypocalcaemia)
- Phenytoin or lignocaine decreases the action potential duration and the refractory period in nonischaemic muscle and is suggested for the control of dysrhythmias. Do not use other class Ia agents.
- A transvenous pacemaker may be used if there is evidence of conduction blockade with wide QRS predisposing to ventricular tachycardia and fibrillation.
- Convulsions seen with severe overdoses of quinidine are controlled with diazepam.
Phenytoin may be required to prevent recurrent seizure.

Class Ib Agents Intoxication

- Establish and maintain vital functions.
- Perform gastric lavage for large ingestions. Avoid emesis.
- Administer activated charcoal
- Treat the seizures initially with diazepam, followed by phenobarbital if necessary. Avoid phenytoin because of its possible synergistic cardiac effects. The seizures may be refractory and require neuromuscular blocking agents, intubation and ventilation. Convulsions may continue even with a therapeutic blood concentration of lignocaine due to elevation of the active but unmeasured metabolites.
- Cardiac dysrhythmias may require pacing and cardioversion.

- Acidosis should be corrected with IV sodium bicarbonate, methaemoglobinaemia should be treated with methylene blue.

Class Ic Agents Intoxication

- Same as for Class Ia Agents.
- Cardiac dysrhythmias such as ventricular tachycardia should be treated with common antidysrhythmic agents, cardioversion and ventricular pacing.

Class III Agents Intoxication

- Same as for class Ia agents.
- GI decontamination with activated charcoal and gastric lavage for large ingestions should be undertaken. Multiple doses of activated charcoal, though not proved, may be useful because of prolonged half-life of amiodarone.
- Treat hypotension and bradydysrhythmias with conventional measures as for class Ia agents.

Laboratory Tests

Class Ia Agents

Monitor vital functions, electrolytes (especially potassium, calcium and magnesium), ECG for QT, QRS or PR prolongation; a 12-lead ECG should be obtained to evaluate the PR, QRS and QT duration intervals; liver function tests (in quinidine intoxication); renal function (in procainamide and disopyramide intoxication); drug concentration in blood.

Class Ib Agents

ECG, blood gas, methaemoglobin level, drug concentration in blood.

Class Ic, II, III, IV, V

Same as Ia agents

4.4 Diuretics

Diuretics are classified according to their site and mechanism of action :

- Loop diuretics: frusemide, ethacrynic acid, bumetanide
- Thiazide diuretics: bendroflumethiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, polythiazide
- Potassium-sparing diuretics: spironolactone, amiloride, triamterene
- Osmotic diuretic: mannitol
- Miscellaneous: acetazolamide, indapamide

Clinical Features

See Table 5.

Management of Toxicity

Frusemide

- Administer activated charcoal. Do not use cathartic if patient is dehydrated.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Monitor fluid and electrolyte status.
- Potassium chloride to replace deficiency.
- Monitor blood glucose level.

Thiazides

- Administer activated charcoal. Do not use cathartic if patient is dehydrated
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Monitor fluid and electrolyte status.
- Potassium chloride or sodium chloride to replace deficiency.

Amiloride

- Administer activated charcoal. Do not use cathartic if patient is dehydrated.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Monitor potassium concentration.
- Administer oral or rectal Resonium A.
- Treat life-threatening hyperkalaemia with IV dextrose, insulin and sodium bicarbonate.

- Cardiac monitoring should be maintained as long as hyperkalaemia exists.
- Not known if amiloride is dialysable.

Spironolactone

- Administer activated charcoal. Do not use cathartic if patient is dehydrated.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Treat life-threatening hyperkalaemia with IV dextrose, insulin and sodium bicarbonate.
- Persistent hyperkalaemia may require dialysis.
- Continuous ECG monitoring.
- Evaluate serum electrolytes and renal and CVS function.

Triamterene

- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Administer activated charcoal. Do not use cathartic if patient is dehydrated.
- Correct electrolyte and fluid imbalances.
- Dialysis may be of some benefit.

Acetazolamide

- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Administer activated charcoal. Do not use cathartic if patient is dehydrated.
- Monitor CVS function.

Indapamide

- Administer activated charcoal. Do not use cathartic if patient is dehydrated.
- Gastric emptying is not necessary if activated charcoal can be given promptly.
- Monitor fluid and electrolyte status.
- Determine blood glucose level.
- Potassium chloride or sodium chloride to replace deficiency.

Antidotes: no specific antidotes

Laboratory Tests: Continuous ECG monitoring, fluid status monitoring, serum electrolytes (particularly sodium and potassium), evaluate renal and CVS function, blood glucose level, uric acid levels, blood pressure, weight, FBC, hearing ability (for loop diuretics)

Table 5. Diuretics

Diuretics	Common Trade Names	Usual Content in Dosage Units	Clinical Features
<i>Loop Diuretics</i> Frusemide	Dirine, Frumid, Frusix, Lasix, Rasitol	Tab 40 mg, Oral solution 10mg/ml, Inj 10 mg/mL	Deafness, paraesthesia, hypotension, tetany, dehydration, electrolyte loss, nausea, vomiting, diarrhoea, acute pancreatitis and skin rash.
Ethacrynic Acid Bumetanide	Edecrin Burinex	Inj 50 mg Tab 1 & 5 mg, Inj 0.5 mg/mL	
<i>Thiazides</i> Bendroflumethiazide Chlorothiazide Chlorthalidone	Pluryle K Saluric Hygroton, Logroton Divitab(+Metoprolol), Tenoret (+Atenolol), Trasitensin (+Oxprenolol)	Tab 2.5 mg Tab 500 mg Tab 12.5, 25 & 50 mg	Potassium loss, chloride loss, lethargy, muscle cramps, acidosis, gastric upset, convulsions and shock. Acute overdose may cause coma.
Hydrochlorothiazide (HDTZ)	Clonuretic (+ Amiloride), Didralin, DiErtride, Hydrochlorzide, Moduretic (+Amiloride)	Tab 25 & 50 mg	
Polythiazide	Nephрил	Tab 1 mg	
<i>Potassium-sparing</i> Spironolactone	Aldactone, Spiridon, Uractonum	Tab 25, 50 & 100 mg	Nausea, vomiting, abdominal pain, drowsiness, confusion, hyperkalaemia, rash and gynaecomastia.

Table 5. (Cont'd)

Diuretics	Common Trade Names	Usual Content in Dosage Units	Clinical Features
Amiloride	Clonuretic (+HDTZ), Kaltan (+HDTZ & Atenolol), Moducron (+HDTZ & Timolol), Moduretic (+HDTZ)	Tab 2.5 & 5 mg	Nausea, vomiting, hypotension, diarrhoea, abdominal pain, hyperkalaemia, bradycardia, paraesthesia, fatigue and flaccid paralysis of the extremities.
Triamterene	Dyazide (+HDTZ)	Tab 50 mg	GIT upset, dry mouth, weakness, tachycardia, hypotension, hyperkalaemia and liver damage.
Mannitol	Osmofundin	Infusion 10% ; 20%	Nausea, vomiting, headaches, chills, dizziness, lethargy, confusion, chest , pulmonary oedema and sometimes hypotension.
<i>Miscellaneous</i> Acetazolamide	Diamox	Tab 250 mg	Papular or erythematous skin eruptions, drowsiness, paraesthesia, fatigue, nausea, acidosis and blood dyscrasias similar to those produced by sulphonamides.
Indapamide	Natrilix	Tab 2.5 mg	Nausea, vomiting, weakness, GI disorders, electrolyte imbalance, hypotension and depressed respiration

4.5 Fibrinolytics

Table 6. Fibrinolytics

Product	Contents
Kabikinase	Purified Streptokinase Inj (100,000 IU, 250,000 IU, 750,000 IU, 1,500,000 IU)
Streptase	Purified Streptokinase Inj (250,000 IU, 750,000 IU, 1,500,000 IU)
Ukidan	Urokinase Inj (5000 IU, 25,000 IU, 100,000 IU, 1 mega IU)
Abbokinase	Urokinase Inj (50,000 IU, 250,000 IU)
Actilyse	Recombinant human tissue-type plasminogen activator Inj (50 mg) (r-TPA)

Toxicity

Uncertain.

Clinical Features

Fever, kidney damage, vascular collapse, localised bleeding and allergic reactions

Management of Toxicity

- Discontinue the drug.
- Treat haemorrhage with fresh blood, tranexamic acid. Aminocaproic acid may be considered if haemorrhage is unresponsive to conventional therapy.
- Treat allergic reactions with adrenaline, antihistamines and corticosteroids.
- Volume expansion may be necessary, but the use of dextrans should be avoided because of their platelet inhibiting effect

4.6 Nitrites And Nitrates

Table 7. Nitrites and Nitrates

Product	Contents
Angised	Glyceryl trinitrate (sublingual tab 0.5 mg)
Apo-ISDN	Isosorbide dinitrate (tab 10mg; sublingual tab 5 mg)
Deponit 5/10	Glyceryl trinitrate (transdermal patch 5 mg, 10 mg)
Elantan	Isosorbide-5-mononitrate (tab 20 mg, 40 mg)
Imdur	Isosorbide-5-mononitrate (durable 60mg)
Ismo 20	Isosorbide-5-mononitrate (tab 20 mg)
Isoket IV	Isosorbide dinitrate (inj 10 mg/10 mL)
Iso-Mack Retard	Isosorbide dinitrate (sustained action cap 20 mg, 40 mg)
Iso-Mack Spray	Isosorbide dinitrate (spray 1.25 mg/0.09 mL dose)
Isordil	Isosorbide dinitrate (tab 10 mg, sublingual tab 5 mg)
Nitro-bid/	Nitroglycerin
Nitro-bid IV	(ointment 2%; inj 5 mg/mL)
Nitrocine	Nitroglycerin (inj 10 mg/mL)
Nitroderm TTS 5/ TTS 10	Total nitroglycerin is 25 mg with a contact surface of 10 cm ² (transdermal patch 5 mg/24hr, 10 mg/24hr)
Nitradisc	Nitroglycerin (patch 5 mg, 7.5 mg, 10 mg)
Soni-Slo	Isosorbide dinitrate (timed-release cap 2.5 mg, 5 mg)
Sorbitrate	Isosorbide dinitrate (tab 5mg, 10mg, 20mg, chewable tab 5 mg, sublingual tab 40 mg)
Suscard	Glyceryl trinitrate (tab 2.5 mg)
Sustac	Glyceryl trinitrate (tab 2.6 mg, 6.4 mg)
Vascardin	Isosorbide dinitrate (tab 10 mg)

Toxicity

Fatal oral dose: Nitrolycerin	-	200 mg - 1200 mg
Sodium nitrite	-	1g

Clinical Features

Headache, flushing of the skin, vomiting, dizziness, collapse, hypotension, reflex tachycardia, cyanosis, convulsions, coma, respiratory paralysis, methaemoglobinaemia, and cyanosis (especially with nitrites).

Management of Toxicity

- Establish airway and maintain respiration.
- Induce emesis followed by administration of charcoal and cathartic.
- Gastric lavage may be useful for large and recent ingestions.
- Administer IV fluid for hypotension and place in Trendelenburg position; if patient is unresponsive, administer dopamine.
- Treat seizures with diazepam.
- Treat methaemoglobinaemia with IV methylene blue.
- Haemodialysis and haemoperfusion are not effective. Severe methaemoglobinaemia in infants not responsive to methylene blue therapy may require exchange transfusion
- Decontamination of inhalation exposure :
Monitor for respiratory distress. Administer 100% humidified supplemental oxygen with assisted ventilation as required.
- Remove poison from skin by scrubbing with soap and water.

Antidotes: Methylene blue for methaemoglobinaemia. See pg 123.

Laboratory Tests: Blood methaemoglobin level (examination must be made quickly as methaemoglobin disappears in standing blood), G6PD assay is indicated in patients who develop methaemoglobinaemia and/or haemolysis; arterial blood gases, FBC should be monitored in symptomatic or cyanotic patients, ECG.

Table 8. Toxicity of beta-blockers

Beta-Blockers	Common Trade Names	Therapeutic Dose	Toxic Conc. or Dose
Acebutolol	ACB100/200/400 Sectral	Oral 400-800 mg/24h (1200 mg max.)	Plasma level of 15 mg/L assoc. with toxicity
Atenolol	Aiti Alomet Antipressan Apo-Atenol Atenol Atenolol 50/100 Stada Atenolol 50/ 100 Trom Atenomel 50/100 Beta-Adalat (+Nifedipine) Blokium Catenol Coroteno-50/100 Cardotab Hypernol Kalten (+amiloride, Hydrochlorothiazide) Nif-Ten (+Nifedipine) Nifetex-TR (+Nifedipine) Normaten Noten Prenolol 50 Pretenol C50/100 (+Chlorothalidone) Pretenol Selobloc Target (+Chlorothalidone) Tenol Tenolol-50 Tenoret 50 (+Chlorothalidone) Tenoretic (+Chlorothalidone) Tenormin Tredol 25/100 Vascoten 50/100 Velorin 50/100	Oral 50-100 mg/24h	above 250 mg /L (assoc. with coma & fatalities)
Betaxolol* Labetalol	Kerlone Trandate, Trantalol	Oral 10-40 mg/24h Oral 200-800 mg/24h (2400 mg max.)	- serum conc. >500 ng/mL
Metoprolol	Apo-Metoprolol Betaloc Betaloc Zok Betazide (+Hydrochlorothiazide) Denex Logroton Divitab (+Chlorothalidone)	Plasma level 0.02-0.34 mcg/mL; Oral 50-200 mg/24h	-

Table 8. (Cont'd)

Beta-Blockers	Common Trade Names	Therapeutic Dose	Toxic Conc. or Dose
Nadolol	Corgard	Oral 80-240 mg/24h (640 mg max.)	Severe toxicity reported at 1.25 nmol/L
Oxprenolol	Transicor Transitsin (+Chlorothalidone)	Oral 40-480 mg/24h	-
Pindolol	Apo-Pindol Barbloc Visken Viskaldi	Oral 2.5-45 mg/24h	-
Propranolol	Angilol Antarol Apo-Propranolol Bedranol Betanol Betascan Corbeta Emforal Hipranol Hopranolol Inderal Indon Inpanol SR JM-Propranolol Nalol Pronol Propa-10/40/SR Synolol	Oral 40-320 mg/24h (640 mg max.)	>4 mcg/mL (highly variable)
Sotalol	Sotacor	Oral 100-600 mg/24h	-
Timolol*	Blocadren-10 Moducuren	Oral 10-60 mg/24h	-

*: Ophthalmic preparation also available

Table 9. Toxicity of antiarrhythmic agents

Antiarrhythmic Drugs	Common Trade Names	Therapeutic Conc./Dose	Toxic Conc./Dose	Clinical Features
Quinidine	Kinidin	1-5 ^a mcg/mL 1-2 g daily	Child : 60 mg/kg Adult : > 1 g >5 ^b mcg/mL	Cinchonism manifested by headache, nausea, vomiting, tinnitus, deafness, diplopia and dilated pupils; confusion, dementia, psychosis, myocardial depression, dysrhythmia, ECG changes, skin rashes, flushing reactions; respiratory depression, convulsions, coma, acidosis, hypoglycaemia and thrombocytopenia have been reported.
Procainamide	Pronestyl	4-10 mcg/mL 1-4 g daily	Adult : > 5 g >10mcg/mL	Hypotension, decreased cardiac output, asystole, AV block, ventricular tachycardia, SLE syndrome, anorexia, nausea, vomiting, diarrhoea.
Disopyramide	Dirytmim Norpace	2-7 mcg/mL 0.4-0.8 g daily	Adult : > 1 g >9 mcg/mL (>4-5 mcg/mL is toxic in some)	Cardiac toxicity similar to that of quinidine, CVS collapse can occur without ECG warning, followed by dysrhythmia, apnoea, and death; respiratory depression or arrest and coma have been reported; anticholinergic activity like dry mouth, urinary hesitancy, constipation, blurred vision, dry eyes, nose and throat, uterine contractions, glaucoma, cholestasis, hypoglycaemia and metabolic acidosis have also been reported.
Lignocaine	Xylocaine	1.5-6.0 mcg/ mL	> 6 mcg/mL	Minor manifestation: Vertigo, drowsiness, dysarthria, perioral numbness, muscle twitching, tinnitus; Major manifestation: psychosis, status epilepticus resulting in metabolic acidosis, severe bradycardia, sinus arrest, arteriovenous heart block, tachyarrhythmias.
Phenytoin	Dilantin Fenitonia Phenilep	10-20 mcg/ mL	> 20 mcg/mL	Nystagmus, dysphagia, cerebral ataxia, dizziness, tremor, visual disturbances, nausea, vomiting, drowsiness, delirium, bizarre behavioural patterns, coma, seizures and death

a Using specific assay

b Great variability among patients

Table 9. (Cont'd)

Antiarrhythmic Drugs	Common Trade Names	Therapeutic Conc./Dose	Toxic Conc./Dose	Clinical Features
Mexiletine	Mexitil mL	0.5-2.0 mcg/ mL	?	Vertigo, paraesthesias, tremor, ataxia, sedation, confusion, coma, convulsions, respiratory depression, cardiac toxicity
Flecainide	Tambocor	200-1000 ng/ mL	> 1000 ng/mL	Proarrhythmic activity leading to ventricular tachycardia, visual disturbances including blurred vision, photophobia, and spots before eyes.
Encainide	Enkaid	> 265 ng/mL	?	Proarrhythmic effect, dizziness, blurred vision, metallic taste, tremor; with acute overdose, cardiac and CNS manifestation, including seizures, bradycardia, hypotension, and ECG changes.
Propafenone	Rythmonorm	90-3000 ng/ mL	?	GI distress, mild CNS depression and ventricular tachyarrhythmias, prolongation of the PR interval and QRS duration has occurred with therapeutic doses greater than 450 mg.
Amiodarone	Cordarone	0.5-2.5 mg/L (or 0.5 - 2.5 mcg/ml)	> 2.5 mg/L (or > 2.5 mcg/ml)	<p>Ocular: Benign yellow brown corneal microdeposits, blurred vision, coloured halos, photophobia (Chronic use)</p> <p>Cardiac: Torsade de pointes arrhythmias, asymptomatic arrhythmias, AV block</p> <p>Pulmonary: Pulmonary fibrosis, pneumonitis manifested by pleuritic chest pain, non-productive cough, low-grade fever and dyspnoea on exertion (Chronic use)</p> <p>Thyroid: Hypo- or hyperthyroidism (Chronic use)</p> <p>Hepatic: Transient elevation of liver function tests, may cause fatal cirrhosis</p> <p>Other: Peripheral neuropathy, tremor, nausea, vomiting, metallic taste, headaches, sleeplessness</p>

Table 9. (Cont'd)

Antiarrhythmic Drugs	Common Trade Names	Therapeutic Conc./Dose	Toxic Conc./Dose	Clinical Features
Bretylium	Bretylol	Child (6 weeks to 10 years) - 5 mg/kg over 8-10 min Adult-Loading: 5-10 mg/kg or continuous infusion Maintenance : 1-2 mg/min	?	Decreased sinus rate, increased PR and QT intervals, hypotension, nausea, vomiting, headache, vertigo, dizziness, light headedness, syncope, and hyperthermia

References

1. *Viccellio, P. Handbook of Medical Toxicology.*
2. *Martindale Extra Pharmacopeia. 31st Edition*
3. *American Hospital Formulary Service, Bethesda. 1998 Edition*
4. *Dreisbach, RH & Robertson, WO. Handbook of Poisoning. 12th Ed.*
5. *Poisindex®, MICROMEDEX, Inc., Englewood, Colorado.*

CHAPTER 5

Central Nervous System Drugs

5.1 Analgesics, Antipyretics And Anti-inflammatory Agents

5.1.1 Analgesics and Antipyretics

A. Paracetamol (acetaminophen)

Paracetamol is widely used as an OTC analgesic, antipyretic, and in cold remedies. It may also be combined with other analgesics such as codeine.

Preparations containing paracetamol

Algesic	Dumin	Paradine
Anarex	Febricol	Paramine
Beaflu	Febs	Paranone
Beserol	Lotemp	Parclorphen
Biogesic	Migraleve	Picapan
Calpol	Naprex	Redon
Cetazone	Norgesic	Relexic
Coritab	Orphenadol	Setamol
Decolgen	Paceco	Sinutab
Dhaflu	Pacofen	Sinuzin-D
Dhamol	Panadeine	Tempra
Disprol Junior	Panadol	Tylenol
Dristan Cold Tablet	Panaflu	Unirhinol

Toxicity

Hepatotoxicity is caused by the reactive metabolite N-acetyl-p-benzoquinoneimine (NABQI) produced by the cytochrome P₄₅₀ enzyme. Normally the NABQI is conjugated with glutathione. In overdose, the excess NABQI reacts with hepatocytes causing necrosis.

Acute toxicity: Acute ingestion of 140 mg/kg in children and 6 g in adult is potentially toxic. Children <10 years are less susceptible to hepatotoxicity. It has been suggested that conjugation of NABQI with glutathione is more efficient in children than in adults. Chronic alcoholics and patients with induced cytochrome P₄₅₀ are more susceptible to hepatotoxicity since there will be an increase production of NABQI.

Chronic toxicity: Children are more susceptible to chronic toxicity presumably because they are less able to clear paracetamol by the other main conjugation pathways due to saturation. In alcoholics, chronic toxicity has been reported with daily consumption of 4-6 g.

Clinical Features

Early signs: anorexia, nausea, vomiting.

After 24 hours: Increase in prothrombin time (PT) and transaminases indicating hepatic necrosis, encephalopathy, metabolic acidosis, renal failure may occur with or without liver failure, myocardial damage, coma.

Management of Toxicity

- Supportive treatment
- Treat spontaneous vomiting so that activated charcoal may be administered orally.
- Support hepatic and renal failure, coma if they occur
- Obtain 4-hour post-ingestion serum sample for paracetamol concentration to assess severity of toxicity (see nomogram on pg 224)
- If paracetamol concentration falls above the treatment line (NB: treatment line is lower for chronic alcoholics, see nomogram) or if serum concentration is not immediately available, start treatment with antidote **N-acetylcysteine**. Early treatment is imperative as antidote is most efficacious within 8 hours of ingestion. However, in view of

recent clinical trials where late N-acetylcysteine was found to be beneficial, the recommendation is that it should be given even when patient is already in liver failure. Nomogram is for acute toxicity and not chronic toxicity.

- Gastric decontamination. Administer activated charcoal and cathartic. Since activated charcoal may adsorb antidote N-acetylcysteine, it is considered prudent to administer N-acetylcysteine by the intravenous route, as opposed to the oral route. Gastric lavage is not necessary if charcoal is given promptly.

Antidote: N-acetylcysteine

Intravenous: 150 mg/kg IV in 200 mL 5% dextrose over 15-30 min followed by 50 mg/kg in 500 mL over 4 h then 100 mg/kg in 1000 mL over 16 h. See pg 89.

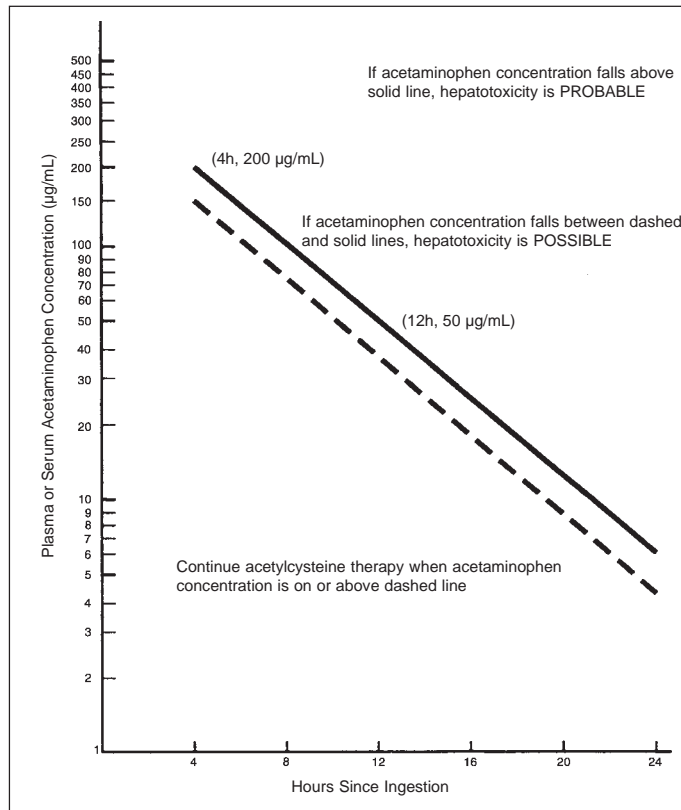
OR

Methionine

Oral: 2.5g initially, followed by 2.5g every 4 hours for another 3 doses.

Note: Methionine is NOT the antidote of choice as its efficacy has not been established.

Laboratory tests: Serum paracetamol concentration with respect to time of ingestion is used to assess severity of toxicity. These levels must be determined immediately. Liver function panel (AST, ALT, bilirubin and PT) should be done daily and for 3 days until they return to normal. Other tests: FBC, creatinine, glucose, electrolytes and BUN.



Nomogram relating plasma or serum acetaminophen concentration and probability of hepatotoxicity at varying intervals following ingestion of a single toxic dose of acetaminophen.

B. Salicylates and their usual contents in dosage forms

Aspirin, salicylic acid, methyl salicylate, glycol salicylates
(2-30% for external use)

Table 1. Preparations containing salicylates

Product	Contents
Algipan	Methyl nicotinate, glycol salicylate, capsaicin
Alka-Seltzer	Aspirin, Na bicarbonate, citric acid
Aspirin 'Bayer'	Aspirin
Aspro	Acetylsalicylic acid
Codis	Aspirin, codeine
Begesic	Methyl salicylate, eugenol, menthol, cajuput
Counterpain	Methyl salicylate, eugenol, menthol
Disprin	Aspirin
Dusil	Aspirin
Flanil	Methyl salicylate, menthol, eugenol
Lloyd's cream	Diethylamine salicylate
Metsal	Menthol, eucalyptus oil, methyl salicylate
Movilisín	Flufenamic acid, hydroxyethyl salicylate, mucopolysaccharide polysulphate
Oil of wintergreen	Methyl salicylate 98%
Reparil N	Aescin, diethylamine salicylate
Transvasin	Ethyl nicotinate, hexyl nicotinate, tetrahydrofurfuryl salicylate
Upha B Liniment	Methyl salicylate, camphor, menthol
Upha Medicated Rub	Nutmeg oil, eucalyptus oil, methyl salicylate, menthol

Toxicity

Toxic oral dose: 300 - 500 mg/kg (salicylates)

Toxic effects appear at varying plasma levels depending on the duration of poisoning but are uncommon below 300mg/L.

Toxic blood levels: >500 mg/L in adults
>300 mg/L in children

Severe poisoning blood levels: >1000 mg/L in adults
>600 mg/L in children

Chronic poisoning: Not well correlated with serum concentrations. Chronic users of salicylates showing confusion and lethargy and levels >600 mg/L require haemodialysis.

Clinical Features

Hyperpnoea, acid-base imbalance, mild pain in throat and stomach, vomiting particularly in infants and children, sweatiness, hypoprothrombinaemia, tinnitus (which may sometimes lead to deafness), delirium, convulsions, oliguria, uraemia, cyanosis, pulmonary oedema, respiratory failure.

Coma is not uncommon and indicates very severe poisoning

Management of Toxicity

- Maintain airway,
- Treat seizures, coma, metabolic acidosis and dehydration if they occur.
- Gastric lavage is not necessary after small ingestions (i.e. <200 - 300 mg/kg) if activated charcoal can be given promptly.
- Administer activated charcoal. Multiple doses of activated charcoal would be reasonably likely to enhance elimination of a significant amount of absorbed salicylate.
- In severe poisoning, begin hydration in the first hour with intravenous fluids 400mL/m². Maintain acid/base balance.
- Treat metabolic acidosis with IV sodium bicarbonate. Do not allow pH to fall below 7.4. See pg 91.
- Forced alkaline diuresis can be considered if plasma-salicylate concentration reaches toxic levels (>500 mg/L). Difficult to achieve in critically ill patients. There are currently other more efficient methods of enhancing elimination, such as multi-dose activated charcoal and haemodialysis.
- Early haemodialysis for rapid removal of salicylates in severe poisoning (levels >1,200 mg/L, severe acidosis in patients with acute ingestion; levels > 600 mg/L and any confusion or lethargy in patients with chronic intoxication)
- Haemoperfusion is also very effective but does not correct acid-base or fluid disturbances. Especially indicated when plasma salicylate levels are very high, i.e. >1000mg/L.

Antidotes: No specific antidotes. Sodium bicarbonate is given to prevent acidaemia and to promote salicylate elimination by the kidneys.

