POISON MANAGEMENT GUIDELINES

POISON TREATMENT CENTRE

NEW YANGON GENERAL HOSPITAL

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Preface

Poisoning is a common medical problem faced by various health care providers working in the different parts of the country. The majority of poisonings are self-deliberated poisonings rather than accidental ones. In a developing country as well as an agricultural country like Myanmar, self-deliberated poisoning with pesticides used in agricultural sector is a major problem.

Among the different types of agricultural poisonings, organophosphate poisoning is a commonest one. It can lead to serious complications like intermediate syndrome and acute respiratory failure requiring ventilator support in the intensive care unit with significant morbidity and mortality. Although paracetamol poisoning is a rare poisoning in the past, it has become gradually commoner and is regarded as one of the commonest poisonings nowadays. Antidote for paracetamol poisoning is easily available with reasonable price and the lives of the patients can be saved if antidote is administered early and correctly. Other common poisonings seen more or less frequently in the Poison Treatment Unit are poisonings with antihistamines, sedatives, narcotics, herbicides, corrosives, rodenticides and methylated sprit.

All the health care providers, working in different regions of the country should be familiar with the management of common poisonings in Myanmar. By the guidance of Union Minister of Health and Sports, Ministry of Health and Sports and by the endeavor efforts of consultants of Poison Treatment Unit, New Yangon General Hospital, Yangon, this guideline was developed from updated evidence based international resources. This guideline is especially meant for the health care providers working in different levels of hospitals in Myanmar in order to manage the common poisonings by locally available resources. I believe that this guideline will be useful for all the health care providers in the management of common poisonings and it should be regularly updated in the future as well.

With best wishes,

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General Management of Acute Poisoning

Poison Treatment Centre, New Yangon General Hospital

Poisoning should be suspected in patients with unexplained illness in previously healthy person, history of psychiatric problem, history of suicidal attempt, recent change in economic and social relationship or working with chemicals.

Assessment of patient

Triage and resuscitation

Vital signs should be assessed immediately and try to identify the poison(s) involved and obtain adequate information about them. Identify the patients at risk of further attempts at self-harm and remove any remaining hazards.

Make sure that airway, breathing and circulation are kept secure and admit the patient to ICU/HDU and consider ventilation if cardio-respiratory support is needed or the patient has recurrent seizures, reduced conscious level (GCS ≤ 8) and respiratory failure (RR < 8/ min or paO2 < 8 kPa when breathing 60% O_2 or paCO2 > 6 kPa).

Identification of Poison

Diagnosis is mainly from the history but the patient may not tell the truth about what has been taken. Take a history from the patient or patient's family to identify the poison.

- What poisons had been taken and how much?
- What time were they taken and by what route?
- Had alcohol or any drug of misuse been taken as well?
- Obtain details of circumstances of the overdose from family friends and ambulance personnel
- Assess suicide risk (full psychiatric evaluation)
- Past medical, drug, allergies, social and family history

Proper physical examination and identifying the physical signs is essential especially when the reliable history can't be taken.

Clinical signs of poisoning by pharmaceutical agents and drugs of misuse

Pupil size

Sign	Possible Poison
Small	Opioids, Clonidine, Organophosphates
Large	Tricyclics, Amphetamine, Cocaine

Cutaneous signs

Sign	Possible Poison
Needle tracks	Heroin, Amphetamine
Bullae	Carbon monoxide, Barbiturates
Hot and dry skin	Anticholinergic agents, Botulism
Hot and sweating	Ecstasy, SSRIs, Salicylates
Hypothermia	CNS antidepressants, Opioids, Chlorpromazine
Diaphoresis	Organophosphates, Mushroom
Alopecia	Arsenic, Mercury, Lead
Erythema	Mercury, Cyanide
Cyanosis	Any CNS depressant drug or agent (N.B. consider methaemoglobinaemia caused by dapsone, amyl nitrite)

Cardiac Signs

Sign	Possible Poison
Tachycardia	Atropine, Aspirin, Cocaine, Amphetamine, Theophylline, Tricyclics, Digoxin, Antihistamines
Bradycardia	Digoxin, Organophosphate, Narcotic, Calcium channel blocker, β blockers
Hypertension	Amphetamine, Cocaine, LSD, α adrenoceptor agonists
Hypotension	Barbiturate, Phenothiazine, Iron, Tricyclics

Oral Signs

Sign	Possible Poison
Salivation	Organophosphate, Strychnine, Corrosive, Salicylates
Dry mouth	Amphetamines, Anticholinergic
Burns	Corrosive, Paraquat
Gum lines	Lead, Mercury, Arsenic
Dysphagia	Corrosive, Botulism

Intestinal signs

Sign	Possible Poison
Diarrhea	Castor seed, Arsenic
Constipation	Lead, Botulism
Cramps	Organophosphate, Arsenic
Epigastric tenderness	Aspirin, NSAID
Right upper quadrant/ renal angle tenderness	Paracetamol hepatotoxicity/ renal toxicity

Respiratory signs

Sign	Possible Poison
Depressed	Alcohol, Narcotic, Barbiturate, Benzodiazepines
Increased	Amphetamine, Cyanide, Carbon monoxide, Salicylates
Pulmonary edema	Organophosphate, Hydrocarbon, Heroin

CNS signs

Sign	Possible Poison
Ataxia	Alcohol, Barbiturates, Phenytoin, Narcotics
Coma	Sedatives, Narcotics, Organophosphates
Hyperpyrexia	LSD, Phenothiazine, Cocaine
Muscle fasciculation	Organophosphate, Theophylline
Muscle rigidity	Phenothiazine, Haloperidol, Metochlopramide
Rhabdomyolysis	Amphetamines, Caffeine
Paresthesia	Cocaine
Peripheral neuropathy	Arsenic, Mercury, Organophosphates
Altered behavior	LSD, Amphetamine, Cocaine

Electrolyte and blood glucose derangement

Sign	Possible Poison
Acidosis with normal lactate	Ethanol, Ethylene glycol, Methanol, Salicylates, Paraldehyde
Acidosis with high lactate	Metformin, Iron, Cyanide, Sodium valproate, CO
Raised plasma osmolality	Ethanol, Ethylene glycol, Methanol
Hypoglycemia	Cocaine, MAOI, Salicylates, OHA
Hyperglycemia	Theophylline, Organophosphates
Hypokalemia	Salbutamol, Salicylates, Theophylline
Hypernatremia	Tricyclics, Phenothiazine

Investigations

- Urea, electrolytes and creatinine
    - in most patients
- Arterial blood gasses
    - in patients with significant respiratory or circulatory compromise
    - poisoning with substances likely to affect acid-base status
- Anion and osmolar gaps
- Identification of poisons in vomitus, blood and urine samples
    - For all unconscious patients, paracetamol and aspirin levels and blood glucose are required.
    - The necessity of other assays depends on the drug taken and the index of suspicion.

