ESSENTIAL CLINICAL TOXICOLOGY

MINISTRY OF HEALTH
SRI LANKA

SLCIM

SRI LANKA COLLEGE OF INTERNAL MEDICINE

Essential Clinical Toxicology

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Message from the Secretary, Ministry of Health, Sri Lanka

It is with great pride and pleasure that I extend my warmest congratulations to the Sri Lanka College of Internal Medicine (SLCIM) on the launch of the book 'Essential Clinical Toxicology'. This collaboration between the Ministry of Health and SLCIM is a huge step forward in ensuring that our medical community has the crucial knowledge needed in clinical toxicology.

As healthcare continues to evolve, the ability to diagnose and manage toxicological emergencies is a critical skill for physicians and healthcare providers. With the increasing exposure to environmental toxins, industrial chemicals, and the misuse of pharmaceuticals, the need for comprehensive knowledge in clinical toxicology has never been greater. This book offers a vital resource to all clinicians, helping them to provide timely and effective care in toxicological emergencies, thereby saving lives and reducing complications.

The Ministry of Health is proud to have supported this project, recognising the importance of advancing medical education and empowering our healthcare professionals with up-to-date knowledge. The collaboration between SLCIM and the Ministry of Health reflects the shared commitment to improving healthcare standards in Sri Lanka.

I trust that this book will serve as an invaluable resource in the continued development of toxicology expertise in Sri Lanka, with benefits to not only medical practitioners and educators, but also to students alike. I commend the editors, contributors, and everyone involved, for their dedication and hard work in making this publication a success.

I wish the Sri Lanka College of Internal Medicine continued success in all its endeavours and look forward to future collaborations that will further enhance healthcare in our nation.

Dr P.G. Mahipala
Secretary
Ministry of Health, Sri Lanka

Message from the Director General of Health Services, Ministry of Health, Sri Lanka

I would like to congratulate the Sri Lanka College of Internal Medicine (SLCIM) on the publication of 'Essential Clinical Toxicology'. This work arrives at a crucial time when managing toxicological emergencies is an indispensable skill for every healthcare provider. Toxicology is not just a subset of medical knowledge; it is a critical domain that intersects with various aspects of patient care. The ability to identify and manage toxicological emergencies profoundly impacts patient outcomes and healthcare systems.

From accidental poisonings to deliberate overdoses, healthcare professionals are on the front lines of these emergencies. By equipping them with essential knowledge and best practices in toxicology, this book empowers them to provide timely and effective care. With chapters on toxidromes and guidance on managing specific toxicities, such as paracetamol, calcium channel blocker overdoses, and agrochemical poisoning such as organophosphates, it covers a wide spectrum of toxicological situations.

The Ministry of Health is proud to support this initiative, confident it will shape a new generation of clinicians, saving lives and improving health outcomes across Sri Lanka.

I extend my heartfelt appreciation to all who have dedicated their time and expertise to producing this invaluable resource. Their commitment to advancing medical knowledge will undoubtedly contribute to saving lives and improving health outcomes across the country.

Dr Asela Gunawardena
Director General of Health Services
Ministry of Health, Sri Lanka

Message from the President

As the President of the Sri Lanka College of Internal Medicine (SLCIM), it is with great pleasure and pride that I welcome you to 'Essential Clinical Toxicology', a comprehensive resource carefully curated by the Toxicology Committee of SLCIM. This book stands as a testament to the hard work, dedication, and expertise of our esteemed committee members, all of whom have contributed their vast knowledge to provide a valuable guide for clinicians.

In an era where the incidence of poisonings and toxic exposures is ever-increasing, the importance of mastering clinical toxicology cannot be overstated. This book is not only an essential tool for physicians, but it also serves as a critical resource for healthcare professionals across all levels, who seek to deepen their understanding of diagnosing and managing toxicological emergencies with confidence and accuracy.

'Essential Clinical Toxicology' reflects the mission of the SLCIM to empower physicians with essential knowledge, practical skills, and a solid foundation in evidence-based medicine. It covers a broad spectrum of toxicological challenges — from commonly encountered cases to rare, complex poisonings — with practical approaches that are easily applicable in day-to-day clinical practice.

I extend my heartfelt gratitude to the authors and contributors from the Toxicology Committee for their remarkable efforts in bringing this book to fruition. Their commitment ensures that our medical community continues to grow stronger in its ability to manage toxicological emergencies effectively and with the highest standards of care.

I am confident that 'Essential Clinical Toxicology' will be an indispensable guide, enhancing the capabilities of all who use it, and ultimately benefiting the lives of countless patients.

Thank you for your dedication to advancing clinical excellence, and I warmly invite you to explore this invaluable resource.

Dr Suranga Manilgama
President
Sri Lanka College of Internal Medicine (SLCIM)

Message from the Editors



The increasing prevalence of poisoning cases poses a significant and growing threat to public health, both globally and particularly in Sri Lanka. Poisoning, whether accidental or intentional, represents a critical concern in emergency departments and intensive care units, demanding immediate and effective intervention. In Sri Lanka, this issue is compounded by a unique epidemiological landscape, where cases of agrochemical poisoning, drug overdoses, and snakebites are alarmingly common. National statistics reveal a staggering estimate of 50,000 poisoning cases reported annually, with agrochemical exposure contributing to a significant proportion of these incidents. These alarming numbers underscore the urgent need to enhance our clinical response to toxic exposures, ensuring that healthcare professionals are equipped with the knowledge and tools necessary to save lives.

'Essential Clinical Toxicology' is a timely and indispensable resource, meticulously published by the Sri Lanka College of Internal Medicine in collaboration with the Ministry of Health. Authored by a distinguished team of experienced internal medicine physicians, this book serves as a beacon of knowledge, delivering an accurate, user-friendly guide that distils the complexities of toxicology into essential core knowledge. It is thoughtfully designed to empower healthcare professionals, particularly those in emergency and internal medicine, in the swift diagnosis and effective management of poisoning cases.

The content is not only highly practical but also engaging, with clear, concise chapters that focus on the most critical aspects of clinical toxicology. It offers clinicians a ready reference to navigate the intricacies of complex cases, ensuring that both common and rare poisonings can be managed with confidence and expertise. Each section emphasises evidence-based practices and real-world application, making it an invaluable tool for healthcare workers across the country. The book's layout is intuitive, allowing for quick access to vital information, which is crucial in high-pressure emergency settings.

In addition to its clinical focus, 'Essential Clinical Toxicology' fosters a holistic understanding of the impact of toxic exposures on individual patients and broader public health. By integrating theoretical knowledge with practical guidelines, this guide not only equips physicians with the skills needed to handle the growing burden of poisoning cases in Sri Lanka but also inspires a collaborative approach to improving patient outcomes.

This guide is an essential addition to the medical community, empowering physicians with the knowledge and confidence they need to combat the rising tide of poisoning incidents. As we confront the challenges posed by toxic exposures, 'Essential Clinical Toxicology' stands as a testament to our commitment to excellence in healthcare, ultimately aiming to protect and preserve lives across Sri Lanka. We would like to acknowledge Professor Anjana Silva and Professor Anuruddhi Edirisinghe for sharing their valuable pictures with us. Some of the images were sourced from the internet.

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Preamble

Book introduction

Title: Essential Clinical Toxicology

Scope:

This book serves as a comprehensive guide to the fundamentals of clinical toxicology, offering a clear and concise exploration of poisons, their clinical presentations, and the systematic approach to managing toxicological emergencies. The content covers a broad spectrum of toxins, including chemical, pharmaceutical, and environmental agents, as well as envenomation such as snake bites and insect stings. Special emphasis is placed on toxidrome identification - clusters of clinical signs that guide early recognition of poisoning syndromes. Additionally, the book includes practical evidence-based guidelines for the management of patients with poisoning, with a particular focus on the clinical challenges and toxicological agents most commonly encountered in Sri Lanka. This makes it an invaluable resource for all healthcare professionals, working even in resource-limited settings.

Key features:

- **Comprehensive overview:** Covers a wide range of poisons and toxins, including both intentional and accidental poisonings
- **Focused on Sri Lanka:** Includes detailed information on the toxicological agents most relevant to the Sri Lankan healthcare context, as well as strategies for managing toxicological emergencies in resource-limited settings
- **Systematic approach:** Provides clear guidance on the assessment, stabilisation, decontamination, and management of poisoned patients
- **Toxidrome identification:** Offers tools for quickly recognising specific poisoning syndromes based on symptom clusters, enabling rapid diagnosis and treatment
- **Practical insights:** Includes tips for managing toxicological emergencies and envenomation in a clinical setting, with guidelines tailored to local epidemiology and healthcare infrastructure

Objectives:

By reading this book, healthcare professionals will develop:

1. **A thorough understanding of the clinical manifestations** of various poisons, with an emphasis on those commonly encountered in Sri Lanka.
2. **The ability to systematically approach toxicological emergencies**, including rapid assessment, stabilisation, decontamination, antidote use, and supportive care.
3. **Proficiency in identifying toxidromes**, enabling quick and accurate diagnosis of poisoning syndromes based on clusters of symptoms and signs.
4. **Skills to differentiate between accidental poisonings and cases of deliberate self-harm**, and apply the appropriate clinical and psychological interventions.
5. **Expertise in managing envenomation**, particularly from snake bites and insect stings, with guidelines tailored to local species and treatment protocols.
6. **The capacity to handle toxicological emergencies** in resource-limited settings, using practical and innovative solutions suited to available resources.

This book provides essential knowledge and practical insights, making it an indispensable resource for healthcare professionals managing toxicological cases in both everyday practice and emergency scenarios.

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1. Basics of Poisoning Management for Healthcare Professionals

Introduction to 'Poison':

Definition:
A **poison** is defined as a substance or object of natural or man-made origin that may be toxic to a living organism and has an injury or fatal effect on the body, whether it is ingested, inhaled, absorbed, or injected through the skin.

Box 1.1

Types of poisons:

Natural poisons: Natural toxins are toxic compounds that are naturally produced by living organisms. These toxins are not harmful to the organisms themselves but they may be toxic to other creatures, including humans.

- **Plant poisons** – e.g.: colchicine from the *Gloriosa superba*, oleander, and mushrooms which can cause multiorgan failure
- **Animal venoms / insect stings** – snakes and other animal bites and insect stings

Synthetic poisons: Encompasses a range of human-made chemicals.

- Pharmaceuticals
- Pesticides – substances that are meant to control pests
    - Insecticides – act against insects
    - Fungicides – act against fungi
    - Nematicides – act against nematodes
    - Rodenticides – act against rodents (mice, rats)
    - Molluscicides – act against molluscs (snails, slugs)
- Herbicides – act against weeds
- Microbicides – act against microbes
- Industrial and household chemicals

LD_{50} value and toxicity classification:

What is LD_{50}?

> LD stands for 'Lethal Dose'. LD_{50} is the amount of a material, given all at once, which causes the death of 50% (one half) of a group of test animals. The LD_{50} is one way to measure the short-term poisoning potential (acute toxicity) of a material.

Box 1.2

Epidemiology of poisoning in Sri Lanka: Trends analysis

Prevalence and impact:

- Approximately 80,000 admissions occur in government hospitals due to poisoning
- Intentional poisoning accounts for 70-75% of cases, while accidental poisoning makes up 25-30%
- Children are more commonly affected in accidental poisonings (approximately 5% of all accidental cases)

Historical trends:

- Pesticide poisoning was the most common type of poisoning before the year 2000 and in the early 2000s

Current trends:

- Household chemical poisoning (including detergents, cleaning materials, acids, alkali substances, mosquito coils, stain removers, and petroleum products), is now the most prevalent type of poisoning in Sri Lanka

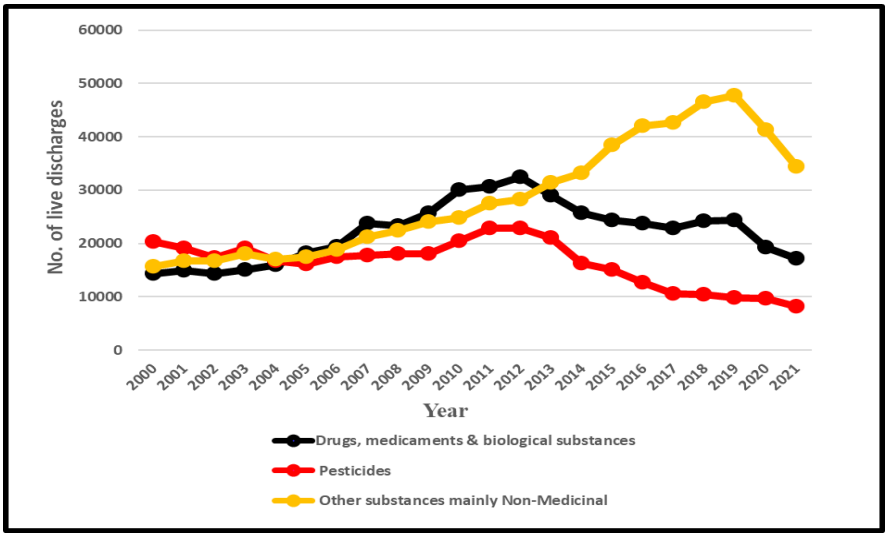

Figure 1.1 - Types of poisoning in the last two decades in Sri Lanka

Epidemiology of poisoning in Sri Lanka: key points

Mortality rates:

- Pesticide-related deaths were a significant issue in the 1980s (Sri Lanka ranked third globally)
- Over the last two decades, there has been a reduction in pesticide-related deaths
- However, a significant number of deaths still occur due to pesticide

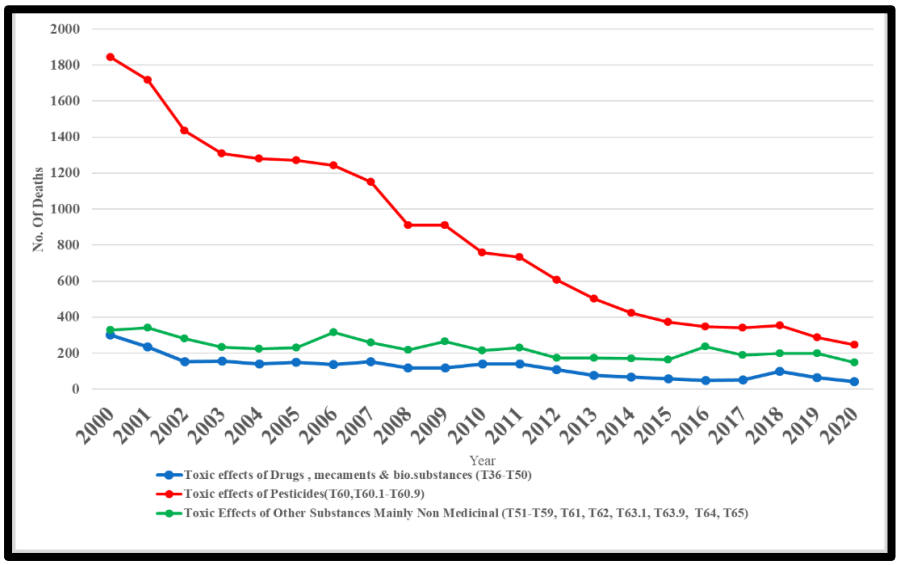

Figure 1.2 - Acute poisoning related deaths in Sri Lanka from 2000 - 2020

Systematic approach to patients with poisoning (ResusRSIDEAD pathway)

Overview: The ResusRSIDEAD pathway provides a structured method for assessing and managing poisoning cases.

Components:

- **Resus:** ABCDE assessment
- **R:** Risk assessment
- **S:** Supportive care and monitoring
- **I :** Investigations
- **D:** Decontamination
- **E:** Enhanced elimination
- **A:** Antidote administration
- **D:** Disposition and follow-up

Box 1.3

ResusRSIDEAD: Resuscitation (ABCDE Approach):

Introduction: The ABCDE approach is a systematic method for the initial assessment and management of life-threatening conditions.

Components:

- **A:** Airway – Ensure the airway is clear
- **B:** Breathing – Assess and support breathing
- **C:** Circulation – Maintain adequate circulation and address shock
- **D:** Disability – Detect and correct hypoglycaemia and seizures, evaluate neurological status including GCS and pupil size
- **E:** Exposure / Environment – Assess for further exposure to toxins and control the environment. By removing clothes contaminated with poison. You may use emergency antidotes if indicated

Box 1.4

In a case of suspected poisoning:

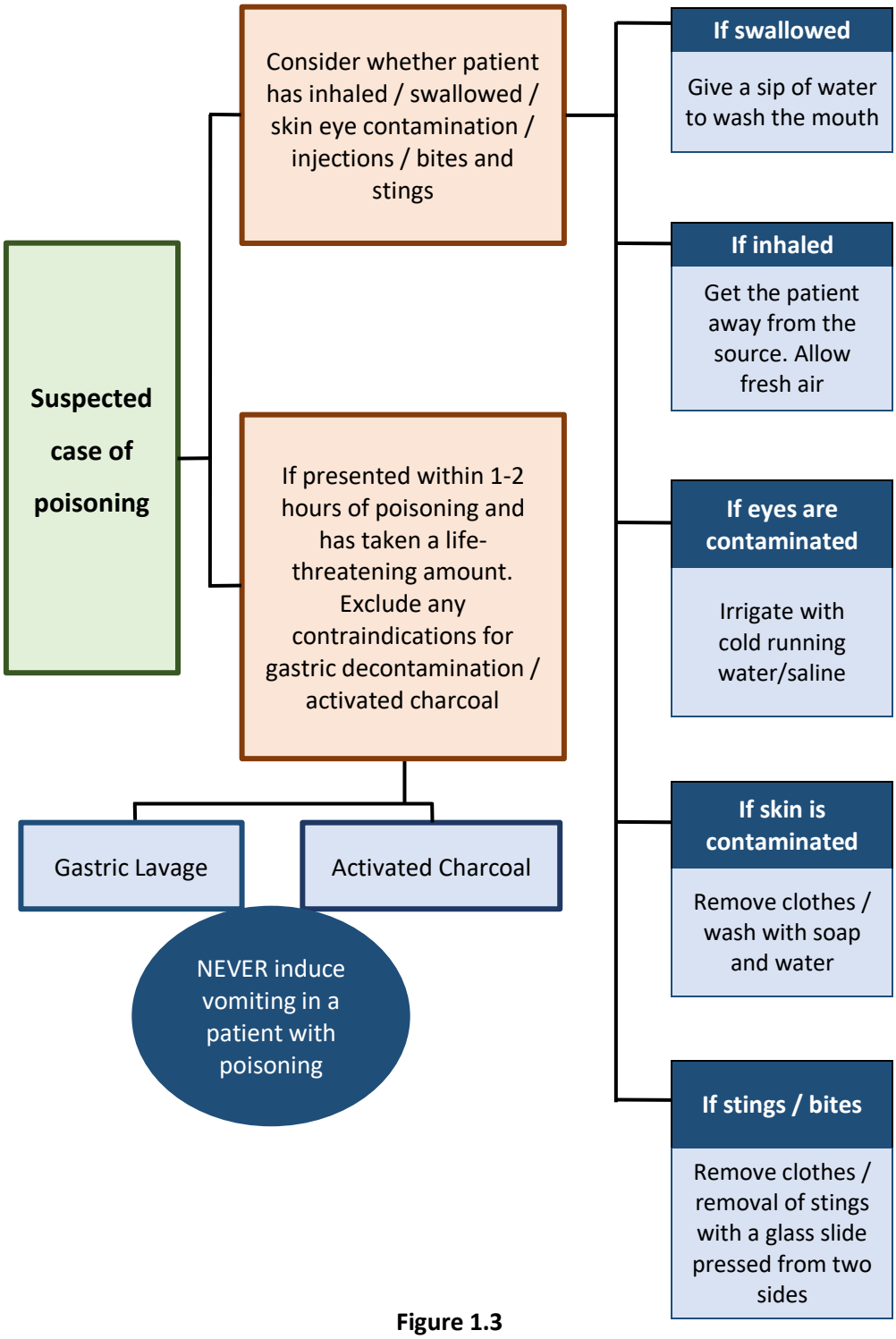

Figure 1.3

ResusRSIDEAD: Risk Assessment

Take relevant history from the patient / bystander and examine the patient to assess the risk.

1. Who (patient identification):

- **Name**: Obtain the patient's full name
- **Age**: Record the patient's age
- **Gender**: Note the patient's gender
- **Weight**: Document the patient's weight (if available)
- **Circumstances at the time of poisoning**: Understand the patient's context, whether the patient was alone, with family, or at work, etc.

2. What (substance details):

- **Name of poison / substance**: Determine the specific toxic agent
- **Amount and route of ingestion**: Quantify the dose ingested and how it was taken (e.g.: oral, inhalation, dermal exposure)
- **Co-ingestions**: Check for any other substances taken concurrently (e.g.: alcohol, medications)

3. When (timeline):

- **Exposure date and time**: Record when the poisoning occurred
- **Deliberate self-harm**: If intentional, document the decision time

4. Where (location):

- **Location of poisoning**: Specify the setting (e.g.: home, workplace, outdoor, etc.)