Laboratory tests: Plasma salicylate levels (obtain stat and serial serum levels), acid-base status (pH of arterial blood), arterial blood gases, urinalysis, FBC, liver function tests, prothrombin time

5.1.2 Narcotic analgesics

Apomorphine, codeine, dextromethorphan, dextropropoxyphene, fentanyl, methadone, nalbuphine, pentazocine, pethidine, morphine, sufentanil

Table 2. Preparations containing narcotic analgesics

Product	Contents
Codis	Codeine phosphate 8 mg, aspirin 500 mg (tab)
Nubain	Nalbuphine 10 mg/ mL (inj)
Panadeine	Paracetamol 500 mg, codeine phosphate 8 mg (tab)
MST Contin	Morphine 10, 30,60, 100 mg (tab)
Parahypnon	Paracetamol 500 mg, codeine phosphate 5 mg, caffeine 10 mg (tab)
Romilar	Dextromethorphan 15 mg (tab)
Talwin	Pentazocine 25 mg (tab), 30 mg (inj)
Physeptone	Methadone 5 mg (tab), 10 mg/mL (inj)

Toxicity

Toxicity is highly variable among the narcotic analgesics

Table 3. Toxicity of narcotic analgesics

Drug	Fatal oral dose (g)*	Clinical Findings (In addition to those listed below)
Apomorphine	0.1	Violent emesis, cardiac depression
Codeine	0.8	Convulsions
Dextromethorphan	0.5	Dizziness
Fentanyl	0.002	Muscle rigidity
Pethidine	1	Fainting, oedema
Methadone	0.1	-
Morphine	0.1	-

Table 3. (Cont'd)

Drug	Fatal oral dose (g)*	Clinical Findings (In addition to those listed below)
Nalbuphine	0.3	Restlessness, hallucinations
Pentazocine	0.2	
Propoxyphene	0.5	Nausea, vomiting, skin rash, ptosis, convulsions
Sufentanil	0.002	-

**Estimated for an adult. May be much higher (up to 10 times) in narcotic addicts and much lower (1/20) in infants. Fatal dose via parenteral administration is much lower*

Clinical Features

- Toxic doses cause unconsciousness; pinpoint pupils (dilated with anoxia); slow, shallow respiration; cyanosis; weak pulse; hypotension; spasm of gastrointestinal and biliary tracts; and in some cases pulmonary oedema, spasticity and twitching of the muscles. Death from respiratory failure may occur within 2-4 hours after oral or subcutaneous administration or immediately after an intravenous overdose.
- Convulsions may accompany codeine, pethidine, apomorphine, propoxyphene.

Management of Toxicity

- Maintain airway
- Treat seizures, coma, shock, hypotension and hypothermia if they occur
- Gastric lavage or emesis. If patient is unconscious or respiration is depressed, emesis is contraindicated. In the case of oral ingestion, gastric emptying should always be undertaken, even after several hours after ingestion. Delayed gastric emptying is characteristic of narcotic analgesics overdose because of the decreased peristaltic activity.
- Administer activated charcoal
Maintain hydration and electrolyte balance by the slow administration of modest amounts of fluids

Antidotes: Naloxone hydrochloride. See pg 127.

Laboratory tests: Drug levels are not generally useful, electrolytes, glucose, arterial blood gas, FBC, chest X-ray

5.1.3 Nonsteroidal anti-inflammatory agents

NSAIDs fall into several subgroups based on chemical structure:

- Acetic acid: diclofenac, fenclofenac, tolmetin
- Anthranilic acids (fenamates): meclofenamate, mefenamic acid
- Indole(indene acetic acid): etodolac, indomethacin, sulindac
- Propionic acids: fenbufen, flurbiprofen, ibuprofen, ketoprofen, naproxen
- Oxicams: piroxicam
- Pyrazolones: phenylbutazone

Table 4. Preparations containing NSAIDs

Product	Contents
Abitren	Diclofenac Na (25 mg)
Anfenax	Diclofenac Na (25 mg)
Asimet	Indomethacin (25 mg)
Almiral	Diclofenac Na (25 mg)
Alka-Seltzer	Aspirin , Na bicarbonate, citric acid
Anacin	Aspirin, caffeine
Aspro	Acetylsalicylic acid
Brexin	Piroxicam- β -cyclodextrin (20 mg)
Brufen	Ibuprofen (200-600 mg)
Cataflam	Diclofenac K (25 mg)
Clinoril	Sulindac (150-200 mg)
Codis	Codeine, aspirin
Hostan,	Mefenamic acid (250 mg)
Indocid	Indomethacin (25 mg)
Lodine	Etodolac (200 mg)
Adamen	Tenoxicam (20 mg)
Olfen	Diclofenac Na (75mg/2mL)
Orudis, Oruvail	Ketoprofen (100mg)
Pericam	Piroxicam (10 mg)
Ponstan	Mefenamic acid (250-500 mg)
Pontyl	Mefenamic acid (250 mg)

Table 4. (Cont'd)

Product	Contents
Rosiden	Piroxicam (10-20 mg tab; 20mg/ml inj)
Sugafen	Ibuprofen (200 mg)
Surgam	Tiaprofenic acid (300 mg)
Synflex	Naproxen Na (275-550 mg)
Tilcotil	Tenoxicam (20 mg)
Toradol	Ketorolac (10 mg tab, 30 mg/mL inj)
Voltaren	Diclofenac (25-50 mg)

Toxicity

Generally, significant symptoms occur after ingestion of more than 5 - 10 times the usual therapeutic dose

Clinical Features

- With most NSAIDs: Anorexia, nausea, vomiting, abdominal pain, haematemesis, drowsiness, lethargy, ataxia, tinnitus, disorientation.
- With more toxic agents e.g. Phenylbutazone and oxyphenbutazone mefenamic acid, piroxicam, and massive ibuprofen overdose: acidosis, hepatic dysfunction, hypoprothrombinaemia, convulsions, cardiopulmonary arrest, renal failure, coma

Management of Toxicity

- Supportive management.
- Administer activated charcoal. Gastric emptying is not necessary for most ingestions if activated charcoal can be given promptly. Perform gastric lavage for massive overdoses.
- Antacids may be used for mild GI upset.
- Management is mainly symptomatic as shown in table 5.

Table 5. Clinical aspects of NSAID poisoning

Organ	Manifestation	Management
Gastrointestinal	Anorexia, nausea, vomiting abdominal pain, gastric mucosal irritation	Nonabsorbable antacids e.g. aluminium and magnesium antacids H ₂ -receptor antagonists, proton pump inhibitors, misoprostol
Hepatobiliary	Hepatic dysfunction, hyperamylasemia	
Respiratory	Hyperventilation Respiratory depression	Mechanical ventilation
Cardiovascular	Sinus tachycardia Hypotension Cardiovascular collapse Cardiac arrest	IV fluids, vasopressors, haemodynamic monitoring
Renal	Haematuria, proteinuria Acute renal failure	Haemodialysis
Haematological	Hypoprothrombinaemia agranulocytosis, leucopenia, thrombocytopenia	Vitamin K
Metabolic	Hyper- and hypothermia Electrolyte abnormalities	Correct imbalance
Neuromuscular	Confusion, disorientation, drowsiness, headache, tinnitus, dizziness, blurred vision, nystagmus, diplopia, ataxia, hypertonia, hyper-reflexia, muscle twitching, convulsions, coma	Anticonvulsants (e.g. diazepam) for convulsions

Antidotes: no specific antidotes. Vitamin K may be used for patients with elevated prothrombin time caused by hypoprothrombinaemia. See pg 138.

Laboratory tests: renal and liver function tests, FBC, electrolytes, blood glucose, PT, urinalysis

5.2 Anticonvulsants / Sedatives

A. Barbiturates

Table 6. Barbiturates

Barbiturates (usual dosage)	Min toxic conc.	Coma conc.
Short acting: ($T_{1/2} = 8-17$ h) Cyclobarbitone (200 mg)	-	20-30 mg/L
Intermediate acting: ($T_{1/2} = 14-32$ h) Amylobarbitone (60-200 mg), Butobarbitone (50-100 mg), Pentobarbitone (30-100 mg),	> 10 mg/L > 10 mg/L > 10 mg/L	20-30 mg/L 20-30 mg/L 20-30 mg/L
Long acting: ($T_{1/2} = 80-120$ h) Phenobarbitone (60-180 mg),	> 30 mg/L	60-80 mg/L

Toxicity

Toxicity is likely when dose exceeds 5-10 times the hypnotic doses.

Fatal oral dose: 2-3 g for shorter acting agents
6-10 g for phenobarbitone

Clinical Features

Generalised CNS depression : drowsiness, ataxia, and dysarthria are soon followed by coma, hypotension, respiratory depression and hypothermia. Pupil constriction. Skin bullae are sometimes seen with barbiturate overdose (but they are not specific for the barbiturates)

Management of Toxicity

- Maintain airway, treat coma, hypothermia, hypotension if they occur
- Gastric lavage if more than 15 tablets or capsules have been taken in the preceding 4 hours or if the patient is unconscious.
- Administer activated charcoal, this has a definitive role in barbiturate poisoning
- Volume expansion with crystalloids and albumin aided by the use of dopamine and dobutamine if patient exhibits arterial hypotension, low cardiac output, or an absolute decrease in plasma volume
- Forced alkaline diuresis may be considered in severe phenobarbitone poisoning
- Charcoal haemoperfusion is the treatment of choice for the small minority of patients with very severe barbiturate poisoning who fail to improve, or who deteriorate despite good supportive care

Antidotes : no specific antidotes

Laboratory tests : Serum concentrations, arterial blood gases, FBC, renal function, blood gases, electrolytes, ECG recordings may be useful in predicting prognosis.

B. Benzodiazepines

Chlorazepate, chlordiazepoxide, clonazepam, diazepam, flurazepam, lorazepam, nitrazepam, oxazepam, temazepam, triazolam, midazolam

Table 7. Preparations containing benzodiazepines

Product	Content
Alzolam	Alprazolam
Valium	Diazepam
Ativan	Lorazepam
Benpine, Librium	Chlordiazepoxide
Domar	Pinazepam
Dormicum	Midazolam
Frisium	Clobazem
Lexotan	Bromazepam
Somese	Triazolam
Tranxene	Chlorazepate
Xanax	Alprazolam

Toxicity

Toxic effects are minimal. In general, large quantities can be taken without causing serious illness and uncomplicated recovery has been reported after ingestion of massive doses. In contrast, respiratory arrest has been reported after ingestion of 5 mg of triazolam. Rapid intravenous injection of benzodiazepines may cause respiratory depression.

Clinical Features

All benzodiazepines produce similar effects. When taken alone, they cause drowsiness, apathy, ataxia, dysarthria, partial ptosis and nystagmus.

Coma seldom deeper than grade 2 and lasting less than 24 hours may follow. Hypothermia may occur.

Mild hypotension, and respiratory depression may occur.

Management of Toxicity

- Maintain airway, treat coma hypotension, hypothermia if they occur.
- Administer activated charcoal. Gastric decontamination is probably valueless unless more than 30 tablets or capsules have been taken within 4 hours.
- Correct dehydration
- Toxic effects of benzodiazepines taken alone are so minimal that little treatment is necessary.

Antidotes: **Flumazenil**, a benzodiazepine antagonist. It reverses the CNS depression, and can be used to confirm suspected diagnosis of benzodiazepine overdose or exclude benzodiazepine intoxication as a cause of CNS depression in an undiagnosed patient. However, flumazenil administration **may precipitate seizures** in poisoning with combinations of benzodiazepines and tricyclic antidepressants. See pg 114.

Laboratory tests: Poor correlation between plasma levels and severity of intoxication; FBC, electrolytes, blood glucose, BUN, creatinine, arterial blood gases.

Note: *Since benzodiazepine overdose is rarely fatal, the role of flumazenil in routine management has yet to be established.*

C. Hydantoins

Dilantin (Phenytoin 30 mg, 100 mg cap, 100 mg/5 ml susp)

Toxicity

The minimum acute toxic oral overdose is approximately 20 mg/kg
Toxic effects are primarily related to serum levels

- 10-20 mcg/mL : Usual therapeutic range
- <15 mcg/mL : Toxic effects not usually seen
- >30 mcg/mL : 50% of patients have side effects (ataxia, tremor, drowsiness, lethargy, coma)
- >95 mcg/mL : Usually associated with fatalities

Clinical Features

- Toxicity from acute ingestion typically consists of the triad of nystagmus, ataxia and drowsiness.
- Toxic effects of chronic phenytoin ingestion are primarily serum-related cerebellar vestibular symptoms. However the classic signs (nystagmus, ataxia and drowsiness) are not always present.
- Other signs of toxicity include, nausea and vomiting, fever, liver and kidney damage, agranulocytosis, adenopathy, aplastic anaemia, pulmonary changes, lupus erythematosus, lymph gland enlargement, epidermal necrolysis, cardiac irregularities, peripheral nerve damage, tremor, drug psychosis, rigidity
- Hyperglycaemia secondary to inhibition of insulin release, transient hemiparesis
- Coma, seizures and apnea

Management of Toxicity

- Maintain airway, treat coma, seizures, arrhythmias and hypothermia if they occur.
- Treat hypotension by fluid infusion or pressor amines
- Complete heart block may be treated by intravenous atropine or a pace maker
- Administer multiple doses of activated charcoal. Gastric emptying is not necessary if activated charcoal can be given promptly.
- Forced diuresis or modification of urine pH is of no benefit.
- Haemodialysis , charcoal haemoperfusion and peritoneal dialysis are ineffective owing to the high protein binding of phenytoin.

Antidotes: no specific antidotes

Laboratory tests: Serum electrolytes and successive phenytoin levels should be obtained. Appreciation of phenytoin kinetics is mandatory for interpretation of results; BUN, creatinine, serum albumin, ECG.

D. Succinimides

Zarontin (Ethosuximide 250 mg cap, 250 mg/5mL syr)

Clinical Features

Toxic effects include lethargy, headache, fatigue, dizziness, hiccups, euphoria and gastrointestinal discomfort.

Idiopathic reactions may include systemic lupus erythematosus, eosinophilia, leucopenia, non-specific rashes, erythema multiforme, behavioural changes and psychoses.

Management of Toxicity

- Maintain airway, supportive therapy is mainstay of treatment.
- Emesis is not recommended due to potential CNS depression
- Perform gastric lavage for large and recent ingestions
- Administer activated charcoal
- Forced diuresis is probably ineffective because of limited renal excretion of the succinimides (1-10%)
- Use of haemodialysis, peritoneal dialysis and exchange transfusion is of questionable value.

Antidotes: No specific antidotes

Laboratory tests: Hepatic and renal function. FBC including platelet counts should be monitored periodically.

E. Miscellaneous

(i) Valproic acid and sodium valproate

Toxic effects are usually associated with daily dose over 1800 mg and blood levels over 100 mcg/mL. Unconsciousness occurs when more than 200 mg/kg has been ingested. Recovery has followed even after an ingestion of 25 g. Plasma concentrations and observed clinical effects are not correlated sufficiently to be of value clinically.

Clinical Features

Gastrointestinal disturbances, CNS depression (confusion, coma with respiratory failure), altered bleeding time, altered liver enzymes, fatal hepatic failure

Management of Toxicity

- Maintain airway, treat coma if they occur
- Gastric lavage for large ingestions followed by charcoal and cathartic administration is recommended
- Naloxone has been reported to reverse valproic acid-induced coma and should be administered if CNS depression is present
- If serum levels increase for 3 days following an ingestion, absorption may be prolonged or valproic acid may be reaching saturable kinetics. Repeated administration of charcoal and cathartic may be indicated

Antidotes: No specific antidotes

Laboratory tests: Serum concentrations, renal and liver function, electrolytes, glucose

(ii) Carbamazepine

Table 8. Preparations containing carbamazepine

Product	Contents
Tegretol	Carbamazepine 200 mg tab, 200 mg CR tab, 100 mg/5 mL syr, 125mg supp
Neurotop Carzepin	Carbamazepine 200 mg cap, 300 mg retard tab Carbamazepine 200 mg tab

Toxicity

Patients have survived ingestion of 80 g but death has also been reported after ingestion of 6-60 g.

Ataxia and nystagmus may occur with levels greater than 10 mcg/mL.

Other toxic manifestations occur at higher doses. Peak serum levels have ranged from 23 to 93 mcg/mL in obtunded or comatose patients.

LD₅₀ (oral) mouse : >500 mg/kg

Clinical Features

- Ingestion of large amounts produces an unpredictable clinical course. Seizures, slurred speech, myoclonus, coma, respiratory depression, apnoea, abnormal deep tendon reflexes, nystagmus, ataxia, encephalopathy, hypertension or hypotension, prolonged PR, QRS and QT intervals, dystonia and ballistic and athetoid posturing have been reported.
- A waxing and waning sensorium, seemingly corresponding to plasma levels may occur a few days following carbamazepine overdose. Cyclic CNS depression and a protracted clinical course should be expected.

Management of Toxicity

- Maintain airway, treat coma, hypertension or hypotension if they occur
- Perform gastric lavage for large and recent ingestions.
- Administer multiple doses of activated charcoal
- Charcoal haemoperfusion may be indicated if there is a worsening of clinical condition in a patient treated with multiple doses of charcoal.
- Haemodialysis and peritoneal dialysis are ineffective due to the high degree of protein binding
- Forced diuresis is of no benefit as only 2% of carbamazepine and 1% of the epoxide metabolite are excreted in the urine.

Antidotes: There are no specific antidotes for overdose. Physostigmine which has been used to diminish dystonic posturing, has little or no effect on other signs or symptoms of poisoning. The dystonic effects are not in any case life threatening and generally resolve spontaneously. Excessive physostigmine may lead to cholinergic toxicity (e.g. bronchospasm). Anticholinergic side effects are not a serious problem in poisoning and there is, therefore, little rationale for use of physostigmine.

Laboratory tests: FBC, vital signs, electrolytes, renal function, liver enzymes, arterial blood gases and ECG should be monitored periodically in the chronically treated patient and for at least 24 hours after admission in the overdose patient.

(iii) Primidone

Primidone is the desoxy derivative of phenobarbitone. It is chemically and pharmacologically related to the barbiturates. Primidone is converted in the body to phenobarbitone.

Table 9. Preparations containing primidone

Product	Contents
Mysoline	Primidone 250 mg tab
Cyral	Primidone
Mylepsin	Primidone
Dilon	Primidone

Toxicity

Toxic effects are observed at doses exceeding 1500 mg/day

Clinical Features

- Symptoms include sedation, vertigo, dizziness, vomiting, ataxia, diplopia and nystagmus
- Massive crystalluria (hexagonal crystals) indicates severe poisoning with primidone. The crystals are the result of primidone precipitation in the urine and this is observed at serum levels above 80 mcg/mL.

Management of Toxicity

- Maintain airway
- Treat coma, seizures if they occur
- Perform gastric lavage for large and recent ingestions.
- Administer multiple doses of activated charcoal
- Fluids and supportive therapy are usually sufficient in the mild to moderate primidone overdose
- Urine alkalisation will enhance the excretion of phenobarbitone
- Peritoneal dialysis, haemodialysis and exchange transfusion have not been evaluated in primidone poisoning
- Haemoperfusion may be indicated for severely intoxicated patients not responding to supportive care (i.e. with intractable hypotension)

Antidotes: no specific antidotes

Laboratory tests: EEG, serum primidone and phenobarbitone levels should be monitored

Therapeutic range: primidone 5 - 12 mg / L; phenobarbitone 15 - 40 mg / L

5.3 Cerebral Stimulants

Amphetamine

Amphetamine and its derivatives are CNS stimulants. They include drugs such as dextroamphetamine, diethylpropion, mazindol, pemoline, phentermine, methamphetamine, 3,4 - methylenedioxymethamphetamine (MDMA, Ecstasy) and methylphenidate.

Toxicity

These drugs have a low therapeutic index, with toxicity at levels slightly above therapeutic doses. Amphetamine is a very toxic substance. Fatalities have been reported following ingestions as low as 1.3 mg/kg of amphetamine.

Clinical Features

- Increased awareness and activity, lessening of fatigue, exhilaration, talkativeness, restlessness, insomnia, irritability, tremors, dizziness, exaggerated reflexes, sweating, mydriasis, flushing or pallor
- Anorexia, dry mouth, nausea, vomiting, diarrhoea
- Fever, chills, dehydration, hyperthermia
- Hyperactivity, purposeless motion, confusion
- Tachycardia or sometimes bradycardia, extrasystoles and other arrhythmias, palpitations, heart block, anginal chest pain, marked hypertension, tachypnea
- Anxiety, headache, hallucinations, paranoid hostile behaviour, delirium, mania, self injury
- Convulsions, coma, circulatory collapse and death

Management of Toxicity

- Treat seizures, hypertension, hyperthermia, coma, if they occur. Continuously monitor the temperature, other vital signs and the ECG for a minimum of 6 hours.
- If the intracranial pressure rises, institute measures to combat cerebral oedema and congestion.
- Avoid inducing emesis because of risk of abrupt onset of seizures.
- Administer activated charcoal. Gastric emptying is not necessary if charcoal can be given promptly.

- A hypertensive crisis may require injection of a short acting alpha adrenergic blocker such as phentolamine or the use of a direct drug such as sublingual glyceryl trinitrate.
- Acidification of the urine may precipitate acute renal failure in patients with myoglobinuria and is not recommended

Antidotes: No specific antidotes

Laboratory tests: FBC, monitor blood electrolytes, ECG, CT scan of the head (if haemorrhage suspected) and urine pH. Monitor temperature carefully, hyperthermia above 40 degrees Celsius indicates a poor prognosis

5.4 Psychotherapeutic Agents

A. Antimanic drugs

Lithium

Table 10. Preparations containing lithium

Product	Contents
Lithosun SR	Lithium carbonate 400 mg SR tab
Camcolit	Lithium carbonate 250 mg, 400 mg tab
Priadel	Lithium carbonate 200 mg, 400 mg SR tab

Toxicity

Acute ingestion of more than 20 tablets by an adult would potentially cause serious toxicity. The serum lithium level is not an accurate predictor of toxicity for acute ingestions and is more relevant for chronic intoxication.

Table 11. Serum lithium and toxic manifestations

Severity of Symptoms	Toxic stage ⁺	Serum lithium concentration (mEq/L)
No toxicity (therapeutic)	0	0.4-1.3
Mild toxicity	I	1.5-2.5
Serious toxicity	II	2.5-3.5
Life threatening toxicity	III	>3.5

NB : Lithium toxicity may manifest even at therapeutic levels, especially in the elderly where the therapeutic level may be 1.2 mEq/L

⁺Classification of Hansen and Amdisen:

Stage I & II : Apathy, tremor, weakness, ataxia, motor agitation, rigidity, fascicular twitching, nausea, vomiting and diarrhoea

Stage III : Latent convulsive movements, stupor, coma

Clinical Features

In patients not previously exposed to the drug or those in whom a single massive ingestion is imposed on chronic therapy, only vomiting and diarrhoea may be provoked initially. Such patients however should be hospitalised because the toxic syndrome may be delayed for a few hours to days after ingestion.

Myocarditis with arrhythmias, prolonged QT interval, ST-T wave abnormalities, cardiovascular collapse; sodium diuresis and nephrogenic diabetes insipidus (polyuria, polydipsia), interstitial nephritis, occasional renal failure; leucocytosis, aplastic anaemia; muscle weakness, ataxia, slurred speech, tinnitus, hyperreflexia, seizures, coma

Management of Toxicity

- Maintain airway
- Treat coma, seizures, CNS depression, hyperthermia if they occur
- Perform gastric lavage or whole bowel irrigation. Activated charcoal is of little use.
- Restore sodium and water balance
- Infusion of mannitol, alkalinisation of urine can increase lithium excretion in patients with good renal function
- Haemodialysis is indicated in severe lithium toxicity. Lithium is the most dialyzable toxin known, in view of its molecular weight, negligible protein binding and behaviour similar to sodium
- Persistent sodium and water loss may occur for days to weeks after lithium intoxication, and patients require careful monitoring of fluid balance during this stage

Antidotes: no specific antidotes

Laboratory tests: Blood plasma lithium levels, FBC, electrolytes, blood glucose, BUN, creatinine and frequent ECG to assess cardiac status

B. Tranquilisers

Phenothiazines: Chlorpromazine, fluphenazine, perphenazine, prochlorperazine, thioridazine, trifluoperazine

Thioxanthenes: Chlorprothixene, thiothixene

Butyrophenones: Haloperidol, droperidol

Toxicity

The toxic dose after acute ingestion is highly variable. Serious CNS depression and hypotension may occur after 200-1000mg of chlorpromazine in children or 3-5g in adults.

Clinical Features

Toxicity causes CNS depression but profound coma and respiratory failure are uncommon. They may produce disproportionately severe hypotension and hypothermia. Some conscious patients show acute dystonic reactions including oculogyric crises, torticollis and orolingual dyskinesias, particularly with trifluoperazine, prochlorperazine and haloperidol. Other parkinsonian features are usually the result of long-term therapy rather than acute dosage. Convulsions may occur.

Tachycardia is often present but conduction abnormalities and dysrhythmias are rare, although well documented particularly with thioridazine. The most common reported dysrhythmias are ventricular tachycardia and fibrillation. Death is usually due to cardiac effects. Neuroleptic malignant syndrome consisting of hyperpyrexia up to 42.2 degrees Celsius may occur.

Management of Toxicity

- Maintain airway
- Treat coma, seizures, hypotension, hyperthermia if they occur
- Treat arrhythmias. Both atrial and ventricular arrhythmias may occur as a result of neuroleptic toxicity. Underlying factors such as acidosis and electrolyte abnormalities should be addressed and corrected if necessary. Torsades de pointes ventricular tachycardia should be treated in the standard fashion (IV magnesium, chemical (IV isoprenaline) or electric overdrive pacing, and correction of hypoxemia and electrolyte disturbances).
- Treat acute dystonic reactions with anticholinergic drugs such as benztropine 1 - 2 mg IV, or diphenhydramine
- Neuroleptic malignant syndrome is a life threatening disorder and should be treated with oral or parenteral dantrolene. Bromocriptine, a dopamine antagonist, has also been successfully employed and theoretically corrects the dopamine depletion within the CNS. The oral dose of bromocriptine is 2.5 mg b.i.d initially, gradually increasing to 5 mg t.i.d. Doses of up to 60 mg per day have been used.
- Perform gastric lavage, regardless of the time that has elapsed from ingestion, since gastric emptying may be delayed by the agent.
- Ipecac emesis is not recommended because of the propensity of neuroleptic drugs to induce rapid sedation or seizures and dystonic reactions.
- Administer activated charcoal. Cathartics should be used with caution in patients with ileus.
- Maintain optimal hydration to ensure adequate urine output.
- Haemodialysis, haemoperfusion and forced diuresis do not appear to enhance elimination because of the extensive tissue and protein-binding.

Antidotes: no specific antidotes

Laboratory tests : ECG, electrolytes, FBC, blood glucose, BUN, creatinine, creatine phosphokinase, arterial blood gases

C. Tricyclic and Tetracyclic Antidepressant Agents

Tricyclics: Imipramine, amitriptyline, doxepin, dothiepin, clomipramine, desipramine, nortriptyline, protriptyline, amoxapine

Related antidepressants: Maprotiline, mianserin, trazodone

Table 12. Preparations containing antidepressants

Product	Description
Anafranil	Clomipramine 10 mg, 25 mg, 75 mg SR tab; 25 mg/5 mL syr
Tofranil	Imipramine 25 mg, 100 mg tab
Janimine	Imipramine 10 mg, 25 mg, 50 mg tab
Norpramin	Desipramine 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg tab
Prothiaden	Dothiepin 25 mg tab, 75 mg cap
Elavil	Amitriptyline 10 mg, 25 mg, 50 mg tab
Tryptizol	Amitriptyline 25 mg, 50 mg tab, 10 mg/5 mL syr
Pamelor	Nortriptyline 10 mg, 25 mg, 50 mg, 75 mg cap, 10 mg/5 mL syr
Sinequan	Doxepin 10 mg, 25 mg, 50 mg tab
Surmontil	Trimipramine 25 mg, 50 mg tab
Ludiomil	Maprotiline 10 mg, 25 mg, 75 mg tab
Asendis	Amoxapine 25 mg, 50 mg, 100 mg tab
Molipaxin	Trazodone 50 mg, 100 mg, 150 mg tab; 50 mg/5 mL syr

Toxicity

The toxic dose varies considerably. Generally, doses of approximately more than 10 times the therapeutic daily dose may produce severe toxicity, and doses of 30 - 40 mg/kg are often fatal in adults. The lowest known fatal dose of amitriptyline is 500 mg, but 1 patient survived after ingesting 10 g of the drug. Although the average acute lethal dose of imipramine has been estimated to be 30 mg/kg, fatalities have occurred in adults who received 500 mg of the drug. Severe symptoms or death occur in children who received more than 20 mg/kg of imipramine. Patients with preexisting cardiac disease and children appear to be somewhat more susceptible to tricyclic antidepressant-induced cardiotoxicity than healthy adults.

Clinical Features

The most important toxic effects of TCA overdoses are hypotension, arrhythmias, coma, seizures and hyperthermia.

Cardiotoxicity results from multiple effects on cardiac cell potential, direct effects on vascular tone, and indirect effects mediated by the autonomic nervous system. Hyperthermia is due to excessive muscular activity in the presence of high cholinergic tone. Central nervous system stimulation, which may result in part from excess anticholinergic activity, occurs usually initially. Symptoms may include agitation, irritation, confusion, hallucinations and hyperpyrexia. Severe CNS depression usually follows the initial stimulation. The patient may exhibit extreme drowsiness, areflexia, hypothermia, respiratory depression, cyanosis, hypotension and coma.