Currently available tests in Myanmar

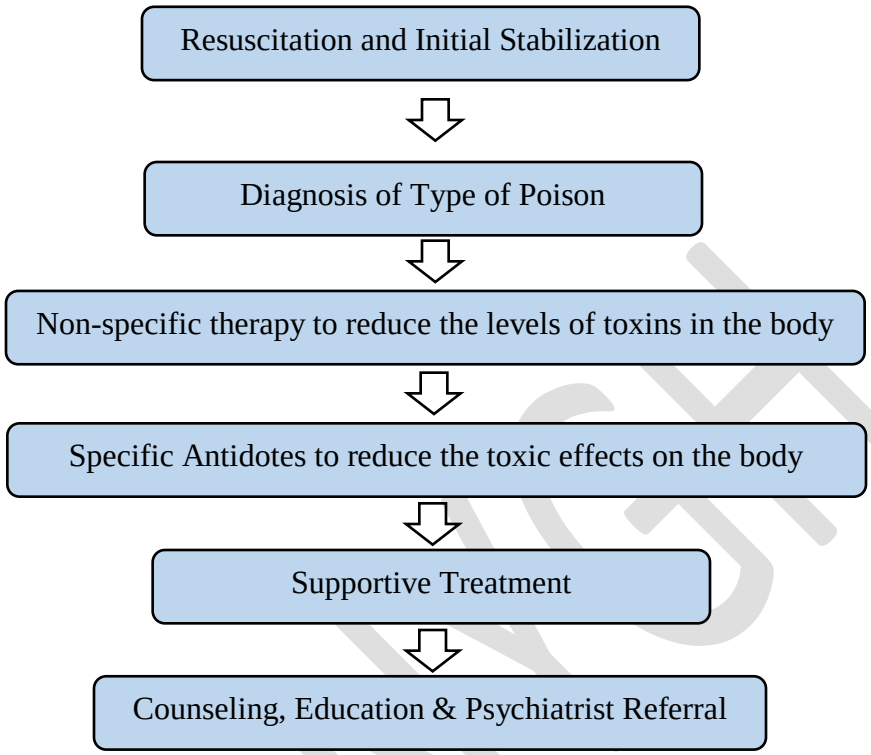
Urine test for identification of the following drugs can be done at Pharmaceutical Toxicology Research Division, National Poison Control Centre, Department of Medical Research, Yangon.

- Acetyl salicylic acid
- Amitriptyline
- Atropine
- Acetaminophen
- Benzodiazepines
- Chlorpheniramine maleate
- Carbamazepine
- Ferrous sulphate
- Haloperidol
- Phenobarbitone
- Phenothiazine
- Propranolol
- Phenytoin

Blood paracetamol level can also be assessed at Pharmaceutical Toxicology Research Division, National Poison Control Centre, Department of Medical Research, Lower Myanmar.

Blood methanol level, carboxyhaemoglobin level and choline esterase level can be assessed at the Occupational and Environmental Health Department.

Steps in Management of Acute Poisoning



Non-specific therapy to reduce the levels of toxins in the body

GI decontamination

It is recommended for many drugs. The treatment of choice is now activated charcoal rather than gastric lavage.

Activated Charcoal

It reduces the absorption of many drugs from the gut when given as a single dose of 50g with water. It is given in repeated doses (50g/4h) to increase elimination of some drugs from the blood.

Poisoning in which activated charcoal should be used	Poisoning in which activated charcoal is NOT effective
• Carbamazepine • Dapsone • Phenobarbital • Phenytoin • Quinine • Theophylline • Salicylates • Paracetamol • Paraquat	• Cyanide • Iron • Ethanol • Methanol • Lithium • Petroleum products • Corrosives • Malathion • Clofenotane

The followings are some important points concerning with the use of activated charcoal.

- It is most effective when taken within 30 min to one hour after poison ingestion. Charcoal given more than 1 hour after ingestion may be of benefit for slow release form of drug poisoning.
- Check for the presence of bowel sounds before administration.
- IV emetics may be required to reduce the risk of vomiting.
- The activated charcoal container should be agitated thoroughly before administration.
- Capsules and tablets should not be used for the treatment of poisoning.

Gastric Lavage

It is rarely used now. Lavage after 30–60min may make matters worse. It is **contraindicated** if petroleum products or corrosives such as acids, alkalis, bleach, descalers have been ingested (*exception:* paraquat), or if the patient is unconscious or unable to protect their airway (unless intubated). Never induce vomiting. If comatose, or no gag reflex, need to have airway protection by endotracheal intubation first. If conscious, get verbal consent.

Steps of gastric lavage

- Monitor O2 by pulse oximetry.
- Have suction apparatus to hand and working.

- Position the patient in left lateral position.
- Raise the foot of the bed by 20cm.
- Pass a lubricated tube (14mm external diameter) via the mouth, asking the patient to swallow.
- Confirm position in stomach.
- Siphon the gastric contents. Check pH with litmus paper.
- Perform gastric lavage using 300–600mL tepid water at a time. Massage the left hypochondrium then siphon fluid.
- Repeat until no tablets in siphoned fluid.
- Leave activated charcoal (50g in 200mL water) in the stomach unless alcohol, iron, lithium, or ethylene glycol ingested.
- When pulling out tube, occlude its end (prevents aspiration of fluid remaining in the tube).

Whole bowel irrigation

It is for ingested packets or slow-release tablets such as iron and lithium that are not absorbed by activated charcoal, but its use is controversial.

It involves the administration of large quantities of osmotically balanced polyethylene glycol and electrolyte solution (1–2 L/hr for an adult), usually by a nasogastric tube, until the rectal effluent is clear.

Contraindications include inadequate airway protection, haemodynamic instability, gastrointestinal haemorrhage, obstruction or ileus. Whole bowel irrigation may precipitate nausea and vomiting, abdominal pain and electrolyte disturbances.

Urinary alkalization

When urine is alkalinized (pH >7.5) with sodium bicarbonate, weak acids (salicylates, methotrexate and herbicides- 2, 4-dichlorophenoxyacetic acid) are highly ionized and their urinary excretion is enhanced. It is currently recommended for salicylate poisoning when the criteria for HD are not met.

Hemodialysis (HD) and haemoperfusion

It is useful in poisonings with small volume of distribution and long half-life.

Poisons effectively eliminated by haemodialysis or haemoperfusion	
Haemodialysis	**Haemoperfusion**
• Ethylene glycol • Isopropanol • Methanol • Salicylates • Sodium valproate • Lithium	• Theophylline • Phenytoin • Carbamazepine • Phenobarbital • Amobarbital

Lipid emulsion therapy

Lipid emulsion therapy, or 'lipid rescue', is being used increasingly for the management of poisoning with lipid-soluble agents, local anaesthetics, tricyclic antidepressants, calcium channel blockers and lipid soluble β-blockers such as propranolol.

It involves intravenous infusion of 20% lipid emulsion (e.g. Intralipid) at an initial dose of 1.5 mL/kg, followed by a continued infusion of 0.25 mL/kg/min until there is clinical improvement.