5. Why (context):

- **Brief Description**: Gather relevant details (e.g.: accidental exposure, suicide attempt)

6. What happened (clinical presentation):

- **Symptoms**: Note any physical or behavioural changes (e.g.: vomiting, drowsiness, seizures)

Box 1.5

Ask	Look
• Time – patient was last seen • Vomited to home • Time – to reach the hospital • Remaining tablets / labels / blister packs / sachets	• Clinic notes of patient / relatives • Suicidal notes • Colour and contents of the vomitus • Any poison particles / tablets in vomitus • Management at the peripheral hospital

Box 1.6

ResusRSIDEAD: Symptomatic / supportive care

Supportive care and monitoring:

- Regularly monitor vital signs (heart rate, blood pressure, respiratory rate, temperature)
- Position the patient in the left lateral or recovery position
- Address associated injuries promptly
- Establish intravenous access for adequate fluid resuscitation which facilitates proper hydration and elimination of poison
- Provide care for unconscious patient
- Attend to bladder, bowel, skin, oral, and eye care

Pain management:

- Assess and manage pain using appropriate analgesics
- Consider non-opioid medications when possible

Psychosocial support:

- Offer emotional reassurance to patients and families
- Involve mental health professionals if necessary

Box 1.7

ResusRSIDEAD: Investigations

Aims of Investigations:

- **Identification**: Confirm the poison and its concentration
- **Risk assessment**: Predict complications and guide management
- **Treatment guidance**: Determine appropriate intervention

Tests selection (based on suspected toxins and clinical presentation):

- Prioritise laboratory tests and imaging based on the patient's symptoms, exposure history, and suspected toxins

Limitations of toxicological investigations:

- **Time sensitivity**: Some tests are most accurate within specific time windows after exposure
- **False negatives /positives**: Test results may not always reflect the actual poisoning status
- **Availability and sensitivity**: Not all substances can be detected reliably
- **Interference**: Other medications or substances may affect test results

Box 1.8

Other relevant investigations:

- Arterial blood gas
- Serum electrolytes
- Ionised calcium and magnesium
- Grouping and DT
- ECG
- Serum creatinine
- SGOT/SGPT
- INR/APTT
- RBS
- FBC
- CPK

Box 1.9

Substances detected in urine analysis (toxicological analysis):

- Urine testing can reveal the presence of various substances
- However, these facilities are not freely available in Sri Lanka
  - Amphetamine
  - Barbiturates
  - Cannabis
  - PCP (Phencyclidine)
  - Opiates
  - Benzodiazepines
  - Propoxyphene
  - Methamphetamine (ICE)
  - Cocaine
  - Methadone
  - MDMA (XTC)

Box 1.10

ResusRSIDEAD: Gastrointestinal Decontamination

Methods of gastric decontaminations are:

- Gastric Lavage
- Activated charcoal
- Whole bowel irrigation

Box 1.11

Induction of emesis

Induction of Emesis - Not recommended (contraindicated)

- Historically used to induce vomiting after ingestion of toxic substances
- Not routinely recommended due to the risk of aspiration
- May cause complications such as oesophageal injury or airway obstruction

Box 1.12

- Induction of emesis is not synonymous with gastric lavage

01) Gastric aspiration and lavage

Indications:

- Usually indicated within first two hours
- However, it could be done even up to 6 to 8 hours if potentially toxic ingestions of sustained-release / enteric-coated drugs, large amount of poison or packaged drug ingestion (body packing / stuffing)
- GCS > 10

Contraindications:

- Oral intake of caustic and corrosive substances
- Increased risk of aspiration – e.g.: hydrocarbon ingestion

Relative contraindications:

- Clinically unstable patients
- Uncooperative patients
- Late presentation
- Inability to protect the airway

- Presence of bradycardia
- Known oesophageal diseases – e.g.: oesophageal strictures
- Concern for decreased peristalsis
- Ingestion of harmless substances or very small quantities

  (If GCS < 10, secure airway with cuffed ET tube and do the gastric lavage via NG tube)

Method:

- Informed verbal consent from patient / relative
- Insert lubricated NG tube (16G-18G) or Ryles tube orally
- Cuffed ET tube – If GCS < 10
- Confirm the correct placement by aspirating the gastric content or inject air with the 50 mL syringe, while auscultating over the epigastrium, (later can confirm the position by X-ray)
- Use a mouth gag to prevent patient from biting the tube
- Collect the first 50 mL of lavage fluid for toxicological analysis or medico-legal purpose
- Use normal saline / water as lavage fluid
- The recommended volume of each aliquot is 200 mL for adults and 10 mL/kg for children
- A total of 3 L of lavage fluid or perform until the return is clear
- The procedure should be supervised by a doctor

Box 1.13

02) Activated Charcoal:

Administration:

- Within 1-2 hours of ingestion
- Orally or via NG tube. The oral route is preferred if the patient is conscious and able to drink

Dose:

- Adults and teenagers: 50-100 g as a single dose (1g/kg) dissolved in 200 mL of water
- Children (1-12 years): 25-50 g as a single dose
- Children under 1 year: Not recommended

Figure 1.4 – Activated charcoal powder

Contraindications for activated charcoal

- Presence of intestinal obstruction is an absolute contraindication
- Decreased peristalsis or partial bowel obstruction is a relative contraindication
- Need for endoscopy (e.g.: significant caustic ingestion)
- For patients with compromised airway reflexes, unless they are intubated
- Oral intake of caustic substances
- Late presentation
- Increased risk and severity of aspiration associated with activated charcoal use (e.g.: hydrocarbon ingestion)

- Toxins poorly adsorbed by activated charcoal (e.g.: metals including iron and lithium, alkali, mineral acids, alcohols)

Box 1.14

03) Whole Bowel Irrigation (WBI):

Indications:

- Used for patients who have ingested toxic doses of medications not absorbed by activated charcoal (e.g.: iron, lithium)
- Potentially toxic ingestions of sustained-release or enteric-coated drugs
- Packaged drug ingestion (body packing/stuffing)

Technique:

- Rapid administration of an osmotically balanced Polyethylene Glycol-electrolytes solution
- Given orally or via nasogastric tube
- Aims at flushing out the entire gastrointestinal tract

Box 1.15

ResusRSIDEAD: Enhanced elimination

Methods of enhanced elimination include:

- Multiple doses of activated charcoal
- Urinary alkalisation
- Urinary acidification
- Various types of dialysis (HD, CRRT, SLED, CVVH)
- Plasmapheresis
- Exchange transfusion
- Therapeutic Plasma Exchange (TPE)

Box 1.16

01) Multiple Dose Activated Charcoal:

- Enhances elimination by interrupting entero-enteric or entero-hepatic circulation

Indications:

- Salicylate
- Quinine
- Verapamil
- Theophylline
- Digoxin / other cardiac glycosides
- Niyangala (*Gloriosa superba*)
- Extended-release preparations
- Slow-release medications (e.g.: theophylline, phenobarbital)
- Phenytoin
- Colchicine
- Dapsone
- Quinines
- Yellow Oleander
- Mushroom
- Carbamazepine

Method:

- Administer additional doses of activated charcoal
- If multiple doses are given – 50 g every four hours for 24-48 hours
- The decision about multiple doses is decided by the treating physician and effectiveness of other treatment methods

Box 1.17

02) Urinary alkalinisation

Rationale:

- Alkaline urine pH promotes the ionisation of highly acidic drugs
- Prevents reabsorption across renal tubular epithelium and promoting excretion in urine
- Alkaline diuresis used in salicylates, MCPA, phenoxyacetate herbicides, mercaptopurine, and phenobarbitone)

Maintenance of urinary pH:

- To achieve alkaline diuresis, urinary pH should ideally be maintained above 7.5, preferably in the range of 8.0 to 8.5

Method:

- Correct dehydration and hypokalaemia if present
- Give IV bolus of 1-2 mmol/kg $NaHCO_3$
- Commence an $NaHCO_3$ infusion of 150 mmol in 1000 mL of 5% dextrose at 250 mL per hour
- Check the urine pH and repeat the dose of $NaHCO_3$ every 4 hourly until the target urine pH of more than 7.5 is achieved
- Can give IV KCl if hypokalaemia is present

Box 1.18

03) Urine acidification

- It is indicated in poisoning with amphetamines, quinine, ephedrine, and flecainide
- However, it is not recommended because of the metabolic acidosis
- It may promote acute kidney injury if there is associated rhabdomyolysis

Box 1.19

04) Dialysis

Common indications and rationale for dialysis in cases of poisoning:

- Acetaminophen (when serum concentration >1000 µg/mL, or 6600 µmol/L)
- Aminoglycoside antibiotics
- Alcohols (ethanol, isopropanol, acetone, methanol, ethylene glycol, propylene glycol, diethylene glycol)
- Chloral hydrate (and metabolite trichloroethanol)
- Valproate (when serum concentration > 1300 mg/L, or 9100 µmol/L)
- Dabigatran
- Disopyramide
- Ethambutol
- Gabapentin
- Heavy metals
- Lithium
- Meprobamate
- Methotrexate
- Nadolol
- Biguanide (e.g.: metformin) when associated with lactic acidosis
- Atenolol
- Baclofen
- Barbiturates
- Bromides
- Caffeine
- Carbamazepine
- Phenytoin
- Pregabalin
- Procainamide
- Salicylates
- Sotalol
- Theophylline

Box 1.20

Indications for dialysis

a) Ethylene glycol and methanol poisoning

- Severe toxicity (even with small ingestions)
- Metabolic acidosis
- Renal failure

b) Lithium Poisoning:

- Symptoms of severe toxicity irrespective of the lithium concentration
- Serum lithium concentration > 5 mEq/L (5 mmol/L)
- Serum lithium concentration > 4 mEq/L (4 mmol/L) with impaired renal function (eGFR < 45 mL/min, serum creatinine of ≥ 2 mg/dL in adults, serum creatinine ≥ 1.5 mg/dL in older adults)

c) Ethanol poisoning:

- Severe cases (organ toxicity) with serum ethanol levels more than 450 mg/dL

d) Salicylates (Aspirin) poisoning:

- Evidence of severe toxicity
    1. Altered GCS – Any alteration in mental status (e.g.: delirium, agitation, lethargy, seizure) attributed to salicylism
    2. Acidaemia – blood pH < 7.2 or pH < 7.3 despite aggressive resuscitation
    3. Renal failure – Presence of acute kidney injury or chronic kidney disease and serial serum salicylate concentrations are relatively unchanged despite bicarbonate infusion. Additional indications for haemodialysis irrespective of clinical findings include the following salicylate threshold concentrations:
        - In acute toxicity with normal kidney function: > 100 mg/dL (> 7.2 mmol/L)
        - In acute toxicity with impaired kidney function: > 90 mg/dL (> 6.5 mmol/L)
        - In chronic toxicity: > 60 mg/dL (> 4.3 mmol/L)
        - Elderly ≥ 60 mg/dL (> 4.4 mmol/L)
    4. Acute pulmonary oedema
- Clinical deterioration (e.g.: cardiovascular collapse, hypotension, ventricular dysrhythmia, worsening metabolic acidosis or a primary respiratory acidosis) despite aggressive and appropriate supportive care
- Urinary alkalinisation is not feasible – Fluid overload that prevents administration of bicarbonate infusion
- Rising serum salicylate levels despite decontamination and urinary alkalinisation

e) Metformin toxicity

- Significant comorbidities
- Critically ill
- pH < 7.1
- Renal insufficiency
- Fluid overload status

Box 1.21

ResusRSIDEAD: Antidotes

Antidotes are used to neutralise or mitigate the harmful effects of toxins, drugs, or other poisonous substances. They can be specific to certain poisons or have a broader application in reducing toxicity.

Poison	Antidote
Acetaminophen	Acetylcysteine, Methionine
Anaesthetics	Lipid emulsion (Fat emulsion)
Aniline	Methylene blue
Anticholinesterases (Organophosphates)	Atropine, Pralidoxime (2-PAM)
Tricyclic antidepressants (TCA)	Sodium bicarbonate, Lipid emulsion
Noncyclic antidepressants (SSRI, SNRI, Bupropion, Venlafaxine)	Sodium bicarbonate, Lipid emulsion
Arsenic	Dimercaprol
Benzodiazepines	Flumazenil
Beta-blockers	Atropine, High Insulin Euglycaemic Therapy (HIET), Calcium, Glucagon, Lipid emulsion
Calcium channel blockers	Atropine, High Insulin Euglycaemic Therapy (HIET), Calcium, Lipid emulsion
Cyanide	Hydroxocobalamin (Cynokit), Sodium thiosulphate
Digoxin	Atropine, Digoxin immune Fab
Ethylene glycol	Fomepizole, Ethanol, Pyridoxine, Sodium bicarbonate
Hydrofluoric acid burns	Calcium gluconate

Iron	Deferoxamine (Desferrioxamine)
Isoniazid	Pyridoxine
Lead	Dimercaprol
Mercury (inorganic or elemental)	Dimercaprol
Methanol	Fomepizole, Ethanol (competitive inhibitors)
Mushrooms (Amanita phalloides) - hepatotoxic	Acetylcysteine
Mushrooms (Gyromitra or Hydrazine containing) - Seizure inducing	Pyridoxine
Nitrates or Nitrites	Methylene blue
Opioids	Naloxone
Propanil	Methylene blue
Salicylates	Sodium bicarbonate
Sodium channel blocking drugs (wide QRS)	Sodium bicarbonate, Lipid emulsion
Sulfonylurea (oral hypoglycaemic)	Octreotide

Table 1.1

Consider antidotes as a first mode of treatment in some cases of overdose such as morphine or organophosphate poisoning (even before gastric decontamination)

Box 1.22

ResusRSIDEAD: Disposition

- Proper disposition of a poisoned patient is crucial for their well-being

Disposition options:

Ward admission:

- If the patient is stable, has mild symptoms, and does not require intensive monitoring or specific antidotes, admission to a general ward may be appropriate

Intensive Care Unit (ICU) admission:

- For severe poisonings, organ failure, altered mental status, or hemodynamic instability, ICU admission may be necessary

Transfer to a tertiary care centre:

- If the local hospital lacks specialised toxicology services or specific antidotes, consider transferring the patient to a tertiary care centre

Box 1.23

Timely transfer:

- Deciding whether to transfer the patient (ward, ICU, or another hospital) ensures timely access to appropriate care.

It is advisable to send the poison bottle with the intact label if available, any empty blister packs / sachets / boxes of medications, specimen (live or dead) in a case of envenomation, with the patient while transferring to another institution.

Box 1.24

Decision for transfer:

Admit to an equipped healthcare facility:

- Transfer the patient to a hospital or healthcare centre with appropriate facilities
- Reasons for admission:
  - **Complex cases:** Some poisonings require specialised management (e.g.: antidote administration, haemodialysis)
  - **Risk of delayed complications:** Even if the patient appears stable initially, complications may arise later (e.g.: delayed organ damage)
  - **Limited resources at the scene:** Pre-hospital settings may lack necessary equipment and expertise

Considerations:

- **Transport time:** Balance the urgency of transfer with the time needed for safe transport
- **Accompanying personnel:** Ensure trained healthcare providers accompany the patient during transfer
- **Supportive equipment:** Bring necessary equipment (e.g.: cardiac monitor, airway supplies, medications, etc.)

Box 1.25

Mode of Transfer:

Ambulance transfer:

- Use an ambulance equipped for medical emergencies
- Dial emergency services (e.g.: 1990) for toll-free ambulance support
- Ambulances provide a controlled environment for monitoring and intervention during transport

Box 1.26

Communication:

- Notify the receiving facility about the patient's condition, suspected poison, and any ongoing treatments
- Provide relevant details (e.g.: vital signs, exposure history, symptoms) where to refer patients in cases of poisoning based on specific indications

Box 1.27

Special referrals

1. **Judicial Medical Officer (JMO) or police:**

Indication:

- Unclear circumstances surrounding the poisoning
- Suspicion of intentional poisoning (homicide)
- Patient death related to poisoning

Action:

- Inform the police or JMO promptly

Box 1.28

2. **Psychiatrist or psychologist:**

Indication: Intentional poisoning (suicidal attempts)

- Address underlying mental health issues

Action:

- Refer the patient for psychiatric evaluation and counselling

Box 1.29

3. Child Protection Authority:

Indication: Child presents with accidental poisoning and concerns about child safety and neglect

Action: Report to the Child Protection Authority for assessment and intervention

Box 1.30

4. Family Education:

Indication: Child comes with accidental poisoning. Need to prevent future incidents

Action: Educate the family on poison prevention, safe storage, and emergency response

Box 1.31

5. Labour Department:

Indication: Poisoning occurs while working in an unsafe environment (e.g.: exposure to chemicals)

Action: Report to the Labour Department for workplace safety investigation

Box 1.32

6. Medical Officer of Health (MOH):

Indication: Food poisoning cases

Action: Notify the MOH for public health surveillance and investigation

Box 1.33

Remember that timely referrals and collaboration with relevant authorities ensure comprehensive care and prevention of future incidents

Consultation with Poison Control Centers:

Contact the National Poisons Information Centres (NHSL Colombo and Peradeniya) for guidance on management and antidotes. When contacting the National Poison Information Centre, it's crucial to provide accurate and relevant information. Here's a comprehensive list of details to include:

1. Caller Details:

- **Name:** Full name of the person making the call
- **Contact number:** Phone number where the caller can be reached
- **Institution or organisation:** If applicable, provide the name of the institution or organisation the caller represents
- **Designation (if applicable)**: If the caller is a healthcare professional, mention their designation (e.g.: HO, Medical officer, ICU nurse, physician)

2. Patient Location:

- **ICU:** If the patient is in the Intensive Care Unit
- **Ward:** If the patient is in a regular hospital ward
- **Home:** If the exposure happened at home
- **Other:** Any other relevant location

3. Patient Details:

- **Name:** Full name of the patient affected by the poisoning
- **Age:** Age of the patient
- **Gender:** Specify whether the patient is male, female, or other
- **Weight:** If known, provide the patient's weight

4. Poison Exposure Details:

- **Type of poison:** If known, mention the specific substance or product name. If unknown describe the poison (e.g.: household chemicals, medications, plants)
- **Amount:** Estimate the quantity of poison ingested or exposed to
- **Co-ingestions:** Mention any other substances the patient might have ingested simultaneously
- **Date and time of exposure:** Provide the exact date and time when the exposure occurred
- **Route of exposure:** Specify how the poison entered the body (e.g.: ingestion, inhalation, skin contact)
- **Circumstances of poisoning:** Intentional (suicidal or homicidal), accidental

5. Suspected poison:

- If unknown, mention the specific substance or product suspected to be the cause of poisoning

6. Symptoms and signs:

- List any observed symptoms or signs related to the poisoning (e.g.: nausea, vomiting, dizziness, difficulty breathing)

7. Emergency measures taken:

- Describe any initial actions taken by the caller or others (e.g.: rinsing eyes, inducing vomiting, administering first aid)

8. Additional notes:

- Include any other relevant information or concerns related to the poisoning incident

Box 1.34

Remember to stay calm and provide accurate details. The poison center staff will guide you further based on the information provided.

HOTLINES:

National Poison Center NHSL Colombo: 011 2 686 143

National Poison Center Peradeniya: 071 102 7076

Box 1.35

REFERENCES

1. Fernando R. Management of Poisoning. 3rd ed. Colombo: The National Poisons Information Centre National Hospital of Sri Lanka; 2007

2. National Poisons Information Service TOXBASE [Internet]. Birmingham (UK): NPIS; c1999 [updated 2024 Jan 10; cited 2024 May 03]. Available from: https://www.toxbase.org

2. Toxidromes

This module is an overview of toxidromes, catering specifically to the context of Sri Lanka while incorporating global best practices.

In this module, we will delve into the fundamental concepts of toxidromes, exploring their key characteristics, diagnostic significance, and clinical relevance.

Toxidrome

- Toxidromes are collections of clinical signs and symptoms associated with different classes of toxins
- They serve as diagnostic frameworks that allow for the rapid narrowing of the toxicological differential diagnosis based on the autonomic effects of the toxin in question

Key characteristics of toxidromes

1. **Clinical signs and symptoms**:
   Toxidromes manifest as characteristic clusters of clinical signs and symptoms, often reflecting the specific actions of the toxin on the body's physiological systems.
2. **Rapid differential diagnosis**:
   By recognising the pattern of signs and symptoms comprising a toxidrome, we could quickly narrow down the potential toxins responsible for a patient's presentation.
3. **Autonomic effects**:
   Toxidromes are based on the autonomic effects of the toxin, which can influence various bodily functions controlled by the autonomic nervous system.

4. **Readily observable findings**:
   Toxidromes rely on readily observable clinical findings, which can be assessed through physical examination. Key areas of assessment include:

- **Vital signs**: changes in blood pressure, heart rate, and respiratory rate
- **Eye**: pupil size, reaction to light, and ocular manifestations
- **Skin**: colour, temperature, moisture, and presence of rashes, or lesions
- **Secretions**: excessive sweating, salivation, lacrimation, or gastrointestinal secretions
- **Mental state**: alterations in consciousness, level of alertness, or psychiatric symptoms

Box 2.1

By integrating these readily observable findings, healthcare providers can effectively recognise and differentiate toxidromes, leading to timely and targeted interventions in cases of poisoning.

Common toxidromes:

- Anticholinergic toxidrome
- Sympathomimetic toxidrome
- Cholinergic toxidrome
- Opioid toxidrome
- Sedative-hypnotic toxidrome

Box 2.2

Other uncommon toxidromes:

- Neuroleptic malignant syndrome
- Serotonin syndrome
- Hallucinogenic toxidrome

Box 2.3

Diagnostic approach to toxidromes

1. Anticholinergic toxidrome

This toxidrome results from the inhibition of the neurotransmitter acetylcholine at muscarinic receptors, leading to a constellation of symptoms.

Common causes of anticholinergic toxidrome

- Atropine
- *Datura stramonium* (Atthana)
- Tricyclic antidepressants (TCA)
- Scopolamine
- Diphenhydramine
- Benztropine
- Trihexyphenidyl
- Some antipsychotics
- Muscle relaxants like cyclobenzaprine
- Some antiarrhythmics

Box 2.4

Clinical features of anticholinergic toxidrome

- **Dilated pupils (mydriasis)**: The pupils are larger than normal, causing blurry vision, and photophobia
- **Delirium**: Patients often present with agitated delirium, which may include hallucinations, incoherent speech, and picking at the air or objects
- **Tachycardia**
- **Dry skin**: Skin appears dry and flushed. Examination may reveal no sweat in the armpits

Box 2.5

Summary of clinical features of anticholinergic toxidrome

Clinical indicator	Finding
Heart rate	Fast
Cardiac rhythm	Sinus tachycardia, tachyarrhythmia
Blood pressure	High
Temperature	High
Respiratory rate	Normal or high
Eyes	Mydriatic
Skin	Dry
Secretions	Dry
Mental status	Normal or agitate

Table 2.1

Mnemonic for anticholinergic toxidrome:

'**Mad as a Hatter'** – delirium and altered mental status
'**Blind as a Bat'** – mydriasis (dilated pupils)
'**Red as a Beet**' – flushed skin
'**Hot as a Hare**' – hyperthermia due to impaired sweating
'**Dry as a Bone**' – dry skin and anhidrosis
'**Full as a Flask**' – urinary retention (due to anticholinergic effects on the bladder)

Box 2.6

Management

Antidote

- The primary antidote used for anticholinergic toxidrome is **physostigmine** (dose – 2 mg IV slow infusion, and could be repeated in 20 min)
- However, physostigmine is not routinely used (e.g.: seizures, dysarrhythmia, severe psychosis) for anticholinergic toxidrome due to several reasons:
    - **Adverse effects**: physostigmine can cause cholinergic excess, leading to symptoms like bradycardia, bronchospasm, and seizures, especially in cases of tricyclic antidepressant (TCA) poisoning
    - **Narrow therapeutic window**: the drug has a narrow therapeutic window
- Alternatives like rivastigmine might be used when physostigmine is not available

- **Specific indications**: It is typically reserved for cases with severe central anticholinergic toxicity where supportive care alone is insufficient

Box 2.7

2. Sympathomimetic toxidrome

This toxidrome results from excessive stimulation of the sympathetic nervous system due to the use or abuse of sympathomimetic substances.

Sympathetic stimulant substances

- Caffeine
- Nicotine
- MDMA (Ecstasy or Molly)
- Amphetamines
- MAO inhibitors
- Cocaine
- Ephedrine
- Pseudoephedrine
- Theophylline
- Withdrawal from benzodiazepines / baclofen

Box 2.8

Clinical features of sympathomimetic toxidromes

- **Dilated pupils (mydriasis)**: The pupils are larger than normal, causing blurry vision, and photophobia
- **Mental state:** Patient may be agitated or normal
- **Tachycardia**
- **Wet skin**: The patient may or may not have diaphoresis. Examination may reveal sweat in the armpits

Box 2.9

Summary of clinical features of sympathomimetic toxidrome

Clinical indicator	Finding
Heart rate	Fast
Cardiac rhythm	Sinus tachycardia, tachyarrhythmia
Blood pressure	High
Temperature	Normal or high
Respiratory rate	Normal or high
Eyes	Mydriatic
Skin	Normal or diaphoretic
Secretions	Normal
Mental status	Normal or agitation

Table 2.2

Most of the clinical features are similar between the anticholinergic toxidrome and the sympathomimetic toxidrome. However, there are few key points to differentiate between the two.