Management

- Maintain airway
- Treat coma, hypotension, seizures if they occur
- Perform gastric lavage for large ingestions (> 20 - 30 mg/kg)
- Administer activated charcoal in multiple doses
- Correct acidosis as it exacerbates TCA toxicity
- Systemic alkalisation with sodium bicarbonate has successfully reversed bradyarrhythmias, multifocal premature ventricular ectopy, ventricular tachycardia, conduction delays, varying degrees of heart block and hypotension
- Haemoperfusion removes only small quantities of the drug due to the large volume of distribution and the high lipid solubility of the cyclic antidepressants

Antidote: Physostigmine has been widely advocated in the past, but it should **not** be routinely administered to patients with tricyclic poisoning; it may aggravate conduction disturbances, causing asystole and may contribute to seizures. See pg 133.

Laboratory tests : ECG monitoring arterial blood gases, FBC, blood glucose, creatine phosphokinase, urinalysis for myoglobin, chest X-ray, electrolytes

D. Monoamine-oxidase inhibitors (MAOIs)

Irreversible MAOIs

Tranlycypromine, phenelzine, isocarboxazid

Reversible MAO-A Inhibitor (RIMA)

Moclobemide

Table 13. Preparations containing MAOIs

Product	Contents
Parnate	Tranlycypromine 10 mg tab
Marplan	Isocarboxazid 10 mg tab
Nardil	Phenelzine 15 mg tab
Manerix	Moclobemide 150 mg, 300 mg tab
Aurorix	Moclobemide 150 mg tab

Toxicity

MAOIs have a low therapeutic index. Acute ingestions of > 2-3 mg/kg should be considered potentially dangerous.

Clinical Features

- The symptoms of overdose may be delayed 6-24 hours and include agitation, irritability, diaphoresis, sweating, tachycardia, muscle rigidity, hyperpyrexia, hypertension and hyperreflexia. Serious reactions involve intracranial bleeding, hypotension, coma, seizures, respiratory distress and fatal malignant hyperthermia

Management of Toxicity

- Maintain airway
- Treat coma, seizures, hypotension, hypertension if they occur
- Perform gastric lavage for large ingestions.
- Administer multiple doses of activated charcoal

- Urinary acidification can enhance elimination of tranylcypromine, but renal excretion probably accounts for only a small fraction of the total drug excretion
- Haemodialysis has not been studied in depth for MAOIs overdoses

Antidotes: no specific antidotes

Laboratory tests : FBC, serum electrolytes, serum creatinine. Urinalysis, serum muscle enzymes, ECG, coagulation profile. Obtain a CT head scan if intracranial haemorrhage is suspected.

E. Selective Serotonin reuptake inhibitors (SSRIs)

Fluvoxamine, fluoxetine, paroxetine, sertraline

Table 14. Preparations containing SSRIs

Product	Contents
Faverin	Fluvoxamine maleate 50 mg, 100 mg tab
Prozac 20	Fluoxetine 20 mg cap
Seroxat	Paroxetine 20 mg tab
Zoloft	Sertraline 50 mg tab

Toxicity

The acute lethal dose in humans is not known.

Clinical Signs

Agitation, restlessness, hypomania, insomnia, tremor and other signs of CNS excitation; nausea and vomiting, tremor; and tachycardia and/or increased blood pressure. Coma has also been reported.

Treatment

- Maintain airway
- Treat seizures, hypotension, coma if they occur
- ECG and vital sign monitoring is essential
- Perform gastric lavage for large ingestions
- Administer activated charcoal
- Haemodialysis does not remove drugs substantially because of the large volume of distribution and the extensive protein binding of the drugs
- Haemoperfusion is also ineffective in reducing substantial quantities of the drug

Antidotes: no specific antidotes

Laboratory tests: Liver function tests, ECG monitoring, electrolytes monitoring

Reference

1. Janes J and Routledge PA. Recent developments in the management of paracetamol poisoning. *Drug Safety* (1992) 7: 170-177.
2. Haddad LM, Winchester JF (ed). *Clinical Management of Poisoning and Drug Overdose*. Saunders, Philadelphia, 2nd Ed, 1990.
3. Ellenhorn MJ, Barceloux DG (ed). *Medical Toxicology: Diagnosis and treatment of Human Poisoning*. Elsevier, New York, 1988.
4. Olson KR (ed). *Poisoning & Drug Overdose*. Appleton & Lange, Connecticut 2nd Ed., 1994.
5. Proudfoot AT. Antidotes: benefits and risks. *Toxicol-Lett* 1995 82-83: 779-783

CHAPTER 6

Gastrointestinal Drugs

6.1 Antacids And Antiflatulents

Drugs containing

Magnesium carbonate, hydroxide, oxide and trisilicate
Aluminium hydroxide
Calcium carbonate
Sodium bicarbonate
Simethicone, dimethicone, polymethylsiloxane, etc.

Some Common Brand Names

Actal and Actal Plus
Alusorb
Alutab
Belcid
Dhalumag
Gaviscon
Gelusil, Gelusil Plus

Toxicity

- Acute ingestion rarely leads to toxicity. Magnesium and aluminium compounds are of low order of toxicity while calcium carbonate and sodium bicarbonate has the potential to cause systemic toxicity. Silicones like simethicone are non-toxic when ingested orally.
- Prolonged ingestion and large doses can lead to cardiovascular and gastrointestinal toxicity as well as imbalance of electrolytes and minerals.

Clinical Features

- Diarrhoea, constipation, obstruction in prolonged and excessive antacid administration. Fluid and electrolyte depletion, hyperaluminemia, hypercalcemia, hypermagnesemia have occurred in chronic renal failure patients.
- Hypermagnesemia: hypotension and bradyarrhythmias, respiratory depression, CNS depression.
- Aluminium: encephalopathy due to accumulation of aluminium in chronic renal patients. Myopathies and osteodystrophies
- Sodium bicarbonate: Congestive heart failure, and risk of alkalosis and sodium overload

Management of Toxicity

- Acute antacid toxicity is unlikely. Gastric decontamination might not be necessary because of poor absorption of most of the antacids.
- Give supportive treatment.
- Monitor fluids, electrolytes, minerals, renal function and ECG especially in symptomatic patients and those with renal impairment.
- Correct fluid electrolyte and mineral imbalance.

Antidotes: no specific antidotes

Laboratory tests: Serum electrolytes, pH, aluminium, calcium, and magnesium levels. ECG and renal function test in patients with renal impairment

6.2 Antidiarrhoeal Drugs

A. Diphenoxylate

Diphenoxylate is an opioid analogue and is commonly formulated with atropine (diphenoxylate HCL 2.5 mg and atropine sulphate 25 µg).

Some Common Brand Names

Dhamotil	Lamofen
Diarase	Lomotil

Toxicity

- Large overdose: Anticholinergic toxicity (due to atropine) followed by opioid toxicity.
- Small overdose: No anticholinergic effects may be observed but delayed onset (6-8 h) of opioid effects should be expected.
- Children with history of potential overdose must be observed for 24 h or longer. Children are more susceptible to toxicity. Six or fewer Lomotil tablets have produced coma, respiratory depression and death in a child.

Clinical Features

Symptoms may occur 6-8 h or longer after ingestion. Ataxia, lethargy, irritability, loss of bowel sounds and urinary retention, respiratory depression, cerebral oedema, seizures and coma

Management of Toxicity

- Give supportive treatment, maintain airway and assist ventilation.
- Treat respiratory depression and coma, if they occur, with antidote naloxone.
- Children (< 6 years) must be in ICU and observed for at least 24 hours.
- Administer activated charcoal and cathartic. Protect airway if gastric lavage is to be performed for large ingestions.
- Catheterise if there is urinary retention.

Antidote : Naloxone. See pg 127.

Laboratory tests: Monitor fluid balance and avoid fluid overload.

B. Loperamide

Tab/cap: 2 mg; Syr: 0.2mg/mL

Some Common Brand Names

Colodium
IMD
Imodium
Loperamil
Lorpa
PMS-Loperamide
Vacontil

Toxicity

- Loperamide is structurally similar to haloperidol and diphenoxylate. Opioid-like effects in children and haloperidol-like dystonic reactions have been reported in overdose.
- Doses of 0.1-2mg/kg have caused respiratory and CNS depression. Children seem to be more susceptible to toxicity than adults.

Clinical Features

Paralytic ileus, necrotizing enterocolitis, bradycardia with ventricular ectopics, respiratory depression leading to acidosis, drowsiness, irritability, personality changes and rarely, dystonic reactions

Management of Toxicity

- Give supportive treatment, maintain airway and assist ventilation.
- Treat respiratory depression and coma, if they occur, with naloxone.
- Treat dystonic reactions, if they occur, with diphenhydramine or benztropine
- Perform gastric decontamination: Administer activated charcoal and cathartic. Protect airway if gastric lavage is to be performed for large ingestions.

Antidote : Naloxone. See pg 127.

Laboratory tests : Blood loperamide levels are not useful in treatment of toxicity

6.3 Antiemetics

A. The antihistamines

Cyclizine (50 mg), dimenhydrinate, (50 mg; 15mg/5mL), meclizine (12.5-25 mg)

Some Common Brand Names

Cyclizine	Marzine, Valoid
Dimenhydrinate	Bonaling A, Dimenate, Dramamine, Gravol, Medramine, Medrinate
Meclizine	Diligan, Navidoxine, Sea-Legs

Toxicity

Either CNS depression or excitation (see Antihistamines pg 147).

Clinical Features

Drowsiness, disorientation, hallucination, stupor, coma, tremors, excitement, hyperthermia, convulsions

Management of Toxicity

- Give supportive treatment.
- Treat seizures and coma if they occur.
- Treat severe anticholinergic CNS symptoms with physostigmine, although supportive management is preferred. See pg 133.
- Perform gastric lavage for large ingestions. Administer activated charcoal and cathartic.

Antidotes : no specific antidote

Laboratory tests : Serum drug levels are only helpful in diagnosis and not for guiding treatment of overdose.

B. Metoclopramide and Domperidone

Metoclopramide (10 mg; Syr: 5mg/5mL; 10mg/2mL inj),

Domperidone (10 mg; Susp: 1mg/mL)

Some Common Brand Names

Metoclopramide	Emeliv, Maxolon, Metocyl, Metolon, Primperan
Domperidone	Motilium

Toxicity

- Overdose is associated with hypertonia and extrapyramidal reactions.
- Acute dystonic reactions are more common in children and young adults whereas tardive dyskinesia and Parkinsonism are more common in the elderly.
- Dystonic reactions usually resolve within 12-48 hours but may last longer. Tardive dyskinesia may last for 6-36 months after termination of chronic therapy.
- Delirium has been observed with 60 mg/day.
- Total daily dose should not exceed 0.5 mg/kg unless it is for chemotherapy-associated nausea and vomiting.

Clinical Features

Oculogyric crisis, dystonic reactions, hypotension, hypertension, cardiac arrhythmias, methaemoglobinemia, agitation, delirium, drowsiness, extrapyramidal symptoms, neuroleptic malignant syndrome, seizures.

Management of Toxicity

- Give supportive treatment.
- Treat seizures, coma if they occur.
- Treat dystonic reactions, oculogyric crisis with benztropine and diphenhydramine.
- Perform gastric lavage for large ingestions. Administer activated charcoal and cathartic.

Antidotes : no specific antidote. Treat dystonic reactions with benztropine and diphenhydramine.

Laboratory tests : Serum metoclopramide concentration of 40 ng/mL peaks after oral ingestion of 10 mg. Levels are not useful in guiding treatment.

6.4 H₂ Receptor Antagonists

Cimetidine (200 & 400 mg tab, 200 mg/2mL inj),
Ranitidine (150 & 300 mg tab, 150mg/10mL syr; 50 mg/2mL inj),
Famotidine (20 mg & 40 mg tab)

Some Common Brand Names

Cimetidine	Cementin, Cimetidin, Cimulcer, Erlmetin, Shintamet, Tagamet, Ulsikur, Xepamet
Ranitidine	Zantac
Famotidine	Famocid, Famodine, Famopsin, Famotin, Famox, Pepcidine, Ulceran

Toxicity

- Cimetidine: 10% of all overdoses had minor effects. Patients have survived 12-24 g. Mild CNS symptoms occurred after 6 and 15 g; mild bradycardia and vomiting after up to 20 g.
- Ranitidine: CNS, endocrine and cardiovascular effects are less pronounced than with cimetidine.

Clinical Features

Bradycardia, hypotension and sinus arrest (rapid IV administration), liver enzyme elevations, reversible renal failure, confusion disorientation, delirium, dizziness, visual hallucinations, respiratory depression and coma. Agranulocytosis, thrombocytopenia may occur with chronic usage of cimetidine and ranitidine.

Management of Toxicity

- Give supportive treatment.
- Administer activated charcoal and cathartic.
- CNS symptoms should subside in 24 hours.
- Monitor ECG in patients with cardiac abnormalities.

Antidote : no specific antidote

Laboratory tests : FBC, liver enzymes and renal function. Serum drug concentrations not useful

6.5 Proton Pump Inhibitors

Omeprazole (Losec: 10 & 20 mg cap; 40 mg vial)

Lansoprazole (Prevacid: 15 & 30 mg cap)

Pantoprazole (Protium: 20 mg & 40 mg cap; 40 mg inj)

Rabeprazole (Pariet: 10 mg tab)

Toxicity

- These drugs are relatively new but appear to have low toxicity.
- Recommended daily dose of omeprazole is 20-60 mg.
- Overdoses between 320-400 mg have been reported with transient clinical effects.

Clinical Features

Transient tachycardia, vasodilation, abdominal pain, increase in serum gastrin levels, somnolence, headache, blurred vision, elevation of liver enzymes, moderate leucocytosis.

Management of Toxicity:

- Give supportive treatment.
- Sinus tachyarrhythmias do not routinely need to be treated unless patient shows haemodynamic instability.
- For large ingestions (>1 g/kg) perform gastric lavage within 60 minutes. Administer activated charcoal and cathartic.

Antidotes : no specific antidote

Laboratory tests : FBC, liver function tests

References

1. *Poisndex*® - Micromedex, Inc Volume 102 Expiratory date: 30/9/99

Gout Preparations

7.1 Allopurinol

Allopurinol is an inhibitor of xanthine oxidase which prevents the *de novo* synthesis of uric acid. It is primarily used in the treatment of hyperuricaemia of gout, but also in several neoplastic and metabolic disorders. Within 2 hours, most of ingested allopurinol is converted to oxypurinol, a less potent inhibitor of xanthine oxidase.

Table 1. Allopurinol tablets

Product	Content
Allopurinol B.P	100 & 300 mg
Allorin	100 & 300 mg
Alloscan	100 mg
Apo-Allopurinol	100 & 300 mg
Aprinol	100 mg
Erloric	100 mg
Mephanol-300	300 mg
Progout-100/Progout-300	100 & 300 mg
Purinol	100 mg
Zyloric/Zyloric-300	100 & 300 mg

Toxicity

- In one case of a massive acute overdose (22.5g), no adverse effects were observed. Toxicity with therapeutic doses is more common in patients with renal failure.
- Serious hypersensitivity reactions can occur at therapeutic doses e.g. Stevens-Johnson syndrome.

Clinical Features

Rash, nausea, vomiting, diarrhoea, fever, eosinophilia, leucopenia and reversible liver impairment. The possibility of cataract formation has been suggested.

Management of Toxicity

- Perform gastric lavage for large and recent ingestions.
- Administer activated charcoal slurry.
- Enhance elimination through urine alkalinisation.
- Although allopurinol and oxypurinol are removed by haemodialysis, its value in overdosage is not established.

Antidotes : no specific antidote.

Monitoring Parameters/Levels

- Serum/Blood
Monitor renal and hepatic function closely if a hypersensitivity reaction is seen. Serum allopurinol levels are not useful.
- Obtain urinalysis.

7.2 Colchicine

Colchicine is used in the treatment of acute gout. Colchicine and Colchicine B.P. are available as 500 µg tablets.

Toxicity

Reported fatal deaths have occurred at oral doses of 7-60mg. A 0.5-0.8mg/kg dose may be fatal.

Clinical Features

- In the early phase after 2-24 hours, overdose causes burning in the throat, abdominal pain, vomiting, watery to bloody diarrhoea, hypotension, electrolyte abnormalities, and volume depletion.
- In the second phase, multisystem failure occurs 24-72 hours post-ingestion. It is manifested as neurological toxicity (confusion, coma, ascending peripheral neuropathy), pulmonary oedema, myocardial depression, hypotension, arrhythmias, respiratory failure, renal/hepatic failure, coagulopathy. Pancytopenia occurs secondary to marrow suppression; cell counts reach a nadir after 4 - 7 days.
- The third phase is one of recovery and is seen at approximately 7 - 10 days post-ingestion. It is characterised by rebound leucocytosis and reversible alopecia. Fever may persist for several weeks.
- Pathological findings in fatal cases are congestion and degenerative changes in the gastrointestinal tract and kidneys.
- Death (within 7-36 hours) from respiratory failure, cardiovascular collapse, or sudden asystole is common. Sepsis is a common cause of death at 3-7 days.

Management of Toxicity

- Perform gastric lavage for large ingestions.
- Administer activated charcoal slurry
- Observe patient for at least 12 hr following history of acute exposure (a latent period of 2-12 hr occurs between exposure and onset of symptoms)
- Treat shock. Give oxygen for cyanosis.
- Treat hypotension. Treat anuria / oliguria.
- Seizures can be managed with diazepam. Manage recurrent seizures with phenytoin or phenobarbitone.
- Manage abdominal cramps with 2-10mg of morphine sulphate as necessary.
- Bone marrow depression.
G-CSF (filgrastim) 300mcg/day is effective in reversing pancytopenia.
- Haemodialysis is not useful due to the large volume of distribution of colchicine.

Antidotes : no specific antidote

Monitoring Parameters/Levels :

- Colchicine levels are not useful. Monitor FBC regularly for signs of marrow suppression.
- Urinalysis may show haematuria, proteinuria or haemoglobin casts.
- Monitor serum creatinine, liver function and CPK.

7.3 Probenecid

Probenecid is a uricosuric agent used in treatment of gout.

Benemid 500 mg tab

Toxicity

No specific toxic dose or serum level has been established.

Clinical Features

Vomiting, tremors, grand mal seizures, visual hallucinations, coma (in later stages), respiratory failure, skin rash and nephrotic syndrome.

Management of Toxicity

- Perform gastric lavage for large ingestions. Ipecac emesis is not recommended because of the potential for CNS depression and seizures.
- Administer activated charcoal slurry
- Treat seizures with phenytoin.

Antidote : no specific antidote

Monitoring Parameters/Levels :

- Due to the potential for blood dyscrasias and kidney malfunction, monitor kidney function and FBC.
- **Urinalysis :** Glucose Test: Probenecid may cause a false positive test when testing for urinary glucose using the Clinitest or Benedict's solution.
Protein : Proteinuria secondary to probenecid-induced nephrotoxicity may develop.
Urinary Function Tests : Should be considered in individuals who have ingested large amounts of probenecid.

7.4 Sulfinpyrazone

Sulfinpyrazone is a pyrazole compound used in the treatment of gout. It is related to phenylbutazone.

Table 2. Sulphinpyrazone tablets

Product	Contents
Anturin	200 mg
Apo-Sulphinpyrazone	100 & 200 mg

Toxicity

Leucopenia occurs in 1% of users, and fatalities from agranulocytosis have followed doses as small as 1g.

Clinical Features

Nausea, vomiting, diarrhoea, epigastric pain, ataxia, anaemia, jaundice, seizures and coma.

Management of Toxicity

- Perform gastric lavage for large ingestions. Ipecac emesis is not recommended because of the potential for CNS depression and seizures.
- Administer activated charcoal slurry
- Treat oliguria
- Treat seizures with phenytoin.
- Alkaline diuresis is of questionable value. Haemoperfusion is not routinely warranted. It may be useful in patients who continue to deteriorate clinically despite conventional treatment.

Antidote : no specific antidote

Monitoring parameters/levels :

- Plasma levels are not useful clinically.
- Obtain FBC, renal and liver function tests, and urinalysis in symptomatic patients.

References

1. *Hande et al : Severe allopurinol toxicity. Description and guidelines for prevention in patients with renal failure. Am J Med 1984;76 : 47-56*
2. *RH Dreisbach and WO Robertson: Handbook of Poisoning. Appleton-Lange, Connecticut, 1987.*
3. *Poisindex® Editorial Staff, Denver, Colorado In : BH Rumack, AJ Hess and CR Gelman (Eds) : Poisindex® System. MICROMEDEX, Inc., Englewood, Colorado (Edition expires December 1999).*

CHAPTER 8

Hormones and Steroids

8.1 Androgens and Anabolic Steroids

Danazol
Nandrolone
Fluoxymesterone
Oxymetholone

Androgens are used as replacement therapy in male hypogonadal disorders and are used in adolescent males with delayed puberty or growth. In females, androgens have been given in the management of disseminated breast carcinoma.

Table 1. Preparations containing androgens and anabolic steroids

Product	Contents
Anapolon 50 Tab	Oxymetholone 50mg
Andriol Cap	Testosterone undecanoate 40mg
Azol Cap 100mg / 200mg	Danazol 100mg / 200mg
Danodiol 200 Cap	Danazol 200mg
Danzol Cap	Danazol 200mg
Deca- Durabolin Inj	Nandrolone decanoate 25mg/ml
Depo Testosterone Inj	Testosterone cyclopentylpropionate 100mg/ml
Freeburn Cap	Danazol 100mg
Halotestin Tab	Fluoxymesterone 5mg
Ladogal Cap	Danazol 50mg/100mg/200mg
Malvinum 25 Tab	Mesterolone 25mg
Nazol Cap	Danazol 200mg
PMS Testosterone Enanthate Inj	Testosterone enanthate 200mg/ml
Provironum Tab	Mesterolone 25mg
Sustanon 250 Inj	Testosterone decanoate 100mg/ml Testosterone isocaproate 60mg/ml Testosterone phenylpropionate 60mg/ml Testosterone propionate 30mg/ml
Testoderm Transdermal System 4mg/day	Testosterone 10mg / 40 sq cm
Testoderm Transdermal System 6mg/day	Testosterone 15mg / 60 cm ²
Testosterone Implant	Testosterone 100mg
Testoviron-Depot Inj 250mg/ml	Testosterone enanthate 250mg/ml

Toxicity

Toxicity is unlikely following acute overdose. Chronic exposure to high doses may result in androgenic effects. The toxic dose is variable depending on the drug and individual.

Clinical Features

Acute: Abnormal liver function tests, salt and water retention, masculinization (particularly of female foetus). Nausea and vomiting. Oesophageal variceal bleeding. Cholestatic jaundice and peliosis hepatitis (reported with therapeutic doses).

Chronic: Hypogonadism has been reported in haemodialysis patients who are taking chronic anabolic steroids therapeutically. Chronic misuse leads to myocardial infarction, thrombosis, sudden cardiac death, choreiform movement, aggravation of nervous tics. Growing children may suffer from premature fusion of epiphyses of long bones, leading to short stature.

Management of Toxicity

- Perform gastric lavage for large, recent ingestions.
- Administer activated charcoal
- Treatment
 - A. In acute single overdosage, toxicity is unlikely.
 - B. In chronic toxicity, discontinue medication. This, together with symptomatic and supportive treatment will be adequate in most situations.
 - C. Patients who chronically misuse anabolic steroids may experience a withdrawal reaction. Steroid withdrawal needs may be treated by detoxication, support during the denial phase, short term rehabilitation/recovery therapy, and long term post-recovery care.

Antidotes : no specific antidote

Monitoring parameters / levels :

Liver-specific isoenzymes (alkaline phosphatases, lactate dehydrogenases) should be used to monitor the liver function. Electrolytes, glucose, BUN, creatinine level.

8.2 Corticosteroids

Betamethasone
 Hydrocortisone
 Hormone Corticotropin (ACTH)
 Methylprednisolone
 Cortisone Acetate

All corticosteroids have mineralocorticoid and glucocorticoid activity to varying degrees.

Table 2. Corticosteroids

Corticosteroid	Approx. equiv. dose (mg)	Relative glucocorticoid potency	Relative mineralocorticoid potency	Plasma $t_{1/2}$ (min)
Short-acting (biologic $t_{1/2}$ < 12 hrs)				
Cortisone	25	0.8	2	30
Hydrocortisone	20	1	2	80-118
Intermediate- acting (biologic $t_{1/2}$ 12- 36 hrs)				
Prednisolone	5	4	1	115-212
Triamcinolone	4	5	0	120-300
Methylprednisolone	4	5	0	78-188
Long-acting (biologic $t_{1/2}$ > 12 hrs)				
Dexamethasone	0.75	20-30	0	110-210
Betamethasone	0.6-0.75	20-30	0	300+

Fludrocortisone has potent mineralocorticoid activity and high glucocorticoid activity (about 15 times as potent as hydrocortisone), but is used only for its mineralocorticoid effects.