Specific Antidotes

Poisons	**Antidotes**
Anticholinergics	Pyridostigmine
Arsenic	Dimercaprol, Penicillamine
Benzodiazepines	Flumazenil
β blockers	Isoproterenol
Calcium antagonists	Calcium gluconate
Cyanide	Dicobalt edentate, Sodium nitrite, Sodium thiosulphate
Digoxin	Digoxin specific antibody

Methanol	Ethanol, Fomepizole
Iron	Desferrioxamine
Lead / Mercury	Dimercaprol, Penicillamine, Sodium calcium edetate
Opioids	Naloxone
Organophosphates	Atropine, Pralidoxime
Paracetamol	N acetylcysteine
Warfarin	Vit K, FFP

Supportive Treatment

For most poisons, antidotes and methods to accelerate elimination are inappropriate or unavailable. Management of the complications is the mainstay of treatment in those cases.

Complications of poisonings and their management	
Coma	Appropriate airway protection and ventilator support Pressure area and bladder care Identification and treatment of aspiration pneumonia
Seizures	Appropriate airway protection and ventilator support IV Benzodiazepines (e.g., Diazepam 10-20 mg, Lorazepam 2-4 mg) Correction of hypoxia, Acid base and metabolic abnormalities
Acute dystonias	Procyclidine, Benzatropine, Diazepam
Hypotension due to vasodilation	IV fluids Vasopressors (rarely indicated)
Hypotension due to myocardial suppression	Optimization of volume status Inotropic agents
Ventricular tachycardia Monomorphic associate with prolonged QRS	Correction of electrolytes, acid base abnormalities and hypoxia Sodium bicarbonate
Torsades depoites associated with QTc prolongation	IV Magnesium sulphate 2 G over 1-2 min, repeated if necessary

Psychiatric assessment and Referral to psychiatrist:

This depends partly on local resources. Refer all with presence of psychiatric disorder or high suicide risk. Consider discussing all presentations with deliberate self-poisoning.

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Organophosphorus Insecticides (Organophosphates) Poisoning Management Guidelines
Poison Treatment Centre, New Yangon General Hospital

Organophosphorus (OP) compounds are widely used as pesticides, especially in developing countries. Case fatality following deliberate ingestion is high (5–20%).

Organophosphorus Insecticides

A variety of organophosphorus insecticides are available.

Dimethyl compounds	Diethyl compounds
• Dichlorvos • Fenthion • Malathion • Methamidophos	• Chlorpyrifos • Diazinon • Parathion-ethyl • Quinalphos

(Thomas, 2018)

Mechanism of Toxicity

The insecticide may be absorbed following ingestion of contaminated food or water, by inhalation, or after dermal or ocular exposure to sprays. Organic solvents may enhance the rate of absorption.

Toxic effects are mainly due to acetylcholinesterase inhibition. Initially, spontaneous hydrolysis of the OP–enzyme complex allows reactivation of the enzyme but, subsequently, loss of a chemical group from the OP–enzyme complex prevents further enzyme reactivation. After this process (termed 'ageing') has taken place, new enzyme needs to be synthesized before function can be restored. The rate of 'ageing' is an important determinant of toxicity and is more rapid with dimethyl (3.7 hrs) than diethyl (31 hrs) compounds.

Features of poisoning

Acute features:

Ingestion: Substantial ingestion may be followed by vomiting and diarrhoea. As organophosphorus insecticides and their solvents may be irritant, burning of the mouth and throat with retrosternal and abdominal pain can occur. The larynx may also be affected causing oedema, airway obstruction and difficulty in clearing excessive bronchial secretions. Systemic

effects may be experienced soon after exposure or over the following hours. Delayed features may occur with very fat soluble insecticides.

Inhalation: Organophosphate vapours rapidly produce mucous membrane and upper airway irritation. Tightness in the chest may occur at an early stage due to local anticholinesterase effects on the bronchi. Systemic features may develop.

Dermal exposure: Irritant. Local neuromuscular effects such as sweating or muscle fasciculations may be seen. Skin absorption may produce systemic effects.

Eye exposure: Local anticholinesterase effects of organophosphate sprays may cause constriction of one or both pupils (miosis). Pain may occur due to spasm of the sphincter muscles of the iris and ciliary body. Lacrimation may be seen. Visual acuity may be reduced for up to a month. The organophosphate, or the organic solvents present in the formulation, may irritate the eye. Serious systemic features are unlikely following ocular exposure, but consideration must be given to the possibility of simultaneous inhalation/dermal exposure of clinically significant amounts.

Systemic features: Cramp-like abdominal pain, vomiting, diarrhoea, sweating, salivation, tightness in the chest and miosis occur. As poisoning progresses, muscular twitching (fasciculations) and generalised muscle weakness (in particular of the respiratory muscles) occur. Bronchial hypersecretion with bronchoconstriction, respiratory depression, ataxia, coma and convulsions may ensue. These effects are termed the **acute cholinergic syndrome**.

Complications of poisoning may result from aspiration or hypoxic brain injury from early loss of consciousness and respiratory failure.

Cardiac effects include sinus tachycardia (sometimes bradycardia), AV block, ST changes, peaked T waves and QT prolongation. Ventricular arrhythmias are an uncommon but recognised cause of death.

Glycosuria and hyperglycaemia may occur in severe cases; leucocytosis and low-grade fever are noted frequently, even in the absence of infection.

A low PaO_2 and metabolic acidosis will be seen in those severely affected and creatine kinase activity may be high.

Delayed and Chronic effects:

Delayed effects may develop, in particular neuromuscular dysfunction that may result in respiratory failure and the need for mechanical ventilation over several weeks. If it occurs 1-4

days after exposure, and after the acute cholinergic toxicity has settled, it is termed the **intermediate syndrome**. Early features include weakness of neck flexors; weakness may progress to involve cranial nerves, brain stem dysfunction and ventilatory failure. It usually resolves within 3 weeks.

Organophosphate-induced delayed polyneuropathy (OPIDN) is a rare complication that usually occurs 2–3 weeks after acute exposure. It is a mixed sensory/motor polyneuropathy, affecting long myelinated neurons especially, and appears to result from inhibition of enzymes other than AChE. It is a feature of poisoning with some OPs such as triorthocresyl phosphate. Early clinical features are muscle cramps followed by numbness and paraesthesiae, proceeding to flaccid paralysis of the lower and subsequently the upper limbs, with foot and wrist drop and a high-stepping gait, progressing to paraplegia. Sensory loss may also be present but is variable. Initially, tendon reflexes are reduced or lost but mild spasticity may develop later. There is no specific therapy for OPIDN. Regular physiotherapy may limit deformity caused by muscle-wasting. Recovery is often incomplete and may be limited to the hands and feet, although substantial functional recovery after 1–2 years may occur, especially in younger patients.

Other delayed features include headaches, anxiety and irritability. Memory and sleep pattern loss may also occur.

The likelihood of full neurological recovery depends mainly on the extent of an individual's exposure, the adequacy of treatment received, and the occurrence of cerebral hypoxic damage.