Key points to differentiate anticholinergic toxidrome and sympathomimetic toxidrome

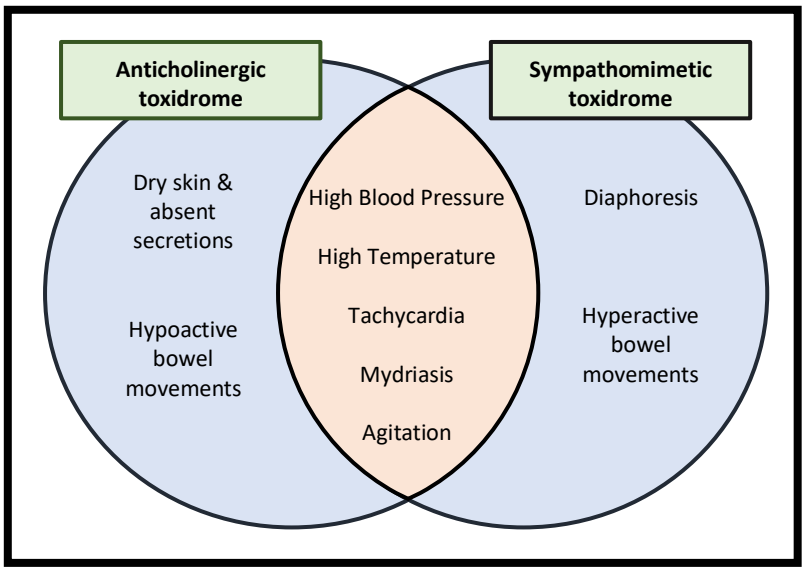

Figure 2.1

Management

- Supportive care
- Management of hyperthermia – consider active cooling methods including IV fluids, tepid sponging, fanning, etc.
- For tachycardia and hypertension,
    - Consider benzodiazepine – it will be effective to control agitation and seizures as well
    - If hypertension and tachycardia persist, consider phentolamine in addition to the benzodiazepines
    - GTN infusion and sodium nitroprusside also can be given after phentolamine
    - Avoid pure beta blockers for tachycardia and hypertension (can cause pure alpha agonism)
- Sedation including intubation if necessary
- Be vigilant about rhabdomyolysis which could be a complication

Box 2.10

3. Cholinergic toxidrome

Cholinergic toxidrome is a constellation of symptoms resulting from acute cholinesterase inhibitor poisoning. It results in overstimulation of the muscarinic and nicotinic receptors due to excess acetylcholine activity in synapses, glands, smooth muscles, and motor end plates where cholinergic receptors are found.

Common causes of cholinergic toxidrome

Organophosphate pesticides:

- E.g.: Parathion, Malathion, Diazinon
- Mechanism: Inhibit acetylcholinesterase, leading to acetylcholine accumulation at neuromuscular junctions

Carbamates:

- E.g.: Carbaryl, Aldicarb, Methomyl, Carbofuran, Baygon, Carbosulfan, Landrin
- Mechanism: Inhibit acetylcholinesterase, typically with a shorter duration than organophosphates

Medications:

- Physostigmine: Treats anticholinergic toxicity but can cause cholinergic effects if overdosed
- Pyridostigmine: Used for myasthenia gravis; overdose can lead to cholinergic symptoms

Chemical warfare agents:

- E.g.: Sarin, Soman and VX – Potent acetylcholinesterase inhibitors, causing severe and rapid cholinergic toxidrome

Certain mushrooms:

- E.g.: Clitocybe, Inocybe species
- Mechanism: Contain muscarine, which directly stimulates muscarinic receptors

Other toxins:

- E.g.: Black widow spider, some marine toxins, and certain snake venoms can cause cholinergic symptoms through various mechanisms affecting acetylcholine

Box 2.11

Clinical features of cholinergic toxidrome

- **Muscarinic symptoms:**

Mnemonic for cholinergic toxidrome: DUMBBELS with 2 killer B and SLUDGE

DUMBELS	SLUDGE
D – **D**iarrhoea	**S** – **S**alivation
U – **U**rination	**L** – **L**acrimation
M – **M**iosis and **M**uscle weaknesses	**U** – **U**rination
B – **B**radycardia and low **B**lood pressure	**D** – **D**efecation
E – **E**mesis (vomiting)	**G** – **G**I Stress
L – **L**acrimation (tearing)	**E** – **E**mesis
S – **S**alivation and **S**weating (diaphoresis)	

Box 2.12

(Respiratory failure and cardiac toxicity are the reason for death)

- **Nicotinic effects**:
  - Neuromuscular junctions: muscle fasciculation, cramps, weakness, and paralysis
  - CNS: tremors, seizures, and altered mental status
  - Tachycardia

- **Muscarinic effects:**
  - Glands: increased salivation, lacrimation, sweating, and bronchial secretions
  - Smooth muscles: bronchoconstriction, bradycardia, and gastrointestinal hypermotility
  - CNS: miosis (constricted pupils), blurred vision, and confusion

Summary of clinical features of cholinergic toxidrome

Clinical indicator	Finding
Heart rate	Slow
Cardiac rhythm	Sinus bradycardia, bradyarrythmia
Blood pressure	Low
Temperature	Normal or low
Respiratory rate	Normal or low
Eyes	Miosis
Skin	Profusely diaphoretic
Secretions	Copious
Mental status	Normal or obtunded

Table 2.3

Management

Antidote – (01) Atropine

- **Initial dose:** 0.6-3 mg IV atropine bolus and double the dose every 3-5 minutes until below target parameters are achieved
- Tachycardia is not a contraindication to give atropine boluses if wet axillae and bronchorrhea are present
- **Target parameters:**
  - Stable heart rate (> 80 bpm)
  - Systolic blood pressure > 80 mmHg
  - Clear lung sounds (no bronchorrhea)
  - Dry mucous membranes and dry axillae
  - Pupils no longer pinpoint
- **After the initial bolus maintenance dose has to be given** – 20% of the initial bolus dose required to achieve the targets and run it as per hourly infusion

e.g.: If the bolus dose needed to achieve targets = 100mg
The maintenance dose would be 20% of 100mg = 20 mg/hour infusion

Parameters to monitor:

Vital signs:

- Heart rate (maintain 80-100 bpm)
- Blood pressure
- Respiratory rate

Review the parameters at:

- Every 30 min for first 3 hours
- Hourly for next 6 hours
- Then 3-6 hourly for 24-48 hours

If atropinisation is lost, give bolus doses of atropine until target parameters are achieved. Add additional 20% of bolus requirement to the existing infusion per hour.

- The duration of atropine infusion is dependent on the clinical parameters of the patient. Sometimes, patients may need continuous infusion over 5-7 days (in the case of fat-soluble organophosphate). The duration of treatment is highly individualised

Laboratory tests:

- Arterial blood gas
- Electrolytes (to monitor for potential imbalances)
- Continuous ECG monitoring (to detect bradycardia or arrhythmias)
- Renal function tests

Fluid balance:

- Monitor for signs of dehydration or overhydration

Neurological status:

- Mental status changes
- Signs of seizures or other CNS effects
    - Give diazepam 10 mg IV (0.1 to 0.2 mg/kg in children), repeat as necessary if seizures occur. Do not give phenytoin

Box 2.13

Antidote – (02) Pralidoxime

- **Indication:** Used in the management of organophosphate poisoning
- **Dosage:** Initial dose of 1-2 g IV, repeat 1 g as needed, or continuous infusion at 8 mg/kg/hour in adults (10 mg/kg/hour in children)
- Atropine must be given before PAM to avoid worsening of muscarinic-mediated symptoms
- It has to be given within 48 hours of the poisoning
- But evidence about the use of oximes to treat organophosphate poisoning is inconsistent, and interpretation is difficult
- **Mechanism of action:**
  - Pralidoxime (2-PAM) reactivates acetylcholinesterase (AChE) that has been inhibited by organophosphates (OPs) by removing the phosphate group from the enzyme
  - It prevents the permanent binding (aging) of organophosphates to AChE, allowing the enzyme to degrade acetylcholine and restore normal function of the nervous system

Box 2.14

4. Opioid toxidrome

The mechanism of opioid toxidrome primarily involves the overstimulation of the brain's mu-opioid receptors. When opioids bind to these receptors, they can cause a range of effects, including analgesia (pain relief), euphoria, and sedation.

Common opioids

- Fentanyl
- Oxymorphone
- Hydromorphone
- Levorphanol
- Methadone
- Oxycodone
- Morphine
- Heroin
- Codeine
- Tramadol
- Laudanum (opium tincture)

Box 2.15

Clinical features of opioid toxidrome

- **Somnolence**: Profound drowsiness or altered consciousness
- **Respiratory suppression:** There will be a quick response to naloxone which will reverse the effects of an opioid toxicity
- **Pupil size**: Classically, small 'pinpoint' pupils. However, severe opioid intoxication can trigger a sympathetic response, leading to normal-sized pupils. Some opioids (like meperidine and tramadol) may even dilate pupils due to serotonergic effects
- **Other signs**:
    - Hypothermia
    - Hypotension

Box 2.16

Summary of clinical features of opioid toxidrome

Clinical indicator	Finding
Heart rate	Normal
Cardiac rhythm	Normal
Blood pressure	Normal or low
Temperature	Normal or low
Respiratory rate	Respiratory depression maybe fatal
Eyes	Miosis
Skin	Normal
Secretions	Normal
Mental status	Sedated / Somnolence

Table 2.4

Management

Antidote - Naloxone

Dose:

1) Age > 12 years

- Give an initial dose 0.4 mg intravenously
- If there is no response after 60 seconds, give a further 0.8 mg
- If there is still no response after another 60 seconds, give another 0.8 mg
- If still no response (after a total of 2 mg), give a further 2 mg dose. Large doses (more than 4 mg) may be required in patients exposed to highly potent opioids and those who are severely poisoned
- Aim for reversal of respiratory depression and maintenance of airway protective reflexes, not full reversal of unconsciousness
- For chronic opioid abuse, use smallest doses (0.1-0.2 mg) to avoid acute withdrawal; titrate to reversal of respiratory depression
- Please use naloxone with caution

2) Age < 12 years

- Give an initial dose of 0.1 mg/kg (maximum dose 2 mg). If no response, repeat at intervals of 60 seconds to a total of maximum 2 mg. Then review diagnosis
- Failure of a definite opioid overdose to respond to large doses of naloxone suggests that another CNS depressant drug or brain damage is present
- Once an adequate response has occurred, monitor arterial blood gases, oxygen saturation, and respiratory rate
- Intramuscular naloxone is an alternative in the event that IV access is not possible or is delayed. The duration of action of naloxone is shorter than that of all opioid analgesics – REPEATED DOSES OF NALOXONE MAY BE REQUIRED
- Intravenous infusions following resuscitation – Start with an hourly infusion rate equal to around 60% of the doses required to adequately reverse respiratory depression

Box 2.17

Complications

- Bradycardia
- Hypotension
- Hypothermia

Box 2.18

5. Sedative - hypnotic toxidrome

This toxidrome results from the central nervous system depression caused by sedative-hypnotic agents.

Mechanism of action

Sedative-hypnotic agents enhance the inhibitory effects of the neurotransmitter gamma-aminobutyric acid (GABA) in the brain.

Common sedative-hypnotic medicines

Benzodiazepines

- Clonazepam
- Lorazepam
- Diazepam
- Alprazolam
- Midazolam

Box 2.19

Clinical features of sedative-hypnotic toxidrome

- Respiratory depression
- Decreased level of consciousness
- Slurred speech
- Hypotension
- Bradycardia
- Hyporeflexia

Box 2.20

Summary of clinical features of sedative-hypnotic toxidrome

Clinical indicator	Finding
Heart rate	Normal
Cardiac rhythm	Normal
Blood pressure	Normal
Temperature	Normal
Respiratory rate	Respiratory depression
Eyes	Normal
Skin	Normal
Secretions	Normal
Mental status	Sedated / Somnolence

Table 2.5

Most of the clinical features are similar between the opioid toxidrome and the sedative-hypnotic toxidrome. However, there are few key points to differentiate between the two.

Key points to differentiate opioid toxidrome and sedative-hypnotic toxidrome

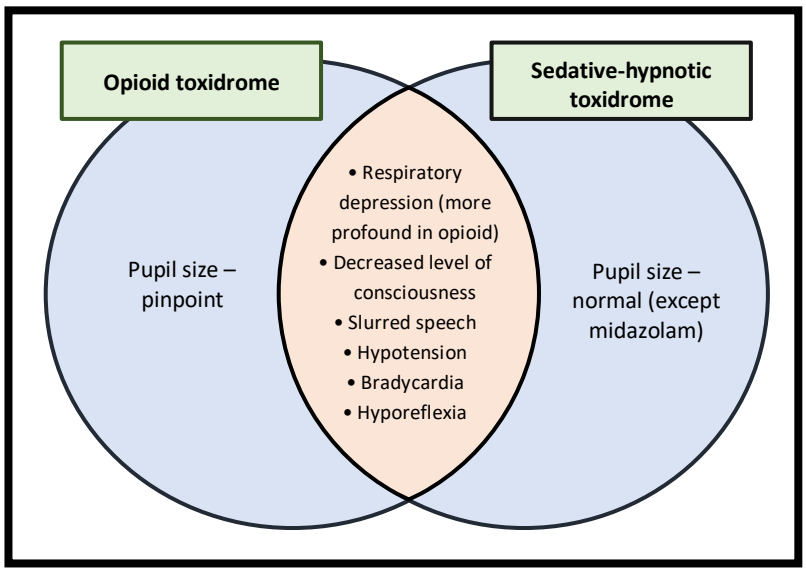

Figure 2.2

Management

Antidote - Flumazenil

- Usually not given because often causes withdrawal seizures especially with long term benzodiazepine use
- Used in severe toxicity and in children
- Contraindicated in patients with prolonged QRS interval
- **Dose**
  - 200 µg intravenously over 15-30 seconds
  - Then 100 µg every 1 minute if recurrent
  - Usual dose is 300-600 µg
  - Maximum dose 1 mg/course

Box 2.21

Common toxidromes in summary

Toxin	HR / BP	Resp	Temp	Eyes	Skin / secretions	Mental status
Sympathomimetic	↑↑	↑	↑	●	Diaphoretic	Agitated
Anticholinergic	↑↑	↑	↑↑	●	Dry	Agitated
Cholinergic	↓↓	↓	↓↓	•	Copiously wet	Somnolent
Sedative Hypnotics	–	– Or ↓	–	●	Normal	Somnolent / Coma
Opioids	–	↓↓	–	•	–	Somnolent / Coma

Table 2.6

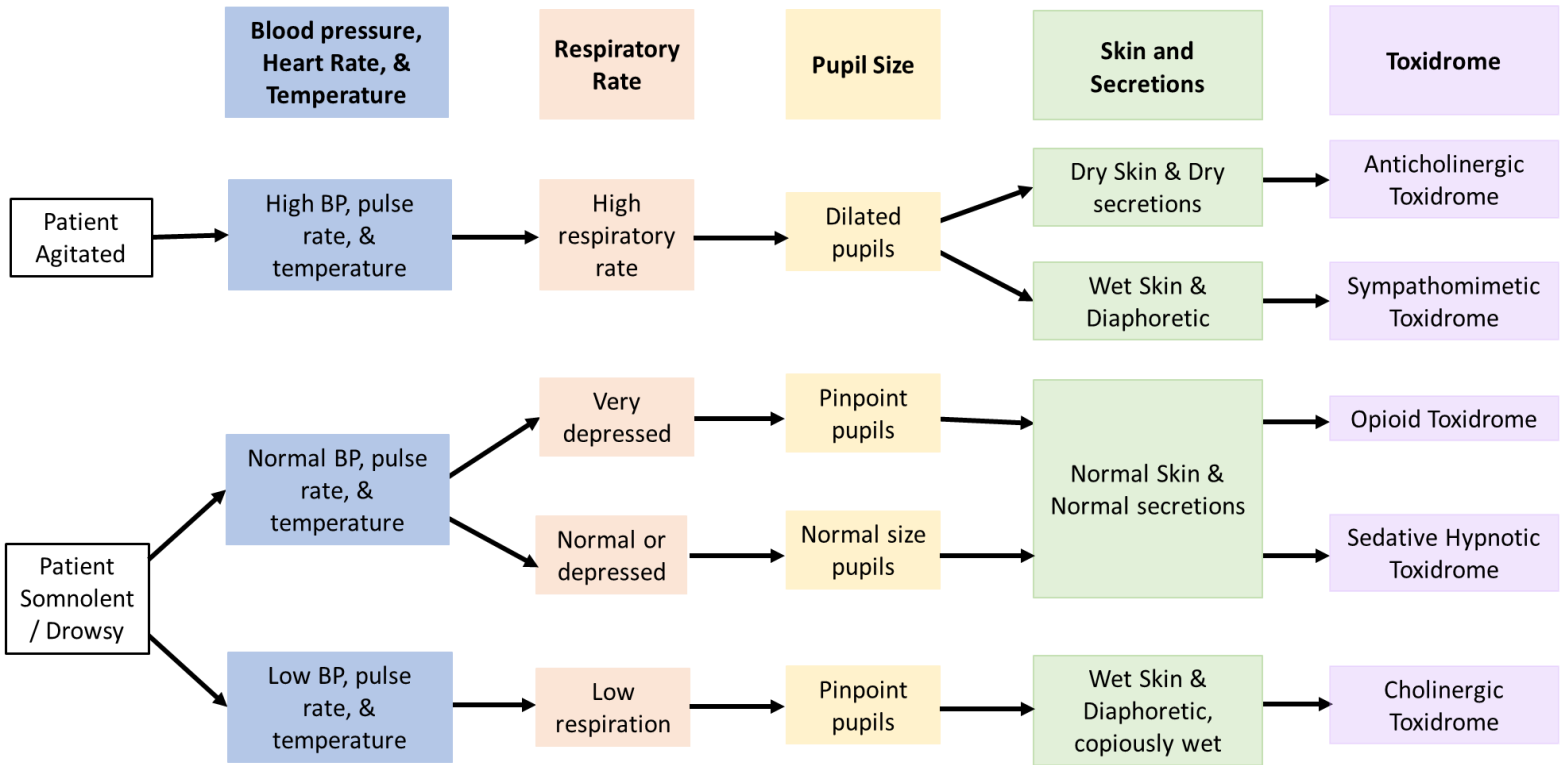

Figure 2.3 – A clinical guide to identifying toxidromes

6. Uncommon toxidromes

Following are the uncommon toxidromes. However, they are very important in clinical practice.

a) **Neuroleptic malignant syndrome**

Common causes of neuroleptic malignant syndrome

A. Neuroleptics:

- Typical antipsychotics – Haloperidol, Prochlorperazine, Chlorpromazine, Fluphenazine, Trifluoperazine, etc.
- Atypical antipsychotics – Risperidone, Clozapine, Olanzapine, Quetiapine, etc.

B. Non-neuroleptics with antidopaminergic activity:
Metoclopramide, Promethazine, Tetrabenazine, Reserpine, etc.

C. Dopaminergic (withdrawal): Dopamine agonists, Levodopa, Amantadine

D. Others: Lithium, Phenelzine, Desipramine, Trimipramine

Box 2.22

- Neuroleptic malignant syndrome (NMS) is an uncommon yet serious reaction to neuroleptic medications.
- It is characterised by tetrad of symptoms:

- Fever (> 38 ^{0}C)
- Muscle rigidity (lead-pipe rigidity)
- Changes in mental state (psychomotor agitation, delirium progressing to lethargy, stupor, coma)
- Dysfunction of the autonomic nervous system

Box 2.23

- In addition to the above tetrad, following clinical symptoms and signs are also seen

- Diaphoresis
- Incontinence
- Dysphagia
- Dyspnoea
- Tremor
- Shuffling gait
- Pallor

Box 2.24

- NMS typically occurs soon after starting neuroleptic treatment or increasing the dosage

Investigations

- CNS infection could also be considered as a differential diagnosis. Therefore, lumbar puncture is important to differentiate

Abnormalities in investigations in NMS

- Leucocytosis (70-98% of cases)
- Thrombocytosis
- Myoglobinaemia
- Increased AST and ALT
- Hyperuricaemia
- Hypocalcaemia
- Decreased serum iron
- Metabolic acidosis
- Increased creatine kinase (50-100% of cases)
- Hyperphosphatemia
- Myoglobinuria
- Increased LDH
- Hyperkalaemia

Box 2.25

Treatment of NMS

- The critical initial step is discontinuing all neuroleptic medications
- Main focus of treatment is to provide supportive care to manage muscle rigidity, elevated body temperature, and to prevent the occurrence of complications such as rhabdomyolysis, respiratory failure, and kidney damage
- Evidence for the usage of dantrolene and bromocriptine to expedite recovery is limited, and other treatment options like amantadine, lorazepam, and electroconvulsive therapy have also been tried
- Patients should be closely monitored, preferably in an intensive care unit (ICU)
- Symptoms generally improve within 1-2 weeks, though NMS caused by long-acting injections could persist for up to a month

Box 2.26

b) Serotonergic toxidrome

Common causes of serotonergic toxidrome

- Selective serotonin reuptake inhibitors (SSRI –antidepressants) e.g.: paroxetine, fluoxetine
- Serotonin noradrenalin reuptake inhibitors (SNRI –antidepressants) e.g.: venlafaxine, citalopram, tricyclic antidepressants
- Monoamine oxidase inhibitors (block serotonin break down – used as antidepressants) e.g.: moclobemide
- Analgesics e.g.: pethidine, tramadol, fentanyl
- Antiemetics e.g.: metoclopramide, ondansetron
- Anticonvulsants e.g.: valproic acid
- Dietary supplements e.g.: St John's wort, ginseng

Box 2.27

- It is a potentially life-threatening condition associated with a collection of signs and symptoms produced by excess serotonin in the central, peripheral and autonomic nervous systems
- Pathogenesis involves excessive stimulation of both peripheral and central postsynaptic 5HT-1A and particularly 5HT-2A receptors
- The syndrome is characterised by a mix of alterations in mental state, increased neuromuscular activity, and heightened autonomic activity
- Serotonin syndrome can develop from the proper use of serotonergic medications, an intentional overdose of such drugs, or commonly, due to a complex interaction between two serotonergic medications that operate through different mechanisms
- Most commonly produces tremor, hyperreflexia, and muscle rigidity especially in the legs. In addition, there may be clonus, opsoclonus, fever, tachycardia, and hypertension

Investigations:

- Serotonin syndrome is a clinical diagnosis
- Serum serotonin concentration levels do not correlate with the clinical symptoms and signs
- However, there could be some non-specific laboratory findings like: elevated white blood cell counts, high creatinine phosphokinase levels, and low serum bicarbonate levels

Box 2.28

Treatment:

- Supportive care – IV fluids, oxygen, management of hyperthermia etc.
- Hyperthermia may need specific management including sedation or intubation
- Role of antidote therapy (cyproheptadine) – If benzodiazepines and supportive care fail to improve agitation and correct vital signs, we suggest antidote therapy with cyproheptadine
- Cyproheptadine is a histamine-1 receptor antagonist with nonspecific 5-HT1A and 5-HT2A antagonistic properties. An initial dose of 12 mg is recommended, followed by 2 mg every two hours until response (normal reflexes) then maintenance dosing being 4-8 mg every 6 hours (maximum dose 32 mg/day)
- Cyproheptadine is only available in an oral form, but it may be crushed and given through a nasogastric or orogastric tub
- Rhabdomyolysis could be another complication due to multifactorial causes. It is recommended to look for any evidence of rhabdomyolysis that needs treatment if identified or confirmed

Box 2.29

Key points to differentiate neuroleptic malignant syndrome and serotonin syndrome

	Neuroleptic malignant syndrome	Serotonin syndrome
Clinical features	• Tachycardia • Raised BP • Hyperthermia • Diaphoresis • Rigidity • Altered mental state • Delirium	• Tachycardia • Raised BP • Hyperthermia • Diaphoresis • Rigidity • Altered mental state
Onset of action	More gradual (days-weeks)	More acute (hours)
Pupil size	Normal	Dilated
Neurological signs	Hyporeflexia, 'lead-pipe' rigidity	Hyperreflexia, clonus, tremor
Gastrointestinal	Normal	Diarrhoea, increased bowel sounds
Creatinine kinase (CK)	Raised; can cause acute kidney injury	Can be raised but generally more associated with neuroleptic malignant syndrome
Management	• Stop antipsychotics • IV fluids • Dantrolene • Bromocriptine	• Stop serotonergic drugs • IV fluids and cooling • Benzodiazepines • Cyproheptadine

Table 2.7

Similarly, there are other clinical conditions that can mimic NMS and serotonin syndrome.