Products

A. Betamethasone

Table 3. Preparations containing betamethasone

Product	Contents
Eye Preparations	
Betoptic Eye Drop 0.1%	Betamethasone sodium phosphate 1mg/ml
Betamethasone Eye-Ear Drop 0.1%	Betamethasone sodium phosphate 1mg/ml
Betnesol Drops for Eye, Ear or Nose	Betamethasone sodium phosphate 1mg/ml
Celestone Eyedrop	Betamethasone disodium phosphate 2mg/ml
Oral Preparations	
Betalone Tablet 0.5mg	Betamethasone 0.5mg
Betamethasone Tablet 0.5mg	Betamethasone 0.5mg
Celestone Tab 0.5mg	Betamethasone 0.5mg
Synmethasone Forte Syrup 0.5mg/5ml	Betamethasone valerate 0.1mg/ml
Synmethasone Forte Syrup 0.25mg / 5ml	Betamethasone valerate 0.05mg/ml
Synmethasone Tab 0.5mg	Betamethasone 0.5mg
Injections	
Bufencom Inj	Betamethasone disodium phosphate 2mg/ml
	Betamethasone dipropionate 5mg/ml
Celestone Inj 4mg/ml	Betamethasone disodium phosphate 4mg/ml
Dibetasol Inj	Betamethasone sodium phosphate 2mg/ml
	Betamethasone dipropionate 5mg/ml
Diprosan Inj	Betamethasone disodium phosphate 2mg/ml
	Betamethasone dipropionate 5mg/ml

Table 3. (Cont'd)

Product	Contents
External Preparations	
Besone Cream 1%	Betamethasone valerate 1mg/g
Betacorten Scalp Application 0.1%	Betamethasone valerate 1mg/ml
Betaderma Cream	Betamethasone valerate 1mg/g
Betaderma Scalp Lotion 0.1%	Betamethasone 17-valerate 1mg/ml
Betalone Cream 0.1%; 0.025%	Betamethasone valerate 1mg/g ; 0.25mg/g
Betalone Ointment 0.1%	Betamethasone valerate 1mg/g
Betamethasone Cream 0.025% ; 0.1%	Betamethasone valerate 0.25mg/g ; 1mg/g
Betamethasone Ointment 0.05%	Betamethasone valerate 0.5mg/g
Betamethasone Skin Ointment 0.1%	Betamethasone valerate 1mg/g
Betamethasone Valerate Cream BP 0.025%; 0.05%; 0.1%	Betamethasone valerate 0.25mg/g ; 0.5mg/g ; 1mg/g
Betamethasone Valerate Lotion USP 0.1%	Betamethasone valerate 1mg/g
Betasone Cream 0.1%	Betamethasone valerate 1mg/g
Betnovate Cream 0.1%	Betamethasone valerate 1mg/g
Betnovate Lotion 0.1%	Betamethasone valerate 1mg/ml
Betnovate Ointment 0.1%	Betamethasone valerate 1mg/g
Betnovate RD Cream 0.025%	Betamethasone valerate 0.25mg/g
Betnovate Scalp Application	Betamethasone valerate 1mg/g
Betoptic Cream 0.1%	Betamethasone valerate 1mg/g
Betoptic Ointment 0.1%	Betamethasone valerate 1mg/g
Camnovate Cream	Betamethasone valerate 1mg/g
Celestoderm V Cream 0.1%	Betamethasone valerate 1mg/g
Cortivate Cream	Betamethasone 17-valerate 1mg/g
Dermasone Cream 0.025% ; 0.05% ; 0.1%	Betamethasone valerate 0.25mg/g ; 0.5mg/g ; 1mg/g
Diprocil Cream 0.05%	Betamethasone dipropionate 0.5mg/ml
Diproderma Cream	Betamethasone dipropionate 0.5mg/ml
Diprosone Cream 0.05%	Betamethasone dipropionate 0.5mg/ml
Diprosone Ointment 0.05%	Betamethasone dipropionate 0.5mg/ml
HD- Betasone Cream	Betamethasone 17-valerate 1mg/g
Medobeta Cream	Betamethasone valerate 1mg/g
Synmethasone Cream	Betamethasone valerate 1mg/g
Temprosone Cream 0.05%	Betamethasone dipropionate 0.5mg/g
Temprosone Gel 0.05%	Betamethasone dipropionate 0.5mg/g
Uniflex 0.025% ; 0.1%	Betamethasone 17-valerate 0.25mg/g ; 1mg/g
Unimethasone Cream 0.1%	Betamethasone valerate 1mg/g

Table 4. Combination preparations containing betamethasone

Product	Contents
Eye Preparations	
Betnesol N Drops for eye, ear or nose	Betamethasone sodium phosphate 1mg/ml Neomycin sulphate 5mg/ml
Garasone Ophthalmic Ointment / Soln	Betamethasone sodium phosphate 1mg/ml Gentamicin sulphate 3mg/g
External Preparations	
Betnovate C cream	Betamethasone valerate 10mg/g Clioquinol 30mg/g
Betnovate N Cream	Betamethasone valerate 1mg/g Neomycin sulphate 5mg/g
Conazole Cream	Betamethasone valerate 1mg/g Gentamicin sulphate 1mg/g Miconazole nitrate 20mg/g
Diprogenta Cream	Betamethasone dipropionate 0.5mg/g Gentamicin sulphate 1mg/g
Diprosalic Ointment	Betamethasone dipropionate 0.5mg/g Salicylic acid 30mg/g
Fucicort Cream	Betamethasone valerate 1mg/g Fusidic acid 20mg/g
Gentrisone Cream	Betamethasone dipropionate 0.5mg/g Gentamicin sulphate 1mg/g Clotrimazole 10mg/g
Myderm Cream	Betamethasone dipropionate 0.5mg/g Gentamicin sulphate 1mg/g Clotrimazole 10mg/g
Quadriderm Cream	Betamethasone valerate 0.5mg/g Gentamicin sulphate 1mg/g Tolnaftate 10mg/g Iodochlorhydroxyquin 10mg/g
Triderm Cream	Betamethasone dipropionate 0.5mg/g Gentamicin sulphate 1mg/g Clotrimazole 10mg/g
Uniflex- N Cream	Betamethasone valerate 1mg/g Neomycin sulphate 5mg/g

B. Dexamethasone

Table 5. Preparations containing dexamethasone

Product	Contents
Oral Preparations	
Decan Tab	Dexamethasone 0.75mg
Dexaltin Oral Paste	Dexamethasone 1mg/g
Dexamed Tab	Dexamethasone 0.5mg
Dexasone Tab	Dexamethasone 0.5mg
Dextrasone Tab / Forte Tab	Dexamethasone 0.5mg; 0.75mg
Erladexone Tab	Dexamethasone 0.5mg; 0.75mg
Injections	
Decadron Inj	Dexamethasone sodium phosphate 4mg/ml
Decan Inj	Dexamethasone 2.2mg/ml
Dexamethasone DBL Inj	Dexamethasone 4mg/ml ; 24mg/ml
Dexasone Inj	Dexamethasone 5mg/ml
Eye Preparations	
Maxidex Eye Drop/Ointment	Dexamethasone sodium phosphate 1mg/ml(drop) ; 1mg/g (ointment)

Table 6. Combination preparations containing dexamethasone

Product	Contents
External Preparations	
Baycuten N Cream	Dexamethasone acetate 0.4mg/g Clotrimazole 10mg/g
Eye / Ear Preparations	
Decadron with Neomycin Eye Drop	Dexamethasone sodium phosphate 1mg/ml Neomycin sulphate 5mg/ml
Dexamytrex Ophthiole Eye Drop	Dexamethasone sodium phosphate 1mg/ml Gentamicin sulphate 5mg/ml
Dexoptic N Eye drop	Dexamethasone sodium phosphate 1mg/ml Neomycin sulphate 5mg/ml
Dextracin Eye /Ear Drop	Dexamethasone sodium phosphate 1mg/ml Neomycin sulphate 5mg/ml
Frakidex Eye Ointment	Dexamethasone sodium phosphate 1mg/ml Framycetin sulphate 5mg/ml
Framoptic-D Eye / Ear Drop	Dexamethasone sodium phosphate 1mg/ml Framycetin sulphate 5mg/ml Gramicidin 0.05mg/ml

Table 6. (Cont'd)

Product	Contents
Maxitrol Eye drop/Ointment	Dexamethasone 1mg/ml (drop); 1mg/g (ointment) Neomycin sulphate 3.5mg/ml(drop); 3.5mg/g (ointment) Polymyxin b sulphate 6000u/ml (drop); 6000u/g (ointment)
Neo-Deca Eye/Ear Drop	Dexamethasone sodium phosphate 1mg/ml Neomycin sulphate 5mg/ml
Neo-Dex Eye Drop	Dexamethasone sodium phosphate 1mg/ml Chloramphenicol 5mg/ml
Polydexa Eye Drop	Dexamethasone sodium metasulfobenzoate 0.5mg/ml Polymyxin B sulphate 10,000u/ml Neomycin sulphate 6500u/ml
Sofradex Eye / Ear Drop/ Ointment	Dexamethasone 0.5mg/ml Framycetin sulphate 5mg/ml Gramicidin 0.05mg/ml
Spersadex Comp Eye Drop	Dexamethasone 1mg/ml Chloramphenicol 5mg/ml
Spersadexoline Eye Drop	Dexamethasone 1mg/ml Chloramphenicol 5mg/ml Tetrahydrozoline 0.25mg/ml
Tobradex Eye Drop / Ointment	Tobramycin 3mg/ml Dexamethasone 1mg/ml

C. Fludrocortisone

Table 7. Preparations containing fludrocortisone

Product	Contents
Florinef Tab	Fludrocortisone acetate 0.1mg

D. Methylprednisolone

Table 8. Preparations containing methylprednisolone

Product	Contents
Solu-Medrol Inj	Methylprednisolone sodium succinate 40mg/ml; 62.5mg/ml
Neo-Medrol Acne Lotion	Methylprednisolone 2.5mg/ml Neomycin sulphate 2.5mg/ml Alcloxa 100mg/ml Sulphur 50mg/ml

E. Prednisolone

Table 9. Preparations containing prednisolone

Product	Contents
Eye preparations	
Blephamide Eye Drop	Sodium sulphacetamide 100mg/ml Prednisolone acetate 2mg/ml Phenylephine hydrochloride 1.2mg/ml
Pred Forte Eye Drop	Prednisolone acetate 10mg/ml
Pred Mild Eye Drop	Prednisolone acetate 1.2mg/ml
Predmycin P Eye Drop	Prednisolone acetate 5mg/ml Polymyxin B Sulphate 5000U /ml Neomycin sulphate 5mg/ml
Oral preparations	
Dhasolone Syrup	Prednisolone 3mg/5ml
Dhasolone Tab	Prednisolone 5mg
Prednisolone Beacons Tab	Prednisolone 1mg; 5mg; 20mg
Prednisolone Jean Marie Tab	Prednisolone 5mg
Prednisolone Sussex Tab	Prednisolone 5mg
Xepasone Tab	Prednisolone 5mg
YSP Prednisolone Tab	Prednisolone 0.5mg
Injections	
Prednisolone Jean Marie Inj	Prednisolone 25mg/ml
Uni P-sone Inj	Prednisolone 25mg/ml
Weimer Prednisolone	Prednisolone 25mg/ml
Others	
Predfoam (Rectal Foam)	Prednisolone 20mg / metered dose

F. Triamcinolone

Table 10. Preparations containing triamcinolone

Product	Contents
External Preparations	
Aristocort-A Cream	Triamcinolone acetonide 1mg/g
Dermacort Cream	Triamcinolone acetonide 1mg/g
Kenalog in Orabase	Triamcinolone acetonide 1mg/g
Oramedy	Triamcinolone acetonide 1mg/g
Injections	
Kenacort A IA/ID	Triamcinolone acetonide 10mg/ml
Kenacort A IM	Triamcinolone acetonide 40mg/ml
Shincort Inj	Triamcinolone acetonide 10mg/ml
Shincort Inj (IM)	Triamcinolone acetonide 40mg/ml
Triamcinolone Lisapharma Inj	Triamcinolone acetonide 40mg/ml
Unicilone Inj	Triamcinolone acetonide 40mg/ml

Table 11. Combination products containing triamcinolone

Product	Contents
Eye/Ear Preparations	
Kenacomb Ear Drop	Triamcinolone acetonide 1mg/g Neomycin 2.5mg/g Gramicidin 0.25mg/g Nystatin 100,000 U/g
External Preparations	
Econazine Cream	Triamcinolone acetonide 1mg/g Econazole nitrate 10mg/g
Kenacomb Ointment/ Cream	Triamcinolone acetonide 1mg/g Neomycin 2.5mg/g Gramicidin 0.25mg/g Nystatin 100,000 U/g
Oracort-E in Orabase	Triamcinolone acetonide 1mg/g Lidocaine hydrochloride 30mg/ml
OralAid Lotion	Triamcinolone acetonide 1mg/ml Lidocaine 25mg/ml Chlorhexidine 5mg/ml
Pevisone Cream	Triamcinolone acetonide 1mg/g Econazole nitrate 10mg/g
Triacomb Cream	Triamcinolone acetonide 1mg/g Neomycin 2.5mg/g Gramicidin 0.25mg/g Nystatin 100,000 U/g

G. Cortisone Acetate

Table 12. Preparations containing cortisone

Product	Contents
Cortisone Acetate USP Tab	Cortisone acetate 25mg

H. Hydrocortisone

Table 13. Preparations containing hydrocortisone

Product	Contents
External Applications	
Cortaid with Aloe	Hydrocortisone 5mg/ml
Derm-Aid Cream	Hydrocortisone 5mg/g
Dhacort Cream	Hydrocortisone 10mg/g
Efficort Cream	Hydrocortisone 1.27mg/g
Efficort Lipocream	Hydrocortisone 1.27mg/g
Egocort Cream	Hydrocortisone 10mg/g
Injections	
Hydro Adreson Aquosum Inj	Hydrocortisone sodium succinate 50mg/ml
Solu-Cortef Inj	Hydrocortisone sodium succinate 50mg/ml; 125mg/ml

Table 14. Combination preparations containing hydrocortisone

Product	Contents
Eye/ Ear Preparations	
Hydrospor Ear Drop	Hydrocortisone 10mg/ml Polymyxin B sulphate 10,000U/ml Neomycin sulphate 3,400U/ml
Kemicort Ear / Eye Drop	Hydrocortisone caprylate 5mg/ml Chloramphenicol 10mg/ml
Kemicort Eye Ointment	Hydrocortisone acetate 5mg/ml Chloramphenicol 10mg/ml
Otosporin Ear Drop	Hydrocortisone 10mg/ml Polymyxin B sulphate 10,000U/ml Neomycin sulphate 3,400U/ml
External Preparations	
Daktacort Cream	Hydrocortisone 10mg/g Miconazole nitrate 20mg/g
Eurax-Hydrocortisone Cream	Hydrocortisone 2.5mg/g Crotamiton 100mg/g
Zaricort cream	Hydrocortisone 10mg/g Miconazole nitrate 20mg/g

Toxicity

- Toxic signs and symptoms rarely occur with acute ingestion or with administration of less than 3 weeks duration over a wide dosage range.
- Systemic effects of toxicity are common with daily usage beyond 3 weeks and appear to correlate roughly with average daily dosage though wide variation in tolerance to the chronic adverse reactions have been observed. Adverse reactions appear to be more common and severe with preparations having long durations of effect or when shorter action preparation are administered in multiple daily doses.

Clinical Features

- Acute Poisoning (via injections)
Anaphylaxis with prostration, rigor, weak pulse, cardiac arrhythmias, loss of consciousness and death
- Chronic Poisoning
Hypertension, oedema, nervousness, sleeplessness, skin eruption, depression, cataracts, amenorrhea, alkalosis, euphoria, decrease in pain sensation
- Repeated intra-articular injection results in destruction of the joint. Death from steroid therapy ordinarily results from either acute adrenal insufficiency or gastric ulcer with haemorrhage or perforation.
- Abrupt withdrawal of adrenocorticoid hormones may cause symptoms of adrenal cortex deficiency: hypotension, coma, weakness and tremor.

Management of Toxicity

- Emesis or gastric lavage is generally not necessary as acute overdose is not associated with high toxicity.
- Administer activated charcoal slurry.
- Treatment

a. Acute overdose - symptomatic and supportive treatment

Treat anaphylaxis with adrenaline and supplementary oxygen

b. Chronic overdose - Avoid chronic daily dosage for durations greater than 3 weeks when possible.

When chronic doses for periods greater than 3 weeks are essential, attempts should be made to manage the underlying disease with alternate day dosage. Single daily doses of shorter acting preparations such as prednisone, prednisolone, or methylprednisolone on alternate mornings may be used.

If toxicity is already present, withdrawal of the corticosteroids and conventional management of peptic ulcers, cataracts, and hypertension is required.

Antidotes : no specific antidote

Monitoring parameters / levels : In chronic toxicity, monitoring of fluid and electrolytes is necessary.

8.3 Oestrogens

Conjugated oestrogens
 Oestriol
 Dienoestrol
 Oestrone

Oestrogens are given for replacement therapy in deficiency states, for menopausal and postmenopausal disorders and for contraception. They may also be used for the treatment of malignant neoplasms of the prostate and of the breast in postmenopausal women.

Table 15. Oestrogenic preparations

Product	Contents
Oral Preparations	
Brevinor Tab	Norethisterone 0.5mg Ethinylestradiol 0.035mg
Diane-35	Cyproterone acetate 2mg Ethinylestradiol 0.035mg
Estrofem / Estrofem Forte Tab	Oestradiol 2mg ; (Forte) 4mg
Gynera Tab	Gestodene 0.075mg Ethinylestradiol 0.03mg
Kliogest Tab	Oestradiol 2mg Norethisterone acetate 1mg
Marvelon Tab	Desogestrel 0.15mg Ethinylestradiol 0.03mg
Menophase Tab	5 Pink Tab: Mestranol 0.0125mg 8 Orange Tab: Mestranol 0.025mg 2 Yellow Tab: Mestranol 0.05mg 3 Green Tab : Mestranol 0.025mg Norethisterone 1mg 6 Blue Tab : Mestranol 0.03mg Norethisterone 1.5mg 4 Lavender Tab : Mestranol 0.02mg Norethisterone 0.75mg
Mercilon Tab	Desogestrel 0.15mg Ethinylestradiol 0.02mg
Microgynon 30 Tab	Levonorgestrel 0.15mg Ethinylestradiol 0.03mg

Table 15. (Cont'd)

Product	Contents
Minulet Tab	Gestodene 0.075mg Ethinylestradiol 0.03mg
Nordette Tab	Levonorgestrel 0.15mg Ethinylestradiol 0.03mg
Nordiol Tab	Levonorgestrel 0.25mg Ethinylestradiol 0.05mg
Norinyl-1 Tab	Mestranol 0.05mg Norethisterone 1 mg
Ovestin Tab	Oestradiol 2mg
Ovulen 50 Tab	Ethinylestradiol Diacetate 1mg Ethinylestradiol 0.05mg
Premarin Tab	Conjugated oestrogen 0.3mg; 0.625mg; 1.25mg; 2.5mg
Prempak Tab	Each 21 Tab: Conjugated equine oestrogen 0.625mg Each 10 Tab: Medrogestone 5mg
Prempak-C Tab	Each 28 Tab: Natural conjugated oestrogen 0.625mg Each 12 Tab: Norgestrel 0.15mg
Progyluton Tab	Each 11 Tab: Oestradiol valerate 2mg Each 10 Tab: Oestradiol valerate 2mg Norgestrel 0.5mg
Progynova Tab	Oestradiol valerate 2mg
Stilboestrol Tab	Stilboestrol 5mg
Trinordiol Tab	Each 6 brown tab: Levonorgestrel 0.05mg Ethinylestradiol 0.03mg Each 5 white tab: Levonorgestrel 0.075mg Ethinylestradiol 0.04mg Each 10 yellow tab: Levonorgestrel 0.125mg Ethinylestradiol 0.03mg
Trisequens Tab	12 blue tab: Oestradiol 2mg 10 white tab: Oestradiol 2mg Norethisterone 1mg 6 red tab: Oestradiol 1mg
Trisequens Forte Tab	12 yellow tab: Oestradiol 4mg 10 white tab: Oestradiol 4mg Norethisterone 1mg 6 red tab: Oestradiol 1mg

Table 15. (Cont'd)

Product	Contents
Triquilar/ Triquilar ED Tab	Each 6 tab: Levonorgestrel 0.05mg Ethinylestradiol 0.03mg Each 5 tab: Levonorgestrel 0.075mg Ethinylestradiol 0.04mg Each 10 tab: Levonorgestrel 0.125mg Ethinylestradiol 0.03mg 7 inactive tab (For Triquilar ED)
Vaginal Preparations	
Ortho-Gynest Vaginal Supp	Oestriol 0.5mg/supp
Premarin Vaginal Cream	Conjugated oestrogen 0.625mg/g
Vagifem Film-coated Vaginal Tab	17- β Oestradiol 0.025mg
Transdermal Preparations	
Estracomb TTS	Estraderm TTS 50 : Oestradiol 4mg Estragel TTS 0.25/50: Oestradiol 10mg Norethisterone acetate 30mg
Estraderm TTS 25; TTS 50	Oestradiol 0.025mg/day; 0.05mg/day
Injections	
Premarin Intravenous	Conjugated oestrogen 5mg/ml
External Preparations	
Oestrogel	17 β -oestradiol 60mg/g
Others	
Oestradiol Implants	Oestradiol 50mg

Toxicity

- Oestrogens are of a low order of toxicity. However, headache, nausea and vomiting, and excessive vaginal bleeding have been reported at therapeutic doses.
- Chronic use may result in oedema, leg cramps, gynaecomastia, porphyria cutanea tarda and chloasma. Exact toxic doses have not been determined.

Clinical Features

Signs and symptoms, other than gastrointestinal effects, are seldom seen following acute overdosage. Hypertension, thromboembolic disorders, elevated liver function tests and cholestatic jaundice are likely. Fluid retention may result from therapeutic doses.

Management of Toxicity

- Emesis or gastric lavage is generally not necessary as acute toxicity is low.
- Administer activated charcoal slurry, followed by oral magnesium sulphate
- Treatment

a. Acute overdosage

In acute single overdosage, toxicity is unlikely and treatment to ease gastrointestinal irritation is all that is required.

b. Chronic overdosage

Discontinue medication. Monitor severe signs of toxicity and treat symptomatically.

Antidotes : no specific antidote

Monitoring parameters : Oestrogen overdose secondary to oestradiol implants should be confirmed by measuring serum oestradiol.

8.4 Antidiabetic Drugs

8.4.1 Insulin

Insulin is a pancreatic hormone involved in the regulation of blood glucose as well as having a role in protein and lipid metabolism. Insulin is given to patients with IDDM to control glycaemia. It may also be necessary in some patients with NIDDM.

Table 16. Insulin preparations

Product	Contents (100i.u./ml)
Actrapid HM Injection	Insulin Human Monocomponent (Soluble)
Actrapid HM Penfill/ Novolet Injection	Insulin Human Monocomponent (Soluble)
Humulin 10/90 Injection	Insulin Human (Isophane) 90% Insulin Human (Regular) 10%
Humulin 20/80 Injection	Insulin Human (Isophane) 80% Insulin Human (Regular) 20%
Humulin 30/70 /Injection	Insulin Human (Isophane) 70% Insulin Human (Regular) 30%
Humulin 40/60 Injection	Insulin Human (Isophane) 60% Insulin Human (Regular) 40%
Humulin 50/50 Injection	Insulin Human (Isophane) 50% Insulin Human (Regular) 50%
Humulin L Injection	Insulin Zinc Suspension Human (Lente)
Humulin N Injection	Insulin Isophane Suspension Human
Humulin R Injection	Insulin Human (Regular)
Humulin U Injection	Insulin Zinc Suspension Human (Ultralente)
Hypurin Lente Injection	Insulin Bovine Highly Purified (Lente)
Hypurin Neutral Injection	Insulin Bovine Highly Purified
Insulatard HM Injection	Insulin Human Monocomponent (Isophane)
Insulatard HM Penfill Injection	Insulin Human Monocomponent (Isophane)
Insulatard Novolet Injection	Insulin Human Monocomponent (Isophane)
Mixtard 10 HM Penfill/ Novolet Injection	Insulin Human Monocomponent 10% (Soluble) Insulin Human Monocomponent (Isophane) 90%
Mixtard 20 HM Penfill/ Novolet Injection	Insulin Human Monocomponent 20% (Soluble) Insulin Human Monocomponent (Isophane) 80%
Mixtard 30 HM Injection	Insulin Human Monocomponent 30% (Soluble) Insulin Human Monocomponent (Isophane) 70%

Table 16. (Cont'd)

Product	Contents (100i.u./ml)
Mixtard 30 HM Penfill/ Novolet Injection	Insulin Human Monocomponent 30% (Soluble) Insulin Human Monocomponent (Isophane) 70%
Mixtard 40 HM Penfill/ Novolet Injection	Insulin Human Monocomponent 40% (Soluble) Insulin Human Monocomponent (Isophane) 60%
Mixtard 50 HM Penfill/ Novolet Injection	Insulin Human Monocomponent 50% (Soluble) Insulin Human Monocomponent (Isophane) 50%
Monotard HM Inj	Insulin Zinc Suspension Human Monocomponent amorphous 30%, crystalline 70%
Ultratard HM Injection	Insulin Zinc Suspension Human Monocomponent

Toxicity

- Hypoglycaemia can occur with therapeutic doses of insulin in diabetics with an uncontrolled diet, with too much exercise or in patients with brittle diabetes. Other causes can be alcohol in combination with insulin or changing insulin types or brands.
- It is difficult to predict the minimum toxic or lethal dose of insulin. Severity of intoxication must be based on clinical findings.

Clinical Features

- Hypothermia, mydriasis, hunger and nausea, diaphoresis and flushing, muscle spasm, tachycardia, palpitations and cardiac arrhythmia (atrial fibrillation) secondary to hypokalaemia, hyperventilation, pulmonary oedema, lethargy, yawning, and irritability, cerebral oedema, generalized seizures, cutaneous bullae, mania, coma.
- Acute insulin overdosage results in hypoglycaemia and resultant seizures, coma, cerebral oedema and permanent brain damage. Initial symptoms preceding coma correlate fairly well with blood glucose levels.

Management of Toxicity

Oral insulin is not absorbed and produces no toxicity, so gastric decontamination is not necessary.

Parenteral exposure

- Respiratory and cardiovascular function should be supported .
- Treat hypoglycaemia
- Treat hypokalaemia and seizures if they occur
- Excision of skin and fat down to muscle wall of an insulin injection site under LA has been utilized in managing of subcutaneously injected insulin overdose.

Antidotes : Glucose or glucagon. See pg 118 & 117.

Monitoring parameters :

- Blood glucose monitoring is diagnostic. Plasma levels of 30mg/dL or lower are common following large overdose.
- Urinary glucose and acetone determinations are diagnostic in diabetic ketoacidosis.
- Monitor for hypokalaemia.

8.4.2 Biguanides

Metformin

Table 17. Preparations containing metformin

Product	Contents
Diabetmin Tab	Metformin HCl 500mg
Diaformin Tab	Metformin HCl 500mg
Diamin Tab	Metformin HCl 500mg
Glucophage Retard Tab	Metformin HCl 850mg
Glucophage Tab	Metformin HCl 500mg
Glycomet Tab	Metformin HCl 500mg
Glycoran Tab	Metformin HCl 250mg
Glycformin 500 Tab	Metformin HCl 500mg
Metformin HCl Tab 500mg	Metformin HCl 500mg
Metformin Tab 250mg (film coated)	Metformin HCl 250mg
Metformin 500mg B.P.	Metformin HCl 500mg

Toxicity

- Lactic acidosis has been reported in patients taking metformin although the incidence is less than that of phenformin. The majority of these patients had significant underlying medical problems such as acute or chronic renal insufficiency, liver disease, sepsis, myocardial infarction or congestive heart failure.
- The minimal acute toxic dose is not well established in the literature.

Clinical Features

Nausea and vomiting, abdominal pain, hypoglycaemia, acute renal failure, mental status depression and hypotension may develop in patients with severe biguanide-associated lactic acidosis. Hypothermia is common in patients who develop CNS depression. Deep, rapid breathing, acute pulmonary oedema, hypotension and shock have also been reported.

Management of Toxicity

- Respiratory and cardiovascular function should be supported
- Perform gastric lavage for large, recent ingestions.
- Administer activated charcoal slurry, followed by oral magnesium sulphate
- Treat hypoglycaemia with glucose. Consider IV diazoxide 0.1 - 2 mg/kg/h infusion if dextrose infusions do not maintain satisfactory glucose concentrations.
- Treat hypokalaemia if it occurs
- Diuresis or haemodialysis are not useful

Antidotes : Glucose, glucagon or diazoxide. See 117 & 118.

Monitoring parameters :

- Blood glucose monitoring is diagnostic. Plasma levels of 30mg or lower are common following large overdose.
- Urinary glucose and acetone determinations are diagnostic for diabetic ketoacidosis.
- Monitor for hypokalaemia.

8.4.3 Sulphonylureas

Chlorpropamide
 Gliclazide
 Glibenclamide
 Glipizide
 Tolbutamide

Table 18. Preparations containing sulphonylureas

Product	Contents
Anti-D Tab	Chlorpropamide 250mg
Apo Chlorpropamide Tab	Chlorpropamide 250mg
Chlomid Tab	Chlorpropamide 250mg
Chlorpropamide Tab	Chlorpropamide 250mg
Chlorpropamide BP Tab	Chlorpropamide 250mg
CPM Tab	Chlorpropamide 250mg
Diabeta Tab	Chlorpropamide 250mg
Diabinese Tab	Chlorpropamide 250mg
Dipamide Tab	Chlorpropamide 250mg
Propamide Tab	Chlorpropamide 250mg
Unipropamide Tab	Chlorpropamide 250mg
Apo Glyburide Tab	Glibenclamide 5mg
Benil Tab	Glibenclamide 5mg
Clamide Tab	Glibenclamide 5mg
D.B.T. Tab	Glibenclamide 5mg
Dalanex Tab	Glibenclamide 5mg
Daomid Tab	Glibenclamide 5mg
Daonil Tab	Glibenclamide 5mg
Debtan Tab	Glibenclamide 5mg
Dilelet Tab	Glibenclamide 5mg
Dicon Tab	Glibenclamide 5mg
Euglucon Tab	Glibenclamide 5mg
G.B.N. Tab	Glibenclamide 5mg
Glibemid Tab	Glibenclamide 5mg
Gliben Tab	Glibenclamide 5mg
Glibenclamide 5 Tab	Glibenclamide 5mg
Glibenclamide Tab	Glibenclamide 5mg
Glibenclamide BP Tab	Glibenclamide 5mg
Glibesyn Tab	Glibenclamide 5mg
Glimel Tab	Glibenclamide 5mg
Glimide Tab	Glibenclamide 5mg
Glitisol Tab	Glibenclamide 5mg

Table 18. (Cont'd)

Product	Contents
Gluben Tab	Glibenclamide 5mg
Melix Tab	Glibenclamide 5mg
Semi-glicon Tab	Glibenclamide 5mg
Diamicon Tab	Gliclazide 80mg
Medoclazide Tab	Gliclazide 80mg
Glipizide Tab	Glipizide 5mg
Glunase Tab	Glipizide 5mg
Melizide Tab	Glipizide 5mg
Minidiab Tab	Glipizide 5mg
Apotolbutamide	Tolbutamide 500mg
Rastinon Tab	Tolbutamide 500mg
Tolbumide Tab	Tolbutamide 500mg
Tolbutamide Tab	Tolbutamide 500mg
Tolmide Tab	Tolbutamide 500mg
Unitamide Tab	Tolbutamide 500mg

Toxicity

The major toxicity of these agents is hypoglycaemia, leading to coma and death. Hypoglycaemia is more common in patients with inadequate carbohydrate stress and in patients with renal and liver insufficiency. Hypoglycaemia can also occur at the recommended therapeutic dosages.

The half lives of sulfonylureas are listed:

Chlorpropamide	35-49 hours
Glibenclamide	2-5 hours
Glipizide	2-4 hours
Tolbutamide	4.8 hours

Clinical Features

- *Chlorpropamide*
Hypoglycaemia, nausea and vomiting, liver damage, exfoliative dermatitis, semi-consciousness, hypotonia, hyperreflexia
- *Glibenclamide, gliclazide, glipizide*
Severe hypoglycaemia, unconsciousness and seizures
- *Tolbutamide*
Hypoglycaemia, nausea and vomiting, weakness, skin eruptions, hyperlipidemia, GI ulceration

Management of Toxicity

- Induction of emesis is not recommended because of the potential for CNS depression and seizures.
- Perform gastric lavage for large, recent ingestions.
- Administer activated charcoal.
- Treat coma and seizures if they occur.
- Treat hypoglycaemia with IV glucose. Consider IV diazoxide 0.1 - 2 mg/kg/h infusion if dextrose infusions do not maintain satisfactory glucose concentrations.
- Perform urine alkalinisation to produce a urine pH of at least 7.5 .
- Diuresis or haemodialysis are not useful.