Management

Emergency management

Maintain a clear airway and ensure adequate ventilation. Give oxygen. Continuous suctioning of the airway may be required because of excessive secretions. Endotracheal intubation and assisted ventilation will be necessary in severe cases. Patients should ideally be cared for in critical care environment. Monitor blood pressure, pulse, respiratory rate, oxygen saturations and cardiac rhythm. **Patients with clinically significant hypoxia, bradycardia, and/or hypotension require oxygen and atropine before decontamination.**

Where the practical expertise exists, consider gastric aspiration/lavage in adults within one hour of ingestion of a potentially life-threatening overdose, who have been resuscitated and received atropine, providing the airway can be protected.

Antidotes

Atropine for anticholinesterases

If the patient develops increased secretions, rhinorrhoea, bradycardia, hypotension, bronchorrhoea, and/or bronchospasm, **urgently** administer atropine 2 mg intravenously in an adult (50-75 microgram/kg in a child), repeated every 5 minutes as necessary, until secretions are minimal and the patient is 'atropinised' (lungs are clear, heart rate is greater than 80/min, and blood pressure is adequate). As the pupils will remain constricted for several days if exposed directly to an anticholinesterase, **pupil size should not be used as an end point for atropinisation**.

A study has shown that in cases of moderate-severe poisoning doubling the dose of atropine every 5-10 minutes until clinical improvement is evident speeds atropinisation and reduces mortality (Abedin et al, 2012). If infusion pump is available, atropine infusion can be given by titration.

Dose of Atropine infusion

Atropine infusion with 50 cc syringe pump (20 amp of atropine 0.6 mg + 30 cc of N/S)		
Dose	**Body weight (kg)**	**Rate of infusion (ml/hr)**
0.02 mg/kg/hr	40 kg	3.3 ml/hr
	50 kg	4.1 ml/hr
	60 kg	5.0 ml/hr
0.04 mg/kg/hr	40 kg	6.6 ml/hr
	50 kg	8.3 ml/hr
	60 kg	10.0 ml/hr
0.06 mg/kg/hr	40 kg	10.0 ml/hr
	50 kg	12.5 ml/hr
	60 kg	15.0 ml/hr
0.08 mg/kg/hr	40 kg	13.2 ml/hr
	50 kg	16.6 ml/hr
	60 kg	20.0 ml/hr

Patients may require prolonged administration of atropine via an infusion. As atropine toxicity (agitation, confusion, urine retention, hyperthermia, ileus and tachycardia) can make management difficult, it is important that the dosing of atropine is titrated to the patient's features and response. The initial bolus loading doses should be followed by an infusion, initially using about 20% per hour of the total bolus dose required for atropinisation.

The infusion rate should be increased (together with additional bolus doses as necessary) or decreased in response to occurrence of clinical features of anticholinesterase or atropine toxicity.

The atropine infusion should be tapered until cholinergic signs no longer appear on stopping atropine. Although atropine will control cholinergic muscarinic features, atropine will not improve muscle weakness.

Oximes

If pralidoxime is available, this should also be given as soon as possible although it is not available in Myanmar currently. All symptomatic patients requiring atropine should be given an intravenous loading dose of pralidoxime chloride 30 mg/kg body weight (2 g in an adult) over 20 to 30 minutes to reactivate phosphorylated enzyme. This is followed by a continuous infusion at 8 mg/kg/hour (i.e. 0.5 to 1 g/hour in an adult) for several days.

Alternatively use Obidoxime: give a loading dose of 4 mg/kg over 20 minutes, followed by an infusion of 0.5 mg/kg/hour. In adults it is usually given as 250 mg loading dose followed by 750 mg every 24 hours.

Subsequent Management

Observe asymptomatic patients for a minimum of 12 hours since onset of clinical features may be delayed. The time taken for development of symptoms will vary with the route of exposure and the particular organophosphorus insecticide.

Review respiratory function frequently by measurement of respiratory rate, oxygen saturation, tidal volume and/or forced vital capacity. Intubate and ventilate patients when the tidal volume or vital capacity fall below 5 mL/kg or 15 mL/kg respectively, apnoeic spells occur, or PaO_2 is less than 8 kPa (60 mmHg) on FiO_2 of greater than 60%.

Review flexor neck strength regularly in conscious patients by asking them to lift their head off the bed and keep it there when pressure is applied to their forehead. Any sign of weakness is a sign that the patient is at risk of developing neuromuscular junction failure (intermediate syndrome) and acute respiratory failure. The tidal volume should be checked in such patients every 4 hours. Values less than 5 mL/kg are an indication for intubation and ventilation.

In patients with agitation and delirium, ensure other causes are excluded (e.g. hypoxia, infection, hypoglycaemia and raised ICP). After excluding those causes, give an initial dose of oral or IV diazepam (10-20 mg) or lorazepam (1-2 mg). Further boluses, given IV, may be administered if the patient remains agitated, provided there is no impairment of respiratory function. If oral and IV routes are not available, give lorazepam IM (1-2 mg) or midazolam IM (5-10 mg) repeated as necessary. Patients with severe agitation may need high doses of intravenous diazepam (total dose in excess of 100 mg given incrementally). These patients need urgent referral to critical care. Haloperidol (5-10 mg IM) may be an adjunct when agitation remains resistant to two or more benzodiazepine doses as described above. Ketamine (1-1.5 mg/kg IV or 5 mg/kg IM) has also been used for uncontrolled agitation but must be used by a practitioner experienced in its use.

In patients with persistent metabolic acidosis after correction of hypoxia and adequate fluid resuscitation, consider correction with intravenous sodium bicarbonate. An initial dose of 50 mmol sodium bicarbonate may be given and repeated as necessary, guided by arterial blood gas monitoring (aim for a pH of 7.44 [Hydrogen ion concentration 36]).

Other measures as indicated by the patient's clinical condition (e.g, treat hypotension, arrhythmias or convulsions if patient develops these complications).

Investigations

Perform a 12-lead ECG in all patients who require assessment. Check cardiac rhythm, QRS duration and QT interval.

Check U&Es, creatinine, magnesium and correct electrolyte abnormalities.

Consider arterial blood gas analysis in patients who have a reduced level of consciousness (e.g. GCS less than 8; AVPU scale P or U) or have reduced oxygen saturation on pulse oximetry.