	Cause	Onset, development, and resolution	Symptoms
Neuroleptic malignant syndrome	Following exposure to dopamine antagonists	Develops over a period of days to weeks; resolution is seen in approximately 9 days with treatment	Neuromuscular hypoactivity manifesting as muscle rigidity and bradyreflexia
Serotonin syndrome	Following exposure to serotonin agonists	Develops within 24 hours following exposure; resolution is seen within 24 hours with treatment	Altered mental status, muscle rigidity especially in the lower extremities, hyperreflexia, diaphoresis, increased bowel sounds
Anticholinergic toxicity	Following exposure to anticholinergic agents	Develops within 24 hours; resolves within hours to days with treatment	Hot and dry erythematous skin, normal muscle tone, normal reflexes, decreased bowel sounds, urinary retention
Malignant hyperthermia	Following exposure to inhalation anaesthetics or depolarising muscle relaxants (succinylcholine)	Develops within minutes or within 24 hours; resolves within 24 to 48 hours with treatment	Rising and tidal CO_2, mottled skin with areas of flushing and cyanosis, muscle rigidity, hyporeflexia

Table 2.8

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3. Paracetamol (Acetaminophen) overdose

- Paracetamol (PCM) poisoning, also known as acetaminophen poisoning, is a common overdose leading to potentially serious liver damage
- This condition arises from ingesting large doses of the medication, often accidentally or intentionally
- Prompt medical intervention is crucial to prevent severe complications and ensure successful treatment

Common modes of toxicity

1. Acute single overdose (most commonly as a deliberate self-harm)
    - > 10 g (20 tablets) or > 200mg/kg can be potentially fatal

2. Repeated supratherapeutic ingestion
    - ≥ 10 g or ≥ 200 mg/kg (whichever is less) over a single 24-hour or
    - ≥ 12 g or ≥ 300 mg/kg (whichever is less) over a single 48-hour or
    - ≥ a daily therapeutic dose* per day for more than 48 hours in patients who also have abdominal pain or nausea or vomiting

      *Total dose of 60 mg/kg over 24 hours and up to a maximum dose of 4 g /day

3. Multiple or staggered immediate release PCM ingestions
    - Any multiple or staggered PCM ingestions over more than 2 hours for the purpose of deliberate self-harm

Box 3.1

Mechanism of action

At therapeutic doses, PCM is primarily metabolised through conjugation (glucuronidation and sulfation) to form water-soluble metabolites that are excreted with urine. However, in cases of overdose exceeding 200 mg/kg, this metabolic pathway becomes saturated. It leads to an increased metabolism of PCM through another minor pathway involving P450 enzymes, mainly CYP2E1. P450 pathway generates a harmful intermediate metabolite known as N-acetyl-p-benzoquinone imine (NAPQ / NAPBQ), which relies on sulfhydryl groups from glutathione for further detoxification. Approximately 8 hours after a significant overdose, glutathione stores become depleted, allowing the toxic metabolite to bind to sulfhydryl groups in cellular membranes and tissue proteins, resulting in cell membrane disruption and ultimately cell death. Any organ containing P450 enzymes, such as the liver, kidneys, heart, and pancreas, can experience toxicity.

PCM metabolism

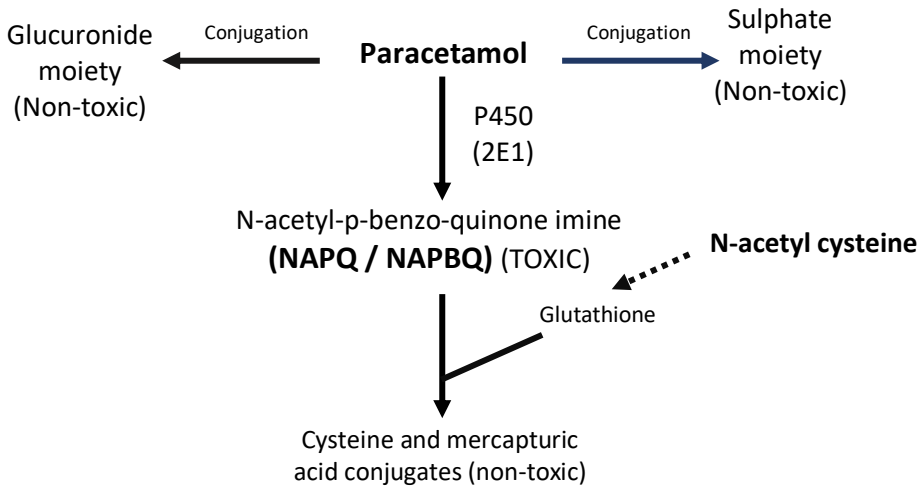

Figure 3.1 - PCM metabolism pathways and breakdown into N-acetyl-p-benzoquinone imine, by cytochrome P450 2E1. N-acetyl-p-benzoquinone imine is the toxic metabolite produced from paracetamol metabolism when the other two conjugation pathways become over-saturated. The resultant toxic N-acetyl-p-benzoquinone imine (NAPQ / NAPBQ) byproduct is converted into nontoxic metabolites by glutathione, which is regenerated by N-acetylcysteine. CYP2E1: Cytochrome P450 2E1; NAC: N-acetylcysteine.

Clinical features - Phases of progression of PCM poisoning

The progression of clinical manifestations in PCM poisoning can be described in four sequential phases:

Phase 1 (½-24 hours)
- Asymptomatic or may report anorexia, nausea or vomiting, and malaise
- Pallor, diaphoresis, fatigue

Phase 2 (18-72 hours)
- Right hypochondrial pain / tenderness, anorexia, nausea, and vomiting

Phase 3 (72-96 hours)
- Hepatic necrosis and dysfunction may manifest as jaundice, coagulopathy, hypoglycaemia, and hepatic encephalopathy
- AKI, death from multiorgan failure

Phase 4 (4 days-3 weeks)
- Possibilities are death due to liver failure or complete resolution of liver damage and recovery

Box 3.2

Initial management of a patient presenting with PCM overdose

- ResusRSIDEAD pathway
    - Gastric lavage and activated charcoal play a role
- Antidote
    - Ideal time to start antidote is within 4–8 hours of ingestion of the toxic dose
    - Since we do not have facilities to check the PCM levels at 4 hours, it is recommended to start antidote as soon as possible if the weight adjusted dose is ≥ 150 mg/kg
- Supportive care and monitoring
- Do not give clotting factors unless the patient is bleeding

Rumack-Matthew nomogram

If the facilities to check the PCM levels are available, check the PCM level after 4 hours of ingestion and plot it on the nomogram. Decisions could be made accordingly.

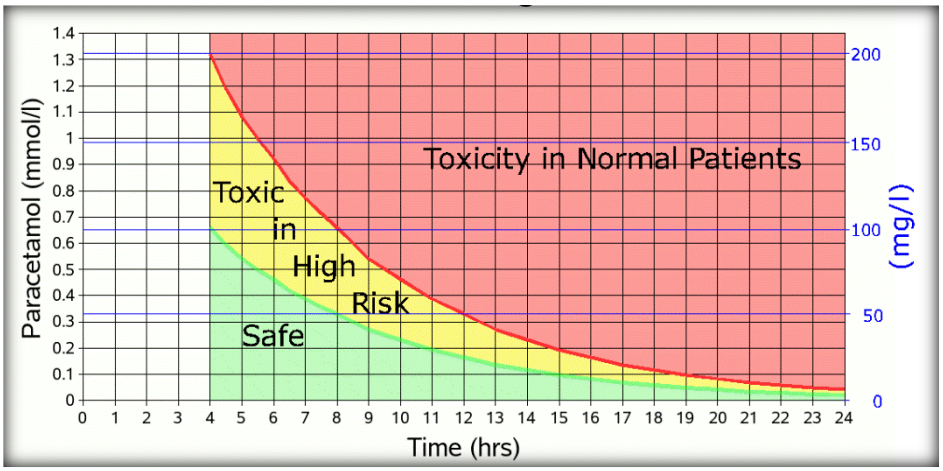

Figure 3.2 – PCM nomogram

- This is not applicable when taken with multiple other medications

Antidote in PCM overdose

- Single overdose of > 10 g (20 tablets) or > 200 mg/kg can be potentially fatal
- If PCM levels are not available, decide as per dose and body weight

Give antidote if the dose adjusted to weight is ≥ 150 mg/kg

Box 3.3

- For example, 50 kg person ingested 18 tablets of PCM. Dose calculation as follows:

  (500 mg x 18)/50 = 900/50 = 180 mg/kg
- Oral methionine or IV / oral N-acetyl cysteine (NAC) are the antidotes for PCM overdose

NAC vs Methionine

- Superiority of NAC over methionine is not proven
- Methionine is as effective as NAC according to available researches
- NAC is expensive
- It is a clinical decision
- NAC is more effective if given within eight hours
- Administer as soon as possible for patients who present > 8 h

Box 3.4

Indications for methionine

- If patient presents within 8 hours
- Asymptomatic patients with a toxic dose (no ongoing vomiting)

Box 3.5

AVOID

- Methionine is **not** recommended to be started later than 10-12 hours after the overdose, or if there is established liver injury

Box 3.6

Indications for NAC

- Patient cannot tolerate methionine
- Patient is symptomatic
- Elevated transaminases or evidence of hepatotoxicity
- If time of ingestion is not known or > 24 hours

Box 3.7

Adverse effects of NAC – Anaphylactoid reactions

- Most common reactions are: nausea, vomiting, and cutaneous systemic hypersensitivity reactions
- Life threatening anaphylaxis is not uncommon

Management of anaphylactoid reaction due to NAC

- Mild reaction usually responds to temporarily discontinuing or slowing down the NAC infusion
- For moderate to severe reactions treat as per anaphylaxis:
    - Stop the NAC infusion and manage as anaphylaxis
    - Then NAC can be recommenced once symptoms settle at half rate for 30 minutes, later continue as per normal protocol

Administration of NAC

- The traditional three bag protocol is associated with a high rate of adverse reactions, ranging from mild to severe. Therefore, it is not practiced nowadays
- **Two-bag method** is preferred

Standard two-bag regimen

- **Initial infusion**
  NAC 200 mg/kg (maximum 22 g) in glucose 5% 500 mL (child, 7 mL/kg up to 500 mL) or sodium chloride 0.9% 500 mL (child, 7 mL/kg up to 500 mL) intravenously, over 4 hours

- **Second NAC infusion**
  NAC 100 mg/kg (maximum 11 g) in glucose 5% 1000 mL (child, 14 mL/kg up to 1000 mL) or sodium chloride 0.9% 1000 mL (child, 14 mL/kg up to 1000 mL) intravenously, over 16 hours

Box 3.8

Criteria to continue the NAC after 2 bag regime (20 hours)

- 2-3 hours before completion of the second bag (at 17 to 18 hours) assess the patient for:
    - Any symptoms and signs of hepatotoxicity (nausea, vomiting, right hypochondrial pain and tenderness)
    - ALT > 50 IU/L
    - INR > 1.3
- If any of above-mentioned features present, continue the NAC at a dose of 100 mg/kg/hour for 24 hours
- Then follow the above-mentioned protocol 2-3 hours before stopping the 24-hour regime (100 mg/kg/hour) and decide on whether to continue the NAC as mentioned above

Box 3.9

- Always assess the patient as above 2-3 hours before completing the NAC infusion and decide about further continuation of NAC

Box 3.10

Criteria to discontinue NAC

- **All** of the following criteria should be present to discontinue NAC:

- Undetectable PCM concentration
- Improving hepatic aminotransferases
- Improving prognostic markers (e.g.: creatinine, lactate, pH, prothrombin time/INR, phosphate)

Box 3.11

- Get expert opinion if necessary

Predictors of poor prognosis

- Decreased pH
- Increased lactate
- Increases in prothrombin time / INR
- Increases in serum creatinine
- Increase in phosphate

Box 3.12

Special situations

1. Very high initial PCM ingestion (> 30 g or > 500 mg/kg or blood PCM level more than double the nomogram line)

- Increase the second infusion NAC dose to **200 mg/kg** (max. 22 g) in 0.9 NaCl or 5% dextrose 1000 mL for 16 hours
- You may continue this high dose as maintenance over 24 hours, after initial 20 hours of infusion if necessary

Box 3.13

2. Pregnancy

- NAC can be given (not contraindicated)
- Calculations should be based on pre-pregnant weight

Box 3.14

3. Repeated supratherapeutic ingestion

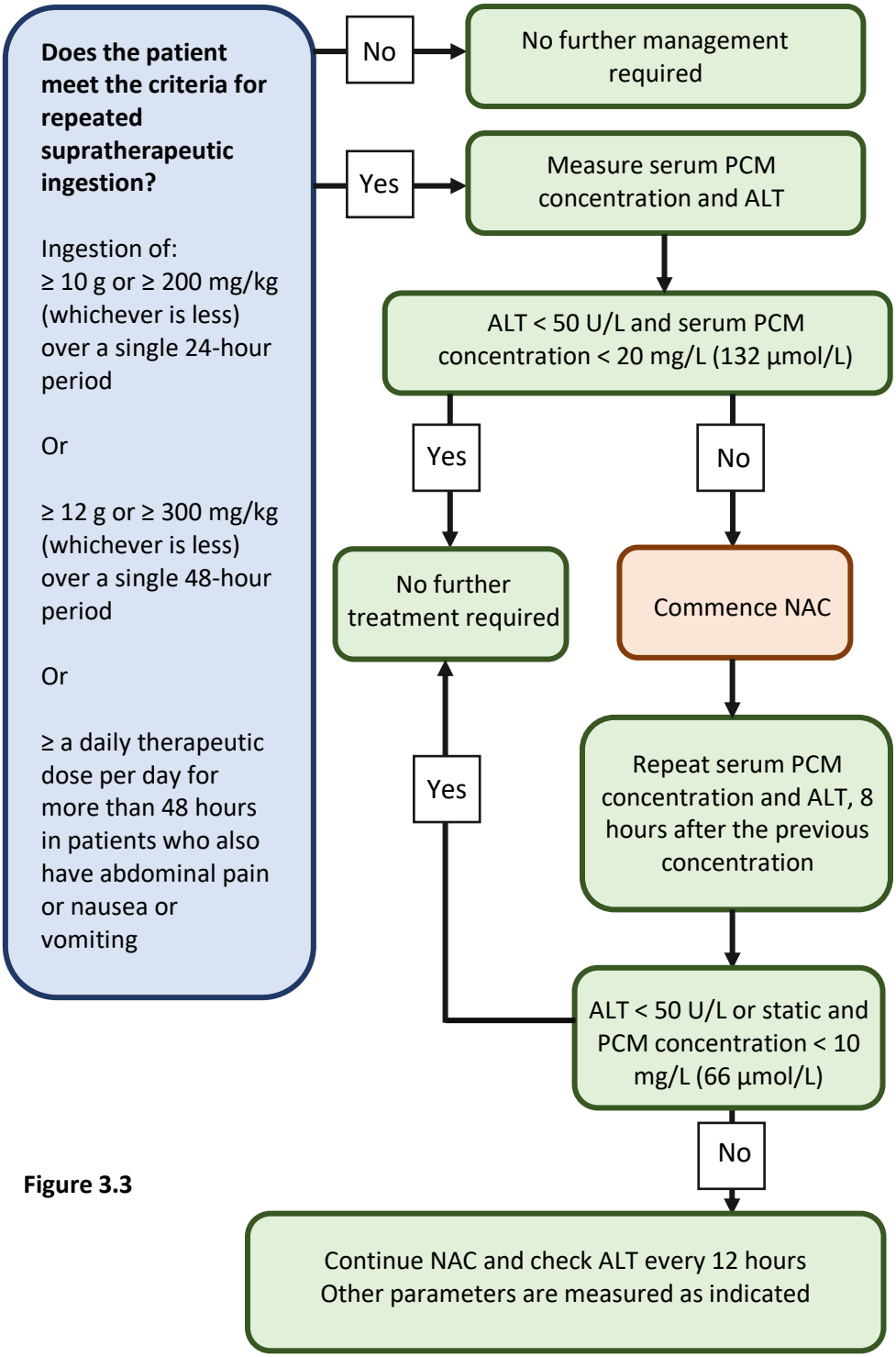

Figure 3.3

- Ideally PCM level and ALT level should be measured to decide about NAC
- However, in Sri Lanka measurement of PCM level is not freely available in government sector
- Therefore, depending on the patient's clinical symptoms and signs, ALT and INR levels, commence NAC. Continue to monitor liver function tests and other prognostic markers

Box 3.15

4. Multiple or staggered immediate release PCM ingestions

- Staggered ingestions should be treated as per acute immediate release PCM ingestion using the earliest time of ingestion for the PCM nomogram
- If it is more than 8 hours since the first dose of PCM or the PCM concentration cannot be obtained within 8 hours, commence treatment with NAC
- If the first PCM concentration was measured within 2 hours of the last ingested PCM dose, it should be repeated after 2 hours to ensure there is no ongoing absorption
- If either concentration is above the nomogram line (using time from the earliest ingestion), start or continue treatment with NAC

6. Acute ingestion of modified release (MR) PCM

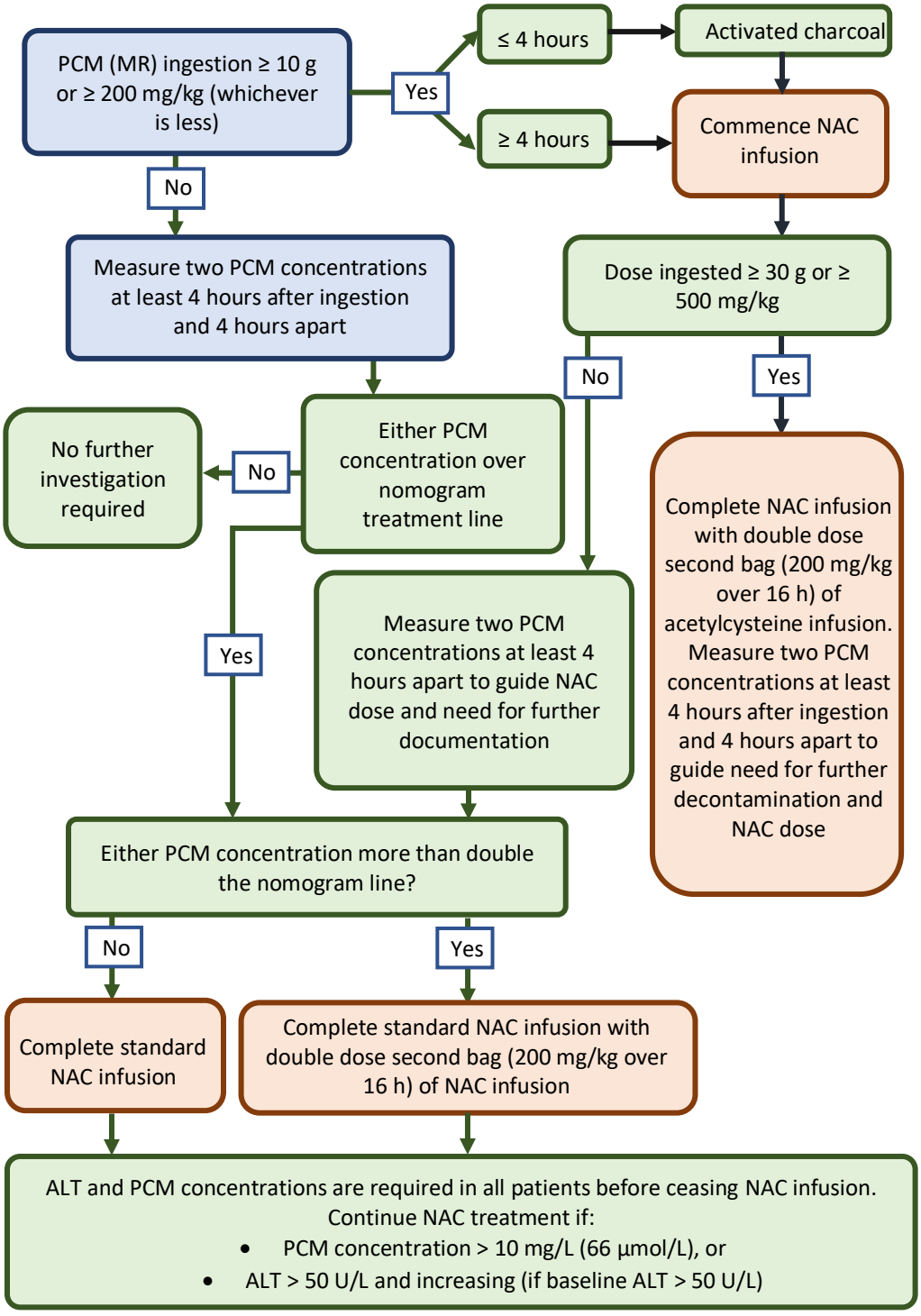

Figure 3.4

The management of acute ingestion of modified-release PCM has been outlined above. However, in Sri Lanka, modified-release formulations are not widely available in either the public or private healthcare sectors. As a result, cases involving this type of ingestion are uncommon in the country.

Cessation of NAC on special situations

- In patients who require NAC beyond 20 hours, NAC can be ceased if **all** the following criteria have been met:
    - ALT or AST are decreasing
    - INR < 2.0; and
    - Patient is clinically well

  And
- For modified release ingestions and patients with an initial PCM concentration greater than double the nomogram line, PCM concentration < 10 mg/L (66 µmol/L)

Antidote – Oral methionine

Adults and children weighing over 20 kg

- 2.5 g initially
- Followed by 3 more doses of 2.5 g given 4 hourly
- The total dose of 10 g

Box 3.16

Children weighing less than 20 kg

- 1 g initially
- Followed by 3 doses of 1 g, 4 hourly
- The total dose is 4 g

Box 3.17

Liver transplantation in PCM overdose

A liver transplantation should be considered when **any of these** criteria are met:

- INR greater than 3.0 at 48 hours or greater than 4.5 at any time
- Oliguria or creatinine greater than 200 µmol/L
- Persistent acidosis (pH < 7.3) or arterial lactate greater than 3 mmol/L;
- Systolic hypotension with blood pressure below 80 mmHg, despite resuscitation
- Hypoglycaemia, severe thrombocytopaenia, or encephalopathy of any degree
- Any alteration of consciousness (Glasgow Coma Scale < 15) not associated with sedative co-ingestions

Box 3.18

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4. Essentials in Tricyclic Antidepressants (TCA) Toxicity

TCA toxicity is common in Sri Lanka. The commonly used TCAs are amitriptyline, clomipramine and nortriptyline.