Antidotes : Glucose, glucagon or diazoxide. See pg 118, 117.

Monitoring parameters : Monitor blood glucose hourly for 24 hours.
Monitor electrolytes.

8.5 Pituitary Drugs

Desmopressin

Desmopressin is a synthetic analogue of vasopressin with prolonged antidiuretic activity and markedly less pressor activity. It is used in the diagnosis and treatment of diabetes insipidus, in the management of nocturnal enuresis, and to boost concentration of factor VIII in patients with haemorrhagic disorders.

Table 19. Preparations containing desmopressin

Product	Contents
Minirin Injection	Desmopressin acetate 0.04 mg/ml
Minirin Nasal Spray	Desmopressin acetate 0.1 mg/ml
Minirin Nose Drops	Desmopressin acetate 0.1 mg/ml
Minirin Tab	Desmopressin acetate 0.1mg ; 0.2mg
Octostim Inj	Desmopressin acetate 0.015 mg/ml

Toxicity

Desmopressin given intranasally has a half life of 0.4 to 4 hours and 90 - 150 minutes after oral ingestions. The toxic dose is not known.

Clinical Features

Mucous membrane irritation, headache, dyspnoea, fluid retention, hyponatraemia

Management of Toxicity

Symptomatic and supportive care

Antidotes : no specific antidote

Monitoring parameters : Serum electrolytes and acid-base balance should be evaluated.

8.6 Thyroid And Antithyroid Drugs

8.6.1 Thyroid Drugs

Levothyroxine (T_4 ; tetraiodothyronine)

Liothyronine (T_3 ; triiodothyronine)

Thyroxine sodium is given by mouth as replacement therapy in the treatment of hypothyroidism and myxoedema. Liothyronine has a faster onset of action and is the active form of thyroxine utilised by the human body.

Table 20. Preparations containing thyroid drugs

Product	Contents
Tertroxin Tab	Liothyronine 0.02mg
Eltroxin Tab	Thyroxine Sodium 0.1mg; 0.05mg
Oroxine Tab	Thyroxine Sodium 0.1mg; 0.05mg
Thyroxine Tab B.P.	Thyroxine Sodium 0.1mg; 0.05mg; 0.025mg
Thyroxine Injection	Thyroxine Sodium 500mcg /vial

Toxicity

- Signs of toxicity may be delayed as long as 5 to 11 days after ingestion with an apparently symptom-free interval between ingestion and toxicity. Thyrotoxicosis is fairly common after chronic overdose, but is virtually rare after acute overdose.
- A large overdose may produce cardiovascular effects and other sequelae (pneumonia, bleeding, murmurs, hypokalaemic alkalosis and coma) for weeks after the exposure.

Clinical Features

Mental confusion, agitation and hyperactivity, mydriasis, tachycardia, tachypnoea and pyrexia, atrial fibrillation, excessive sweating and diarrhoea.

Management of Toxicity

- Perform gastric lavage for large, recent ingestions.
- Administer activated charcoal slurry
- Treat hypotension, tachycardia
- Enhanced elimination : plasmapheresis, charcoal plasma perfusion and charcoal haemoperfusion are effective in removing levothyroxine.

Antidotes : Partial inhibition of metabolic conversion of T_4 to T_3 can be obtained using propylthiouracil.

Monitoring parameters :

- Blood pressure and cardiac function should be monitored closely.
- Plasma level of T_3 and T_4 level should be assessed 6 to 12 hours after ingestion.

8.6.2 Antithyroid Drugs

Carbimazole

Propylthiouracil

Both carbimazole and propylthiouracil are thiourea anti-thyroid agents given by mouth in the management of hyperthyroidism.

Table 21. Antithyroid preparations

Product	Contents
Camazol Tab	Carbimazole 5mg
Camazol Tab	Carbimazole 5mg
Carbimazole B.P. Tab	Carbimazole 5mg
Carbiroid Tab	Carbimazole 5mg
Cazole Tab	Carbimazole 5mg
Neo-Mercazole Tab	Carbimazole 5mg
Propylthiouracil BP Tab	Propylthiouracil 50mg

Toxicity

Carbimazole is rapidly and completely converted to methimazole which has a half life of 3 to 6 hours while propylthiouracil has a half-life of 1 to 2 hours. Only one acute overdosage has been reported with raised ALP but there was no clinical evidence of liver toxicity. Only about 1-5% of patients developing agranulocytosis or leukopenia from antithyroid drugs have died.

Clinical Features

- In the first few weeks of therapy, skin reactions, joint pain, fever, sore throat, anorexia, malaise and agranulocytosis have occurred.
- Methimazole, a metabolite of carbimazole, has been reported to cause toxic neuropathy on chronic use. Hypoprothrombinemia with purpura has been reported during propylthiouracil therapy.

Management of Toxicity

- Perform gastric lavage for large, recent ingestions.
- Provide symptomatic and supportive management

Antidotes : no specific antidote

Monitoring parameters :

- Although blood levels of T_3 , T_4 and protein-bound iodine may be markedly elevated, both with and without clinical signs of toxicity, these values are virtually no help in treatment or prognosis of overdose.
- Monitor BP, HR and take ECG.
- FBC may reveal reduction or absence of granulocytes,

Sodium Iodide

Potassium Iodide

Iodides are essential for normal thyroid activity and is used in combination with thiourea antithyroid agents in the pre-operative management of hyperthyroidism, in the treatment of thyroid storm, and to protect the thyroid against radio-iodine. They can also be used in the treatment of iodine deficiency disorders. They are used in external preparations for their antibacterial activity.

Table 22. Iodide preparations

Product	Contents
Sodium Iodide Injection 10%	Sodium Iodide 100mg/ml
Vitrealent Eye Drops	Sodium Iodide 3mg/ml
	Potassium Iodide 3mg/ml
Lugol's Iodine Solution	Iodine 5%, potassium iodide 10%

Toxicity

- The mean fatal dose of iodine is 2-4 g. If the patient survives 48 hours after ingestion of iodine, recovery is likely although stricture of the oesophagus may be a complication.
- In hypersensitivity reactions involving parenteral iodine compounds, survival is likely if the patient lives past the first hour.

Clinical Features

Vomiting, collapse and coma, abdominal pain, thirst, metallic taste, fever, anuria, delirium, uraemic coma. Application to the skin causes weeping, crusting, blistering and fever.

Management of Toxicity

- Gastric lavage can be done but ipecac emesis is not recommended due to the possibility of oesophageal injury.
- Administer activated charcoal slurry, followed by oral magnesium sulphate
- Give milk every 15 minutes, followed by a starch solution (15g of corn starch to 500ml of water).
- Treat hypotension.
- Enhanced elimination: The renal excretion of ionic iodine can be increased by osmotic diuresis, chloruretic diuresis and salt loading.

Antidotes : There is no specific antidote. However, 100ml of sodium thiosulphate 1% solution given orally will immediately reduce iodine to iodide.

Monitoring parameters :

- Plasma iodine levels are not clinically useful, but may aid in diagnosis.
- Monitor fluid and electrolyte status carefully in severely symptomatic patients.
- Monitor acid-base status, serum electrolytes and FBC.
- Monitor renal function tests and urinalysis for patients with significant exposure.

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CHAPTER 9

Oxytocics

9.1 Ergot Alkaloids

The ergot alkaloids include ergometrine maleate (synonym ergonovine) and ergotamine. The ergot alkaloids are clinically used to relieve pain of migraine and to contract the post-partum uterus.

Table 1. Ergot alkaloid preparations.

Products	Contents
Cafergot® tablets	Ergotamine tartrate 1mg Caffeine 100mg
Migril® tablets	Ergotamine tartrate 2mg Cyclizine HCl 50mg Caffeine hydrate 100mg
Ergometrine maleate Injection	Ergometrine maleate 500 mcg/ml
Syntometrine® Injection	Ergometrine maleate 500mcg/ml Oxytocin 5 units/ml

Toxicity

- Ergot and its alkaloids stimulate the smooth muscles of the arterioles, intestines, and uterus. While no fatalities with ergotamine or other purified derivatives have been reported, therapeutic doses can be fatal in those with underlying cardiovascular or other predisposing conditions. All accidental or intentional ingestions should be considered potentially toxic.
- A dose of 40mg of ergotamine tartrate over 5 days has caused impending gangrene in all 4 extremities.

Clinical Features

- Manifests as focal or generalised arterial spasm with extremity or organ ischaemia. In acute overdose, patients present with nausea, vomiting, coma, seizures, and spontaneous abortion. Vascular insufficiency may cause extremity gangrene or organ infarction.
- Symptoms of ischaemia may be delayed 12-24 hours following an acute overdose. Arterial spasm may persist for as long as 3 days. Ischaemic neurological deficits may be present or slowly resolve over a period of weeks to months.

Management of Toxicity

- Gastric lavage if it is soon after ingestion. Ipecac emesis is not recommended because of the potential for CNS depression and seizures.
- Administer activated charcoal slurry.
- Treat seizures, hypotension if they occur
- To reverse peripheral ischaemia secondary to vasoconstriction and to treat hypertension, administer IV sodium nitroprusside 1-2 mcg/kg/min while monitoring vital signs regularly. Prostaglandin E₁ and I₂, both potent vasodilators, have been given by direct arterial infusion to treat arterial spasm.
- Anticoagulant therapy with IV heparin is useful in patients with evidence of ischaemia.
- Abdominal cramps can be managed with atropine.

Antidote : no specific antidote.

Monitoring parameters/levels :

- Frequent vital signs and cardiac monitoring (ECG) is recommended for all patients.
- Toxic effects may persist despite undetectable blood levels.

9.2 Oxytocin

Products	Contents
Syntometrine® injection	Oxytocin 5 units/ml Ergometrine maleate 0.5mg/ml
Syntocinon® injection	Oxytocin 10 units/ml
Oxytocin injection	Oxytocin 10 units/ml

Toxicity

- Water intoxication may occur due to an antidiuretic effect independent of ADH. This effect is measurable at an infusion rate of 15 milliunits/min (maximal at 45 milliunits/min).
- Accidental ingestion in the home is unlikely.

Clinical Features

Large doses of oxytocin have a minimal effect on the uterus except near the end of pregnancy. Blood pressure changes, fluid and electrolyte imbalance, and possible seizures (secondary to water intoxication) may occur. Administration has resulted in uterine rupture and fetal damage.

Management of Toxicity

- Hypertonus of the uterus can be managed readily with β -adrenergic agonists eg. salbutamol.
- Treat seizures.
- Water intoxication is managed by fluid restriction and promotion of diuresis. Intravenous hypertonic saline may be necessary.

Antidote : no specific antidote

Monitoring parameters/levels :

- Monitor heart rate, seizures, water intoxication-induced CNS effects.
- Monitor serum electrolytes, especially sodium.

- Monitor urine volume and osmolality.
- Check foetal heart rate, resting uterine tone, and the frequency, duration and force of uterine contractions.

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CHAPTER 10

Skin And Mucous Membrane Agents

10.1 Astringents

Bismuth Subgallate

Bismuth subgallate is lipophilic and a potentially neurotoxic compound.

Toxicity

Blood bismuth measurements do not correlate with symptoms of toxicity. A bismuth level of 14.6mcg/dL was associated with symptoms in 1 patient. One patient was reported to develop bismuth encephalopathy after ingesting 120mg/day for 1 year.

Clinical Features

- Ulcerative stomatitis, pyorrhoea, loss of sense of taste, anorexia, nausea, vomiting, diarrhoea, encephalopathy, hepatic damage, kidney damage.
- Bismuth encephalopathy has 2 phases. The early phase may last weeks to months and involve primary affective and cognitive changes. The secondary phase has an onset of 24 to 48 hours, and includes confusion, dysarthria, ataxia, and pseudotremor with mild clonic jerking.

Management of Toxicity

Ingestion

- Support respiratory and cardiovascular function.
- Gastric lavage may be considered.
- Dimercaprol may be useful if severe renal lesion is anticipated.
- Haemodialysis may be necessary for those with renal or liver failure.
- Mobilization and excretion of bismuth may be enhanced by ammonium chloride.
- Control seizures with diazepam, phenytoin or phenobarbital

Laboratory tests : Liver and kidney function should be monitored.

10.2 Miscellaneous

A. Eusol

Eusol contains not less than 0.25% w/v of available chlorine.

Contents:

Boric acid 1.25%

Chlorinated lime 1.25%

Toxicity

The ingestions of solutions with “available chlorine” concentrations as low as 0.5% is rarely if a threat to life. Although no exact clinical data are available, solutions with 4 to 6% available chlorine are probably lethal to adults only in oral doses of many mL. However, as little as 30 mL may be dangerous if the concentration is 15% or more.

Clinical Features

Pain, inflammation, erosion of mucous membranes. Red or coffee-ground vomitus. Circulatory collapse, with cold and clammy skin, cyanosis and shallow respirations. Confusion, delirium, coma, oedema of pharynx, glottis and larynx with stridor and obstruction.

Management of Toxicity

- Administer milk, aluminium hydroxide or magnesium trisilicate. Do not induce vomiting or use acidic antidotes.
- Mixture magnesium trisilicate 30mL may be left in the stomach to act as a mild antacid, adsorbent, demulcent and cathartic.
- Provide symptomatic and supportive treatment.

B. Methyl Salicylate

Table 1. Methyl salicylate preparations

Product	Content
Begesic	Per 100g Methyl salicylate 11g and other ingredients
Flanil	Per 100g Methyl salicylate 10.2g and other ingredients
Metsal	Per g Methyl salicylate 283mg and other ingredients
Methyl salicylate Liniment	Per 1000mL Methyl salicylate 250mL

Toxicity

- Significant toxicity may result from single doses of greater than 300 to 500mg/kg of salicylates.
- Chronic ingestion of greater than 100mg/kg/24 hrs of salicylates for 2 or more days have been associated with toxicity.
- 95-150mg/kg for 2 weeks have been associated with toxicity in children.

Clinical Features

Nausea, vomiting, lethargy, agitation, confusion, fever, tinnitus, sweating, thirst, diarrhoea, metabolic acidosis, rapid pulse and respiration, dyspnoea, kidney damage, oliguria, hepatic injury, seizures, coma, toxic nephritis may develop, pulmonary oedema, death from respiratory failure.

Management of Toxicity

- Maintain airway,
- Treat seizures, coma, metabolic acidosis and dehydration if they occur.
- Gastric lavage is not necessary after small ingestions (i.e. <200 - 300 mg/kg) if activated charcoal can be given promptly.
- Administer activated charcoal. Multiple doses of activated charcoal would be reasonably likely to enhance elimination of a significant amount of absorbed salicylate.

- Early haemodialysis for rapid removal of salicylates in severe poisoning (levels >1,200 mg/L, severe acidosis in patients with acute ingestion; levels > 600 mg/L and any confusion or lethargy in patients with chronic intoxication)
- Haemoperfusion is also very effective but does not correct acid-base or fluid disturbances. Especially indicated when plasma salicylate levels are very high, i.e. >1000mg/L.

Antidotes: No specific antidotes. Sodium bicarbonate is given to prevent acidaemia and to promote salicylate elimination by the kidneys.

Laboratory tests: Plasma salicylate levels (obtain stat and serial serum levels), acid-base status (pH of arterial blood), arterial blood gases, urinalysis, FBC, liver function tests, prothrombin time.

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Vitamins And Iron Preparations

11.1 Vitamins

A. Vitamin A

A history of megadose vitamin therapy most commonly precedes the development of toxicity.

Toxicity

Acute toxicity is reported in

- adults after oral ingestion of 1,000,000 IU
- children after oral ingestion of 300,000 IU

Chronic toxicity usually develops after ingestion of 10 times the RDA for prolonged periods of time which due to patient variables such as age, diet and health may be weeks to years.

RDA of Vitamin A in the different age groups

Adults & Children > 4 yrs	5,000 IU
Children < 4yrs	2,500 IU
Infants (0-12 mths)	1,500 IU

Clinical Features

- **Acute ingestion**
Headache, vomiting, blurred vision, irritability and other effects associated with increased intracranial pressure
- **Chronic ingestion**
Vomiting, anorexia, fatigue, irritability, diplopia, headache, bone pain, alopecia, skin lesions, cheilosis, increased intracranial pressure mimicking brain tumour and papilloedema; laboratory findings include elevated liver function tests, prolonged PT, hypercalcaemia, elevated erythrocyte sedimentation rate and periosteal calcification on X-ray.

Management of Toxicity

- Withholding all vitamin A supplementation and the elimination of liver from the diet is the mainstay of therapy.
- Treat vitamin-A induced elevated intracranial pressure (if it occurs) with mannitol, dexamethasone and hyperventilation.

Laboratory Tests : Serum aminotransferase levels, bilirubin, INR or PT and calcium levels for chronic overdose; plasma vitamin A levels is useful in diagnosis.

B. Vitamin D (Calciferol)

Normal Vitamin D level: 10-50ng/mL

Toxicity

Limited data is available for toxicity due to single overdose; one report suggests that 100 times RDA (40,000 IU) is necessary to produce acute hypercalcemia.

Chronic ingestion in excess of 2,000 IU/day in children and of 75,000 IU/day in adults may produce toxicity.

Clinical Features

Anorexia, lassitude, nausea, vomiting, diarrhoea, polyuria, nocturia, albuminuria, polydipsia, sweating, headache, thirst, vertigo, hypertension, renal failure and high cholesterol level. Hypercalcaemia, cardiac arrhythmia, myocardial infarction, polyneuropathy, extreme depression, apathy, confusion and fatigue, normocytic/normochromic anaemia may be seen with chronically high ingestion.

Management of Toxicity

- Withhold all Vitamin D supplements.

- Treat hypercalcaemia :
 - initiate low calcium diet
 - administer ascorbic acid to lower urine pH thereby enhancing calcium excretion
 - administer IV frusemide to enhance calcium excretion by forced diuresis
 - replace lost fluids, sodium and potassium by IV infusions
 - administer prednisolone to decrease plasma calcium
 - severe hypercalcaemia not responding to other therapies has been treated with sodium EDTA or mithramycin
 - Cholestyramine may be effective in lowering serum calcium

Laboratory Tests : Serum calcium and phosphate levels, urinalysis (proteinuria), BUN, creatinine.

C. Vitamin E

Toxicity

- Toxicity following acute overdosage with a multiple vitamin preparation is unlikely unless a massive dose has been ingested.

Clinical Features

- GI disturbances, headache and fatigue, abnormalities of prothrombin and bleeding times have been noted.

Management of Toxicity

- Discontinuance of megadose therapy is indicated.

Laboratory Tests : PT

D. Vitamin B₆ (Pyridoxine)

Toxicity

- Neuropathy has been most commonly reported after chronic oral ingestion of 200-6000 mg/day for several months or years. Minimum acute oral toxic dose for human is unknown but 1 patient was reported to develop reversible neuropathy after approximately 140mg/kg IV dose.

Clinical Features

- Sensory neuropathies characterized by burning pains and paraesthesias, often associated with ataxia or clumsiness; seizure

Management of Toxicity

- Discontinuation of Vitamin B₆ leads to resolution of symptoms. Total recovery can take months.

Laboratory Tests : Serum pyridoxine level (above 20ng/mL), neurological testing.

E. Vitamin B₃ (Niacin)

Toxicity

- Acute ingestion of more than 100mg may cause dermal flushing.

Clinical Features

- Cutaneous flushing, pruritus, wheezing. Chronic large doses lead to hepatotoxicity.

Management of Toxicity

- Symptomatic treatment of sensitivity reactions with oral or intramuscular diphenhydramine.

F. Vitamin C**Toxicity**

- Toxicity of water-soluble vitamin C is rare. In a single case, a man given an IV dose of 45g suffered from acute renal failure and death. Nephropathy has occurred with chronic ingestion of >4g/day and acute IV administration of 1.5g.

Clinical Features

- Diarrhoea with amounts up to 10g or more daily.

Management of Toxicity

- Treatment of effects of diarrhoea eg. dehydration.

11.2 Iron Preparations

Toxicity

- Ingestion of 20-60mg/kg of elemental iron is potentially toxic.
- Fatalities have occurred following paediatric ingestions of 1200 to 4500 mg of elemental iron. The lowest reported lethal dose in an adult is 2g of elemental iron with delayed deferoxamine treatment.
- Normal serum values range from 50 to 175µg/dL, peak levels of < 350µg/dL are not considered toxic; toxic serum iron level is > 500µg/dL.

Clinical Features

GI system	Nausea, vomiting, diarrhoea and haemorrhagic necrosis
CVS system	Tachycardia, hypotension, circulatory collapse and cardiac failure
Respiratory	Pulmonary oedema
Metabolic	Acidosis, hyperglycaemia
Hepatic	Necrosis
Genitourinary	Renal failure
Neurologic	Lethargy, restlessness or confusion, convulsions and coma may occur in later phases

The clinical effects of serious iron poisoning have been described as appearing in phases :

- Phase I (0.5-2hrs) includes vomiting, haematemesis, abdominal pain, diarrhoea, haematochezia, lethargy, shock, acidosis and coagulopathy. Necrosis to the GI tract occurs from direct effect of iron on GI mucosa.
- Phase II (after Phase I) includes a period of apparent recovery and may give a false sense of security. Observe closely.
- Phase III (2-24 hours after Phase I) includes profound shock, severe acidosis, cyanosis, fever, worsening of GI haemorrhage, severe lethargy, coagulation defects, renal insufficiency secondary to poor perfusion.

- Phase IV (2 to 4 days) includes possible hepatotoxicity.
- Phase V (days to weeks) includes GI scarring and strictures.

Management of Toxicity

- Maintain airway and circulation.
- Treat shock with IV crystalloid fluids and replace blood if needed, place patient in Trendelenburg position. If unresponsive, administer dopamine or norepinephrine.
- Correct electrolyte balance.
- Perform gastric lavage for patient with recent ingestion of 20mg/kg or more OR symptomatic patient. Ipecac emesis is controversial but may be indicated in recent substantial ingestions (most effective if initiated within 30 min of ingestion).
- IV Deferoxamine is indicated if :
 - free serum iron is present;
 - patient is symptomatic and a serum iron cannot be readily obtained;
 - peak serum iron exceeds 350-500µg/dL.
 - The recommended dose is continuous IV infusion of up to 15mg/kg /hr with the maximum daily dose up to 80mg/kg. The total duration of therapy has not been established, however, the generally accepted recommendations include continuation of desferoxamine until :
 - (a) 24 hours after the patient's urine has turned clear
 - (b) Serum iron falls to <100µg/dL
 - (c) Patient is asymptomatic.
- Correct coagulopathy, treat coma, seizures and metabolic acidosis if they occur.

Antidotes : Deferoxamine. See pg 100.

Laboratory Tests : Obtain FBC, electrolytes, blood sugar, serum iron (at 2-hour intervals for the first 6-8 hours; serum electrolytes), arterial blood gases and bicarbonate level (important in assessing metabolic acidosis) and abdominal radiograph (to reveal tablet or diffuse densities within the gut). Perform liver function test, obtain transaminases, bilirubin and coagulation profiles to detect liver abnormalities. Baseline PT, PTT and LFT's should be obtained in severe overdoses.

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S E C T I O N **C**

**HOUSEHOLD, INDUSTRIAL AND
METALLIC POISONING**

CHAPTER 1

Household Chemicals

1.1 Anticoagulant Rodenticides

In Singapore, all household rodenticides that are available for sale in local retail stores and supermarkets are anticoagulants. Other types of rodenticides are available for use under licence only.

Table 1. Commonly sold anticoagulant rodenticides

Common Name	Synonymous/Trade name
Coumatetralyl	Racumin, Endox Endrocid
Warfarin	Warf, Dethmor, Warfat, Dethnel, Rosex, Sifar, d-CON, Rattunal, Mar-Frin, Ratorex, Coumatene, Zoocoumarin, Kypfarin, Warficide, Tox-Hid, Sorexa-Plus, Biotrol
Prolin	Banarat, Final, Erazze, Warfarin-S
Coumarfuryl	Fumarin, Ratafin, Fumasol, Krumkil, Rat-A-Way, Tomarin Lurat
Coumachlor	Tomorin, Ratilan
Brodifacoum	Talon, PP-581, Volak, Klerat, Havoc, Volid, Matikus
Difenacoum	Ratak, Neosorexa

Toxicity

All these compounds inhibit hepatic synthesis of vitamin K. The toxic dose is highly variable. Single small doses of these compounds will not cause serious intoxication, as most of the preparations found in the market contain only small amounts of active ingredient.

Clinical Features:

Epistaxis, intraocular bleeding, haemoptysis, bleeding gums, blood in urine and faeces, occasional paralysis due to cerebral haemorrhage

Management of Toxicity:

- Administer activated charcoal and a cathartic. Gastric emptying is not necessary if activated charcoal can be given promptly. These measures are not effective beyond 4 hours post-ingestion.
- Oral cholestyramine can be used as an alternative to activated charcoal. Dosage: 4g 3 times daily for 10 days.
- Provide symptomatic and supportive treatment.

Antidote: Slow IV or SC phytonadione 0.1mg/kg. Fresh whole blood in serious cases. See pg 138.

Laboratory tests: Prothrombin time (PT), FBC. Anticoagulant levels in blood are not available.

1.2 Boric Acid and Borates

Boric acid and borates are used in baby talcum powders, anti-cockroach/ant products, eye washes, and laundry soaps.

Toxicity

Acts as cellular poison. They concentrate in tissues such as kidneys and cause problems there.

Points to note

- chronic exposure carry a high mortality rate in infants and children.
- dermatologic manifestations may take 3-5 days to fully develop.

Fatal oral dose : 0.1g to 0.5g/kg

Toxic dose : Highly variable, but serious poisoning could occur with as little as 5g ingestions.

Note : About 50% of the amount absorbed is excreted in the urine within 12 hours; the remaining is excreted over 5 to 7 days.

Normal blood level : < 5mg/l

Clinical Features

- Vomiting, diarrhoea (emesis & diarrhoea may have a blue green colour), hyperpyrexia, jaundice, erythematous (boiled lobster) rash, blistering, desquamation, excoriation seen especially on palms, soles and buttocks, exfoliative rash, nausea, convulsions, tremors, lethargy, weakness, CNS depression, collapse, coma, renal failure, cardiovascular collapse.

Management of Toxicity

- Maintain airway and assist ventilation if necessary.
- Treat coma, convulsions, hypotension and renal failure if they occur
- Induce emesis or perform gastric lavage for large ingestions.
- Administer activated charcoal.
- Elimination of boric acid or borates from the blood can be enhanced by haemodialysis.

Antidotes : none

Laboratory tests : Useful to do FBC, electrolytes, glucose, BUN, creatinine, urinalysis.

Note: Serum boric acid levels may not correlate accurately with the severity of intoxication.

1.3 Carbon Tetrachloride

Carbon tetrachloride is found in degreasers, spot removers, fire extinguishers, and dry cleaning solvent. However, its usage has been curtailed due to hepatotoxicity and carcinogenicity.

Toxicity

Carbon tetrachloride is a central nervous system depressant and a potent hepatic and renal toxin.

Fatal oral dose : 3 to 5ml

Toxic dose : An air level of 300 ppm is immediately dangerous to life.

Note : Toxicity may arise from inhalation or absorption through skin.

Clinical Features

Nausea, vomiting, abdominal pain, headache, visual disturbances, dizziness and confusion. Also coma, cardiac arrhythmias, renal and hepatic damage, if exposed to large amounts of carbon tetrachloride

Management of Toxicity

Inhalation

- remove from exposure and give oxygen.

Skin

- remove contaminated clothing and wash affected skin with large amounts of soap and water.

Eye

- irrigate exposed eye with normal saline or water.

Ingestion

- perform gastric lavage.
- do NOT induce emesis.
- administer activated charcoal and cathartic.

General

- maintain airway and assist ventilation.
- treat coma, and arrhythmias if they occur.
- provide symptomatic and supportive treatment.
- there is no role for enhanced removal procedures.

Antidotes : No specific antidote available. However acetylcysteine injection could be used to minimise the hepatic and renal toxicity of carbon tetrachloride. If possible it should be given within 12 hours after exposure. See pg 89.

Laboratory tests : Useful to do FBC, electrolytes, glucose, BUN, creatinine, LFT, prothrombin time, ECG.

1.4 Chlorates

The usual forms of chlorates are sodium chlorate, potassium chlorate, and barium chlorate. They are found in:

- match heads (20 wooden matches contain 330mg, 2 books of paper matches contain 220mg)
- fireworks, weedkillers, gargles and mouth washes

Toxicity

Chlorates are oxidising agents that can cause haemolysis with methaemoglobin; they are also nephrotoxic.

Fatal oral dose : 7.5 - 35g (Adults). 2g (Children).

Clinical Features

- Abdominal pain, vomiting, diarrhoea, haemolysis, methaemoglobinaemia, renal failure, confusion, convulsions

Management of Toxicity

- Maintain airway and assist ventilation if necessary
- Treat coma, hyperkalaemia, and renal or hepatic failure if they occur
- Treat haemolysis
- Induce emesis or perform gastric lavage for large ingestions.
- Give milk to relieve gastric irritation
- Administer activated charcoal and cathartic
- Haemodialysis if there is renal insufficiency

Antidotes: methylene blue injection 1-2mg/kg (0.1-0.2ml/kg of a 1% solution for methaemoglobinaemia. See pg 123.