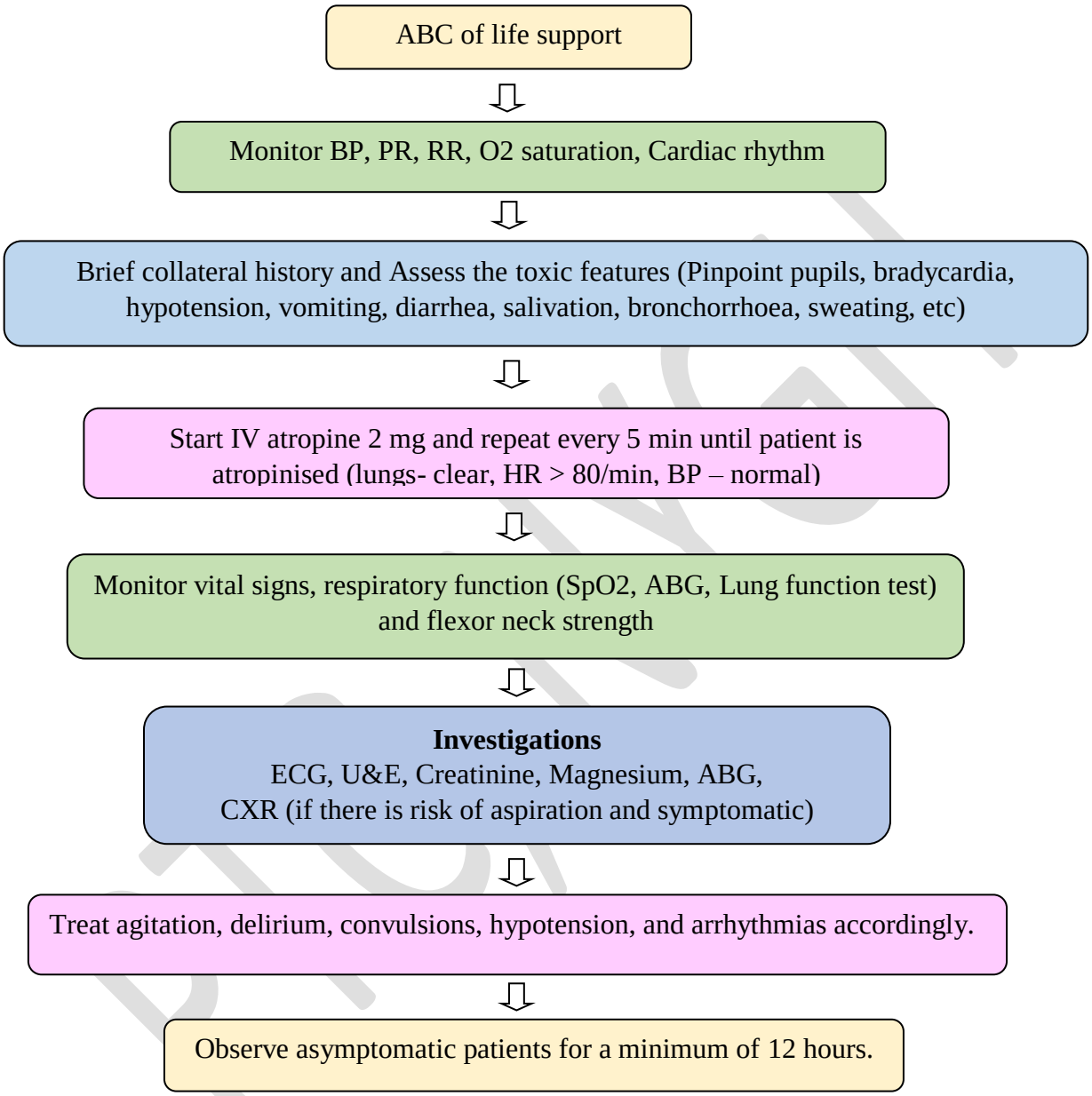
In symptomatic patients, perform a chest X-ray to exclude aspiration.

Diagnosis confirmation should be done by measuring erythrocyte and plasma cholinesterase activities but currently diagnosis is usually done by history of poison exposure and clinical features. Plasma cholinesterase can be measured at the Department of Occupational and Environmental Health, Myanmar but it is only used for public health purposes.

Prognostic factors

Metabolic acidosis indicates poor prognosis.

Workflow for Acute Management of Organophosporus Insecticide Poisoning



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Ingestion/systemic toxicity of Paraquat

1. **The benefit of gastric decontamination is uncertain.** Consider activated charcoal (charcoal dose: 50 g for adults; 1 g/kg for children) if the patient presents within 1 hour and the airway can be protected. Efficacy declines rapidly with time since ingestion but there may be some potential benefit from later use.
2. Alternatively consider gastric aspiration or lavage in adults who have ingested a potentially lethal dose within 1 hour of ingestion. Beware mediastinal perforation from the corrosive effects of ingested paraquat.
3. Monitor vital signs and cardiac rhythm; check the capillary blood sugar.
4. In all patients, check ECG, FBC, U&Es and LFTs.
5. Avoid giving supplemental oxygen, if possible, as this may enhance the toxicity of paraquat.
6. Replace lost fluids and electrolytes intravenously.
7. Anti-emetics may be given for symptomatic treatment.
8. In symptomatic patients, perform a chest X-ray and measure arterial blood gases.
9. Hypotension

   Ensure adequate fluid resuscitation. Treat brady and tachyarrhythmias appropriately. Consider early referral to critical care for patients with fluid-resistant hypotension, as these patients can deteriorate extremely rapidly. Vasopressors and inotropes can be initiated in an emergency through peripheral venous access.
10. Drooling, dysphagia, vomiting, severe pain, haematemesis, stridor and extensive oropharyngeal burns are associated with more severe injuries.

    Corrosives - investigation

    Features of severe tissue injury (severe abdominal pain, abdominal distension, circulatory collapse or lactic acidosis) may indicate the presence of bowel necrosis or perforation. Immediate surgical assessment is recommended urgently because early resection of necrotic tissue and intraluminal stenting has been shown to improve survival and reduce the risk of oesophageal stricture formation.

    Both CT scan and fibreoptic endoscopy have been shown to be useful in assessing the

severity of injury, risk of mortality and risk of subsequent stricture formation. These 2 imaging modalities are complimentary and combined provide the best understanding of the injury and risk. If there are severe clinical features then endoscopy is best performed by a surgeon capable of undertaking definitive treatment.

Grading of corrosive injury by endoscopy is based on the **Zargar grading system** and is important to guide further management:

Patients with grade 1 burns (erythema, oedema) to the gastrointestinal tract may be discharged if they are able to take oral fluids.

Those with grade 2a (localised superficial ulceration, friability and blisters) or 2b (circumferential or deep ulceration) burns should be admitted for observation in case of deterioration and kept nil by mouth. Parenteral nutrition may be required.

Patients with grade 3a (multiple deep ulcerations and scattered areas of necrosis) should be managed as those with 2a/2b.

The presence of grade 3b (extensive necrosis) lesions in the oesophagus and/or stomach is potentially life threatening and all cases should be managed at a facility with upper GI surgical expertise.

Urgent laparotomy is strongly advised in those with grade 3b involvement of the stomach and oesophagus or stomach alone. For gastric lesions this can be clarified by direct vision at laparoscopy or laparotomy, direct vision of the oesophagus is not possible. CT should therefore be performed *in addition to endoscopy* in those with grade 3b lesions of the oesophagus to more accurately determine the depth of necrosis and the need for oesophagectomy.