Mechanism of action of TCA

- Na channel blocking
- Anticholinergic activity
- Antihistamine effect
- Noradrenaline and serotonin reuptake inhibition
- GABA inhibition
- Alpha blocking

Box 4.1

Complex toxicological effects of TCA

- Onset of toxicity occurs usually in 2-3 hours after ingestion
- Patients can remain asymptomatic during the early hours of toxicity

- Nausea, vomiting, and abdominal discomfort
- Elevated body temperature and flushed skin
- Dry mouth and decreased bowel sounds
- Urinary retention
- Altered mental status, agitation, and seizures
- Pupillary dilatation, nystagmus
- Clonus, tremor, hyperreflexia
- Sinus tachycardia to broad complex tachydysrhythmias
- Hypotension
- Metabolic acidosis

Box 4.2

Investigations

- ABG – metabolic acidosis
- ECG
    - Sinus tachycardia
    - PR prolongation
    - QRS widening >100 ms
    - Dominant R wave of > 3 mm in aVR
    - R/S ratio > 0.7 in aVR
    - Prolonged QT interval
    - Others – RBBB, VT, VF, asystole, right axis deviation, Brugada like pattern
- Metabolic panel – LFT, RFT

Box 4.3

Management

- ResusRSIDEAD pathway
- Prompt fluid resuscitation with crystalloids to target serum sodium around 150 -155 mmol/L
- Early intubation, when GCS < 12 is needed; as the onset and progression of coma is abrupt. Need to maintain a hyperventilation mode
- IV bolus of 8.4% sodium bicarbonate administration as an antidote until QRS is normalised (See Box 4.5 below)
- Target the pH > 7.5
- Consider noradrenaline to manage hypotension
- IV benzodiazepam, barbiturates, and propofol are the drugs to manage seizures
- Consider IV lignocaine, phenytoin, and magnesium sulphate to manage dysrhythmia
- Cardioversion and defibrillation are usually ineffective
- Severe toxicity needs prolonged resuscitation

Box 4.4

Bicarbonate dose and preparation

- Initial dose of the bicarbonate:
  - 1-2 mmol/kg of sodium bicarbonate is given as an IV bolus over 1-2 minutes
  - Usually, this is equal to 50-100 mL of an 8.4% sodium bicarbonate solution in adults
- Repeat doses:
  - Repeat boluses over every 3-5 minutes until the QRS duration narrows to less than 100 ms or there is an improvement in blood pressure and arrhythmias
  - Multiple repeat boluses are often required, depending on the patient's response
- Maintenance of infusion (if necessary):
  - After the boluses, an infusion of sodium bicarbonate may be started to maintain the serum pH more than 7.5
  - The infusion is usually prepared by adding 150 mmol of sodium bicarbonate in 1 litre of 5% dextrose, and the rate is adjusted according to the patient's clinical response and blood gas analysis
- Sodium bicarbonate could lead to hypokalaemia due to intracellular shifting of potassium. Therefore, it is recommended to monitor serum potassium levels while on treatment and correct if necessary

Box 4.5

AVOID

- Type 1a antiarrhythmics due to Na channel blocking effect (contraindicated)

Box 4.6

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5. Essentials in Calcium Channel Blockers (CCB) Toxicity

Severe CCB overdose is highly fatal and aggressive management approach is necessary for the successful outcome.

Mechanism of action of CCB

- Non-dihydropyridine group of CCB (diltiazem and verapamil) mainly block 'L-type voltage-gated' calcium channels in myocardium
- Dihydropyridine group of CCB (nifedipine, amlodipine, cilnidipine, etc.) mainly block 'L-type voltage-gated' calcium channels in vascular smooth muscles and cause peripheral vasodilation
- Cardiac toxicity is multifactorial
    - Excessive negative inotropic effects lead to myocardial depression
    - Negative chronotropic effects lead to bradycardia / bradyarrhythmia
    - Negative dromotropic effects lead to AV nodal blockade
- Effects on the vascular system lead to,
    - Reduced afterload
    - Systemic hypotension
    - Coronary vasodilatation
- Other effect
    - Hyperglycaemia is another cardinal clinical manifestation due to,
        - CCB acting on the pancreatic beta cells and reducing the insulin release via L-type voltage-gated calcium channels
        - CCB increases transient insulin resistance

Box 5.1

Complex toxicological effects of CCB

- Onset of toxicity occurs usually in 1-2 hours after ingestion of standard CCB preparations
- Patients can remain asymptomatic for many hours (up to 12 hours) if ingestion of slow-release CCB preparations

- Nausea, vomiting
- Heart block, hypotension (even refractory) and bradyarrhythmia
- Seizures (rare, if present suspect co-ingestion)
- Hyperglycaemia (level of hyperglycaemia proportional to the mortality and morbidity)
- Non-cardiogenic pulmonary oedema
- Acute kidney injury
- Abdominal pain (due to mesenteric ischaemia)
- Rare complications – myocardial infarction and stroke

Box 5.2

Investigations

- ABG – metabolic acidosis, high lactate level
- ECG – bradyarrhythmia or 1^{st} ,2^{nd} ,3^{rd} degree heart blocks
- Serum calcium (low)
- Metabolic panel – LFT, RFT
- Chest X-ray

Box 5.3

Management

- ResusRSIDEAD pathway
- Gastric lavage and activated charcoal are effective within 1 hour of ingestion. However, they can be considered even after 1 hour up to four hours if large dose of ingestion or ingestion of extended-release preparation of CCB
- Whole bowel irrigation with poly-ethylene glycol (PEG, at a rate of 1-2 L/hour for 4-6 hours or until rectal effluent becomes clear) can be considered if patient has ingested a large dose of CCB especially sustained-release preparations.
- However, whole bowel irrigation is absolutely contraindicated if bowel sounds are absent
- Fluid resuscitation – normal saline 20 mL/kg boluses can be given 2-3 times followed by normal saline infusion of 120 mL/hour
- After initial fluid resuscitation if the MAP remains less than 65 mmHg consider bedside USS or echocardiogram to visualise the contractility of the heart and the status of the inferior vena cava (IVC). If IVC is collapsed and the cardiac contractility is good, can give further fluid boluses. If IVC is distended or cardiac contractility is less, start on inotropes
- Inotropes / vasopressor – first choice is will be noradrenaline. Other choices would be adrenaline / dobutamine
- IV Cal gluconate to maintain Ca^{2+} upper limit of normal
    - 10% calcium gluconate IV bolus 30-60 mL over 10-15 mins, or 10% calcium chloride 20 mL (calcium chloride should be given via a central line)
    - Repeat boluses every 10-20 mins up to three times
    - Then continue calcium gluconate IV infusion to maintain the serum calcium more than 2 mmol/L for at least three days
- Atropine is often effective to manage the bradycardia in addition to the calcium gluconate especially when there is associated hypotension
- High-dose insulin euglycaemic therapy (HIET)
- IV $NaHCO_3$ for severe metabolic acidosis (8.4% $NaHCO_3$ 50-100 mL bolus). Then repeat ABG / VBG and decide about further doses of $NaHCO_3$
- The dose of IV glucagon would be initial bolus of 5-10 mg and continue infusion at a rate of 5-10 mg/hour
- Methylene blue
    - Methylene blue is not a first-line treatment. It should be considered in refractory vasodilatory shock
    - Dosage: 1-2 mg/kg as an IV bolus over 5-10 minutes, followed by a continuous infusion of 0.25-0.5 mg/kg/hour if necessary

Box 5.4

HIET (High-dose Insulin Euglycemic Therapy) – Gold Standard

Box 5.5

HIET - general protocol

- To be started early stage of haemodynamic instability
- Peak action gets after 1 hour later
- Short acting insulin (soluble insulin) 1 Unit/kg is initiated
- May need to be stepped up to 10 Unit/kg gradually for refractory cases
- Glycaemic correction by 10% dextrose / 25% dextrose
- If there is hypoglycaemia it has to be corrected with dextrose, preferably 25% and continue the HIET
- HIET may precipitate hypokalaemia. Serial monitoring of serum electrolytes (every 20-30 mins) and maintain potassium at the normal range. IV KCl may need to be started
- HIET to be continued until clinical parameters are stable while correcting metabolic panel

Box 5.6

HIET – pathophysiology

- CCB toxicity – metabolic starvation of myocardium
- HIET increase glucose and lactate uptake by myocardium
- Increase calcium entry to mitochondria / ATP production
- Improve myocardial function (positive ionotropic effect)
- Promote excitation and contraction

Box 5.7

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6. Essentials in Metformin Toxicity

Introduction

Excessive intake of metformin, particularly doses exceeding 10 g, can be toxic in healthy individuals and is even more dangerous for patients with organ failure. This toxicity manifests as severe lactic acidosis, which can progress to coma or death. Metabolic acidosis arises from metformin inhibiting the liver's ability to absorb lactate, while increasing lactate production at the cellular level. Since the unmetabolized drug is excreted by the kidneys, any impairment in kidney function can exacerbate the toxic effects.

Metformin toxicity can be divided into three categories:

1. **Metformin induced lactic acidosis (MILA)** – lactic acidosis that occurs as a result of an overdose of metformin.

2. **Metformin associated lactic acidosis (MALA)** – lactic acidosis that develops in patients who are chronically on metformin therapy.

3. **Metformin unrelated lactic acidosis (MULA)** – lactic acidosis in patients taking metformin, but arising from causes unrelated to metformin.

Box 6.1

Mechanism of action

- Metformin is used therapeutically to inhibit gluconeogenesis and enhance peripheral glucose uptake
- In toxic doses, metformin can lead to severe lactataemia and metabolic acidosis
- Metabolic acidosis results from metformin inhibiting hepatic lactate absorption and increasing lactate production at the cellular level
- The exact mechanisms are not fully understood, but inhibition of gluconeogenesis, which requires lactate, contributes to this condition

- In healthy individuals, lactate is usually excreted in the urine, but in cases of impaired renal function or acute overdose, excess lactate can accumulate, leading to serious complications
- Lactic acidosis associated with therapeutic metformin use has a high mortality rate, and it is crucial to address any underlying causes, such as sepsis
- Lactic acidosis usually occurs in individuals who are susceptible (renal, cardiac, or respiratory failure), or in patients who have ingested or are on medications that impair cardiac and renal function

Box 6.2

Complex toxicological effects

- Metformin peak levels occur at 2 hours of ingestion
- Metformin monotherapy alone does not cause hypoglycaemia, but it may occur secondary to lactic acidosis

- Gastrointestinal symptoms – nausea, vomiting, and diarrhoea, epigastric pain
- Hypothermia, hypertension progressing to vasopressor refractory shock
- Delirium, reduced consciousness

Box 6.3

Investigations

In metformin toxicity there is evidence of metabolic acidosis and hyperlactataemia

- ABG – high anion gap metabolic acidosis and hyperlactataemia
- CBS
- 12 lead ECG
- Serum lactate levels
- SE – Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}
- Renal functions
- Other metabolic panels – AST, ALT

➢ Doing serum PCM level is worth when suspect a co-ingestion, if facilities are available

Box 6.4

Management

- ResusRSIDEAD pathway
- Severe acidosis and hyperkalaemia may require the administration of 8.4% sodium bicarbonate 1-2 mmol/kg intravenous infusion
- Fluid resuscitation
- Correct electrolyte abnormalities
- Mechanical ventilation
- In cases of hypoglycaemia manage it with dextrose
- If the patient is on therapeutic doses of metformin, stop further administration and look for an underlying cause e.g.: sepsis, acute kidney injury

Box 6.5

Place for Haemodialysis

- Haemodialysis is needed in worsening acidosis and clinical instability
- Haemodialysis removes both the lactate and metformin
- Metformin induced severe lactic acidosis needs Continuous Renal Replacement Therapy (CRRT) / Sustained Low Efficiency Dialysis (SLED)
- Conventional intermittent haemodialysis is effective in metformin toxicity but the plasma level increases at the end of the procedure due to redistribution. Therefore, SLED (done over 16 hours) is useful in haemodynamically unstable patients
- CRRT and Continuous Venovenous Haemodialysis (CVVH) also has a place
- CRRT is considered more suitable for haemodynamically unstable patients but metformin clearance is less when compared to haemodialysis
- SLED with bicarbonate containing dialysate produce a higher clearance of metformin as haemofiltration or haemodiafiltration

Usual indications for dialysis:

- Significant comorbidities
- Critically ill
- pH < 7.1
- Failure of supportive care
- Renal insufficiency
- Fluid overload

Box 6.6

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7. Essentials in Lithium Toxicity

Lithium is used to treat bipolar affective disorder and it has a narrow therapeutic index.

There are two types of lithium toxicity:

1. Acute toxicity
2. Acute on chronic toxicity

Lithium accumulation could occur due to excessive intake or reduced excretion of lithium.

1. **Excessive intake may be due to,**
   - intentional overdose
   - accidental ingestion of large quantities of lithium tablets, leading to acute or acute-on-chronic overdose
   - dosage adjustments in patients who are on long-term lithium therapy

2. **Impaired excretion may be due to,**
   - conditions that cause sodium and fluid depletion which can increase lithium reabsorption in the kidneys (e.g.: vomiting, diarrhoea, renal insufficiency, febrile illnesses, congestive heart failure, excessive exercise, water restriction, excessive sweating, a low-sodium diet)
   - medications that reduce the glomerular filtration rate which can contribute to chronic lithium toxicity

Box 7.1

Mechanism of action

- Physiological role and mechanism of action of Lithium are not well established. Several theories are proposed for its mechanism of action:
  - Brain inositol depletion – results in decreased responsiveness to alpha adrenergic stimulation
  - Inhibition of adenylate cyclase and G-proteins essential for ion channel opening – causes decreased neuronal responsiveness to neurotransmitters
  - Stimulation of serotonin release

Box 7.2

Complex toxicological effects

GI symptoms:

E.g.: vomiting, diarrhoea

- Usually occurs within the first hour of ingestion
- Predominantly seen in acute ingestions

Neurological symptoms and signs:

E.g.: coarse tremors, nystagmus, hyperreflexia, ataxia, agitation, reduced consciousness ranging from mild confusion to delirium, coma

- CNS redistribution occurs in large acute intoxication
- Neurotoxic features are predominantly seen in chronic toxicity
- The earliest sign seen is tremors
- Seizures may lead to permanent CNS damage

Renal toxicity:

E.g.: nephrogenic diabetic insipidus, sodium-losing nephritis, nephrotic syndrome

- More commonly seen with chronic toxicity

Cardiac toxicity:

- Cardiovascular effects of lithium toxicity are usually mild and non-specific
- Most frequently reported conduction defect is sinus node dysfunction

Endocrine effects:

- Inhibition of thyroid hormone synthesis leads to hypothyroidism
- Hyperthyroidism too can be seen, but less commonly

Box 7.3

Investigations

- ECG - minor ST/T changes, T-wave flattening, QT-prolongation, U-waves
- Serum electrolytes
- Renal functions
- Ca^{2+} level
- Plasma glucose levels
- Plasma lithium levels
  - Poorly correlates with severity
  - Used to confirm the ingestion, monitor progression, and to optimise resuscitation
  - Normal range of serum lithium level is approximately 0.6 to 1.2 mmol/L
  - To prevent misinterpretation of pre-distribution levels, serum measurements should be conducted at least 6 to 12 hours after the last therapeutic dose
- TSH levels
- Metabolic panel

Box 7.4

- In chronic intoxications, patients are at risk of renal insufficiency, indicated by elevated blood urea nitrogen and creatinine levels

Complications

- Lithium can cause serotonin syndrome
- The severity of lithium toxicity is commonly classified into three categories:

Mild (Serum lithium concentration between 1.5 - ≤2.5 mmol/L)	Moderate (serum lithium concentration between >2.5-3.5 mmol/L)	Severe (serum lithium concentration more than 3.5 mmol/L)
Lethargy	Confusion	Coma
Fatigue	Agitation	Seizures
Nausea	Delirium	Hyperthermia
Vomiting	Tachycardia	Hypotension
Tremors	Hypertonia	

Figure 7.1

Management

- ResusRSIDEAD pathway
- Decontamination
    - Activated charcoal is not indicated as lithium does not effectively adhere. However, if there is a co-ingestion with an unknown substance, activated charcoal should be used
    - Gastric lavage is considered, especially with regular-release formulations of lithium and for the patients who present early
    - Whole bowel irrigation has a place in massive ingestions or with sustained release preparations of lithium
- Elimination – most suitable method for the removal of lithium is haemodialysis, especially if there are symptoms and signs of severe lithium toxicity or the patient has renal failure
- Support care
- Monitoring vitals and urine output
- In acute toxicity, haemodialysis is needed only if neurocardiac instability is present
- Most symptomatic chronic patients need haemodialysis

Indications for haemodialysis:

- Serum lithium levels >2.5mmol/l
- Neurocardiac instability
- Symptomatic chronic lithium toxicity irrespective of the serum level

Box 7.5

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8. Common Pesticide Poisonings

- Pesticide self-poisoning is one of the most common means of suicide globally and accounts for 20% of the global burden of suicide
- Late presentations and inability to identify the poisons are the common causes for deaths

1. Organophosphate poisoning

- There are three different common modes of presentation
  1. Acute organophosphate (OP) poisoning
  2. Intermediate syndrome
  3. Long-term effects of OP poisoning (organophosphate induced delayed polyneuropathy)

Lipid soluble organophosphates

E.g.: dichlofenthion, fenthion, malathion

- Mechanism of action:
  - Rapid adipose fat uptake
  - Delayed redistribution from the fat stores
- Delayed onset of symptoms (up to five days)
- Prolonged illness (greater than 30 days)

Clinical features

- Clinical features are similar to cholinergic toxidrome
- Please refer the cholinergic toxidrome in chapter 2

Box 8.1

Management

- ResusRSIDEAD pathway
- Atropine is the crucial antidote. In addition, pralidoxime also can be considered. Please refer the cholinergic toxidrome
- Atropine should be considered at the beginning of the resuscitation process

Box 8.2

Intermediate syndrome in organophosphate poisoning

- Usually occurs in between 2-4 days
- Causes neck and proximal limb weakness – check tidal volume / check one breath count (single breath count) / spirometry
- Die due to type II respiratory failure
- Treatment: immediate intubation and ventilation

AVOID

- Succinylcholine must be avoided as it may prolong the paralysis

Box 8.3

2. Carbamate poisoning

- Derivative of carbamic acid (organophosphate – phosphoric acid)
- Similar mechanisms of organophosphate except reversible cholinesterase inhibition
- Shorter duration of action due to rapid metabolism

Clinical features

- Clinical features are similar to cholinergic toxidrome
- Please refer the cholinergic toxidrome

Box 8.4

Management

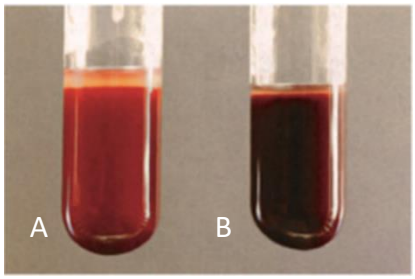
- ResusRSIDEAD pathway
- Atropine is the crucial antidote. Pralidoxime is not indicated

Box 8.5

3. Propanil poisoning

- The mortality rate of propanil poisoning is 10.7%
- It is the most lethal herbicide in Sri Lanka after paraquat
- Poison effect is due to methaemoglobinaemia
- The onset of the development of methaemoglobinaemia is said to be proportional to the level of toxicity
- Methaemoglobinaemia is clinically evident when SpO_2 is low and PaO_2 is high in ABG

- In addition, blood will be chocolate brown in colour (Coca-Cola colour) when methaemoglobinaemia develops (figure 8.1)



A - normal blood
B - chocolate brown coloured blood in methaemoglobinaemia

Figure 8.1 - Chocolate brown colour blood in methaemoglobinaemia

Clinical features

- Abdominal pain
- Nausea and vomiting
- Cyanosis due to methaemoglobinaemia

Box 8.6

Clinical presentations according to the level of methaemoglobin

Methaemoglobin Concentration	% Total Haemoglobin*	Symptoms**
< 1.5 g/dL	10%	None
1.5-3.0 g/dL	10-20%	Cyanotic skin discolouration
3.0-4.5 g/dL	20-30%	Anxiety, light headedness, headache, tachycardia
4.5-7.5 g/dL	30-50%	Fatigue, confusion, dizziness, tachypnoea, tachycardia
7.5-10.5 g/dL	50-70%	Coma, seizures, arrhythmias, acidosis
> 10.5 g/dL	> 70%	Death

*Assumes haemoglobin = 15 g/dL. Patients with lower haemoglobin concentrations may experience more severe symptoms for a given percentage of methaemoglobin level
** Patients with underlying cardiac, pulmonary, or haematological disease may experience more severe symptoms for a given methaemoglobin concentration

Table 8.1

Methaemoglobin level is not freely available in Sri Lanka. Therefore, following bedside colour charts would help to assess the level of methaemoglobinaemia. Usually, in resource poor setting take a few drops of patient's blood on a blotting paper or wadding paper and compare the colour with the standard colour chart (see figure 8.2)

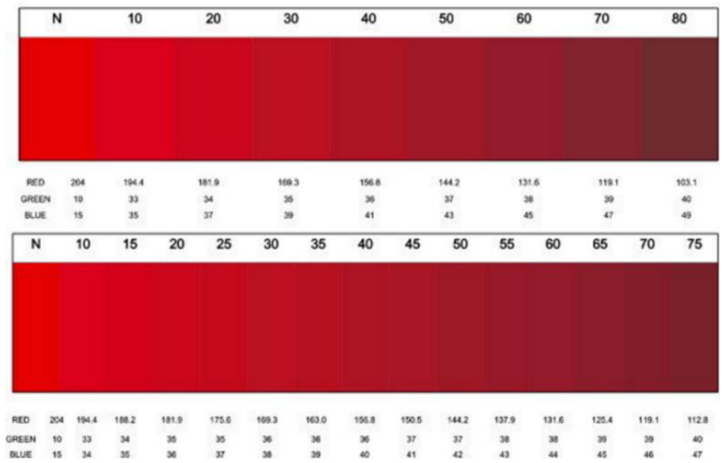


Figure 8.2 – Bedside colour chart to determine methaemoglibin %

Management

- High flow oxygen
- Methylene blue should be started when methaemoglobin level reaches around 20% in a symptomatic patient
- Methylene blue should be considered when methaemoglobin level reaches 30% in an asymptomatic patient
- Patients with anaemia or cardiorespiratory problems should be treated at lower levels
- The recommended dose of **methylene blue** is **1 mg/kg for adults** diluted in 1% sterile aqueous solution **infused over 5 min**
- Excessive use of methylene blue give rise to worsening of methaemoglobinaemia
- The dose can be repeated hourly up to a **maximum of 7 mg/kg over 24 hours**
- **Ascorbic acid is not of much use in acute methaemoglobinaemia**
- **Consider plasmapheresis in refractory cases**