Laboratory tests : useful to do FBC, plasma free haemoglobin, electrolytes, glucose, BUN, creatinine, methaemoglobin level, LFT, prothrombin time, urinalysis.

1.5 Detergents

Detergents are synthetic surface active agents classified as:

- anionic/nonionic type (used in soap powders, shampoo, bar soap and liquid detergents).
- cationic type (used in antiseptic and disinfectant products, fabric softeners).

Many such products may contain bleaching agents, anti-bacterial or enzymatic agents.

1.5.1 Anionic/Nonionic Detergents

Toxicity

- Anionic/nonionic detergents are only mildly irritating.
- Cationic detergents may be caustic and more hazardous.
- Fatal dose: No information available.
- Mortality and morbidity are rare.

Clinical Features

- Nausea, vomiting, diarrhoea, intestinal distension
- Rarely, dehydration and electrolyte abnormalities.

Management of Toxicity

- Give oral fluids in small amounts, allow vomiting to occur.
- Administer IV fluids to correct dehydration and electrolyte imbalance if necessary.
- If corrosive injury is suspected, consult a gastroenterologist for possible endoscopy.
- If symptomatic hypocalcaemia occurs administer IV calcium
- Activated charcoal is ineffective.

Antidotes : None.

Laboratory tests :

- There are no specific blood or urine levels.
- It is useful to perform FBC and test for electrolytes, glucose, calcium & phosphate (after ingestion of phosphate-containing products).

1.5.2 Cationic Detergents

Table 2. Common cationic detergents

Pyridinium compounds	Cetalkonium chloride Cetrimide Cetrimonium bromide Cetylpyridinium chloride Stearalkonium chloride
Quaternary ammonium compounds	Benzalkonium chloride Benzethonium chloride
Quinolinium compounds	Dequalinium chloride

Toxicity

Deaths have been reported with doses of between 30mg/kg to 400mg/kg depending on which cationic detergent was ingested.

Clinical Features

- Corrosive burns of mouth, pharynx and oesophagus.
- Nausea, vomiting, diarrhoea, pulmonary oedema, hypotension, metabolic acidosis, CNS depression, convulsions

Management of Toxicity

- Maintain airway
- Administer milk or water to dilute
- Administer activated charcoal followed by cathartic .
- Do not perform gastric lavage or emesis because of corrosive effects.

- If methaemoglobin occurs, administer methylene blue.
- Monitor and treat seizures, hypotension, pulmonary oedema
- If corrosive injury is suspected, consult a gastroenterologist for endoscopy
- Dialysis and diuresis are not effective

Antidote: None

Laboratory test :

- There are no specific blood or urine levels.
- It is useful to perform FBC and test for electrolytes, glucose, calcium & phosphate (after ingestion of phosphate-containing products).

1.6 Hydrogen Peroxide

Hydrogen peroxide is an oxidising agent used in mouth washes, bleaching solutions, antiseptics, and hair bleach

Nomenclature: 10 volumes hydrogen peroxide is equivalent to 3% v/v hydrogen peroxide. (i.e 1 volume is about 0.3%v/v)

Toxicity

It is an oxidising agent which breaks down to oxygen and water.

Points to note:

- most ingestions of household strength (3 to 5%) hydrogen peroxide e.g. antiseptic or mouth washes are benign and mild irritation is self limited.
- ingestion of solutions with concentrations above 5% are potentially corrosive.
- vapours are irritating to the eyes, nose and throat

Fatal oral dose : 1.5 g/kg (30% soln)

Toxic dose : up to 5% strength, low toxicity; higher strengths are corrosive.

Clinical Features

A. Household Strengths (3 to 5%)

- vomiting and diarrhoea are common after ingestion.
- mild irritation to mucous membrane and skin

B. High (Industrial) Strength (over 5%)

Ingestion or contact

- severe burns to mucous membranes, skin, eyes and gastrointestinal mucosa, coma, seizures, gas embolisation, shock and cardiac arrest
- the patient may complain of a stinging sensation accompanied by whitening of skin
- prolonged contact may result in slow-healing burns

Inhalation

- severe mucous membrane irritation & inflammation, pulmonary oedema, shock, coma & seizures

Management of Toxicity**A. Household Strengths (3 to 5%)**

- Give water to dilute, if ingested. Activated charcoal and cathartics are not effective.
- Irrigate eyes & skin with copious amounts of water. Remove contaminated clothing.

B. High (Industrial) Strength (over 5%)

- Avoid emesis.
- Monitor airway for swelling and intubation, if necessary.
- Monitor patient for seizure, burns to gastrointestinal tract, ruptured colon, gas embolisation.
- Monitor for respiratory distress (after inhalation)
- Irrigate eyes and skin with copious amounts of water.
- Tissue injuries from severe burns are treated as thermal or chemical burns

Antidotes: None.

Laboratory tests : Blood gases, electrolytes and ECG may be useful.

1.7 Naphthalene

Naphthalene is found in mothballs, toilet bowl fresheners, insecticides, and air fresheners.

Toxicity

It causes gastrointestinal upset and may cause central nervous system stimulation.

Note: It may produce haemolysis, especially in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Fatal oral dose : 50-100mg/kg body weight.

Toxic dose : Less than one naphthalene ball (200-500mg) may cause haemolysis especially in G6PD deficient children.

Clinical Features

- On ingestion, nausea, vomiting and diarrhoea are common. Some hours later, oliguria, dysuria and haematuria. Later, anaemia and jaundice from haemolysis especially in G6PD deficient individuals.
- On ingestion of large amounts, excitement, convulsions and coma may occur.
- On inhalation of fumes of boiling naphthalene, headache, confusion, nausea, vomiting, extensive sweating and visual disturbances may occur.
- Occasionally dermatitis, corneal irritation and lens opacity.

Note : Characteristic mothball smell around the mouth and vomitus.

Management of Toxicity

- Maintain airway and assist ventilation if necessary.
- Treat coma and seizures if they occur.
- Treat haemolysis and resulting haemoglobinuria if they occur, by intravenous hydration and urinary alkalinisation.
- Perform gastric lavage for recent, large ingestions

- Treat methaemoglobinaemia with methylene blue.
- Administer activated charcoal and cathartic.
- Haemodialysis is not routinely recommended but may be needed for supportive care.
- Withhold fatty foods

Antidotes : none

Laboratory tests

- FBC, blood gases, electrolytes and ECG
- If haemolysis suspected, check for haptoglobin, free haemoglobin, and urine haemoglobin.
- Blood levels of naphthalene are not available

1.8 Oxalic Acid and its Salts

Oxalic acid is found in bleaches, metal cleaners and rust removers.

Toxicity

- Oxalic acid solutions are highly irritating and corrosive.
- Ingestion and absorption of oxalate causes acute hypocalcaemia resulting from precipitation of the insoluble calcium oxalate salt.
- Calcium oxalate crystals may deposit in the brain, heart, kidneys and other sites, causing serious systemic damage.

Fatal oral dose : 5 to 15g (adult) (oxalic acid)

Clinical Features

Nausea, vomiting, weakness, tetany, convulsions, cardiac arrest due to hypocalcaemia, corrosion of pharynx and oesophagus, renal failure

Management of Toxicity

- Protect airway, administer oxygen and assist ventilation
- Treat coma, seizures, arrhythmias, if they occur.
- Monitor ECG and vital signs for at least 6 hours after exposure.
- Do NOT induce emesis.
- Administer orally calcium gluconate or lactate or carbonate (150mg/kg body weight) to precipitate the ingested oxalate in the stomach.
- Maintain high volume urine flow to help prevent calcium oxalate precipitation in the tubules.
- Treat symptomatic hypocalcaemia with 10% calcium chloride or gluconate.
- Monitor patient for at least 6 - 8 hrs after ingestion

Antidotes : calcium chloride or gluconate. See pg 94.

Laboratory tests : FBC, electrolytes, glucose, BUN, creatinine, calcium, urinalysis and ECG monitoring.

1.9 Paradichlorobenzene

Paradichlorobenzene is found in mothballs and toilet bowl fresheners. It is less toxic than naphthalene and has been used to replace naphthalene in mothballs and related products.

Toxicity

- It causes gastrointestinal upset and may cause central nervous system depression.
- The vapour can cause irritation to the skin, eyes and throat.

Toxicity is low. Up to 20g ingestions have been well tolerated in adults.

Clinical Features

Nausea, vomiting, diarrhoea, abdominal pain, anaemia and methaemoglobinaemia (rare)

Management of Toxicity

- Maintain airway and assist ventilation if necessary.
- Gastric lavage and activated charcoal are not necessary unless a massive dose has been ingested
- Other enhanced elimination techniques play no role

Note: Withhold fatty foods, oils, milk for several hours post ingestion to minimise absorption.

Antidotes : none

Laboratory tests : Useful to do FBC, electrolytes, glucose, BUN, creatinine, calcium, ECG, urinalysis

1.10 Phenol and Related Compounds

Phenol (carbolic acid) and related compounds (such as creosote, creosol, hydroquinone, eugenol and dinitrophenol) are found in antiseptics, disinfectants, local anaesthetics.

Phenol is obtained from coal tar; lysol and creosol are mixtures of phenolic compounds and other compounds obtained by the destructive distillation of wood or coal.

Toxicity

Phenol denatures protein and penetrates tissues well. It is a potent irritant that may cause corrosive injury to eyes, skin and respiratory tract. Systemic absorption causes central nervous system stimulation.

Fatal oral dose : adults - 2g or less for phenol and creosol
infants - 50 to 500mg

Toxic dose : not available

Urine phenol level : < 20 mg/L (normal)

Clinical Features

Contact

- skin becomes white, then turns red and finally brown.
- ocular burns.

Ingestion

- nausea, vomiting, bloody diarrhoea, abdominal cramps, burning pain in mouth and throat, profuse sweating, cyanosis, CNS stimulation, hypersensitivity, convulsions, followed by depression of CNS and stupor, hypotension, pulmonary oedema, pneumonia, oesophageal stricture, haemolysis, methaemoglobinemia, jaundice, renal failure.

Management of Toxicity

Ingestion

- gastric lavage is contraindicated in the presence of oesophageal injury.
- do **NOT** induce emesis
- administer activated charcoal and cathartic
- do not dilute with liquids
- maintain airway and assist ventilation if necessary
- treat coma, seizures, hypotension, and arrhythmias if they occur.
- treat methaemoglobinaemia with methylene blue.

Contact

- wash skin with copious amounts of water for at least 15 minutes and apply olive oil or mineral oil.
- flush eyes with copious amounts of water or saline.

Antidotes : none

Laboratory tests : FBC, electrolytes, glucose, BUN, creatinine, and ECG

1.11 Sodium Hypochlorite

Sodium hypochlorite is used as household bleach, and in deodorisers and disinfectants. Its action is due to the presence of chlorine. Household bleach contains 3-5 %v/v sodium hypochlorite, while swimming pool and industrial strength cleaners contain up to 20%v/v.

Toxicity

Sodium hypochlorite has corrosive actions, especially at higher strengths.

Household strength bleach causes burning in mouth and throat but no serious injury. However higher strengths cause severe injury.

Clinical Features

Inhalation

- burning of eyes, nose, throat, coughing, pulmonary oedema.

Ingestion

- burning of mouth, throat, oesophageal and gastric burns, dysphagia, drooling, throat, chest, abdominal pain, vomiting, oedema of mouth and pharynx, hypotension, delirium, coma

Contact

- burning of eyes, skin irritation.

Management of Toxicity

Inhalation

- give humidified oxygen
- intubate the trachea if there is upper airway obstruction
- administer bronchodilators for wheezing
- treat pulmonary oedema

Ingestion

- do NOT induce emesis,

- do **NOT** use activated charcoal
- do **NOT** use acidic antidotes
- give water or milk to dilute
- perform gastric lavage after concentrated liquid ingestion
- perform endoscopy to evaluate serious oesophageal or gastric injury
- perform a chest X-ray to look for mediastinal air which suggests oesophageal perforation.

Contact

- flush with copious amounts of water
- irrigate eyes with water or saline

Antidotes : None

Laboratory tests : FBC, electrolytes, arterial blood gas, chest and abdominal X-rays.

1.12 Turpentine

Turpentine, an oleoresin derived from plant, is found in paints, waxes and polishes, deodorisers and liniments.

Toxicity

Turpentine is a central nervous stimulant and can cause seizures after ingestion. Death is usually due to respiratory failure

Fatal oral dose : 140ml (Adult).

Toxic oral dose : 15ml (Child).

Clinical Features

Ingestion

- burning, abdominal pain, vomiting, diarrhoea, tachycardia, dyspnoea, cyanosis, fever, excitement, seizures, coma, respiratory failure.

Inhalation

- irritation to mucous membrane, hyperpnea, vertigo, tachycardia, seizures.

Management of Toxicity

Ingestion

- Maintain airway and assist ventilation if necessary.
- Support cardiovascular function.
- Gastric lavage if large ingestion
- Monitor for aspiration and treat if necessary.
- Administer activated charcoal as soon as the gastric tube is placed.

Laboratory tests : FBC, electrolytes, glucose, arterial blood gases (if patient is comatose or in status epilepticus).

1.13 Paraquat and Diquat

Paraquat and diquat are herbicides used primarily for weed control.

Toxicity

Both are extremely toxic, although diquat is less so.

Clinical Features

Nausea, vomiting, abdominal pain. Renal failure, pulmonary fibrosis, massive gastroenteritis, pulmonary oedema and cardiogenic shock.

Management of Toxicity

- Maintain airway and assist ventilation, avoid excessive oxygen supplementation in paraquat poisoning.
- Perform gastric lavage, give activated charcoal. Bentonite 7%, 200mL every 2 hourly for 24 hours may be used instead of charcoal.
- Early haemoperfusion (within 4 hours) may be useful.

Antidotes : None

Laboratory tests : Paraquat serum levels, electrolytes, glucose, urinalysis, chest x-rays, arterial blood gases.

CHAPTER 2

Industrial Poisons

2.1 Acids and Acid-Related Corrosives

A variety of acid and acid-like chemicals are used for various purposes. The common ones are listed in Table 1.

Toxicity

Ingestion of 1 mL of corrosive acid may cause death. Acids destroy tissues by direct chemical action. The tissue protein is converted to acid proteinate. The estimated fatal doses of some of these compounds are listed in Table 1.

Clinical Features

Inhalation

- Acids readily dissolve fluids of mucous membrane and lung tissue to produce inflammation leading to:
 - acute chemical pneumonitis, pulmonary oedema manifested by cough, chest pain, cyanosis, dyspnoea, haemoptysis; blood pressure may be high or low
 - chronic cough with bronchopneumonia

Ingestion

- corrosive burns of the oropharynx, oesophagus and stomach accompanied by burning pain, vomiting with or without blood, fever, rigid abdomen, stricture of pylorus and oesophagus
- oxalate ingestion may also produce convulsions, respiratory collapse and renal stones with or without anuria

Contact

- skin: severe pain and brownish or yellowish stains
- eyes: conjunctival oedema and corneal destruction, pain and tearing

Management of Toxicity*Inhalation*

- maintain respiration
- treat shock with infusion fluids
- treat pulmonary oedema
 - decrease respiratory rate with IM morphine 10 mg
 - give oxygen
 - IV infusion, aminophylline 250-500 mg for bronchoconstriction
 - reduce oedema with oral or IV frusemide 20 - 80 mg
- treat pneumonia with antibiotics

Ingestion

- give water or milk (120 mL to 240 mL in adults; 60 mL to 120 mL in children); for oxalic acid, give milk, calcium lactate or calcium carbonate to precipitate oxalate
- avoid emesis and gastric lavage
- if perforation is suspected, give Nil By Mouth until endoscopic examination.
- treat asphyxia
- treat shock - maintain BP by infusion fluids
- reduce pain with morphine 5 - 10 mg 4 H prn
- in oxalic acid poisoning, give fluids up to 4 L daily to prevent precipitation of oxalate stones in renal tubules

Contact

- eye contact
 - flood eye with running water for 15 minutes
 - relieve pain with analgesic, bandage and refer to ophthalmologist
- skin contact
 - flood area with running water for 15 minutes
 - relieve pain with analgesic and treat burns

Antidote : Do not use chemical antidote eg. bicarbonates

Laboratory Tests : FBC, electrolytes, glucose, arterial blood gases, chest X-ray, abdominal X-ray

Table 1. Toxicity level of acids and acid-related corrosives

Name	Estimated fatal dose (g or mL)	Corrosive effect
Acetic acid	5	3 (>10%)
Acetic anhydride	5	3
Acetyl chloride	1	4
Acrylic acid	5	3
Amyltrichlorocyclane	1	4
Benzyl chloride	1	4
Benzotrighloride	1	4
Bromine	1	4
Calcium chloride	-	1
Chlorine	-	4
Chlorine dioxide	-	4
Chloroacetylchloride	1	4
Chlorosulfonic acid	1	4
Dibutylphosphate	10	2
2, 2 Dichloropropionic acid	1	4
Ethylchlorocarbonate	1	4
Formic acid	30	2
Furoyl chloride	1	4
Hydriodic acid	1	4
Hydrobromic acid	1	4
Hydrochloric acid	1	4
Hydrofluoric acid	15	4 (>10%)
Hydrogen bromate	1	4
Hydrogen iodate	1	4
Lactic acid	1	4
Maleic anhydride	10	2
Methacrylic acid	10	3
Methyl silicate	1	4
Methyltrichlorosilane	1	4
Oleum	-	-
Osmic acid	1	4

Table 1. (Cont'd)

Name	Estimated fatal dose (g or mL)	Corrosive effect
Oxalic acid	5-15	4 (>10%)
Peracetic acid	1	4
Perchloric acid	1	4
Phenylmagnesium chloride	5	3
Phosphoric acid	1	4
Phosphorus pentachloride	1	4
Phosphorus pentafluoride	-	-
Phosphorus trichloride	1	4
Phthalic anhydride	1	3
Propionic acid	30	2
Sulphuric acid	1	-
Sulfamic acid	5	3
Sulfosalicylic acid	10	3
Tartaric acid	30	1
Thioglycolic acid	1	3
Titanium tetrachloride	1	4
Trichloroacetic acid	1	4

Legend : (for corrosive effect)

- 1 Mild irritation and reddening. Cough
- 2 Strong irritation and erythema, blistering
- 3 Superficial destruction of skin or mucous membrane
- 4 Complete destruction of skin or mucous membrane

2.2 Alcohols and Glycols

Ethanol

Ethanol is used as a solvent, an antiseptic, a beverage and in a variety of chemical synthesis. It is commonly found in alcoholic beverages, colognes, perfumes, mouthwashes, food flavourings and pharmaceutical preparations.

Toxicity

A central nervous depressant, the fatal oral dose for adults is 300 - 400 mL in 1 hr; for children, 3 g / kg. Toxic blood level is 300 - 500 mg / dL.

Clinical Features

CNS depression, marked muscular incoordination, blurred, double vision, hypothermia, hypoglycaemia, rigidity, convulsion, slow respiration, unconsciousness, death

Management of Toxicity

- If ingestion was recent (within 30 - 45 minutes), ipecac emesis or gastric lavage or activated charcoal may be attempted.
- Protect and maintain adequate airway
- Give glucose and thiamine. See pg 136 & 118.
- Maintain body temperature, treat coma and seizures
- IV infusion dextrose 5% if hypoglycaemic
- Perform haemodialysis if blood ethanol level above 500 mg / dL
- Avoid depressant drugs

Antidote: slow IV naloxone 2-5 mg. Naloxone may antagonise the depressant effects following acute ethanol overdose.

Laboratory Tests: ethanol level, glucose, electrolytes, BUN, creatinine, liver transaminases, arterial blood gases, magnesium.

Ethylene Glycol

Ethylene glycol is the main ingredient found in antifreeze.

Toxicity

Ethylene glycol is metabolised to glycolic, glyoxylic and oxalic acids. Tissue injury is caused by these chemicals. Fatal oral dose for adults is 100 mL. Serum levels higher than 50 mg / dL are associated with serious intoxication.

Clinical Features

Nausea, vomiting, headache, coma, convulsions, ophthalmoplegia, depressed reflexes, acidosis, hypocalcaemia, tachycardia, pulmonary oedema, bronchopneumonia, cardiac failure

Management of Toxicity

- Maintain airway, treat coma, convulsions, arrhythmias and metabolic acidosis if they occur
- Perform gastric lavage as quickly as possible.
- Administer IV or IM pyridoxine 50 mg every 6 hours, IV folic acid 50 mg every 4 hours (for 6 doses) and slow IV or IM thiamine 100 mg every 6 hours.
- Correct acidosis: IV infusion sod bicarbonate 4.2%
- Give IV infusion of calcium gluconate 10% 10 ml in dextrose 5% 1 L for hypocalcaemia
- Give fluids up to 4 L or more to increase glycol excretion
- Give a slow IV infusion of dextrose 5% if hypoglycaemic
- Give slow IV diazepam 10 mg for convulsions
- Perform haemodialysis
- Avoid CNS depressant drugs

Antidote: Administer ethanol to saturate the enzyme alcohol dehydrogenase and prevent metabolism of ethylene glycol to its toxic metabolites. See pg 113.

Laboratory Tests: ethylene glycol level, electrolytes, glucose, BUN, urinalysis, serum osmolality and osmolar gap, creatinine, calcium, hepatic transaminases, arterial blood gases, ECG monitoring.

Isopropyl Alcohol

Isopropyl alcohol is widely used as a solvent, an antiseptic, a disinfectant, and as rubbing alcohol (70% solution).

Toxicity

A central nervous system depressant, ingestion or inhalation may lead to coma and respiratory arrest. Fatal ingestion dose for adults is 250 mL.

Clinical Features

Marked muscular incoordination, dizziness, nausea, vomiting, gastric haemorrhage, headache, confusion, hypothermia, circulatory collapse, stupor, coma, respiratory failure

Management of Toxicity

- Maintain airway, treat coma, hypotension if they occur
- Perform gastric lavage for large ingestions and give activated charcoal
- Maintain body temperature
- Give an IV infusion of dextrose 5% if hypoglycaemic. See pg 118.
- Perform haemodialysis if blood isopropyl alcohol level above 500 mg / dL; avoid depressant drugs.

Antidote: there is no specific antidote

Laboratory Tests: isopropyl alcohol level, electrolytes, glucose, BUN, creatinine, arterial blood gases

Methanol

Methanol is used as a solvent, a denaturant, a paint remover and in a variety of chemical synthesis.

Toxicity

Methanol is metabolised to formaldehyde and subsequently to formic acid. These metabolites may cause metabolic acidosis, blindness and death. The fatal dose of methanol is estimated to be 60 - 250 ml. Toxic blood level varies; concentrations higher than 20 mg / dL should be considered toxic.

Clinical Features

Fatigue, nausea, vomiting, headache, CNS depression, blurred vision, dilated pupils, blindness, acidosis, cyanosis, fall in BP, coma, respiratory failure, death. Severe symptoms usually present after a latent period of up to 18-24 hours.

Management of Toxicity

- Maintain airway, treat coma and seizures, if they occur
- Perform gastric lavage
- Treat acidosis with IV infusion sodium bicarbonate 4.2%
- Maintain adequate urine output with 4 L fluids daily
- Control delirium by slow IV diazepam 10 mg
- Perform haemodialysis if no response to above, or if blood methanol exceeds 50 mg / dL

Antidote: administer ethanol to saturate the enzyme alcohol dehydrogenase and prevent the formation of methanol's toxic metabolites. See pg 113. Folic acid may enhance conversion of formic acid to carbon dioxide. See pg 116.

Laboratory Tests: methanol level, ethanol level, lactate level, electrolytes, glucose, BUN, creatinine, arterial blood gases, serum osmolality and osmolar gap.

2.3 Alkalis and Other Alkali-Related Corrosives

A variety of alkali agents are used for various purposes. The common ones are listed in Table 2.

They are commonly used in the manufacture of soaps and cleansers and in chemical synthesis.

Toxicity

Alkali agents cause corrosive injury by reaction with protein and fat in the tissue producing necrotic, deeply penetrating damage. There is no specific toxic dose or level, because the concentration of corrosive solutions potency of caustic effect vary widely.

Clinical Features

Inhalation

- irritation, inflammation of respiratory tract and eyes, swelling of lips, conjunctiva, temporary blindness, tightness in chest, swelling, pulmonary oedema, cyanosis, rapid weak pulse

Ingestion

- severe pain, bloody vomitus, diarrhoea, collapse
- patient may improve for 2 - 4 days, then suffer pain and rigidity with rapid fall in BP (GIT perforation)
- oesophageal stricture may occur weeks to months later

Contact

- skin: alkali penetrates slowly; prolonged contact causes pain and burns
- eye: conjunctival oedema, corneal destruction, blindness

Management of Toxicity

Inhalation

- maintain airway
- treat shock with infusion fluids
- treat pulmonary oedema
- decrease respiratory rate with IM morphine
- give oxygen
- IV aminophylline 250-500 mg for bronchoconstriction
- reduce oedema with oral or IV furosemide 20 mg
- treat pneumonia with antibiotics

Ingestion

- give small quantities of water or milk to dilute alkali (<250 mL in adults, <180 mL in children)
- avoid emesis and gastric lavage
- perform oesophagoscopy as soon as possible; give Nil By Mouth until oesophagoscopy has been done
- treat metabolic alkalosis

Contact

- eye contact: flood eye with running water for 15 mins; irrigate with normal saline for 30 - 60 mins. Relieve pain with analgesics, bandage and refer to ophthalmologist
- skin contact: flood with running water until skin is free of soapiness; treat burns if any

Antidote: in most cases, there is no specific antidote; for phosphate ingestion, treat hypocalcaemia with slow IV calcium gluconate 10%, 5 ml

Laboratory Tests: check for specific chemical test with laboratory; other useful laboratory tests - FBC, electrolytes, glucose, arterial blood gases, chest X-ray, abdominal X-ray

Table 2. Toxicity level of alkalis and basic compounds

Name	Estimated fatal dose (g or mL)	Corrosive effect
2-Aminobutane	10	2
2-Aminopropane	10	2
Ammonium hydroxide 25%	30	-
Butylamine	20	3
Calcium chloride	-	2
Calcium hydroxide	-	2
Calcium oxide	-	3
Cement	60	3
Cesium hydroxide	15	2
Cyclohexylamine	30	2
2-N-Dibutyl aminoethanol	30	2
Diethanolamine	20	2
Diethylamine	20	2
Diethylaminoethanol	20	2
Diethylene triamine	20	2
Diisopropylamine	20	2
Dimethylamine	10	2
Ethanolamine	50	2
Ethylamine	20	2
Ethylenediamine	10	2
Isopropylamine	20	2
Lithium hydride	5	4
Lithium hydroxide	5	4
Methylamine	50	1
Potassium carbonate	20	3
Potassium hydroxide	5	4
Sodium bicarbonate	30	3
Sodium hydroxide	5	4
Sodium phosphate	50	2
Sodium silicate	50	2
Tetrasodium pyrophosphate	50	2
Triethanolamine	50	2
Triethylamine	20	2
Tri(hydroxymethyl)-aminomethane	50	1

Legend : (for corrosive effect)

- 1 Mild irritation and reddening
- 2 Strong irritation and erythema, blistering
- 3 Superficial destruction of skin or mucous membrane
- 4 Complete destruction of skin or mucous membrane

2.4 Carbon Disulphides

Carbon disulphide is used mainly as a solvent.

Commonly used: solvents for waxes and resins, grease remover, disinfectant, insecticide

Toxicity

Exposure to carbon disulphide at concentrations of 60 to 100 ppm causes toxic symptoms. Ingestion of 0.5-5 g/kg is fatal.

Clinical Features

Inhalation

- restlessness, irritation of mucous membrane, blurred vision, nausea, vomiting, headache, unconsciousness and paralysis of respiration

Ingestion

- vomiting, headache, cyanosis, respiratory depression, fall of BP, loss of consciousness, tremors, convulsions, death

Contact

- reddening and burning, cracking and peeling of skin, 2nd degree burn if liquid remains in contact with skin for several minutes

Management of Toxicity

Inhalation

- remove patient to fresh air
- give artificial respiration with oxygen

Ingestion

- maintain airway, treat seizures if they occur
- perform gastric lavage
- administer activated charcoal
- IV or oral pyridoxine 25 mg / kg

Antidote: Pyridoxine, 25 mg / kg IV can also be used as a sulphide acceptor

Laboratory Tests: blood level not available; FBC, electrolytes, glucose, arterial blood gases, chest X-ray

2.5 Corrosive Gases and Oxidising Agents

Boron Trichloride

Boron trichloride is a general chemical agent commonly used in chemical processes.