CT scan scoring system for corrosive injuries:

Grade 1 – no definite swelling of the oesophagus wall

Grade 2 – oedematous wall thickening without peri-oesophageal soft tissue infiltration

Grade 3 – oedematous wall thickening with peri-oesophageal soft tissue infiltration plus well demarcated tissue interface

Grade 4 - oedematous wall thickening with peri-oesophageal soft tissue infiltration plus blurring of tissue interface or localised collection of fluid around oesophagus or descending aorta

Patients with symptoms other than those described above as severe (i.e. where emergency surgery is not a consideration) should undergo fibre optic endoscopy as a planned procedure, in

hours with experienced staff in an endoscopy unit. This should be performed preferably within 24 hours. Asymptomatic patients do not require further imaging.

11. Adequate analgesia and local anaesthetic preparations may be required to alleviate discomfort from oropharyngeal burns.

12. **Convulsions**

Give oxygen, check blood glucose, U&Es and ABG. Correct acid base and metabolic disturbances as required. Single brief convulsions do not require treatment.

Control convulsions that are frequent or prolonged with intravenous diazepam (10-20 mg in adults; 0.1-0.3 mg/kg body weight in children).

Further doses of benzodiazepines may be needed in adults; refer to intensive care. In children seek consultant paediatric input.

If unresponsive to the above measures, the patient should be referred urgently to critical care. If convulsions persist, consider the need for referral to intensive care, general anaesthesia, intubation and ventilation. There may continue to be epileptiform activity and measures to monitor and control this are necessary.

Inhalation - Maintain a clear airway and ensure adequate ventilation. Endotracheal intubation, or rarely tracheostomy may be required for life-threatening laryngeal oedema. Perform a chest X-ray if symptomatic. If features of systemic toxicity are present, manage as per ingestion.

Dermal exposure - Decontaminate the patient. If features of systemic toxicity are present, manage as per ingestion.

Ingestion/systemic toxicity of Paraquat

Within 1 hour → activated charcoal 50 g or gastric aspiration or lavage

↓

Monitor vital signs, ECG, RBS, FBC, U&Es and LFT

↓

Avoid giving supplemental oxygen

↓

Replace lost fluids and electrolytes intravenously

Treatment for vomiting, hypotension, arrhythmias, mucosal erosions, pain and convulsion

In symptomatic patients, perform a chest X-ray and arterial blood gases

↓

Assess the severity of corrosive injury by CT scan and fibreoptic endoscopy

Presence of bowel necrosis or perforation → refer to surgeon

Chlorphenamine maleate Overdose
Management Guidelines
Poison Treatment Centre, New Yangon General Hospital

Type of Product

Chlorphenamine is the first generation sedating H1 antihistamine used in the treatment of allergic conditions and as an ingredient in cold and flu medications.

Synonyms

Chlorpheniramine maleate

Ingredients

Chlorphenamine maleate

Syrup - 2 mg/5 mL

Tablets - 4 mg

Injection – 10 mg/mL

May be found as an active ingredient in combination products such as Decolgen (Paracetamol 500 mg, Phenylpropanolamine HCl 25 mg, Chlorphenamine maleate 2 mg).

Mechanism of Toxicity

Antihistamines act by competing with histamine for H1 receptor sites on effector sites. They prevent, but do not reverse, responses mediated by histamine alone. Toxicity manifests principally as sedation with central and peripheral anticholinergic (atropine like) symptoms.

Studies in man and experimental animals indicate that chlorphenamine maleate is rapidly absorbed from gut. After therapeutic doses peak plasma concentrations occur at 2.5 - 6 hours. Plasma half-life values of 2 - 43 hours have been reported with most excreted in the urine. These pharmacokinetic values may be shortened in children.

Probable lethal dose (Human) – 5-50 mg/kg

Features of Poisoning

Key features include sedation and anti-cholinergic effects (delirium, cardiotoxicity, coma, and convulsions).

Common features include drowsiness, nausea, vomiting, flushing, dilated pupils, blurred vision, dry mouth and tongue, hot dry skin, fever, decreased bowel movements, urinary retention, sinus tachycardia, hypertension, ataxia, nystagmus, agitation, delirium and visual hallucinations.

Uncommon features include myoclonic jerking, muscle rigidity, hypotonia, convulsions, coma, psychosis, cardiac conduction abnormalities including both QRS and QT prolongation, ventricular dysrhythmias including torsade de pointes, cardiorespiratory instability, hyperkalaemia, metabolic acidosis and rhabdomyolysis. Less commonly than anticholinergic toxicity, serotonin toxicity may occur.

Management

Emergency Management

Maintain a clear airway and ensure adequate ventilation. Monitor vital signs, cardiac rhythm and check capillary blood sugar.

The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose: 50 g for adults; 1 g/kg for children) only if the patient presents within 1 hour of ingestion of a toxic dose or more, provided the airway can be protected.

All patients should be observed for at least 6 hours. Following mixed overdoses involving cardiac/cardiotoxic agents, asymptomatic patients should be monitored for at least the longest period recommended in any of the individual TOXBASE® entries.

Antidotes

There is no specific therapy. Treatment is along general symptomatic and supportive lines.

Subsequent Management

Check pulse and blood pressure frequently. Monitor cardiac rhythm. Repeat ECGs should be performed. In symptomatic patients, or patients with an abnormal ECG, consider early discussion with HDU/ITU.

In patients with hypoxia and hypercapnia, assisted ventilation is indicated. Treat the complications accordingly (e.g., hypotension, convulsions, agitation, delirium, hypertension, hyperthermia, metabolic acidosis, rhabdomyolysis, etc).