The antidote for propanil poisoning is Methylene Blue

Figure 8.3 – bottle of methylene blue

Box 8.7

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9. Common Household Poisons

1. Poisoning with Kerosene

- Kerosene is a combustible hydrocarbon and is a solvent of many substances including a few pesticides
- Accidental ingestion of kerosene is common in Sri Lanka

Clinical features

- Nausea and vomiting
- Irritation of mouth and throat
- Coughing, fever, choking, dyspnoea, wheezing, cyanosis, tachypnoea, tachycardia, and crepitations. It can lead to chemical pneumonitis followed by secondary bacterial pneumonia – if aspirated
- Fatal haemorrhagic pulmonary oedema – in extreme cases
- Neurotoxicity following hypoxaemia and pneumonia
- Pneumothorax, cardiac arrhythmias, convulsions and coma
- Rarely, multiorgan dysfunction (e.g.: acute kidney injury, disseminated intravascular coagulation)

Box 9.1

Investigations

- Full blood count may show polymorphonuclear leucocytosis
- Chest X-ray findings include bilateral, punctate, mottled densities in perihilar areas and mid lung fields. Later, patchy densities and large areas of consolidation, atelectasis and emphysema can be observed

Management

- ResusRSIDEAD pathway
- Avoid induction of emesis and gastric lavage
- Avoid charcoal
- Protect airway if there is low GCS
- Oxygen / ventilation if there is respiratory compromise
- Correct electrolytes and support organ systems
- Anticipate chemical pneumonitis. However, there is no solid evidence for steroids as treatment
- Prevent / treat secondary bacterial pneumonia with intravenous antibiotics
- Management of arrhythmia and convulsions

Box 9.2

2. Poisoning with corrosive agents

Different types of corrosive agents encountered

	Acids	Alkali
Necrosis	Coagulative (Denaturation of proteins)	Liquefactive (Saponification of fats)
Damage	Eschar formation – perforation	Oedema – small vessel thrombosis
Timeline	Delayed	Minutes
Structures involved if ingested	Upper aerodigestive structures	Stomach
Examples	• Sulphuric Acid – Battery acid • Nitric acid – Toilet bowl cleaner/ rust remover • Hypochlorous acid – bleach • Hydrogen peroxide – mildew remover	• Sodium hydroxide – oven/ pipe cleaner • Ammonia – bleach/ household cleaner

Table 9.1

Clinical features

- Nausea and vomiting
- Irritation of mouth and throat
- Abdominal pain, haematemesis, and diarrhoea
- Cardiac arrhythmias and shock
- Chemical pneumonitis and mediastinitis
- Hoarseness of voice, stridor, and respiratory distress may occur due to laryngeal and epiglottic oedema
- Metabolic acidosis, acute renal tubular necrosis and acute kidney injury
- Haemolysis
- Late complications include oesophageal strictures and pyloric stenosis

Box 9.3

Management

- ResusRSIDEAD pathway
- Decontaminate by removing of contaminated clothes
- Irrigate aggressively in case of contact with skin, eyes, and other mucosal tissues
- Keep nil per oral
- Do not induce emesis or administer charcoal
- Do not give counteractive acids / alkali
- Injury to skin should be managed as per burn injury
- Ensure good hydration and nutrition
- May need prophylactic antibiotics

Box 9.4

3. Cyanide poisoning

Cyanide is present in plants like Hondala (*Adenia hondala*) and Manioc (*Manihot utilissima*). Both hydrogen cyanide and cyanide salts are highly toxic. Cyanide ions deactivate the cellular respiratory enzyme cytochrome oxidase, leading to cellular hypoxia, which causes the symptoms of cyanide poisoning. In the case of manioc poisoning, these symptoms result from the release of cyanide from glycosides, such as linamarin, found in the skin of the root.

Poisoning symptoms may appear 15 minutes to 2 hours after exposure. Linamarin, found in manioc / tapioca / cassava, is converted into cyanide through the action of linamarase, an enzyme in ginger. Therefore, as a precaution, ginger is not used in combination with manioc / tapioca / cassava.

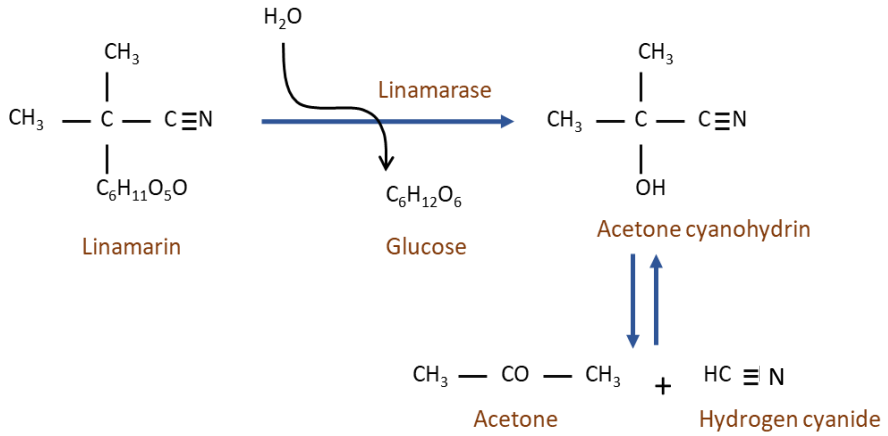


Figure 9.1 - Hydrolysis of linamarin by linamarase to produce hydrogen cyanide

Other circumstances of cyanide poisoning

- Industrial cyanide – plastic, synthetic rubber, metal processing, gold plating, fumigation, photography
- Suicidal agents

Clinical features of cyanide toxicity

- Headache, vomiting, dizziness, drowsiness, palpitations, and weakness
- Dyspnoea and tachypnoea
- Diaphoresis
- Hypotension, shock, arrhythmia, and conduction defects
- Hyperglycaemia, cerebral oedema, convulsions, and metabolic acidosis
- Bitter almond smell in breath due to hydrogen cyanide
- Chronic cyanide poisoning can cause ataxia, peripheral neuropathy, optic atrophy, and deafness
- Severe acute cyanide poisoning can result in sudden unconsciousness and death from respiratory arrest

Box 9.5

Management

- Supplemental oxygen
- Activated charcoal
- Gastric lavage in cases of large doses of ingestion

Consider one of the following antidotes:

- Sodium thiosulphate ($Na_2S_2O_3$) 50 mL of 25% solution IV over 10 minutes
- Dicobalt edetate (Kelocyanor) 20 mL (300 mg) IV over 1 minute
- Hydroxycobalamin 10 mL (4 g) of 40% solution over 20 minutes
- Sodium nitrite ($NaNO_2$) 10 mL of 3% solution over 5-20 minutes

Box 9.6

4. Accidental ingestion of a disc battery

Disc batteries are used in digital watches, calculators, toys, and cameras, etc. They often contain heavy metals such as mercury, silver, lithium, and manganese, along with aqueous potassium hydroxide. Accidental swallowing is very common in children.

Clinical features of accidental ingestion of a disc battery

- Mostly, there are no symptoms and signs, and the intact battery is expelled in the stool within 2 to 4 days
- If the battery is lodged in the oesophagus, it may lead to fever, difficulty in swallowing, vomiting, and loss of appetite
- Electrical current passing through tissues can result in tissue necrosis, ulceration, or potentially fatal conditions like tracheo-oesophageal fistula and perforation into the aorta
- On rare occasions, the battery may become impacted in the intestines
- If a mercury battery is opened up in the gastrointestinal tract, it can result in systemic mercury absorption

Box 9.7

Management

- ResusRSIDEAD pathway
- Whole bowel irrigation has a place
- Do a chest and abdominal X-ray to locate the position of disc battery. Abdominal X-rays should be conducted every 24 to 48 hours to assess the battery's transit
- Endoscopic retrieval if the object presents in oesophagus or has impacted
- Observe for fever, vomiting, abdominal pain and tarry stools. These features are suggestive of possible perforation of the intestine
- Objects found further in distal position usually will be passed in faeces. Parents should be advised to monitor stools to confirm the passage of the battery

Box 9.8

5. Detergent poisoning

Prinso / Penso /Sun Shine is a detergent comprised of 2 separate powders. The white powder is oxalic acid (may cause soreness and ulceration of aerodigestive tissues and breathlessness). The purple / pink powder is Condy's crystals (Potassium permanganate – $KMnO_4$).

Front and back of Penso packet:

Figure 9.2

Figure 9.3

Oxalic acid is found in other substances such as star fruit, biling, alocasia, dumbcane and caladium

Figure 9.4 – Star fruit

Figure 9.5 – Biling

Figure 9.6 – Alocasia

Figure 9.7 – Dumbcane

Figure 9.8 – Caladium

Clinical features of detergent poisoning

- Severe intoxicated poison patients manifest, electrolyte imbalances, hypocalcaemia, acute kidney injury, and have intense corrosive effect on their gastrointestinal tract
- QT prolongation may be observed in ECG
- Patients who have ingested the Condy's crystals can have the same symptoms including methaemoglobinaemia, purplish stained oral mucosa, necrosis and rarely perforation of oesophagus

Box 9.9

Management

- Administer orally calcium containing solutions to precipitate oxalate such as calcium gluconate, lactate, chalk or milk
- Administer 10% IV calcium gluconate 10 mL over 10 min if delayed
- Replace fluids and correct electrolyte imbalance
- Antidote methylene blue is useful in treatment for Methaemoglobinaemia

Box 9.10

6. Poisoning with spirits

Spirits consist of various chemicals including ethyl alcohol (ethanol), isopropyl alcohol (isopropanol), methyl alcohol (methanol), and ethylene glycol. Ethyl alcohol (ethanol) and isopropyl alcohol (isopropanol) are commonly used in the healthcare institutions as antiseptic agents.

Clinical features and antidotes

	Ethyl Alcohol (Ethanol)	Isopropyl Alcohol (Isopropanol)	Methyl Alcohol (Methanol)	Ethylene Glycol
Found in	Alcoholic beverages	Hand rub solutions, solvents mouth washes	Illicit alcohol – *Kassippu* Paint thinner Photocopier fluid	Anti-freeze Radiator fluid Brake fluid/oil
Key feature	CNS depression	CNS depression **Fruity breath (acetone)**	**Retinal damage and loss of vision** (formaldehyde/ formic acid – damage ETC)	**Renal failure** **Oxaluria** (crystals) **Hypocalcaemia**
Metabolic Acidosis	Usually no	No	Yes	Yes
High Anion Gap	Usually no	No	Yes	Yes
Osmolar gap	Yes	Yes	Yes > 20	Yes > 20
Treatment	Supportive	Similar to ethanol	Alcohol Fomepizole (if available)	Alcohol Fomepizole (if available)

Table 9.2

- Revise the biochemical basis of metabolism of these agents to relate to pathogenesis

The pathway of ethanol metabolism

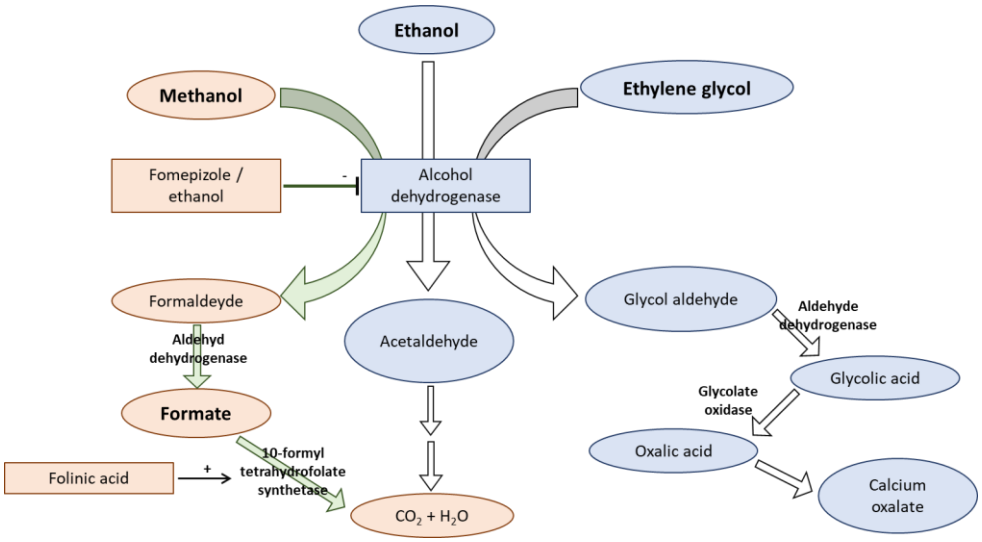


Figure 9.9

- Methanol and ethylene glycol are metabolised by alcohol dehydragenase (ADH) and generate formaldehyde and glycol aldehyde respectively. These metabolites are highly toxic agents
- Ethanol and fomepizole are competitive inhibitors of the enzyme ADH i.e. they compete with methanol and ethylene glycol for binding to ADH
- However, ethanol metabolism by ADH generate less toxic agent i.e. acetaldehyde
- This process helps to mitigate the dangerous effects of methanol and ethylene glycol while the body eliminates them

Initial Mangement

- If available, send blood samples for methanol or ethylene glycol level analysis
- Do not induce vomiting. Consider gastric lavage or using a flexible nasogastric tube to aspirate ingested liquids if the presents within 1 hour
- If the patient has impaired consciousness, insert a cuffed endotracheal tube before performing gastric lavage
- Administer oxygen and assisted ventilation if respiration is compromised
- Monitor fluid balance and address dehydration and electrolyte imbalances
- Administer intravenous sodium bicarbonate to correct metabolic acidosis

Comparison of the specific management principles of these agents `

Ethyl alcohol/ Isopropyl alcohol	Methanol	Ethylene Glycol
Gastric lavage when appropriate (it is rapidly absorbed Correct hypoglycaemia Correct dehydration and electrolyte imbalance Alcohol ketoacidosis – 5% dextrose IV Thiamine 100 mg (Give before IV glucose)	Gastric lavage $NaHCO_3$ IV to correct metabolic acidosis Correct dehydration and serum electrolytes Ethanol per orally to block metabolization (Fomepizole is the antidote if available) IV Thiamine 100 mg 6 hourly IV / IM Pyridoxine 50 mg for 2 days Folinic acid (if available)	Gastric lavage $NaHCO_3$ IV to correct metabolic acidosis Correct dehydration and serum electrolytes. Correct calcium up to lower limit normal. Ethanol per orally to block metabolization (Fomepizole is the antidote if available) IV Thiamine 100mg 6 hourly IV/IM Pyridoxine 50 mg for 2 days

Table 9.3

How to give ethanol in methanol and ethylene glycol poisoning?

- Ethanol is the antidote for methanol poisoning. Administer ethanol orally or intravenously to maintain a blood ethanol level of 100-150 mg/dL, which inhibits the metabolism of methanol
    - In mild cases, oral ethanol is sufficient. For intravenous administration, give 10% ethanol at 7.5 mL/kg over 30-60 minutes as a loading dose
    - The maintenance dose for non-drinkers is 1 mL/kg/hour of 10% ethanol IV; for chronic ethanol users, the dose is 1.96 mL/kg/hour
    - If the patient is undergoing haemodialysis, the maintenance dose increases to 3 mL/kg/hour
- A 10% ethanol solution can be prepared by mixing 60 mL of absolute alcohol with 500 mL of 5% dextrose for intravenous use

- A 10% ethanol solution can be prepared by mixing 60 mL of absolute alcohol with 500 mL of 5% dextrose for intravenous use
- If IV ethanol is unavailable, oral ethanol may be administered. Dilute ethanol to concentrations below 20% to prevent gastric irritation
    - A loading dose of 95% ethanol at 0.8 mL/kg followed by a maintenance dose of 0.1 mL/kg/hour can be given orally or via a nasogastric tube
    - During haemodialysis, increase the maintenance dose to 0.2 mL/kg/hour
    - For chronic ethanol drinkers, the maintenance dose is 0.2 mL/kg/hour
- In the absence of ethanol, arrack or whisky (40%) can be given **orally** as a substitute
    - Administer 1.8 mL/kg as a loading dose and 0.2 mL/kg/hour as a maintenance dose, diluted in water or fruit juice
    - During haemodialysis, the maintenance dose increases to 0.7 mL/kg/hour
    - For chronic ethanol drinkers, the maintenance dose is 0.45 mL/kg/hour
- Keep in mind that ethanol has a specific gravity of approximately 0.8, meaning that 95% ethanol is about 76 g/100 mL, not 95 g/100 mL
- The treatment should be continued for 3 to 4 days, or until the plasma methanol concentration drops below 20 mg/dL, unless contraindicated
- Blood ethanol levels should be monitored hourly at first, then at longer intervals based on available facilities
- Prolonged ethanol use can lead to hypoglycaemia, especially in children, so monitor blood glucose levels and provide oral glucose or intravenous dextrose (5% or 50%) as needed
- If seizures occur, administer diazepam 5-10 mg IV (paediatric dose: 0.2 mg/kg), repeating if necessary
- Administer folic acid or folinic acid at 50 mg IV (1 mg/kg) every 4 hours for a total of six doses (paediatric dose: 1 mg/kg every 4 hours
- In severe cases, haemodialysis is life-saving, as it can remove both methanol and its metabolites

Box 9.11

7. Naphthalene poisoning

Naphthalene is the chemical agent found in moth balls. The usual circumstances of poisoning of Naphthalene include accidental ingestion among children and also inhalation or skin exposure are possible.

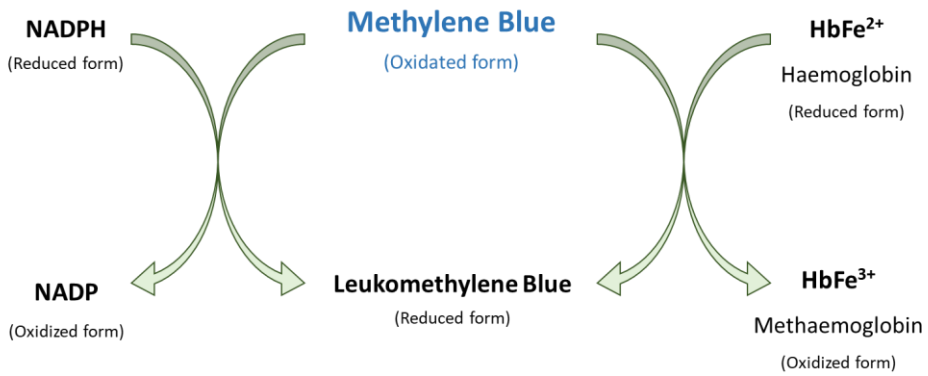
Toxic effects of naphthalene

- Abdominal pain, nausea, vomiting, diarrhoea and headache
- Oxidation of haemoglobin by α-naphthol to methaemoglobin
- Intravascular haemolytic anaemia
- Cyanosis
- Hypotension, tachycardia, hyperkalaemia, dysuria, oliguria

➢ *Patients with G6PD deficiency are more susceptible*

Box 9.12

Biochemical basis of pathogenesis



Methylene blue act as an electron shuttle, facilitating the reduction of methaemoglobin by NADPH. This mechanism, enables a single methylene blue molecule to reduce multiple methaemoglobin molecules.

Figure 9.10 - Mechanism of action of methylene blue

Management

- Activated charcoal
- Gastric lavage if appropriate
- Good hydration and diuresis
- May need dialysis
- Haemolysis – may need blood transfusion
- Cyanosis – bed rest and oxygen supplementation
- Check methaemoglobin levels
- If Methaemoglobin level are more than 30% or if cyanosis is present, 1% methylene blue intravenous 0.1 mL/kg slowly should be administered. If the IV preparation is not available oral methylene blue 300 mg daily can be used. If methylene blue is unavailable oral ascorbic acid 1 g bd can be used

Box 9.13

8. Poisoning with rodenticides

Poisoning with rodenticides is common. Patients may present with ingestion of following rodenticides:

- Pellets – Usually coumarins (indandiones and brodifacoum)
- Powder – Zinc phosphides

Clinical features of coumarin ingestion

Coumarins Inhibit hepatic synthesis of Vitamin K dependent coagulation factors (II, VII, IX, X). Patients are most of the time asymptomatic. However mild to severe degree of bleeding can occur ranging from epistaxis, gingival bleeding, petechiae, purpura, haematuria and malaena. When one has *abdominal pain and backache internal bleeding should be considered.*

Specific considerations in management of coumarin poisoning

- Administer activated charcoal
- Avoid induction of emesis / lavage
- Check PT/INR (It may take 48 hours to show abnormalities

No bleeding. But prolonged INR	Vitamin K 10-50 mg PO bd-qds. May need prolonged treatment.
Mild bleeding. Prolonged INR	Vitamin K 10 mg SC daily. Repeat daily until INR is corrected.

Table 9.4

Key features of zinc phosphide poisoning

Zinc phosphide is hydrolysed in stomach to phosphine which inhibits cytochrome oxidase. Nausea, vomiting abdominal pain and headache can present. Chest tightness, dyspnoea, thirst, agitation, arrhythmia and pulmonary oedema are significant symptoms.

Management

- Gastric lavage with 1:5000 potassium permanganate/ sodium bicarbonate

Box 9.14

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10. Snake Bites

Snake envenomation is a potentially fatal condition that occurs due to the bite of venomous snakes. Identification of the snakes and symptoms and signs of snake bite are mandatory in managing such patients.