Toxicity

Information not available

Clinical Features

Hydrolysis of the liquid produces hydrochloric acid fumes which upon inhalation will result in oedema and irritation of the upper respiratory tract

Management of Toxicity

- If lungs are affected, give antibiotics prophylactically.
- Rest is important
- Observe for pulmonary oedema

Antidote: no specific antidote

Laboratory tests: no specific blood level available; electrolytes, arterial blood gases, chest X-ray

Corrosive Gases

The common corrosive gases are chlorine, nitrogen oxides, sulphur oxides. They are used as general chemical agents.

Toxicity

These are oxidising agents that form strong acids when dissolved in mucous fluids but all of them produce an inflammatory reaction of the respiratory tract when inhaled. Fatal dose for nitric acid is 110 mg/kg. Exposure level (level considered immediately dangerous to life or health) for the other gases are Chlorine 30 ppm, Nitric acid (vapour) 100 ppm, Nitric oxide 100 ppm, Nitrogen dioxide 50 ppm, Sulphur dioxide 100 ppm.

Clinical Features

As described for Acids. See pg 349

Management of Toxicity

Treat as for Acids. See pg 350

Antidote: no specific antidote

Laboratory Tests: no specific blood level available; electrolytes, arterial blood gases, chest X-ray

Potassium Permanganate

Potassium permanganate is an oxidising agent. The crystalline form and concentrated solution are corrosive. It is commonly used as antiseptics and disinfectants.

Toxicity

Potassium permanganate is a strong oxidising agent. Concentrated solutions of this chemical may cause corrosive burns. Lethal oral dose - 10 g.

Clinical Features

Corrosive burns on the skin and mucous membranes, and oropharyngeal, oesophageal or gastric injury may occur. Brown discoloration and oedema of the mucous membranes, laryngeal oedema, cough, stridor, bradycardia and hypotension may occur.

Management of Toxicity

Treat as for acids. See pg 350, however may consider gastric lavage for large and recent ingestions of within 60 minutes. Potassium permanganate may cause methaemoglobinaemia.

Antidote: no specific antidote

Laboratory Tests: no specific blood level available; electrolytes, arterial blood gases, chest X-ray

Iodine

The chief use of iodine is in antiseptics.

Toxicity

Iodine is corrosive and the lethal oral dose is 2 - 3 g of free iodine or 1 - 2 ounces of strong iodine tincture.

Clinical Features

Inhalation

- severe pulmonary irritation, pulmonary oedema

Ingestion

- corrosive gastroenteritis, abdominal pain, vomiting, haematemesis, diarrhoea, fever, anuria, delirium, collapse, coma and death
- the patient may also complain of thirst and a metallic taste

Contact

- severe corrosive burns, dermal necrosis (for strong iodine tincture comprising 7% iodine, 5% potassium iodide in 83% ethanol).

Management of Toxicity

Treat as for acids. See pg 350, however may consider gastric lavage if it can be performed within 60 minutes of ingestion.

Antidote: no specific antidotes. After small ingestions of less corrosive products (eg USP iodine tincture, povidone), administer a starchy food (potato, corn flour) or milk to lessen gastrointestinal irritation. These products will convert iodine to nontoxic iodide in the stomach.

Laboratory Tests: no specific blood level available; other useful laboratory tests - electrolytes, arterial blood gases, chest X-ray

Silver Nitrate

Silver nitrate is used as a local styptic and antiseptic.

Toxicity

Silver nitrate causes a local corrosive effect, and the lethal oral dose may be as low as 2 g.

Clinical Features

Pain and burning in the mouth, abdominal pain, blackening of skin and mucous membranes, vomiting, diarrhoea, anuria, collapse, shock, coma and death. The patient may also have hypochloraemia and hyponatremia.

Management of Toxicity

- Maintain airway, treat seizures if they occur
- Give milk or water (120 mL to 240 mL in adults, not more than 15 mL/kg in children)
- Perform gastric lavage for large ingestions.
- Give activated charcoal
- Treat shock
- Treat methaemoglobinaemia
- Do NOT induce emesis as silver nitrate is caustic

Antidote: no specific antidote

Laboratory Tests: no specific blood level available; electrolytes, arterial blood gases, chest X-ray

Boranes

Boranes are a group of chemicals used in various industries. These compounds are far more toxic than borates. The common ones are diborane, pentaborane and decaborane.

Commonly used: fungicide, bactericide, fuel, chemical synthesis

Toxicity

Inhalation of diborane may cause irritation of lungs, pulmonary oedema, pentaborane and decaborane have primarily neurologic toxicity. Exposure limit - diborane 0.1 ppm, pentaborane 0.005 ppm, decaborane 0.05 ppm.

Clinical Features

Ingestion of these products is unusual. Most exposures occur either by inhalation or dermally. High exposure produces symptoms resembling metal fume fever characterised by chills, fever, malaise, general aches, dry cough, nausea and vomiting.

Management of Toxicity

- Maintain airway, treat seizures, hyperthermia if they occur
- Perform gastric lavage if poisoning is by ingestion, but beware of bleeding or perforation.
- Administer activated charcoal
- Wash affected areas with copious amounts of cool water

Antidote: no specific antidote

Laboratory Tests: blood boron level may be elevated; other useful laboratory tests - electrolytes, arterial blood gases, chest X-ray, renal and liver function tests

Fluorine, Hydrogen Fluoride, Sulphur Tetrafluoride and Derivatives

These are a group of chemicals with diverse uses including chemical synthesis, fumigant, insecticides and petroleum industry.

Common uses: fluorine - organic synthesis, petroleum industry and in etching glass fluorides - in many industrial processes, dental applications and as rodenticides methylsulfonyl fluoride - as a fumigant

Toxicity

Exposure limits

chlorine trifluoride	0.1 ppm
fluoride salts	2.5 mg / m ³
fluorine	1 ppm
hydrogen fluoride	3 ppm
nitrogen trifluoride	10 ppm
sulphur tetrafluoride	0.1 ppm

Fatal oral dose

Fluoride	5 - 10 mg / kg
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Clinical Features

Inhalation

- cough, choking, chills lasting 1 - 2 hrs after exposure, cyanosis, pulmonary oedema
- sulfuryl fluoride causes narcosis, convulsions, pulmonary irritation
- nitrogen trifluoride causes methaemoglobin formation

Ingestion

- salivation, nausea and vomiting, diarrhoea, abdominal pain, weakness, tremors, shallow respiration, spasm, convulsions, death by respiratory paralysis; absorbed fluoride ions chelate calcium leading to tetany, hypocalcaemic convulsions, ventricular tachycardia and fibrillation

Contact

- fluoride skin burns are usually deep, exceedingly painful and may result in profound hypocalcaemia within 2 - 3 hours
- skin or mucous membrane contact with hydrogen fluoride solution results in damage depending on concentration
- concentration above 50%: severe, extremely painful burns which are deep and heal slowly
- concentration less than 50%: slight immediate irritation of skin or none at all

Management of Toxicity*Inhalation*

- maintain airway, treat shock, pulmonary oedema if they occur

Ingestion

Hydrogen fluoride

- treat as acid ingestion. See pg 350.

Natural fluoride

- maintain airway, treat shock if it occurs
- perform gastric lavage for large ingestions.
- administer slow IV calcium gluconate 10% 10 ml for hypocalcaemia; repeat until symptoms disappear
- oral calcium lactate 10 g in 250 ml water and magnesium sulphate 30 g in 200 ml water to precipitate and remove fluoride
- give milk and cream every 4 hourly to relieve irritation of oesophagus and stomach
- haemoperfusion and haemodialysis unlikely to be beneficial

Contact

- skin or mucous membrane burns
- wash with copious flow of water for 15 - 60 mins
- coat the burn with glycerin; open all blisters
- for hydrofluoric acid burns (6-11%)-application of calcium gluconate gel to the damaged surface reduce the risk of fluoride intoxication and also give some pain relief

- continued tissue destruction and associated pain may be minimised by subcutaneous administration of calcium gluconate, for every sq cm of burns, inject (with local anaesthetic) calcium gluconate 10% 0.5 ml under the skin area. See pg 95
- treat systemic effect

Eye burns

- wash with copious flow of water for 15 mins
- irrigate the eye with normal saline for 30 - 60 mins
- cover eyes with sterile bandages
- treat pain with systemic analgesics
- do not use chemical antidotes

Antidote: IV calcium for hypocalcaemia. See pg 95
IV magnesium sulphate for hypomagnesemia

Laboratory Tests: blood or serum fluoride level may be elevated; other useful laboratory tests - electrolytes (especially magnesium, calcium, potassium) albumin (to assess free calcium), ECG

2.6 Aldehydes, Ethers And Ketones

Acetaldehyde, Metaldehyde, Paraldehyde

These are a group of chemicals with diverse uses including chemical synthesis, insecticides and pharmaceutical preparations

Common uses: acetaldehyde - reagent in chemical synthesis
metaldehyde - snail bait
paraldehyde - in pharmaceutical preparations

Toxicity

Exposure Limits

Acetaldehyde	25 ppm
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Fatal oral dose

Metaldehyde	400 mg / kg
Paraldehyde	25 mL

Clinical Features

Acetaldehyde

Exposure

- severe irritation of mucous membrane, reddening of skin, coughing, pulmonary oedema, narcosis

Ingestion

- nausea, vomiting, diarrhoea, narcosis, respiratory failure

Metaldehyde

Ingestion

- nausea, vomiting, abdominal pain, increase in temperature, muscular rigidity, hyperventilation, hyperreflexia, convulsions, coma, death from respiratory failure

Paraldehyde

Ingestion

- lethargy, stupor and coma.
- oral doses above 25 mL - death from respiratory and circulatory failure

Management of Toxicity

Ingestion

- Maintain airway, treat coma, hypotension, metabolic acidosis, pulmonary oedema and convulsions if they occur
- Perform gastric lavage for large, recent ingestions.
- Administer activated charcoal
- Treat acidosis by administering sodium bicarbonate or other alkalisating agents
- Dialysis is ineffective

Antidote: no specific antidote

Laboratory Tests: check for blood or serum level if available; electrolytes, glucose, arterial blood gases, renal and liver function tests

Acetone

Acetone is used in the production of lubricating oils and industrial solvents. It is also found in some fingernail polish removers.

Toxicity

Lethal concentration: 550 mcg/ml (in human blood)
2 - 3 ml/kg (children)

Clinical Features

Eye and mucous membrane irritation, nausea, vomiting, haematemesis, sedation, dizziness, coma.

Management of Toxicity

Ingestion

- Perform gastric lavage for large, recent ingestions and give activated charcoal
- Give symptomatic support

Antidote: None

Laboratory Tests: blood and urine ketone concentrations, arterial blood gases, glucose.

Acrolein

A flammable liquid with a very pungent odour, acrolein is used in a number of manufacturing industries. It is commonly used in making plastics, perfumes and in organic synthesis.

Toxicity

Air level considered immediately dangerous to life or health (IDLH): 5 ppm

Clinical Features

Inhalation

- pneumonia and nephritis with death from cardiac failure

Ingestion

- severe gastrointestinal distress, pulmonary congestion, and oedema

Contact

- severe skin irritation, vesiculation and burns

Management of Toxicity

- Remove from exposure
- Maintain airway
- Give oxygen
- Treat pulmonary oedema

Ingestion

- maintain airway
- perform gastric lavage for large, recent ingestions.
- administer activated charcoal
- give slow IV diazepam 10 mg for convulsions
- provide symptomatic and supportive treatment

Antidote: no specific antidote

Laboratory Tests: no specific blood or serum level available; electrolytes, glucose, BUN, creatinine, liver transaminases, ECG monitoring

Ethylene Oxide

Ethylene oxide is a gas and is widely used in hospitals to sterilise medical equipment and supplies. It is also used widely in the chemical industry. It is sometimes used as a fumigant.

Toxicity

Ethylene oxide is an alkylating agent and reacts directly with proteins to cause cell damage. It is also probably mutagenic, teratogenic and carcinogenic in humans. The air level considered immediately dangerous to life or health (IDLH) is 800 ppm

Clinical Features

Intense skin irritation leading to blisters, pulmonary oedema, central depression, respiratory arrest, liver and kidney damage leading to death.

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, convulsions, shock, pulmonary oedema, bronchospasm, if they occur
- Give oxygen

Antidote: no specific antidote

Laboratory Tests: no specific blood or serum level available; arterial blood gas, chest X-ray

Formaldehyde

Formaldehyde is a gas with a pungent odour and is a chemical that is widely used in the industries. Formaldehyde aqueous solution (formalin) is used in varying concentrations as a disinfectant and tissue fixative. Other common uses of formaldehyde and formalin are as antiseptics, deodorants, embalming fluids, in paper processing and urea foam manufacturing.

Toxicity

Formaldehyde causes necrosis and shrinking of the mucous membrane. It metabolises to form formic acid, which may accumulate and produce metabolic acidosis.

The air level considered immediately dangerous to life or health (IDLH) is 30 ppm. Ingestion of 30 mL of 37% formaldehyde solution has been known to cause death in an adult.

Clinical Features

Inhalation

- severe irritation of the upper respiratory tract, cough, wheezing, noncardiogenic pulmonary oedema

Ingestion

- severe corrosive oesophageal and gastric injury, lethargy, metabolic acidosis, coma

Management of Toxicity

Inhalation

- Remove from exposure
- Maintain airway, treat coma, convulsions, shock, pulmonary oedema, bronchospasm, if they occur
- Give oxygen

Ingestion

Treat coma, shock if they occur

- Administer activated charcoal
- Treat metabolic acidosis with sodium bicarbonate
- Perform gastric lavage. Do not induce emesis
- Give milk or tap water to dilute.

Antidotes: no specific antidote

Laboratory Tests: no specific blood or serum level available; liver function tests, arterial blood gases, chest X-ray

Propylene Oxide

Propylene oxide is used as a soil fumigant, herbicide and preservative.

Commonly used: fumigants, herbicides

Toxicity

Propylene oxide is a toxic chemical. Air level immediately dangerous to life or health (IDLH) : 2000 ppm

Clinical Features

Inhalation

- severe irritation to eyes, lungs and mucous membrane, pulmonary oedema

Ingestion

- nausea, vomiting, diarrhoea, ataxia, CNS depression; a carcinogen

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, shock, pulmonary oedema, bronchospasm, if they occur
- Give oxygen
- Perform gastric lavage for ingestions. Do not induce emesis.
- Administer activated charcoal
- Give slow IV diazepam 10 mg for convulsions

Antidote: no specific antidote

Laboratory Tests: no specific blood or serum level available; other useful laboratory tests - arterial blood gas, chest X-ray, pulmonary function tests, liver function tests

Triorthocresyl Phosphate

Triorthocresyl phosphate (TOCP) is used in lubricants, fireproofers, and as a plasticizer in plastic coating.

Commonly used: plastics, lubricants, fireproofers

Toxicity

TOCP interrupts the nervous system of the body causing paralysis. The fatal dose for TOCP is 1 g / kg and the toxic dose is 6 mg / kg. The exposure limit is 0.1 mg / m³.

Clinical Features

Weakness of distal muscles progressing to foot drop, wrist drop and loss of plantar reflex. Laryngeal, ocular and respiratory muscles are affected in severe poisoning. Death from respiratory paralysis.

Management of Toxicity

- Maintain airway
- Perform gastric lavage for ingestion. Do not induce emesis.
- Administer activated charcoal.
- Provide symptomatic and supportive treatment
- Slow IV diazepam 10 mg for convulsions

Antidote: no specific antidote

Laboratory Tests: electrolytes, glucose, BUN, creatinine, liver transaminases, arterial blood gas, chest X-ray, electromyograms & nerve conduction velocity studies.

2.7 Mercaptans

Ethyl Mercaptan, Methyl Mercaptan, Perchloromethyl Mercaptan

Mercaptans are released in petroleum refining and are used as warning odours in liquid propane, butane and natural gas.

Toxicity

Exposure limit :

Ethyl mercaptan	0.5 ppm
Methyl mercaptan	0.5 ppm
Perchloromethyl mercaptan	0.1 ppm

Clinical Features

Cyanosis, convulsions, haemolytic anaemia, fever, coma, irreversible depression of cerebral function

Management of Toxicity

Inhalation

- Remove patient to fresh air
- Give artificial respiration with oxygen

Ingestion

- Perform gastric lavage. Do not induce emesis.
- Provide symptomatic and supportive treatment

Antidote: no specific antidote

Laboratory Tests: no specific blood / serum level available

2.8 Halogenated Hydrocarbons

Dichloromethane (Methylene Chloride) Trichloromethane (Chloroform)

Dichloromethane is used in paint removers and as an industrial solvent. Chloroform is used as a raw material in the production of Freon and as a chemical and pharmaceutical solvent.

Toxicity

Depress the CNS and may potentiate arrhythmias by sensitising the myocardium to catecholamines.

Oral toxic dose : 0.5 - 5 ml/kg (dichloromethane)
 10 - 100 mL (chloroform)

Clinical Features

Inhalation / Ingestion

- mucous membrane and skin irritation; pulmonary oedema, cardiac arrhythmias, CNS depression with respiratory arrest, hepatic and renal toxicity. Corrosive GIT injury occurs with dichloromethane ingestion.

Contact

- erythema, blistering, defatting of skin epithelium

Management of Toxicity

Inhalation

- Remove from exposure
- Maintain airway, treat coma, pulmonary oedema, treat arrhythmias if they occur
- Give oxygen

Ingestion

- Perform gastric lavage if the patient presents within 30-60 minutes or has ingested a large dose and administer activated charcoal
- Do NOT give adrenaline or other stimulants that may cause ventricular arrhythmias
- Control seizures with IV diazepam.
- Haemodialysis and haemoperfusion has not been shown to be effective

Antidote : if carboxyhaemoglobin level is elevated - administer 100% oxygen

Laboratory Tests : monitor carboxyhaemoglobin level; FBC, electrolytes, creatinine, liver transaminases, glucose, ECG monitoring

Epichlorohydrin

Epichlorohydrin is used for various gums, resins and cellulose. It is also used in varnish, paint, nail polish and insect fumigants.

Toxicity

Extremely irritating upon contact and may cause severe burns. Exposure limit: 2 ppm

Clinical Features

Irritation of mucous membrane, skin, lungs and cornea, cyanosis, muscular relaxation on paralysis, tremor, convulsions, death in respiratory failure. Animal studies suggest a potential for liver and kidney injury.

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, pulmonary oedema, hypotension, seizures if they occur
- Administer 100% humidified supplemental oxygen as required.
- Perform gastric lavage for large, recent ingestions. Emesis is not recommended. Activated charcoal may be given.

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; other useful laboratory tests - FBC, electrolytes, creatinine, liver and kidney function tests, blood glucose, ECG monitoring

Ethylene Chlorohydrin

Used as a general chemical agent and as a cleaning solvent.

Toxicity

Ethylene chlorohydrin hydrolyzes to an acid causing cell damage.

Fatal oral dose : Highly variable. >1ml is potentially fatal.

Exposure limit : 1 ppm

Immediately dangerous to life or health air concentration (IDLH) : 10ppm

Clinical Features

Nausea, vomiting, headache, abdominal pain, excitability, dizziness, delirium, fall of BP, twitching of muscles, cyanosis and coma. Death from respiratory and circulatory failure.

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, pulmonary oedema, if they occur
- Perform gastric lavage for large, recent ingestions. Give activated charcoal
- Provide supportive and symptomatic treatment

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; FBC, electrolytes, creatinine, liver transaminases, glucose, ECG monitoring

Ethylene Dichloride

Used as a solvent in the rubber, plastic and insecticide industries; rubber and plastic cement for hobby and household use.

Toxicity

Ethylene dichloride causes damage to all cells.

Fatal oral dose : 30-70g

Exposure limit : 10 ppm

Clinical Features

Cyanosis, fall of BP, vomiting, diarrhoea, cardiovascular collapse, coma, respiratory difficulty. Severe kidney and liver damage has been reported.

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, pulmonary oedema, if they occur
- Wash affected skin carefully with water
- Perform gastric lavage for large, recent ingestions. Do not induce emesis. Dilute with milk or water. Activated charcoal can be given.
- For convulsions: slow IV diazepam 2 - 10 mg at 1 mg / min
- Provide supportive and symptomatic treatment

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; FBC, electrolytes, creatinine, liver and kidney function tests, blood glucose, ECG monitoring

Methyl Bromide, Methyl Chloride, Methyl Iodide

General chemical agents commonly used in chemical synthesis, fumigants and refrigerants.

Toxicity

These chemicals cause cell damage.

Exposure limit :

methyl bromide	5 ppm
methyl chloride	50 ppm
methyl iodide	2 ppm

Clinical Features

Nausea, vomiting, blurred vision, vertigo, weakness or paralysis, drowsiness, confusion, pulmonary oedema. Severe hepatic injury may occur with methyl iodide.

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, pulmonary oedema, seizures if they occur
- Wash affected skin carefully with water
- If ingested, dilute with milk or water. Do not induce emesis. Gastric lavage for large, recent ingestions, and administration of activated charcoal is possible.
- For convulsions: slow IV diazepam 2 - 10 mg at 1 mg / min
- Supportive and symptomatic treatment

Antidote: no specific antidote

Laboratory Tests: no specific blood / serum level; liver panel tests, FBC electrolytes, creatinine, glucose, BUN, arterial blood gases, chest X-ray

Phosgene

Used in the manufacture of dyes, resins and pesticides

Toxicity

Phosgene hydrolyses to hydrochloric acid in the body and causes cell damage . Exposure limit - 0.1 ppm.

Clinical Features

Inhalation and Contact: burning sensation in the throat, tightness in the chest, feeling of oppression, dyspnea, cyanosis, pulmonary oedema, death from respiratory and circulatory failure

Management of Toxicity

- Remove from exposure
- Maintain airway, give artificial respiration. Use 100% humidified supplemental oxygen if necessary.
- Treat pulmonary oedema
- Supportive and symptomatic treatment

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; arterial blood gases, chest X-ray

Polychlorinated Biphenyls (PCBs) or Arochlor

Used in heat exchangers and electrical condensers as di-electric solvents, hydraulic and lubricating fluids. Because of its carcinogenicity, it is now largely replaced by silicone oil.

Toxicity

PCBs are irritating to mucous membranes. They are mutagenic and teratogenic and also human carcinogens.

Exposure limit:

1 mg / m³ (42% chlorine),
0.5mg/m³ (54% chlorine)

Acute toxicity after ingestion is unlikely; the oral LD50 is 1-10g/kg

Clinical Features

Chronic exposure causes pinhead to pea-sized papular acne-like eruption on skin (chloracne). Skin pigmentation and porphyria may occur.

Management of Toxicity

- Remove from further exposure
- Treat bronchospasm if it occurs
- Monitor for elevated hepatic enzymes; and nonspecific eye, gastrointestinal and neurological symptoms
- For ingestion, give activated charcoal. Induce emesis if it can be given within a few minutes of exposure.
- Dialysis, haemoperfusion and repeat dose charcoal are not effective

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; BUN, creatinine, liver enzymes

Tetrachloroethane

Tetrachloroethane is an industrial solvent.

Toxicity

A toxic chemical with an exposure limit of 1 ppm. Immediately dangerous to health and life air concentration (IDLH) is 150ppm.

Clinical Features

Irritation of the eyes and nose, headache, cyanosis, CNS depression, coma. May cause hepatic or renal injury.

Management of Toxicity

As for carbon tetrachloride. See pg 331.

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; liver function tests, blood gases, electrolytes, ECG

Tetrachloroethylene (Perchloroethylene)

Tetrachloroethylene is used as a solvent in commercial dry cleaning and degreasing.

Toxicity

Exposure limit : 25-50 ppm.

Immediately dangerous to health and life air concentration : 500ppm.

Clinical Features

Headache, dizziness, loss of inhibitions, ventricular premature beats

Management of Toxicity

As for trichloroethylene. See pg 391.

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; electrolytes, creatinine, glucose, BUN, arterial blood gases, chest X-ray, liver function test.

Trichloroethylene

Used in industrial solvents and household cleaners for walls, clothing, rugs.

Toxicity

Fatal dose : 5mL

Exposure limit : 50 ppm.

Immediately dangerous to life and health air concentration (IDLH) is 1000ppm.

Clinical Features

Headache, dizziness, nausea and vomiting, loss of consciousness, pulmonary oedema. May cause liver damage and sensitise the heart to the arrhythmogenic effects of adrenaline

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, pulmonary oedema, if they occur
- Wash affected skin carefully with water
- For convulsions, give slow IV diazepam 2 - 10 mg at 1 mg / min
- Provide supportive and symptomatic treatment

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; other useful laboratory tests - electrolytes, creatinine, glucose, BUN, arterial blood gases, chest X-ray

1,1,1-Trichloroethane (Methyl chloroform)

Used as a solvent for cleaning and degreasing in crafts and paint removers.

Toxicity

Fatal oral dose : 500-5000 mg/kg

Exposure limit : 350 ppm

Immediately dangerous to life and health air concentration : 1000ppm

Clinical Features

Headache, dizziness, nausea, fainting, loss of consciousness, respiratory depression, arrhythmias, fall of BP, renal and liver damage.

Management of Toxicity

- Remove from exposure
- Maintain airway, treat coma, seizures, and arrhythmias if they occur
- Perform gastric lavage and administer activated charcoal
- Wash affected skin carefully with soap and water
- Supportive and symptomatic treatment

Antidote : no specific antidote

Laboratory Tests : no specific blood / serum level; electrolytes, creatinine, blood glucose, BUN, arterial blood gases, chest X-ray, liver enzymes.

2.9 Hydrogen Cyanide & Derivatives

Acrylonitrile
Cyanamide
Cyanogen Chloride
Cyanogenetic Glycosides
Nitroprussides

These compounds are all cyanide-releasing substances.

Common uses:

Hydrogen cyanide	:	fumigant and chemical synthesis
Acrylonitrile	:	production of synthetic rubber
Cyanamide	:	fertiliser and source of hydrogen cyanide
Cyanogen Chloride	:	chemical synthesis
Cyanide salts	:	metal cleaning, hardening, refining and recovery of gold from ores
Nitroprussides	:	chemical synthesis

Toxicity:

Cyanides	:	Super toxic
Nitroprusside	:	Extremely toxic
Acrylonitrile	:	Extremely toxic
Cyanamide	:	Moderately toxic
Cyanogenic glycosides	:	Very toxic

Lethal oral dose : Cyanide > 5mg/kg; 200-250mg of sodium or potassium salt.

Clinical Features:

Inhalation (Acrylonitrile)

- nausea, vomiting, diarrhoea, weakness.

Ingestion :

- dizziness, rapid respiration, vomiting, flushing, headache, drowsiness, fall in BP, rapid pulse, unconsciousness, convulsion, death.

Contact :

- epidermal necrolysis.

Management of Toxicity:

- Remove contaminated clothing and rinse contaminated skin thoroughly
- Maintain airway, provide cardiovascular support
- Perform gastric lavage
- Treat metabolic acidosis if it occurs.
- Administer activated charcoal and cathartic.
- IV sodium nitrite 3% 10mls at 2.5-5ml/min
- IV sodium thiosulphate 25% 50 ml over 10 mins using the same needle and vein.
- Repeat using half the initial dose if necessary.
- Empty stomach by aspiration and lavage with sodium thiosulphate 5% solution (20g to 400ml). Leave 200ml of sodium thiosulphate 25% solution in the stomach.
- Provide symptomatic and supportive treatment.

If patient is tending to lose consciousness or is unconscious, give IV infusion of dicobalt edetate, 300mg (20mL) over 1-5 minutes, followed by 50mL of IV infusion of glucose 50%. If response inadequate, a 2nd dose of both may be given; if no response after further 5 minutes, a third dose of both may be given.

Antidote : Sodium nitrites, thiosulphate and dicobalt edetate. See pg 128, 137, 110.

Laboratory tests : Electrolytes, glucose, serum lactate, arterial blood gas.

2.10 Nitrogen Compounds

Aniline
Dimethylaniline
Ethyleneimine
Hydrazine
Nitroazine
Nitroaniline
Nitrobenzenes
Propylene imine
Toluidine

Used in printing inks, cloth making inks, paints, paint removers and in the synthesis of dyes and other chemicals.

Toxicity:

Exposure limit :

Aniline	2ppm
Dimethylaniline	5ppm
Nitrobenzene	1ppm
Ethyleneimine	0.5ppm
Propylene imine	2ppm
Hydrazine	0.1ppm

Clinical Features:

Methaemoglobinaemia, cyanosis, headache, tachypnoea, dizziness, hypotension, lethargy, stupor, convulsions, coma.

Management of Toxicity:

- Maintain airway and circulation.
- Treat coma and seizures if they occur

- Perform gastric lavage to remove ingested poison, followed by activated charcoal.
- Provide symptomatic and supportive treatment.
- Remove poison from skin by washing thoroughly with soap and water.

Antidote : For severe methaemoglobinaemia (level >30%): slow IV methylene blue 1% 1-2mg/kg.

Laboratory tests : Blood methaemoglobin, liver function, electrolytes, glucose, BUN, creatinine, and arterial blood gases.

2.11 Organic Peroxides

Cumene hydroperoxide

Di-t-butylperoxide

Methylethyl ketone peroxide

t-butyl hydroperoxide

General industrial chemicals that are potentially explosive. Detonation may be caused by heat, shock or friction. They are commonly used in chemical synthesis.