Investigations

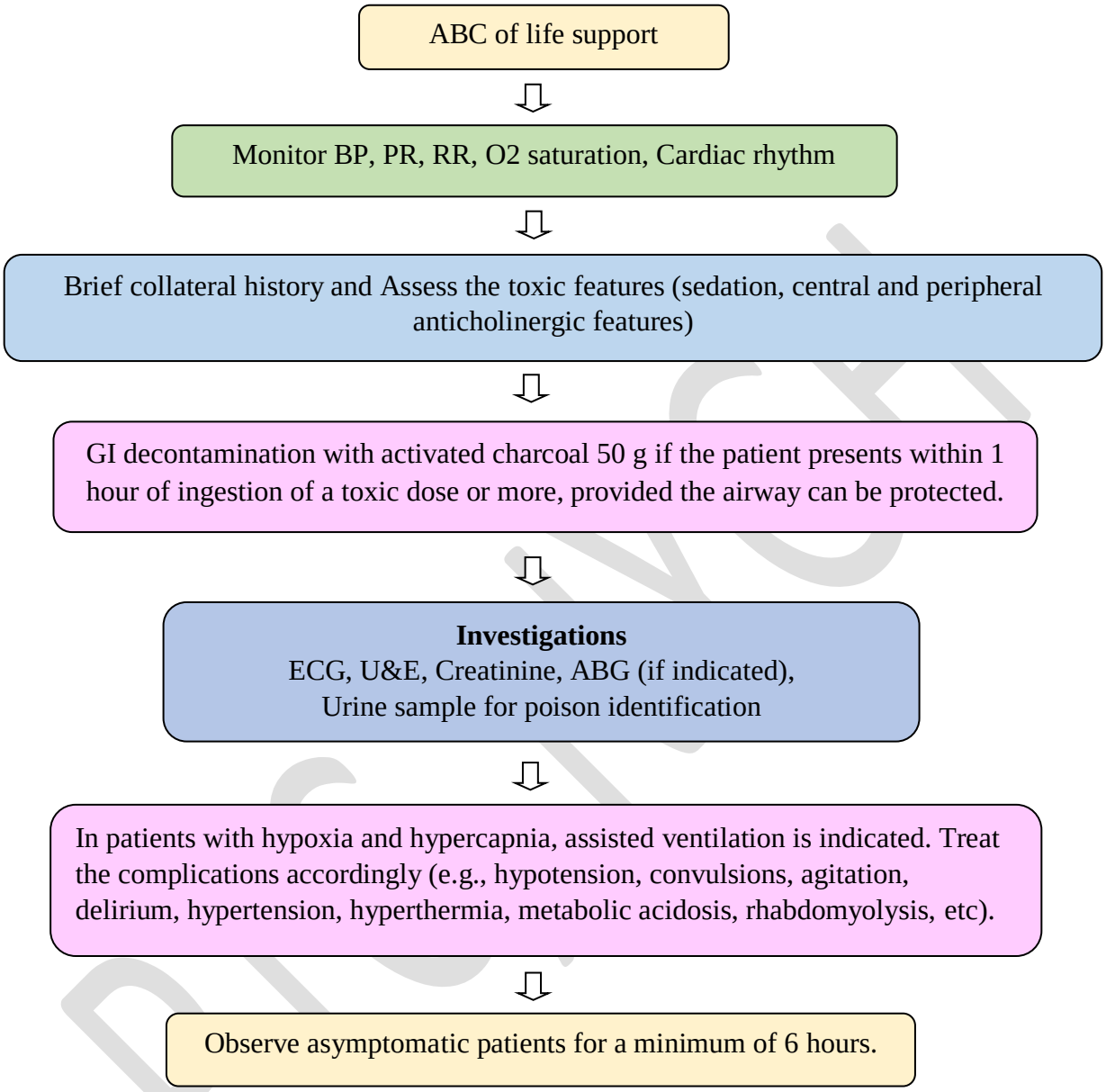
This agent is cardiotoxic and careful assessment of the ECG is required. Perform a 12-lead ECG in all patients who require assessment. Repeat 12-lead ECGs are recommended, especially in symptomatic patients or in those who have ingested sustained release preparations. Check cardiac rhythm, QRS duration and QT interval.

In symptomatic patients check U&Es and CK.

Consider arterial blood gas analysis in patients who have a reduced level of consciousness (e.g. GCS less than 8; AVPU scale P or U) or have reduced oxygen saturation on pulse oximetry.

Urine for chlorphenamine maleate can be tested at National Poison Control Center, DMR, but it is only a qualitative test. Currently, blood levels can't be measured in Myanmar.

Workflow for Acute Management of Chlorphenamine maleate Overdose

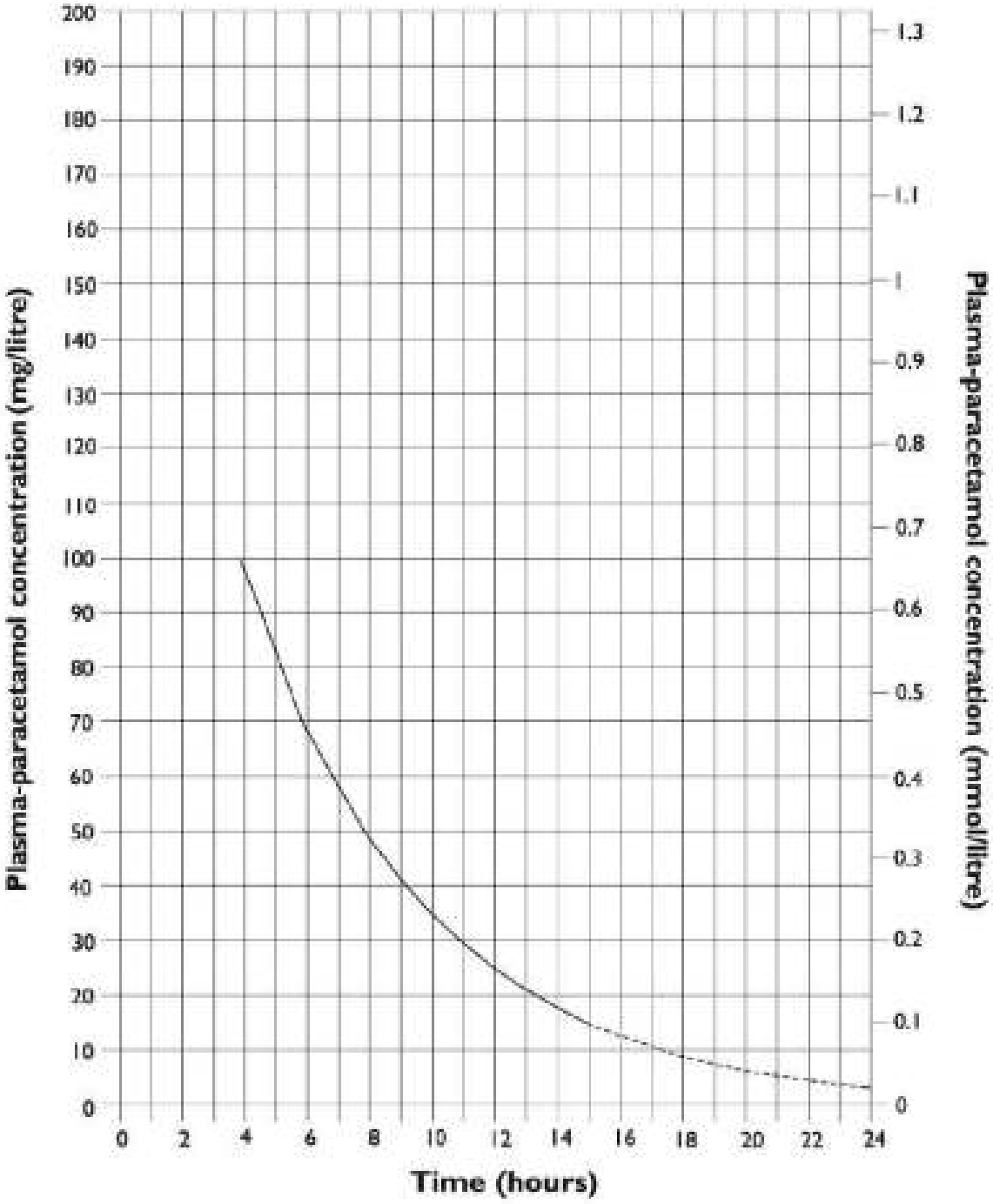


References

1. TOXBASE®. Chlorphenamine maleate poisoning - features and management updated 6/2015; Available from: http://www.toxbase.org.
2. Gosselin RE, Smith RP, Hodge HC. Clinical Toxicology of Commercial Products 5th Ed. Baltimore: Williams and Wilkins, 1984, 11-15.