Highly venomous snakes in Sri Lanka

Cobra

Figure 10.1 – Sri Lankan Cobra

- Circumstances
  - Bites are possible even inside the house and near water filled areas
  - Commonly occur in rural and agricultural areas
- Toxic effects
  - Local effects – swelling, tissue necrosis
  - Neurotoxicity – ptosis, external ophthalmoplegia, respiratory paralysis, limb paralysis
  - No coagulopathy

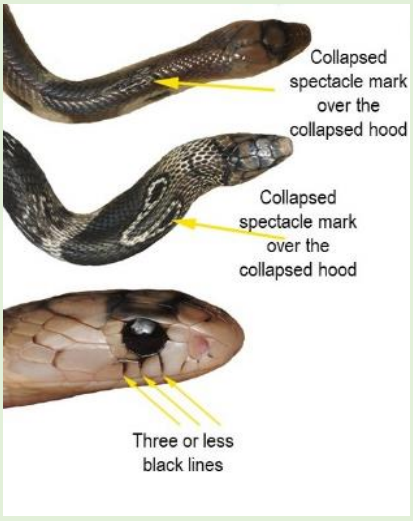


Figure 10.2

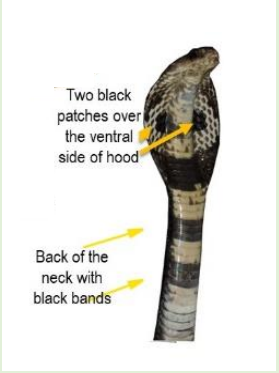


Figure 10.3

Figure 10.4

Box 10.1

Krait

Figure 10.5 – Sri Lankan Krait

- Circumstances
  - Mostly occur during the night, while sleeping on the floor
  - Bites are possible even in the groin and axillary areas

Figure 10.6 – Common / Indian Krait

- Toxic effects
  - No local effects
  - Neurotoxicity – ptosis, external ophthalmoplegia, respiratory paralysis, limb paralysis, coma
  - No coagulopathy

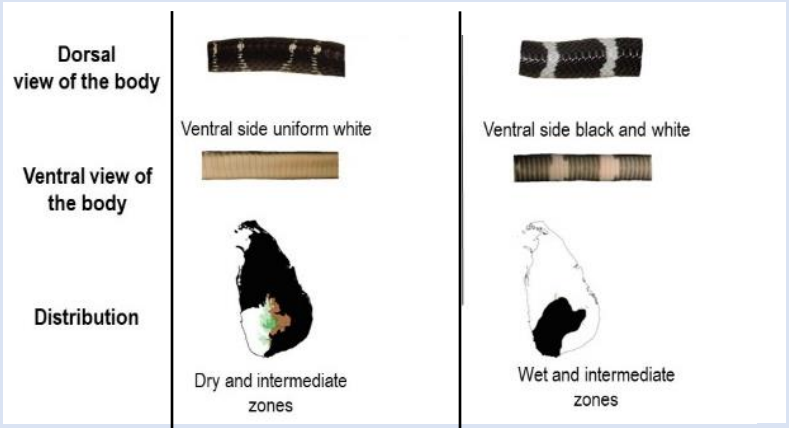


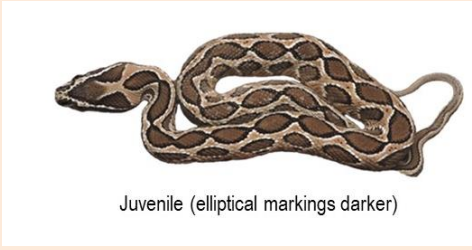
Figure 10.7 Common / Indian Krait Sri Lankan Krait

Box 10.2

Russell's viper

Adult (elliptical markings lighter)

Figure 10.8



Juvenile (elliptical markings darker)

Figure 10.9

- Circumstances
  - Common during harvesting season
- Toxic effects
  - Local swelling
  - Abdominal pain, faintness, nausea, and vomiting are common early non-specific systemic features of envenomation
  - Neurotoxicity – ptosis, external ophthalmoplegia
  - Coagulopathy – dark urine, prolonged clotting time, incoagulable blood, DIC
  - Cardiac toxicity – hypotension, tachycardia

Box 10.3

Hump-nosed viper

Variation in dorsal body colouration (Note the two rows of triangular blotches either side of midline)

- Merrem's hump-nosed pit-viper (*Hypnale hypnale*), Lowland hump-nosed pit-viper (*Hypnale zara*) are highly venomous and Sri Lankan hump-nosed pit-viper (*Hypnale nepa*) is potentially highly venomous
- Most commonly causes only local swelling
- Haemorrhagic blister at the bite site
- Tender regional lymphadenopathy
- Systemic effects of coagulopathy, microangiopathic haemolytic anaemia (MAHA), mild neurotoxicity, and acute renal failure

- Management of MAHA includes 15 mL/kg FFP twice a day 2-3 days depending on the clinical situations
- Plasmapheresis does not have proven survival benefits
- Haemorrhagic blister may end up with osteomyelitis / gangrene later. Therefore, it is advisable to rupture and drain the tensed blister under strict aseptic conditions at the early stage and cover with IV antibiotics

Figure 10.10

Box 10.4

Potentially highly venomous snakes

Green pit viper

Figure 10.11 – Green pit viper

- Circumstances
  - Bites are commonly seen in tea, cinnamon, and nutmeg plantations
  - Commonly bitten during daytime on hands and feet

- Toxic effects
  - Mostly local envenoming – pain, swelling, bleeding, regional lymphadenopathy, and haemorrhagic blisters
  - Systemic envenoming is rare – mostly venom induced consumption coagulopathy (VICC) and acute kidney injury

Box 10.5

Differentiating wolf snake from a Sri Lankan krait

There can be difficulty in identification between the krait and the wolf snake. These are the ways to identify a wolf snake from a Sri Lankan krait:

Wolf snake - Often confused with kraits as both have single bands

- Have broader and flatter heads, slightly thicker bands
- Vertebral scales and the other scales are similar in size and have no separate appearance

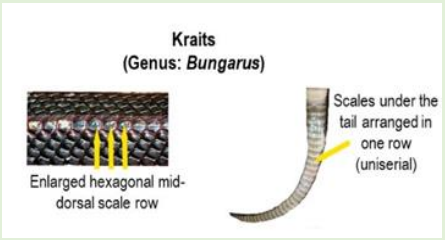


Figure 10.12 – Sri Lankan krait

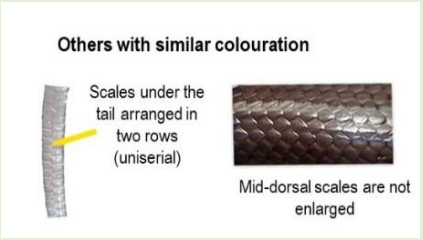


Figure 10.13 – Wolf snake

Box 10.6

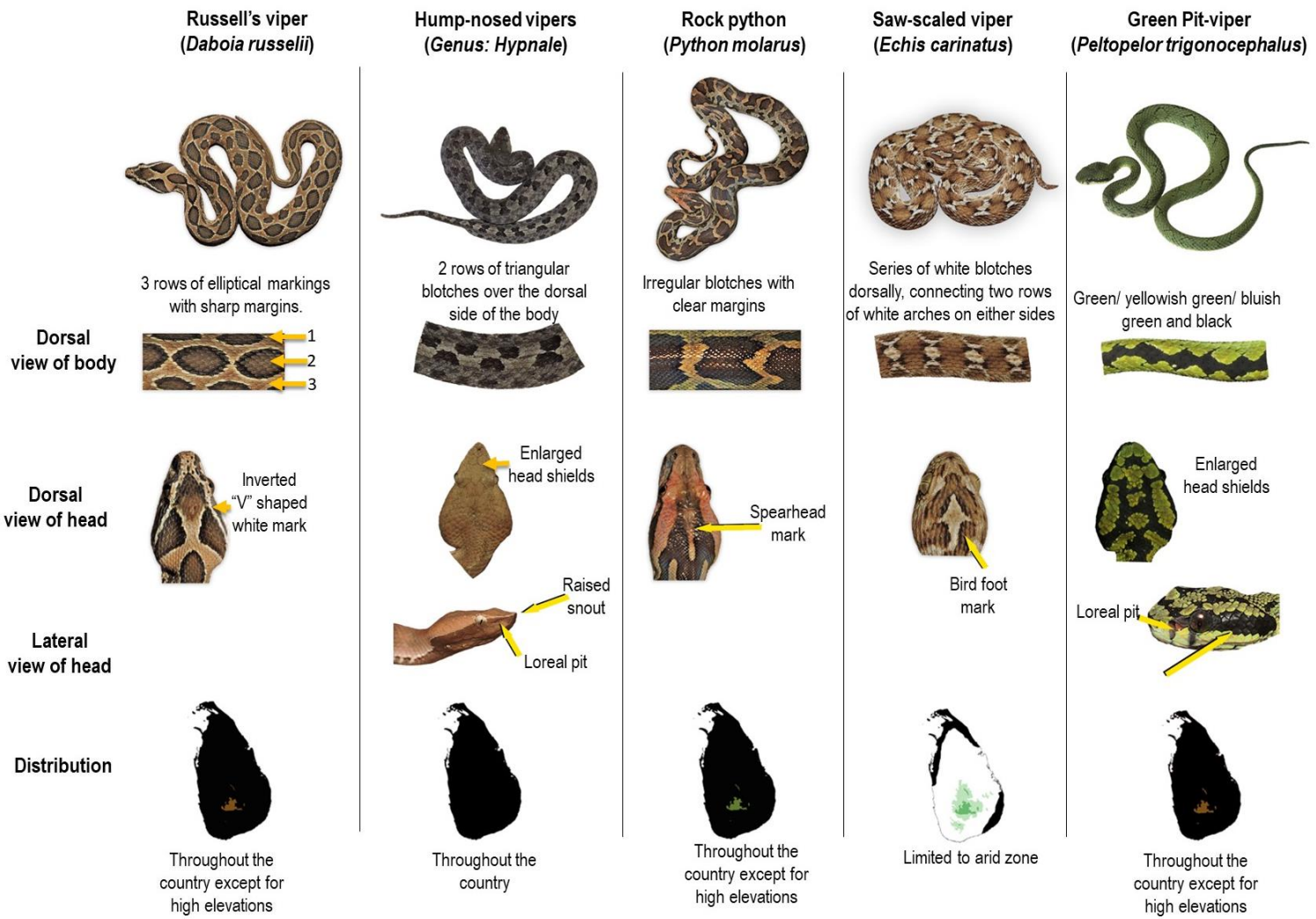

Russell's viper
(Daboia russelii)
Hump-nosed vipers
(Genus: Hypnale)
Rock python
(Python molarus)
Saw-scaled viper
(Echis carinatus)
Green Pit-viper
(Peltopelor trigonocephalus)
Dorsal view of body
3 rows of elliptical markings with sharp margins.
1
2
3
2 rows of triangular blotches over the dorsal side of the body
Irregular blotches with clear margins
Series of white blotches dorsally, connecting two rows of white arches on either sides
Green/ yellowish green/ bluish green and black
Dorsal view of head
Inverted "V" shaped white mark
Enlarged head shields
Spearhead mark
Bird foot mark
Enlarged head shields
Lateral view of head
Raised snout
Loreal pit
Loreal pit
Distribution
Throughout the country except for high elevations
Throughout the country
Throughout the country except for high elevations
Limited to arid zone
Throughout the country except for high elevations

Figure 10.14

What to do if the snake cannot be identified?

When the snake is not brought or could not be identified with a picture, identification could be done by clinical features and circumstance of the bite.

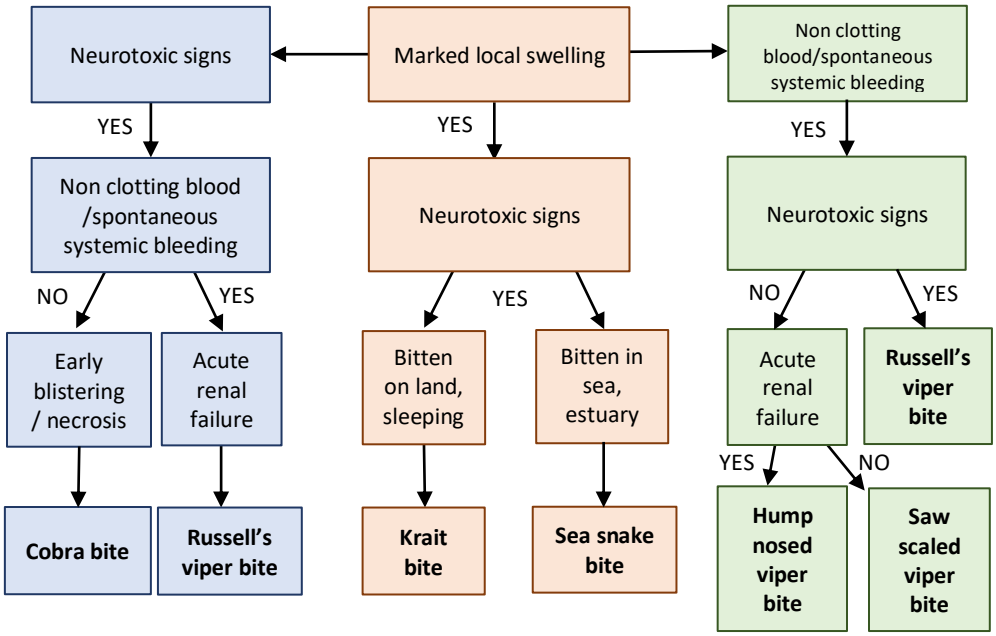


Figure 10.15 – Syndromic approach to identifying an unknown snake envenomation

Management of snake bites

1. First aid
   - Wash the bitten area with soap and water
   - Do not apply any tourniquet
   - Remove rings, threads, anklets, etc. as early as possible before swelling develops
   - Try to immobilise the limb area
   - Do not cut or try to aspirate the bitten area
2. Admit, reassure and assess general condition
3. Resuscitate if necessary
4. Assess signs of envenomation
5. Identify the snake
6. Monitor
7. Antivenom therapy if indicated
8. Monitor for complications

Box 10.7

Signs of envenomation

Local effects	Systemic effects	
	Nonspecific features	Specific features
Swelling	Abdominal pain	Neurotoxicity
Blistering	Nausea, Vomiting	Spontaneous systemic bleeding
Tissue necrosis	Hypotension	Rhabdomyolysis with myoglobinuria
	Polymorphonuclear leucocytosis	Coagulopathy

Table 10.1

Initial assessment of a snake bite victim (ABC)

- **A**irway – Maintain clear airway
- **B**reathing – Weak cough and reduced neck muscle power are the early signs of impending respiratory failure. Keep the instruments ready to ventilate
- **C**irculation – Monitor pulse rate, blood pressure. Gain IV assess
- Hypotension – Normal saline 20 mL/kg bolus. If still hypotensive repeat the same dose once more
- Look for local and systemic signs of envenomation

What are the parameters to be monitored in a patient bitten by a snake?

- Level of consciousness
- Pulse rate
- Blood pressure
- Oxygen saturation
- Respiratory rate and tidal volume
- Temperature
- Urine output
- Fluid balance

Box 10.8

Investigations

- The most important bedside investigation would be to arrange a 20WBCT (20-minute Whole Blood Clotting Test) to detect coagulopathy
- If facilities are available
- PT/INR
- Serum creatinine, Serum electrolytes – to assess and monitor renal functions
- ECG – if cardiotoxicity is suspected

AVOID

- NSAIDS including Aspirin
- IM injections
- Concurrent administration of sera other than AVS
- Narcotics and other respiratory depressants

Box 10.9

20WBCT

How to perform:

- 1 mL of blood should be collected into a clean, dry 5 mL borosilicate glass test tube with an internal diameter of 10 mm
- Allow it to stand undisturbed for 20 minutes
- Then tilt the tube and check for clot formation

➢ Tap water should be used to clean the glass test tube (detergents or soap should not be used when cleaning the test tube. Because they may interfere with the 20WBCT)

Interpretation:

- If the blood is not clotted, there is coagulopathy (envenomed) – it is called POSITIVE 20WBCT
- If the blood is clotted, there is no coagulopathy (not envenomed) – it is called NEGATIVE 20WBCT
- If any doubt – repeat the test (in **one hour**- depending on the suspicion of snake)
- PT/INR would be more reliable in this situation, if it is available urgently

Box 10.10

Antivenom therapy

- Most important investigation to do before commencing antivenom therapy is 20WBCT
- Coagulopathy is diagnosed if the 20WBCT is positive

Indications to give Antivenom therapy:

- Commence immediately if systemic envenomation is present in bites of Russell's viper, cobra, krait and saw scaled viper
- Local envenomation in cobra bites
- Severe abdominal pain in krait bite in the absence of neurotoxicity
- In Russell's viper bites, even if 20WBCT is negative, if abdominal pain and faintness are present and the snake is identified as a Russell's viper, have to start on antivenom without delay

Box 10.11

The indications for antivenom in snake bite:

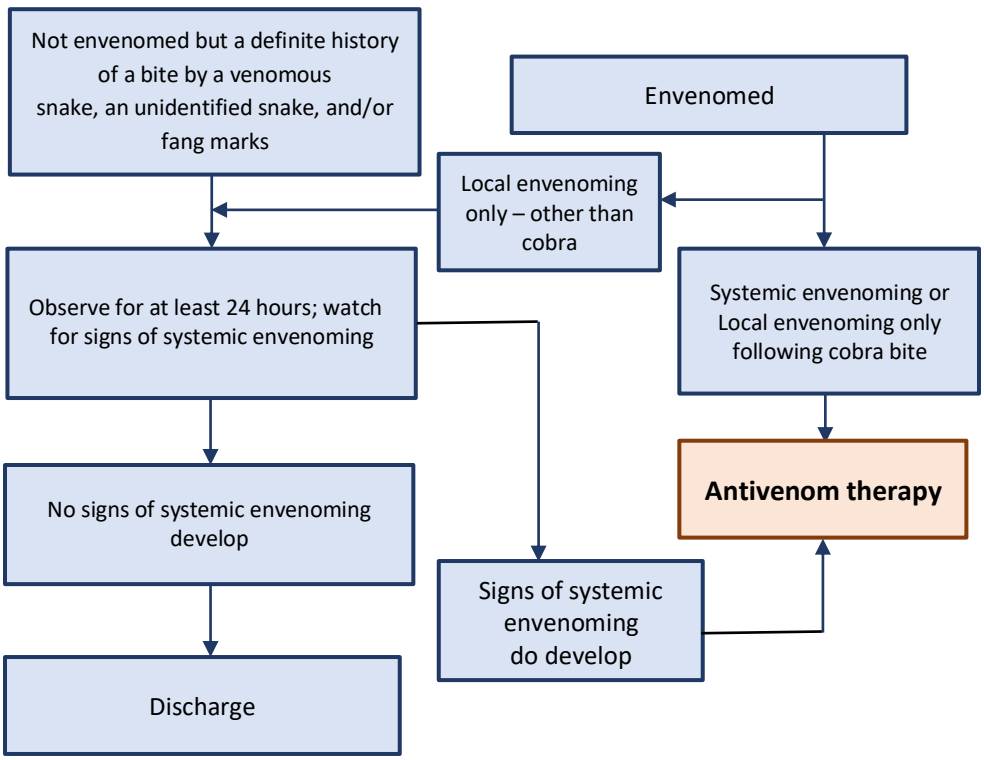


Figure 10.16

No benefit of antivenom therapy for bites of:

- Hump nosed viper
- Green pit viper
- Sea snakes

Do not give antivenom for those snake bites

Box 10.12

- Commence antivenom as soon as systemic envenoming is detected
- Dose:
  - Russell's viper bites – 20-30 ampoules as first dose. May repeat in 6 hours at a dose of 10 ampoules if coagulopathy persists
  - Cobra bites – one dose of 10 ampoules
  - Krait bites – one dose of 10 ampoules
- 100-200 mL (10-20 ampoules) or more of Indian polyspecific antivenom in normal saline (total volume should be 500 mL) over 1 hour
- When preparing the antivenom, do not shake the bottle. First introduce the negative pressure before adding the distilled water. Then gently rotate the bottle in between the palms to dissolve the antivenom. This will avoid froth formation leading to anaphylaxis
- In acute severe envenomation of Russel's viper bites up to 40 ampoules can be given, if coagulopathy persists FFP can be given to correct the coagulopathy (The dose of FFP is 10 mL/kg IV twice a day)
- Persistent neurological signs alone are not an indication to repeat antivenom therapy
- Once antivenom is given repeat 20WBCT 6 hourly until blood clots up to 24 hours
- If first 20WBCT is negative, repeat the 20WBCT 2-4 hourly, in the first 24 hours

Box 10.13

Premedication to prevent or reduce the reactions to antivenom

- Adrenaline 0.25 mg (0.25 mL of 1:1000 solution) SC given just before starting antivenom has proven benefits in preventing major reactions
- A dose for children is 0.005 mL/kg of BW in solution SC 1:1000
- When IV adrenaline is given, there can be worsening of existing myocardial ischaemia and hypertension. It can also cause arrhythmias

Box 10.14

- Early detection and vigorous treatment are more important

Treatment of Anaphylaxis

- Stop the antivenom
- Adrenaline:
  - Adults – (0.5 mg) 0.5 mL of 1:1000 solution
  - IV if in shock or collapsed
  - IM if not in shock or collapsed (on the lateral middle third of the thigh)
  - Children – 0.01 mg/kg
- Chlorpheniramine: 10 mg IV
- Hydrocortisone: 200 mg IV
- Start on IV normal saline bolus if blood pressure is low

Box 10.15

Causes of death in patient with a snakebite

- Respiratory arrest – Hypoxia
- Hypotension
- Complications secondary to antivenom and snakebite
- Respiratory muscle paralysis (causing type II respiratory failure) – A major problem after cobra and krait bites
- Hypovolemia
- Direct effects of cardio toxins
- Venom induced anaphylaxis
- Acute kidney injury

Box 10.16

Management of allergic reactions

- IM adrenalin can be given one after the other may be 2-3 times
- In severe shock – not responding to IM Adrenalin
    - Intravenous infusion of Adrenaline
    - 10-20 µg (1-2 mL of a 1:100,000 solution) per minute IV infusion
    - Adults 1 mg (1.0 mL of 0.1% solution in 250 mL 5% dextrose or 0.9% saline) infused at the rate of 15-60 drops/min; the rate maybe increased up to twice as fast if necessary, depending on the response
    - Or 0.75-1.5 µg/kg of 1:100,000 solution IV infusion
- Persistent hypotension / shock – Dopamine infusion
    - Dose: 400 mg in 500 mL in 5% dextrose or 0.9% saline infused 2-5 µg/kg/min
- Resume antivenom infusion once the reaction has settled and give the full dose in remaining time
- Anaphylaxis can occur for up to 3 hours following antivenom therapy. Therefore, continue monitoring
- Hydrocortisone is given for long term protection – no evidence for benefit
- In mild allergic reactions (e.g.: rash, dry cough, etc.) only chlorpheniramine is adequate

Box 10.17

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11. Miscellaneous Faunal Poisoning

1. Beetles

Local reactions can occur following contact of certain beetles, mainly due to cantharidin in insect fluid.

Blister beetle **Figure 11.1**

Figure 11.2

Key clinical features

- Dermatitis and keratoconjunctivitis
- Burning sensation of the mouth, abdominal pain, dysphagia, nausea, and haematemesis
- Dark coloured urine, gross haematuria, and dysuria
- Renal dysfunction can result in acute tubular necrosis
- Priapism, seizures, and cardiac abnormalities are less commonly reported
- Respiratory failure and a 'Guillain-Barre-like' syndrome

Box 11.1

Management of this condition is symptomatic.

Box 11.2

2. Scorpions

More than 650 species of scorpions have been identified worldwide. Annually, 1.2 million scorpion bites are reported globally, leading to more than 3000 fatalities. Eighteen scorpion species have been identified in Sri Lanka. Among them, the most commonly found species is the black scorpion (Heterometrus species). Although these species are not known to cause fatal stings, the Indian red scorpion (*Hottentotta tamulus*) has recently been linked to fatal envenoming in the Jaffna Peninsula.

Types of scorpions found in Sri Lanka

Figure 11.3 - Black Scorpion
Heterometrus gravimanus

Figure 11.4 - Red (White) Scorpion
Hottentotta tumulus

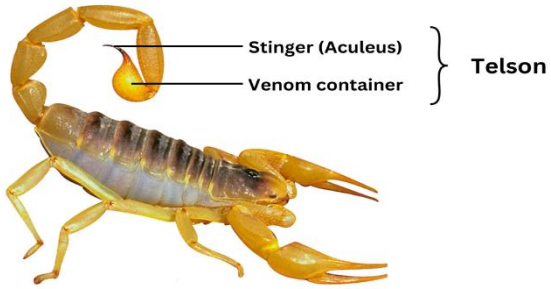


Figure 11.5 – Anatomy of the scorpion stinger

Clinical features

- The toxin in the telsons cause local reactions such as wheals, pain, and swelling
- In red scorpion envenomation there is overactivation of autonomic nervous system. This may lead to tachycardia, blood pressure fluctuations, diaphoresis, excess salivation, piloerection and priapism
- Other complications include myocardial infarction, acute pancreatitis, shock, and death

Box 11.3

Oral prazosin is useful to control hypertension in the bites of Red Scorpions.