Toxicity:

Fatal oral dose: 50 - 100 mL (methylethyl ketone peroxide 35% soln)

Clinical Features:

Irritation of skin and eye except for di-t-butylperoxide.

Inhalation of vapour causes weakness and tremors of head and neck in animals. CNS depression may occur.

Ingestion of ketone peroxides usually result in pharyngitis and oesophageal necrosis. Complications include gastric perforation, acute renal failure, interstitial pneumonia and hepatic coma.

Management of Toxicity:

- Maintain airway and circulation.
- Treat coma and seizures if they occur
- Give small amounts of milk or water to decontaminate oral mucosa, if no respiratory compromise is present.
- Provide symptomatic and supportive treatment.
- Remove poison from skin by washing thoroughly with soap and water.

Antidote : No specific antidote.

Laboratory tests : Electrolytes, glucose, BUN, creatinine, and arterial blood gases, renal and liver function test.

2.12 Hydrocarbons

Hydrocarbons or petroleum distillates, are widely used industrially as solvents, degreasers, fuels and pesticides. There are many types of hydrocarbons: aliphatic (saturated carbon structures); alicyclic (ring compounds); aromatic (containing one or more benzene ring); halogenated; alcohols; ethers; ketones, etc.

Toxicity :

Highly variable, systemic toxicity can result from ingestion or inhalation of gas or vapour:

- petroleum jelly, motor oil, gasoline, kerosene, petroleum naphtha, petroleum, gasoline, diesel oil, kerosene, petroleum ether have low risk of systemic toxicity after ingestion as they are poorly absorbed from GIT.
- camphor, phenol, halogenated and aromatic hydrocarbons (eg. benzene, toluene, xylene) have high systemic toxicity: 10 - 20 mL ingestion can be fatal.

Clinical Features:

Nausea, vomiting, haemorrhagic gastroenteritis. Most hydrocarbons are capable of inducing chemical pneumonitis if aspirated.

Confusion, ataxia, lethargy, syncope, coma, respiratory arrest, arrhythmias (for the more toxic hydrocarbons)

Management of Toxicity:

Ingestion

- For low toxicity agents, do not induce emesis or perform gastric lavage
- For systemic toxins, do not induce emesis, give activated charcoal; perform gastric lavage for recent large ingestions
- Give supportive treatment

Antidote : No specific antidote

Laboratory tests : Arterial blood gases, chest x-ray, electrolytes, glucose, BUN, liver transaminases, ECG.

CHAPTER 3

Metallic Poisons

3.1 Antimony & Stibine

Antimony is a metal with many applications. It is commonly used in alloys, ant paste, batteries, ceramics, foil, safety matches and textiles. Stibine (antimony hydride) is a colourless gas and is an ore industry by-product.

Toxicity:

Highly toxic. Minimum lethal oral dose: 15 mg/kg (antimony)

Clinical Features:

Antimony ingestion causes nausea, vomiting, severe diarrhoea with mucous and blood, haemorrhagic nephritis and hepatitis. Stibine inhalation causes acute haemolysis, resulting in anaemia and renal failure.

Management of Toxicity:

- Perform gastric lavage or ipecac emesis.
- Administer activated charcoal.
- Provide symptomatic and supportive treatment.
- Blood transfusion may be needed after massive haemolysis.

Antidote : No specific antidote.

Laboratory tests : Specific serum and urine antimony levels, FBC, electrolytes, BUN, creatinine, urinalysis for free haemoglobin, liver transaminases, bilirubin, prothrombin time (PT).

3.2 Arsenic & Arsine

Arsenic compounds may be organic or inorganic. When absorbed the chemical disrupts enzymatic reactions vital to cellular metabolism. Arsine is a gas which when absorbed into the body forms a complex that results in massive intravascular haemolysis.

Arsenic compounds are used in a variety of industries and commercial products. Arsine is a colourless gas and is used in the microelectronic industry.

Many marine organisms may contain organic triemethylated arsenic compounds which are basically non-toxic.

Toxicity :

Highly toxic. Fatal oral dose (trivalent arsenic compound) : 100-300mg. Arsine is the most toxic form of arsenic. Fatal dose (exposure): 25-50ppm.

Clinical Features:

Burning oesophageal pain, vomiting, copious watery or bloody diarrhoea, cold, clammy skin, hypotension, convulsions, coma and death from circulatory failure. Massive haemolysis, oliguria and acute renal failure occur within 1 - 3 days of arsine exposure.

Management of Toxicity:

- Treat coma, shock, and arrhythmias if they occur.
- Perform ipecac emesis or gastric lavage, followed by administration of oral magnesium sulphate 30g solution as a cathartic.
- Perform haemodialysis in severe poisoning.
- Provide symptomatic and supportive treatment.

Antidote : For arsenic poisoning, IM dimercaprol 3mg/kg 4 H for 2 days then oral penicillamine 100mg/kg/day (max. 1g/day) in 4 divided doses. Discontinue antidote when urine arsenic falls below 50mcg/L. Treatment should not be longer than 1 week. See pg 104.

Laboratory tests : Urine arsenic level, FBC, electrolytes, glucose, BUN and creatinine, liver enzyme, ECG, CPK, abdominal & chest x-rays.

Note: BAL & other chelators are not useful for arsine poisoning.

3.3 Beryllium

Beryllium is commonly used as alloys for electrical and other equipment. It is present in some fluorophors used in cathode ray tubes. Exposure to beryllium causes chronic granulomatous disease. The lung is the primary target organ.

Toxicity

Exposure limit : 0.002mg/m³

Clinical Features

Inhalation :

- Acute pneumonitis, chest pain, bronchial spasm, fever, dyspnoea, cyanosis, cough, blood-tinged sputum, nasal discharge.

Contact :

- Dermatitis, skin granulomas, and ulcers.

Management of Toxicity :

- Complete bed rest.
- Cyanosis: give at least 40% oxygen by mask or intratracheal tube.
- Bronchial spasm: SC adrenaline 0.2mg or IV aminophylline 250mg - 500mg
- Symptomatic or supportive treatment.

Laboratory tests : FBC, electrolytes, glucose, BUN, creatinine, arterial blood gases, chest x-ray, CT scan.

3.4 Cadmium

Used as pigment stabilizers in plastics, in alloys, in solders, and in the plating industries, cadmium is damaging to all cells. Inhaled cadmium is far more toxic than the ingested form. The fumes may cause chemical pneumonitis. Ingestion may cause liver damage and renal failure.

Toxicity

Highly toxic. Exposure limit: $0.05\text{mg}/\text{m}^3$; lethal oral dose ranges from 350 to 8900 mg.

Inhaled cadmium is 60 times more toxic than the ingested form.

Clinical Features

Inhalation :

- metallic taste in the mouth, shortness of breath, pain in the chest, cough with foamy or bloody sputum, weakness, pain in the legs.

Ingestion :

- nausea, vomiting, diarrhoea, headache, salivation, abdominal pain, shock, liver damage, renal failure.

Management of Toxicity

Inhalation :

- remove patient from further exposure.
- maintain adequate ventilation and oxygenation.
- treat wheezing and pulmonary oedema.

Ingestion :

- perform gastric lavage, administer activated charcoal. Do not induce emesis.
- give milk every 4 H.
- perform catharsis with oral magnesium sulphate 30g solution, but not if the patient has diarrhoea.
- provide symptomatic and supportive treatment.

Antidote : IM or slow IV infusion of calcium disodium edetate 15-25mg/kg (max 75mg/kg/day) in dextrose 5% 250-500ml over 1-2 hours every 4 to 6 hours for up to 5 days with a rest period of at least 2 days between courses. Each course should not exceed a total of 500 mg/kg. (For acute exposure only). See pg 109.

Laboratory tests : Blood cadmium levels, FBC, electrolytes, glucose, BUN, creatinine, arterial blood gases, chest x-ray.

Note: Some authors report that there is no evidence that chelation therapy (eg. with BAL, EDTA or penicillamine) is effective.

3.5 Chromium

Chromium metal is relatively non toxic. Chromic (chromium III) or chromous (chromium II) have little significant toxicity. However hexavalent chromium salts such as chromium trioxide, chromic anhydride, chromic acid, dichromate salts are toxic. They are irritating and destructive to all cells of the body. Chromium is commonly used in chemical synthesis, electroplating, leather tanning, radiator anti-rust, and steel making.

Toxicity

Lethal oral dose: 1 - 2 g (chromic acid)
6 - 8 g (potassium dichromate)

Clinical Features

Dizziness, intense thirst, abdominal pain, methaemoglobinaemia vomiting, shock, death from uraemia.

Management of Toxicity

- Perform gastric lavage, administer activated charcoal.
- Provide symptomatic and supportive treatment.
- Administer oral ascorbic acid for hexavalent chromium ingestions (1 g per 0.135 g of elemental chromium).

Antidote : None

Laboratory tests : Urine chromium levels, FBC, electrolytes, glucose, BUN, creatinine, liver transaminases, arterial blood gases, chest x-ray.

3.6 Lead

Lead is a soft, malleable metal. The metal has a wide variety of applications, with lead storage batteries accounting for most of the commercial uses.

Commonly used : Brass alloys, gasoline, electric cable covering, industrial paint, rubber, solder, storage batteries, toys and type metal.

Toxicity

Toxicity from lead normally occurs through long term exposure rather than oral ingestion. However with lead compounds, especially the organic lead compounds (alkyl compounds) the toxicity is much higher. Fatality was reported for an ingestion of 15g of lead oxide. Exposure to organic lead such as tetraethyl lead or tetramethyl lead accounts for the majority of acute poisoning.

Exposure limit : tetraethyl (or tetramethyl) lead 0.1mg lead/m³.

Clinical Features

Metallic taste, abdominal pain, vomiting, diarrhoea, black stools, oliguria, collapse, coma.

Management of Toxicity

- Maintain airway and circulation.
- Treat coma and seizures if they occur
- Perform gastric lavage to remove ingested soluble lead compounds. Ipecac emesis is possible.
- For cerebral oedema, give IV mannitol 25% 5ml/kg at a rate of 1ml/min and IM/IV dexamethasone 10mg, then 4mg 6 H.
- Withhold oral fluid, food, medication for at least 3 days.
- Do not use catharsis or enemas in the presence of severe symptoms.
- Provide symptomatic and supportive treatment.

Antidote : Calcium EDTA. See pg 109.
Use IM dimercaprol as adjunctive treatment in encephalopathy.
See pg 104.

Laboratory tests : Whole blood lead level, free erythrocyte protoporphyrin,
urine lead level, stomach x-ray.

*Note: Lead encephalopathy is a medical emergency. Patient should be hospitalised
in an intensive care setting.*

3.7 Manganese

Manganese is mainly used in the steel industries and in the manufacturing of alkaline batteries. Exposure is normally through chronic occupational exposure rather than acute exposure.

Toxicity

Inorganic manganese is poorly absorbed from the GIT. Thus acute exposure is normally through inhalation exposure in work places. Permissible exposure limit for manganese dusts is $5\text{mg}/\text{m}^3$. The metal causes disturbance to the neurotransmitter, but the precise mechanism is not known.

Clinical Features

Irritant-type pneumonitis. Chronic exposure results in patients with an effective psychiatric disorder, parkinsonism and other extrapyramidal movement disorders.

Management of Toxicity

- Remove victim from exposure and give oxygen.
- Treat bronchospasm and noncardiogenic pulmonary oedema.
- Treat chronic CNS symptoms with the usual psychiatric & antiparkinsonian drugs.

Antidote : Nil

Laboratory tests : Serum and urine manganese level, arterial blood gases, chest x-ray.

3.8 Mercury

Mercury comes in three primary forms, elemental, inorganic and organic. Mercury has a wide range of industrial application as amalgam, and in the manufacturing of chlorine and caustic soda. It can be found as constituents in batteries, electrical apparatus, explosives, felt, lamps, paints and thermometers.

Toxicity

Elemental mercury and organic mercury are toxic to the central nervous system. Inorganic mercuric salt is corrosive and nephrotoxic. Lethal oral dose of mercuric chloride : 1 -4 g.

Liquid mercury pose little toxicity in acute ingestion as it is poorly absorbed in the GIT, except in cases of abnormal gut motility where normal faecal elimination is delayed.

Clinical Features

Inhalation:

- dyspnoea, cough, fever, nausea, vomiting, diarrhoea, stomatitis, salivation, metallic taste, bronchiolitis, pneumonitis, pulmonary oedema and pneumothorax.

Ingestion

- metallic taste, thirst, severe abdominal pain, vomiting, bloody diarrhoea, oesophageal, gastric or intestinal stenosis, death from uraemia.

Management of Toxicity

Ingestion

- Maintain airway and circulation.
- Treat coma and seizures if they occur
- For inorganic and organic mercury, perform gastric lavage to remove ingested poison, give activated charcoal.
- For metallic mercury, no need for gut decontamination except in extremely large ingestions, or in patients with abnormal gut motility or intestinal perforation. Multiple-dose cathartics, whole bowel irrigation or surgical removal may be necessary.
- Symptomatic and supportive treatment.

Antidote : For inorganic mercury, use IM dimercaprol. See pg 104.
For organic and metallic (elemental) mercury, use oral DMSA 10 mg/kg every 8 hours for 5 days, then 10 mg/kg every 12 hours for 2 weeks.
Alternatively oral penicillamine can be used. See pg 131.

Laboratory tests : Whole blood, and urine mercury level, electrolytes, glucose, BUN, creatinine, liver transaminases, urinalysis; chest x-ray and arterial blood gases.

Note: Dimercaprol is contraindicated in methyl mercury poisoning.

S E C T I O N **D**

PESTICIDE POISONING

CHAPTER 1

Carbamates

Carbamate insecticides are moderately hazardous.

Clinical Features

As for organo-phosphorus compounds but of lesser intensity. See pg 419.

Management of Toxicity

- Maintain airway, treat coma and seizures if they occur.
- Perform gastric lavage for large ingestions.
- Wash contaminated skin with soap and water.
- Irrigate eyes with water or saline.
- Give IV saline to correct dehydration and electrolyte imbalances.
- Keep patient under constant observation for at least 24 hours.

Caution :

- Ensure cyanosis and severe hypoxia are corrected before atropinization.
- Pralidoxime is generally not recommended for carbamate poisoning.
- Avoid CNS depressants such as reserpine, chlordiazepoxide and phenobarbitone which may potentiate carbamate poisoning.

Antidote : Administer IV atropine 2-5 mg and repeat every 15 mins until mydriasis occurs. See pg 90.

Laboratory tests : Red blood cell cholinesterase, electrolytes, glucose, BUN, creatinine, arterial blood gasses.

Table 1. Carbamate insecticides

Type	Brand Names	Description	Toxicity		
			Oral LD50	Dermal LD50	WHO/FAO ADI*
Bendiocarb	Garvox	Systemic insecticide and aphicide with contact and stomach action. Cholinesterase inhibitor.	55mg/kg	566-800mg/kg (rat)	0.04mg/kg
BPMC	BPMC Hopcin BPMC 40WP BPMC 50EC	Insecticide with controlling sucking insects, bugs and weevils. Cholinesterase inhibitor.	350 mg/kg	>5000mg/kg(rat)	
Carbaryl	Carbaryl 85WP Servin Avin Sevtos Sevin	Insecticide with contact and stomach action. Also acts as a plant growth regulator. Cholinesterase inhibitor.	300mg/kg	>2000mg/kg	0.01mg/kg
Carbofuran	Furadan Carbofuran	Systemic insecticide, acaricide and nematocide with stomach and contact action. Cholinesterase inhibitor.	8mg/kg	2550mg/kg	0.01mg/kg
Dioxacarb	Elocron	Insecticide with contact and stomach action. Control of chewing and sucking foliar insect pests on a range of crops. Cholinesterase inhibitor.	90mg/kg	1950mg/kg (rabbit)	
Isoprocarb	Mode (MPIC)	Insecticide with contact and stomach action. Control of various insects on crops. Cholinesterase inhibitor.	450mg/kg	>500mg/kg (rat)	
Methiocarb	Mesuroil Methiocarb	Non-systemic insecticide-acaricide with contact and stomach action. Molluscicide with stomach action. Bird repellent. Cholinesterase inhibitor.	20mg/kg	350mg/kg (rat)	0.001mg/kg
Propoxur	Propoxur Shelltox (Advance) Super Raid	Non-systemic insecticide with strong contact action giving rapid knock-down. Cholinesterase inhibitor. Control of insect pests in food storage areas, houses, animal houses. Control of sucking and chewing insects on a range of crops.	95mg/kg	>1000mg/kg	0.02mg/kg

* WHO/FAO ADI: World Health Organisation/Food & Agricultural Organisation Acceptable Daily Intake.

CHAPTER 2

Inorganic Insecticides

Phosphine and Aluminium Phosphide

Phosphine is a colourless gas and is produced from aluminium phosphide for fumigation purposes of stored grains. It is highly hazardous.

Brand Name :

Phostoxine

Toxicity

Lethal oral dose : < 500 mg (aluminium phosphide)

Clinical Features*Ingestion :*

- nausea, vomiting, diarrhoea, garlic odour of breath and excreta. Death in coma or cardiac arrest.

Inhalation :

- phosphine or phosphide: Nausea, vomiting, fatigue, cough, jaundice, ataxia, hypotension, pulmonary oedema, convulsion, coma.

Contact :

- may cause severe dermal or ocular burns.

Management of Toxicity*Ingestion :*

- maintain airway, treat coma and seizures if they occur.
- perform gastric lavage, give activated charcoal.
- give IV calcium gluconate 10%, 10ml to maintain serum calcium.
- provide symptomatic and supportive treatment.

Contact :

- remove from skin or eyes by copious irrigation with tap water.

Antidote : No specific antidote.

Laboratory tests : No specific tests recommended. Other tests include BUN, creatinine, liver transaminases, arterial blood gases, chest x-ray, ECG.

CHAPTER 3

Organo-Chlorine Insecticides

Chlordane, Lindane

These are non-systemic insecticides with stomach, contact and respiratory actions. Organochlorine insecticides are generally banned in Singapore. Chlordane and Lindane are for termite extermination. They are moderately hazardous.

Toxicity :

Oral LD₅₀ (animals): >50mg/kg

Clinical Features

Nausea and vomiting, paraesthesia of the tongue, lips, face and hands, apprehension, disturbance of equilibrium, muscle weakness, tremors, convulsion, coma, death due to respiratory failure or ventricular fibrillation.

Management of Toxicity

- Maintain airway, treat coma, seizures if they occur.
- Perform gastric lavage for large, recent ingestions. Give activated charcoal.
- Sedate patient, if necessary and ensure complete rest.
- Observe patient for hydrocarbon pneumonia.
- Provide symptomatic and supportive treatment.

Antidote : No specific antidote.

Laboratory tests : Electrolytes, glucose, BUN, creatinine, hepatic transaminases, prothrombin time (PT), ECG monitoring.

CHAPTER 4

Organophosphorus Compounds

Organophosphorus compounds range from slightly to highly hazardous.

Clinical Features

Anorexia, nausea, headache, anxiety and restlessness, mental confusion followed by bradycardia, respiratory distress, vomiting, abdominal cramps, excessive cold sweating, salivation and finally muscular twitching, urinary incontinence, 'pin-point' pupils and coma. Death is normally due to respiratory failure.

Management of Toxicity

- Maintain airway, treat coma, seizures and hydrocarbon pneumonitis if they occur.
- Perform gastric lavage, administer activated charcoal and a cathartic. Do not induce emesis.
- If skin is contaminated, it should be washed with alkaline soap which will not only remove but also help to hydrolyse the phosphate ester.

Antidote :

- Administer IV atropine 2-4mg; repeat every 15mins until the pupils start to dilate. Then give IV pralidoxime 1-2g (25-50mg per kg body weight for children) over 2 mins. Another 1-2 dose can be given if necessary. Max. dose 12g/24hrs. See pg 134.
- Maintain atropinization.
- Give the following supportive treatment if necessary:
 - administer slow IV diazepam 5-10mg (0.2-0.5mg for children) for convulsions, extreme restlessness and excitement.
 - give IV saline drips continuously.
 - remove bronchial hypersecretion by repeated bronchial aspiration and postural drainage.
 - give oxygen if breathless.
 - sample blood for cholinesterase activity.
 - monitor for at least 24 hours.

Caution:

- ensure cyanosis or severe hypoxia is corrected before atropinization.
- do not give morphine, aminophylline and phenothiazines such as promazine and chlorpromazine.

Laboratory tests:

Cholinesterase level, electrolytes, glucose, BUN, creatinine, hepatic transaminases, prothrombin time (PT), ECG monitoring.

Table 1. Organophosphorus insecticides

Type	Brand Names	Description	Toxicity		
			Oral LD ₅₀	Dermal LD ₅₀	WHO/FAO ADI*
Acephate	Acephate Orthene Acephatom	Systemic insecticide with stomach action. Cholinesterase inhibitor. Controls a wide range of chewing and sucking insects.	945mg/kg	> 2000mg/kg	0.003mg/kg
Azamethiphos	SNIP	Used for control of flies and other insect pests in stables, mosquitoes, tsetse flies, cockroaches and other public hygiene pests. Cholinesterase inhibitor.	1010mg/kg	>2150mg/kg	
Chlorpyrifos	Chlorpyrifos Lorsban Chlorpycin Phantom	Non-systemic insecticide for control of soil insects and some foliar insect pests on a wide range of crops. Cholinesterase inhibitor.	135mg/kg	2000mg/kg	0.01mg/kg
Diazinon	Diazinon Basudin Fezudin Trisudin	Insecticide and acaricide with contact, stomach and respiratory action. Cholinesterase inhibitor.	300mg/kg	540-600mg/kg	0.002mg/kg
Dichlorvos	DDVP	Insecticide and acaricide which gives rapid knock down. Used for control of household and public health insect pests, stored product pests, sucking and chewing insects, and spider mites in a wide range of crops. Cholinesterase inhibitor.	56mg/kg	107mg/kg	0.004mg/kg
Dimethoate	Dimethoate Roxion Dimet Rogor Chemathoate Rantox Triluxon	Systemic insecticide and acaricide. Remains active for 2 to 3 weeks. For control of a wide range of insects and mites on many crops. Also used for control of flies in animal house. Cholinesterase inhibitor.	15-30mg/kg	255-300mg/kg	0.01mg/kg

Table 1. (Cont'd)

Type	Brand Names	Description	Toxicity		
			Oral LD ₅₀	Dermal LD ₅₀	WHO/FAO ADI*
Fenrothion	Fenitrothion Folithion Dust Kendi	Non-systemic insecticide for control of chewing, sucking and boring insects on a range of crops. Also used as a public health insecticide. Cholinesterase inhibitor.	250mg/kg	890-1300mg/kg (rat)	
Fenthion	Fenthion Lebaycid Baytex	Contact, stomach, respiratory and systemic action insecticide for agricultural and public health uses. Cholinesterase inhibitor.	180-250mg/kg	330mg/kg (rat)	0.001mg/kg
Heptenophos	Hostaquick	Systemic insecticide with contact, stomach, and respiratory action, for control of sucking insects (aphids) and certain Diptera. Also used for control of animal ectoparasites. Cholinesterase inhibitor.	96mg/kg	2925mg/kg	
Malathion	Malathion Fyanon Mondane Trinon	Insecticide and acaricide with predominantly contact action, but also has some stomach and respiratory action. Offers broad spectrum control of sucking and chewing insects and spider mites and of insect pests in stored products. Also used in public health. Cholinesterase inhibitor.	1000 -2800 mg/kg	2925mg/kg	
Methamidophos	Methamidophos Tamaron Laser 600 Tamaron SL600	Systemic insecticide with contact and stomach action. Absorbed by the roots and leaves. Used for control of chewing and sucking insects, and spider mites on a wide range of crops. Cholinesterase inhibitor.	30mg/kg	118mg/kg	0.0006mg/kg
Methidathion	Methidathion	Contact and stomach action insecticide and acaricide for control of a wide range of sucking and chewing insects and spider mites in many crops. Cholinesterase inhibitor.	25mg/kg	200mg/kg	0.005mg/kg

Table 1. (Cont'd)

Type	Brand Names	Description	Toxicity		
			Oral LD ₅₀	Dermal LD ₅₀	WHO/FAO ADI*
Mevinphos	Phosdrin 24EC	Systemic insecticide and acaricide with short residual activity. Used for control of chewing and sucking insects, and spider mites on a wide range of crops. Cholinesterase inhibitor.	4mg/kg	16-33mg/kg	0.0015mg/kg
Monocrotophos	Monocrotophos Bullet Azodrin 60	Systemic stomach and contact action insecticide and acaricide. Used for control of a broad spectrum of pests including chewing and boring insects and spider mites on a wide range of crops. Cholinesterase inhibitor.	8-23mg/kg	130-250mg/kg	0.0006mg/kg
Omethoate	Omethoate 50S Folimat 50EC	Systemic insecticide and acaricide with contact and stomach action. Cholinesterase inhibitor.	50mg/kg	700mg/kg (rat)	0.0003mg/kg
Profenofos	Selecron	Non-systemic insecticide and acaricide with contact and stomach action. Used for control of insects on maize, soyabean and vegetables. Cholinesterase inhibitor.	358mg/kg	472mg/kg	
Quinalphos	Bayrusil	Insecticide and acaricide with contact and stomach action. Used for control of a wide range of insects. Cholinesterase inhibitor.	62mg/kg	1750mg/kg	
Temephos	Abate	Non-systemic insecticide for the control of larvae; used in public health and agriculture. Cholinesterase inhibitor.	4204-10000 mg/kg		
Triazophos	Hostathion	Insecticide and acaricide with contact and stomach action. Cholinesterase inhibitor.	57-59mg/kg	1100mg/kg	
Trichlorfon	Trichlorfon Dipterex Triden	Non-systemic insecticide with contact and stomach action. Used for control of pests in agriculture, forestry, food storage, household, and animal husbandry. Also controls a wide range of insects. Cholinesterase inhibitor.	250mg/kg	2000mg/kg	0.01mg/kg

* WHO/FAO ADI: World Health Organisation/Food & Agricultural Organisation Acceptable Daily Intake.

CHAPTER 5

Pyrethrum Derivatives

Alphamethrin, cypermethrin, deltamethrin, fenvalerate, permethrin, pyrethrins, s-bioallethrin

Pyrethoid insecticides are general insecticides with contact and stomach action. The toxicity of these compounds is lower than those of organophosphorus compounds. The toxic oral dose in mammals is greater than 100-1000mg/kg and the potentially lethal oral dose is 10-100g.

Brand Names :

Ambush	Hickson antiborer
Anti ant powder	Kudos
Aqua reslin	Landsect
Baythroid	Peripel
Cislin	Permacal
Coopex	Permethrin
Cymbush	Pestigas
Cypermethrin	Responsar
Decamethrin	Ripcord
Decis	Sumicidin
Delatmethrin	Sunmerin
Fastac	Super Raid
Fenvalerate	

Toxicity

Oral LD₅₀ - 100mg/kg - 1000mg/kg

Clinical Features

Local irritation of mucous membranes, vomiting, diarrhoea, chemical pneumonitis with dyspnoea and cyanosis. CNS depression, drowsiness, stupor, convulsion and coma occur with large ingestions (200 - 500 mL of concentrated solution).

Management of Toxicity

- Maintain airway, treat coma, seizures if they occur.
- Administer saline cathartic or activated charcoal. Gastric lavage is not necessary if activated charcoal can be given promptly.
- Give symptomatic treatment.
- Extracorporeal methods of elimination not recommended as these compounds are rapidly metabolised by the body.

Antidote : No specific antidote.

Laboratory tests : These compounds are rapidly metabolised in the body. Electrolytes, glucose, arterial blood gases.

CHAPTER 6

Thiocarbamates

Tetramethyl Thiuram Disulfide, Metallo-Dimethyl-Dithiocarbamates, Metallo-Ethylene-Bis-Dithiocarbamates

Systemic insecticide with stomach and contact action. Cholinesterase inhibitor. Used for control of chewing & sucking insects. Also used as foliar fungicide. Compounds of this class usually have low acute toxicity.

Brand Names :

Agrithane	Polyram
Antracol	Polytox
Bisectrex	Pomasol Z
Cartap	Propineb
Dithane	Suntap
Farmtapol	Tersam
Febram	Thiram
Mancozeb	Trifungol
Maneb	Tripomol
Manzineb	Tritogol M
Naban	Vapam
Pandan	Zineb
	Ziram

Toxicity

Oral LD₅₀ 325mg/kg

WHO/FAO ADI: 0.1mg/kg

(World Health Organisation/Food & Agricultural Organisation Allowable Daily Intake)

Clinical Features

Irritation to skin, eye and mucous membrane, allergic eczema, anorexia, nausea, headache, anxiety, mental confusion.

Management of Toxicity

- Treatment is symptomatic and supportive
- Maintain airway
- Perform gastric lavage for large ingestions.
- Wash contaminated skin thoroughly for 15 mins.

Caution :

- Avoid fats, oils and lipids.
- Abstain from alcohol for at least 10 days.

Antidote : No specific antidote.

Laboratory tests : No specific parameter for monitoring. Other useful tests: Electrolytes, glucose, BUN, creatinine, liver transaminases.

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