Box 11.4

3. Centipedes

Centipedes live inside caves and among foliage and dirt. They are predators and mainly active at night. They are distributed widely, especially in warm, temperate and tropical regions. 24 species of centipedes have been recorded in Sri Lanka.

Figure 11.6 -

Garuda centipede

Features of centipede sting

- The injury results from forcipules in the head. It causes intense local pain, swelling, and redness, and necrosis
- Vomiting, sweating, constitutional symptoms, and enlargement of regional lymph nodes are other recognised features

Box 11.5

Management

- They are not usually deadly unless anaphylaxis sets in
- Ice packs application to the site of envenomation is useful along with antihistamines
- Promethazine 25 mg or chlorpheniramine 4 mg orally can be administered
- The use of analgesics is advocated

Box 11.6

4. Spiders

Spiders (Araneae) form a vast group of widely distributed arthropod predators found in various environments. In Sri Lanka, it is estimated that just over 400 species of spiders exist. While their bites can lead to significant morbidity, often causing muscle spasms, they rarely result in fatalities.

Black widow spider

The venom of the black widow spider (Latrodectus mactans) exerts its neurotoxic effects on motor end-plates by attaching to gangliosides and glycoproteins at synaptic junctions. This interaction triggers the release of acetylcholine and noradrenaline, while also blocking their reuptake, leading to excessive stimulation of the motor end-plates. The bites of black widow spiders in Sri Lanka are not usually deadly.

Figure 11.7 – Black widow spider

Clinical features

- Symptoms can appear within 15 minutes to 6 hours following the bite. Symptoms peak around 4 hours and usually subside within 24 to 48 hours, but can occasionally last for weeks
- Clinical features include
  - Pain and swelling of bitten part (pain at the bite site may radiate to larger muscle groups)
  - Bite site may show:
    - Two small red fang marks (≈1 mm apart) with mild swelling
    - Later development of urticaria and pruritus
  - It also can cause chest, abdominal, and muscular pain
  - Autonomic symptoms – sweating, salivation and vomiting
  - Restlessness and difficulty in breathing
  - Hyperaesthesia, ptosis, and convulsions can occur rarely

Box 11.7

Management

- Bed rest
- Wash the bitten area
- Apply cold packs
- Do not incise, suck the venom, or put tourniquets
- Tetanus prophylaxis if indicated
- Administer 10% calcium gluconate IV slowly, starting with 2 mL
- Increase the dose up to 10 mL based on symptom relief
- To relieve muscle spasms, give diazepam 2 to 10 mg intravenously
- Analgesics for pain relief e.g.: paracetamol or codeine
- In some countries, specific antivenin for the venom is available

Box 11.8

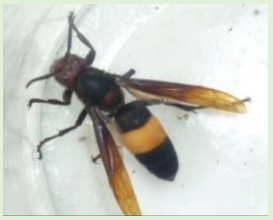
5. Insect stings

Hymenoptera order

Wasps, bees, and ants are members of the Hymenoptera order. Unpublished data indicate that thousands of hospitalisations and between 15 to 30 fatalities occur each year in Sri Lanka due to insect stings.

- Stings can be fatal
- Wasps – usually multiple stings and do not leave the stinging apparatus
- Bees and giant honey bees – usually single sting and leave the stinging apparatus behind

Apis dorsata
Giant Honey bee (S. Bambara)



Vespa tropica
Hornet / Wasp (S. Debara)

Apis cerana
Honey bee (S. Meemassa)

Figure 11.8

Clinical features of envenomation of insects of the Hymenoptera order

- The venom of these insects contains dopamine, histamine, phospholipase A2, hyaluronidase and toxic peptides (a haemolysin, a neurotoxin and a mast cell degranulator). This results in burning pain, swelling, and pruritus
- Nausea, vomiting, diarrhoea, tightness of chest, malaise, urticaria and facial oedema also can settle in
- Severe anaphylactic reaction with hypotension, bronchospasm, and laryngeal oedema
- Rarely, oliguria, renal failure, seizures, and rhabdomyolysis may occur
- Serum sickness may occur up to 10 to 14 days after envenomation
- **Kounis syndrome** – Acute coronary syndrome in the setting of allergic reactions, usually secondary to allergic coronary vasospasms and/or plaque rupture
- Arterial spasm can lead to formation of gangrene as well

Box 11.9

Management

- Apply ice packs to reduce pain and absorption of venom
- As bees and giant honey bees leave the stinger, it should be carefully scraped with a glass slide or a credit card, taking care not to squeeze the attached venom sac
- Antihistamines such as promethazine 25 mg IM are useful
- Anaphylaxis should be anticipated and managed
    - In cases where severe systemic symptoms are observed, administer 0.5 to 1.0 ml of 1:1000 adrenaline either subcutaneously or intramuscularly
    - For paediatric patients, the dose is 0.01 mL/kg, up to a maximum of 0.3 mL
    - Additionally, administer 200 mg of hydrocortisone intravenously and 25 mg of promethazine either intramuscularly or intravenously (paediatric dose: 6.25 to 12.5 mg). Continue oral prednisolone (1 mg/kg/day) for 3-5 days
    - If the response to treatment is insufficient, adrenaline can be repeated after 3 minutes. In life-threatening situations, adrenaline can be administered intravenously. For hypotension, elevate the foot end of the bed and administer IV fluids rapidly
    - If bronchospasm occurs, give 250 mg of aminophylline intravenously at a slow rate or 2.5 mg of salbutamol via nebulizer

- Renal failure may require dialysis
- It is noteworthy that Kounis Syndrome is associated with envenomation. Primary focus of treatment of Kounis syndrome should be directed towards allergic insult and removal of the offending allergen and sometimes it may need the treatment of the acute coronary event
- Bee sting induced hepatotoxicity could also occur
- Management of rhabdomyolysis if necessary

Box 11.10

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12. Plant Poisoning

1. *Gloriosa superba* (S. Niyangala, T. Illankalli / Kartikai, E. Glory Lilly)

Figure 12.1 – *Gloriosa superba*

- **Poison**: Highly active alkaloids such as colchicine, gloriosine, superbrine (a glycoside), chelidonic acid and salicylic acid
- All parts of the plant are poisonous, especially the tubers
- Accidental poisoning also common
- Colchicine is a spindle poison which affects rapidly proliferating cell lines such as intestinal epithelium, hair follicles, bone marrow cells, etc.
- Lethal dose: about 6 mg/kg body weight
- The usual fatal period is about 12-72 hours after the ingestion

Toxic effects

Phase 1 (2-24 hours)

- Burning sensation of mouth, excessive salivation, pain in throat, dysphagia, nausea, vomiting, colicky abdominal pain, and mucoid diarrhoea. Later progress to haemorrhagic diarrhoea, and dehydration. Even death is possible due to severe electrolyte imbalance and haemodynamic instability

Phase 2 (24 -72 hours)

- Bone marrow suppression, delirium, convulsions, oliguric renal failure, electrolyte imbalance, acid-base disturbance, shock, liver failure, coagulation disorders and DIC, diffuse haemorrhage, acute respiratory distress syndrome, arrhythmias, cardiovascular collapse, encephalopathy, and rhabdomyolysis. Because of the bone marrow suppression and the other toxic effects, the patient may have high risk of infection and septic shock. Due to all of the above multifactorial causes, death is possible during this phase

Phase 3 (1-3 weeks)

- Non pruritic dermatitis, polyneuropathy, sensory disturbance, muscle pain, and weakness, ascending motor paralysis, and non-scarring alopecia. Recovery typically occurs within few weeks of ingestion with above features

Box 12.1

Management

- General management of the patient with poisoning
- ResusRSI-DEAD pathway
- Gastric lavage is recommended
- Activated charcoal with requirement of multiple doses
- Symptomatic and expectant management
- Broad Spectrum Antibiotics to start early to prevent sepsis
- GM-CSF if neutropaenic
- Haemodialysis is indicated if there is acute kidney injury (it is not for the removal of the toxin)

Box 12.2

2. Pink Oleander (*Nerium oleander)* or Yellow Oleander *(Thevetia peruviana)* (S. Kaneru, T. Alari)

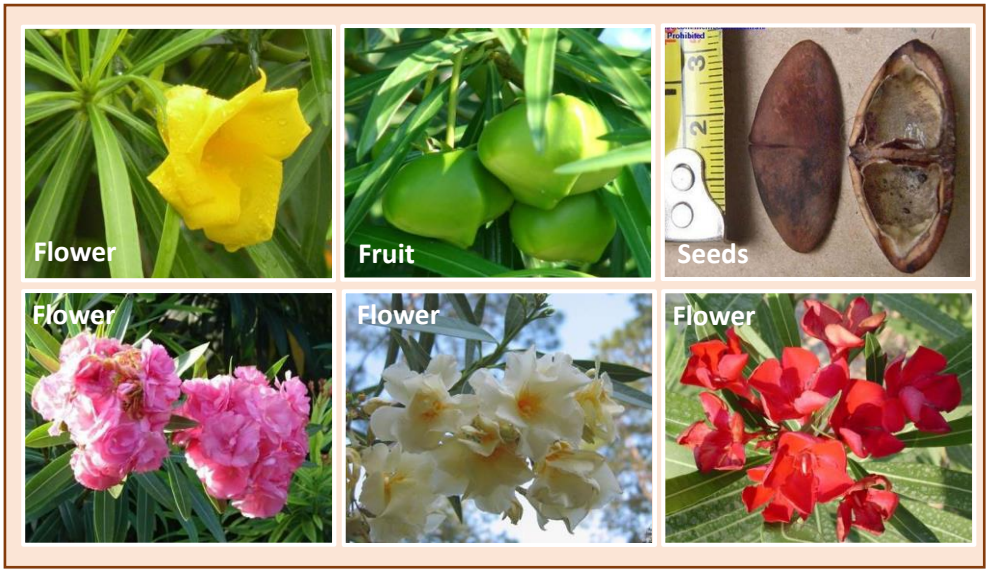

Figure 12.2 – Oleander

- **Poison** – Cardiac glycosides, Thevetin A & B, Neriifolin
- Toxins inhibit the Na-K-ATPase pump
- All parts of the plant are toxic, especially the fruit and seed
- Severity of the yellow oleander poisoning and clinical presentation are not correlating with the number of seeds ingested

Mimickers of poisoning of pink / yellow oleander

- The foxglove plant (*Digitalis sp.*) also gives rise to similar clinical presentation due to analogous chemical digoxin

Figure 12.3

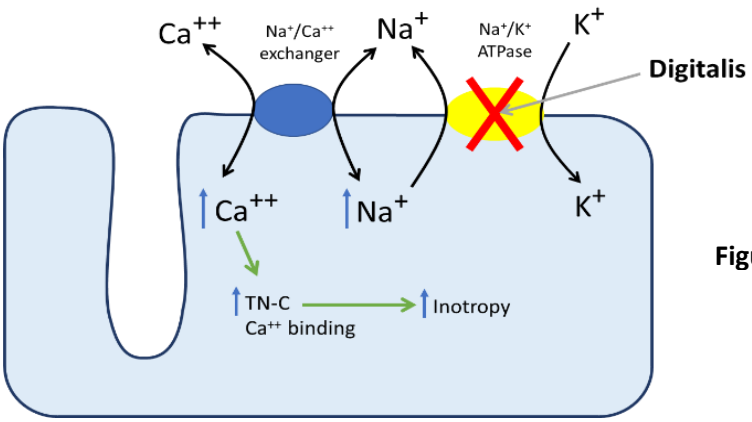

Figure 12.4

Other mimickers:

- Diyakaduru poisoning
- Drug toxicity by beta blockers, calcium channel blockers and digoxin

Toxic Mechanism

- Digoxin works by inhibiting the Na-K-ATPase pump in cell membranes, which leads to higher intracellular sodium levels, increase intracellular calcium, and elevated extracellular potassium
- Rise in intracellular calcium enhances cardiac contractility, and boosts vagal tone which reduces the conduction at SA and AV nodes, resulting in various arrhythmias

Toxic effects

- Nausea and vomiting as early signs due to gastric irritation. Persistence of the symptoms along with diarrhoea and abdominal pain suggest significant absorption
- ECG may show bradycardia, varying degrees of heart blocks, atrial and ventricular ectopics/ arrythmias, T inversions, ST depressions or characteristic reversed tick appearance
- Hyperkalaemia secondary to inhibition of Na-K-ATPase pump
- Hypokalaemia due to diarrhoea and vomiting
- Other symptoms such as xanthopsia (yellow vision), anxiety, convulsions, and coma

Box 12.3

Management

- ResusRSIDEAD pathway
- Monitor pulse rate, blood pressure, respiratory rate, and oxygen saturation and maintain a fluid balance chart
- Maintaining a good hydration is beneficial in these patients
- Continuous cardiac ECG monitoring for the first 24 hours is recommended
- Give activated charcoal and repeat 25-50g every 4 hours
- Check serum electrolytes four hourly. Correct hypo/hyperkalaemia. Hypokalaemia should be corrected with intravenous KCl as it worsens the toxicity of the poison. Calcium gluconate is not recommended usually for hyperkalaemia due to the risk of cardiac arrhythmias
- For second- or third-degree heart block with bradycardia (<40 per minute and hypotension), urgent temporary pacemaker (TPM) insertion is lifesaving. Bridging with intravenous boluses (0.6-3 mg) or infusion of atropine (10 vials in 500 mL 0.9% of sodium chloride titrated to maintain heart rate between 60 and 90 bpm) until TPM insertion could be tried
- Avoid tachycardia. If features of atropine toxicity develop, stop atropine infusion
- Give 5-10 mg of IV diazepam if there are convulsions

- ***KaneruTab*** **- Anti-Digoxin Fab Antibody Fragments can also be used** *800 mg in 100 mL of 0.9% NaCl over 20 min*

  Indications
  - Third degree heart block
  - Sick Sinus syndrome
  - Atrial/Ventricular tachycardia
  - Ventricular fibrillation/ ventricular tachycardia
  - Hyperkalaemia > 5.5 mmol/L

  Contraindications
  - Known allergy, albumin allergy
  - Possibly in pregnancy

Box 12.4

3. *Datura stramonium* (S. Attana, T. Ayigam / Umatthai, E. Datura)

Figure 12.5 – *Datura*

- **Poison:** Alkaloid atropine, hyoscine and hyoscyamine, scopolamine
- All parts of the plant are poisonous, especially the seeds
- Even one seed is fatal
- Effects are mainly due to anticholinergic toxidrome. Datura toxin competes with Acetylcholine (Ach) at muscarinic receptors and inhibit parasympathetic drive
- It can lead to hallucinogenic and euphoric effects
- Similar kind of toxicity is seen in patients presenting with Angel's trumpet poisoning

Figure 12.6 - Angel's trumpet

Toxic effects

- Refer cholinergic toxidrome
- The toxic effects usually last for 24-48 hours

Box 12.5

Management

- ResusRSIDEAD pathway
- Supportive care
- Please refer anticholinergic toxidrome – **Box 2.7**

Box 12.6

4. Kaduru

- There are three different types of Kaduru

Different types of Kaduru


Goda kaduru (S)
Eddukkoddai (T)
Bitter nut


Divi Kaduru (S)
T. Nathiyawaddai (T)
Eve's Apple


Diya kaduru/ Gon kaduru/ Wel kaduru (S)
Natchukkai (T)
Sea Mango

Figure 12.7

Goda kaduru (S) Eddukkoddai (T) Bitter nut	Divi kaduru (S) T. Nathiyawaddai (T) Eve's Apple	Diya kaduru/ Gon kaduru/ Wel kaduru (S) Natchukkai (T) Sea Mango
Stychnos nux vomica	*Tabernaemantana dichotoma*	*Cerbera manghas*
All parts are toxic, mainly seeds, bark, and leaves	Latex, seed, and fruits are toxic	All parts of the plant are poisonous, especially the kernel
Poison: Strychnine, brucine, and loganin	**Poison: Atropine and Strychnine (small amount)**	**Poison: cardiac glycosides (Cerberin, Odollum, Thevetin)**
Mechanism of action: acts as a competitive antagonist at the post synaptic glycine receptors	Mechanism of action: Similar to atropine	Mechanism of action: Similar to cardiac glycosides
The fruit is green and round in shape. It turns out to be soft orange in colour when ripe.	Fruit is pendulous, wedge shaped, and paired usually. It turns out to be yellowish orange in colour when ripe.	The fruit is green and oval in shape usually. It tuns out to be pink or yellow in colour when ripe.
Toxic effects		
• Anxiety • Muscle twitching • Hyper-reflexia • Painful contractions • Risus sardonicus • Trismus • Opisthotonus • Convulsions • Hyperthermia • Lactic acidosis • Rhabdomyolysis • Acute kidney injury • Death	• Dryness of mucosa • Thirst • Mydriasis • Flushing • Tachycardia • Delirium • Convulsion • Coma	• Nausea • Vomiting • Diarrhoea • Abdominal pain • Cardiotoxicity with bradycardia, varying degrees of heart blocks and hypotension, atrial and ventricular ectopics / arrythmias • Hyperkalaemia

➢ Similar to tetanus	➢ Similar to Datura / atropin toxicity	➢ Similar to kaneru
Management		
• ResusRSIDEAD pathway • Mainly supportive care including fluid and electrolyte replacement • Management of contractions and seizures (Benzodiazepines and barbiturates could be used) Treatment of rhabdomyolysis	• ResusRSIDEAD pathway • Mainly supportive care including fluid and electrolyte replacement • Management of contractions and seizures (Benzodiazepines and barbiturates could be used) Treatment of rhabdomyolysis	• ResusRSIDEAD pathway Management similar to Kaneru (Yellow oleander)

Table 12.1

5. Miscellaneous Plant Poisons

a) Castor

- There are two varieties of castor

1. Ricinus communis. S. Beheth Endaru T. Amanakku

Figure 12.8 – *Ricinus communis*

2. Jatropha curcas S. Weta Endaru T. Adalai

Figure 12.9 – *Jatropha curcas*

- **Poison:** ricin (*Ricinus)* and curcin *(Jatropha)*
- Ricin and Curcin are toxalbumins
- The toxic part is the seed. Even 2-6 seeds may be fatal
  - Poisoning seen after several hours (usually after 4-12 hours)
  - Castor oil in small amounts is used to induce diarrhoea, but larger amounts may be toxic

Toxic effects

- Nausea, vomiting, epigastric and abdominal pain, diarrhoea
- Dehydration and electrolyte disturbances
- Shock
- Hypoglycaemia
- Retinal haemorrhages
- Haematuria
- Renal and liver toxicity

Box 12.7

Management

- ResusRSIDEAD pathway
- Decontamination
- Fluid and electrolyte replacement
- Anticipate renal and hepatic involvement
- Alkalinisation of urine

Box 12.8

b) Hondala –– *Adenia palmata* (S. Hondala T. Kondala)

Figure 12.10 – *Adenia palmata*

- **Poison:** cyanogenic glycoside and toxalbumin
- The appearance is closely similar to passion fruit

Clinical Features

- Toxalbumin induced abdominal pain, diarrhoea, vomiting, fever, and agitation are the features of toxicity during first phase
- During the second phase, toxalbumin induced necrotising enterocolitis presents with blood and mucous diarrhoea and right iliac fossa pain
- Third phase of clinical features are due to hypersensitivity reaction, which occurs 2-3 weeks after the ingestion. Most common clinical features include myocarditis, tender hepatomegaly, retinopathy, and papilloedema

Box 12.9

Management

- ResusRSIDEAD pathway
- Blood transfusions may be indicated with or without antibiotics for necrotising enterocolitis
- There may be a place of steroids for the clinical features due to hypersensitivity reaction during the third phase

Box 12.10

c) Jequirity - *Abrus precatorius* (S. Olinda, T. Kundumani)

Figure 12.11 – *Abrus precatorius*

- **Poison:** abrin (glycoprotein, toxalbumin) and abric acid (glycoside)
- The toxic part is the seed
- They inhibit protein synthesis and cause cell death

Clinical features

- Nausea, vomiting, diarrhoea, and abdominal pain
- Haematemesis and melaena due to mucosal erosions
- Hepatotoxity
- Haemaglutination and haemolysis
- Acute kidney injury
- Retinal haemorrhages

- Neurological features including encephalopathy, and arrhythmias are less common

Box 12.11

Management

- ResusRSIDEAD pathway
- Symptomatic treatment
- Monitoring the renal functions is compulsory
- If there is evidence of haemolysis, forced diuresis may be tried to maintain the urine output

Box 12.12

d) Alocasia (*Alocasia macrorrhiza* (S. habarala, T. saembu, shamakkilangu)

Figure 12.12 – Alocasia

- **Poison**: calcium oxalate
- The toxic parts are the leaves and stems

Clinical features

- Profuse salivation
- Mucosal irritation and blistering
- Oedema of the aerodigestive tract
- Necrotising oesophagitis
- Gastric bleeding
- Acute kidney injury
- Hypocalcaemia

Box 12.13

Management

- ResusRSIDEAD pathway (Gastric lavage is indicated)
- Symptomatic treatment is by mucosal washes and antihistamines
- May need endotracheal intubation or tracheostomy insertion if there is laryngeal oedema
- 10% Calcium gluconate may be needed to manage hypocalcaemia

Box 12.14

- Other analogous plants of alocasia include:

Ketala / Kotakimbula /Dumb cane

Figure 12.13

Caladium/ Heart of Jesus/
Elephant Ear (*Caladium sp.)*
S. Rathu habarala

Figure 12.14

e) Manioc / Cassava / Tapioca - Manihot utilissima (S. Manyokka T.Maravalli)

Figure 12.15 – Manioc / Cassava / Tapioca

- **Poison:** cyanogenic glycoside
- Toxic parts include leaves and roots (especially the skin of the root)
- Manioc toxicity is due to the release of cyanides from glycosides such as linamarine in the skin of the root
- Severity of the toxicity increases due to improper cooking such as damaging the mature root (skin) and closing the lid of the pot while cooking the manioc

Clinical Features

- Dizziness and headache
- Respiratory depression
- Hypotension and collapse
- Abdominal pain
- Drowsiness
- Diarrhoea
- Vomiting

Box 12.15

Management

- ResusRSIDEAD pathway
- In severe poisoning sodium thiosulphate and dicobalt edetate IV are used

Box 12.16

f) Purging Croton - *Croton tiglium* (S. Japala Aeta, T. Nervalam)

Figure 12.16 – Purging Croton

- **Poison:** crotonoleic acid, glyceryl crotonate, crotonic acid, crotonic resin and carcinogenic phorbols
- Poisonous part is seed
- The seeds are commonly used to treat constipation after the seeds have undergone a traditional Ayurvedic detoxification process with cow's milk
- The major toxic manifestation is diarrhoea
- Management is symptomatic

g) Nutmeg - *Myristica fragrans* (S. Sadikka, T. Sadikkai)

Figure 12.17 – Nutmeg

- **Poison:** myristicin
- Clinical features are similar to datura but with miosis
- The toxic parts are seeds and to a lesser extent the aril. Mace (S. Wasawasi) is the spice made out of aril

- Treatment is symptomatic or expectant treatment

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Essential Clinical Toxicology is a concise yet comprehensive guide designed to meet the needs of healthcare professionals managing poisoned patients in clinical settings. This book offers critical insights into the diagnosis and treatment of toxic exposures, including pharmaceuticals, chemicals, and environmental agents.

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