Management of Paracetamol Overdose

Normogram



NAC infusion (Body weight ≥ 40 kg)

First infusion over 1 hour - 150 mg/kg of NAC (max 16.5 g) + 200 ml of 5%DW or NS
Second infusion over 4 hours - 50 mg/kg of NAC (max 5.5 g) + 500 ml of 5%DW or NS
Third infusion over 16 hours - 100mg/kg of NAC (max 11 g) + 1 L of 5%DW or NS

NAC prescription (each ampoule = 200 mg/ml NAC)						
Regimen	First infusion		Second infusion		Third infusion	
Infusion fluid	200 ml 5% DW or NS		500 ml 5% DW or NS		1000 ml 5% DW or NS	
Duration of infusion	1 hour		4 hours		16 hours	
Drug dose	150 mg/kg NAC		50 mg/kg NAC		100 mg/kg NAC	
Patient weight	Ampoule volume	Infusion rate	Ampoule volume	Infusion rate	Ampoule volume	Infusion rate
kg	ml	ml/hr	ml	ml/hr	ml	ml/hr
40-49	34	234	12	128	23	64
50-59	42	242	14	129	28	64
60-69	49	249	17	129	33	65
70-79	57	257	19	130	38	65
80-89	64	264	22	131	43	65
90-99	72	272	24	131	48	66
100-109	79	279	27	132	53	66
≥ 110	83	283	28	132	55	66

NAC infusion (Body weight <40 kg)

First infusion over 1 hour

- Prepare a 50 mg/ml solution by diluting each 10 ml ampoule of NAC (200 mg/ml) + 30 ml 5%DW or NS = 40 ml

Second infusion over 4 hours

- Prepare a 6.25 mg/ml solution by diluting each 10 ml ampoule of NAC (200 mg/ml)+ 310 ml 5%DW or NS =320 ml

Third infusion over 16 hours

- Prepare a 6.25 mg/ml solution by diluting each 10 ml ampoule of NAC (200 mg/ml) + 310 ml 5%DW or NS =320 ml

Paediatric NAC prescription (each ampoule = 200 mg/ml NAC)						
regimen	First infusion		Second infusion		Third infusion	
NAC dose	150 mg/kg NAC		50 mg/kg NAC		100 mg/kg NAC	
Duration of infusion	50 mg/ml for 1 hour		6.25 mg/ml for 4 hours		6.25 mg/ml for 16 hours	
Infusion rate	3 ml/kg/h		2 ml/kg/h		1 ml/kg/h	
Patient weight	Vol	Infusion rate	Vol	Infusion rate	Vol	Infusion rate
kg	ml	ml/hr	ml	ml/hr	ml	ml/hr
1	3	3	8	2	16	1
2	6	6	16	4	32	2
3	9	9	24	6	48	3
4	12	12	32	8	64	4
5	15	15	40	10	80	5
6	18	18	48	12	96	6
7	21	21	56	14	112	7
8	24	24	64	16	128	8
9	27	27	72	18	144	9
10-14	38	38	100	25	208	13

15-19	53	53	140	35	288	18
20-24	68	68	180	45	368	23
25-29	83	83	220	55	448	28
30-34	98	98	260	65	528	33
35-39	113	113	300	75	608	38

Management of Adverse reaction of NAC

Relatively common features are nausea, vomiting, flushing, urticarial rash, angioedema, tachycardia, bronchospasm. Hypotension and collapse are uncommon.

A history of anaphylactoid reactions is not a contraindication to IV NAC when clinically indicated.

1) Temporarily stopping NAC may be all that is required.

2) Consider IV Chlorpheniramine 10 mg and Neb Salbutamol if bronchospasm is present.

3) It is essential that NAC is restarted once the reaction has settled. Consider slowing the infusion rate (e.g., Administer the first bag over 2 hours rather than 1 hour before resuming the normal infusion rate for the second and third bags).

Prophylactic management of patients with previous anaphylactoid reactions to NAC

- Consider giving the first bag more slowly than normal eg.over 2 hours. The normal infusion rate can be used for bags 2 and 3.
- Prophylactic treatment with H1 and H2 antihistamines should be considered.

Pretreatment with nebulized salbutamol may be considered in those patients with a history of bronchospasm following NAC.

- Systemic corticosteroids have no role.

Staggered paracetamol overdose (non-therapeutic ingestions of excessive paracetamol over a period of >1 hour)

1. Treatment with acetylcysteine should be commenced without delay in ALL patients who have ingested a staggered overdose.
2. Check blood tests **at least 4 hours** after the last paracetamol ingestion. Check paracetamol

concentration, CP, U&Es, creatinine, LFTs, and INR.

3. Clinically significant hepatotoxicity is unlikely if at least 4 hours or more after the most recent paracetamol ingestion:
    - the paracetamol concentration is less than 10 mg/L, **AND**
    - the ALT is within the normal range, **AND**
    - the INR is 1.3 or less, **AND**
    - the patient has no symptoms suggesting liver damage.

    Acetylcysteine can be discontinued

Therapeutic excess (ingestions of excessive paracetamol with intent to treat pain or fever and without self-harm intent - ≥ 75 mg/kg/24hrs)

1. Patients with clinical features of hepatic injury such as jaundice or hepatic tenderness should be treated urgently with acetylcysteine.
2. In other patients, management is determined by the maximum dose of paracetamol ingested in any 24-hour period. Clinicians should be aware that reported doses may be unreliable and should take this into account when making judgements about the need for further assessment.
3. The underlying clinical reason for the chronic excess dosage should be considered.

Maximum dose > licensed 24-hour dose (e.g. 4 g in an adult) but < 75 mg/kg/24 hours over the preceding 2 or more days

Risk of clinically important hepatotoxicity is extremely small, but blood tests may be considered, especially

(a) if there is doubt about the doses used, OR

(b) other factors are present that may increase risk of hepatotoxicity, such as:

- long term treatment with carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, St John's Wort or other drugs than induce liver enzymes
- regular consumption of ethanol in excess of recommended amounts
- likely glutathione depletion e.g. eating disorders, cystic fibrosis, HIV, starvation, cachexia

Clinically significant hepatotoxicity is unlikely if at least 4 hours or more after the most recent paracetamol ingestion:

- the paracetamol concentration is less than 10 mg/L, AND
- the ALT is within the normal range, AND
- the INR is 1.3 or less, AND
- the patient has no clinical features suggesting liver damage.

Management of IV overdose

The paracetamol treatment nomogram cannot be directly applied when managing such cases.

1. **Single acute overdose**: Give intravenous acetylcysteine to all patients if > 60 mg/kg body weight paracetamol has been administered.
2. **Repeated dosing**: In the case of repeated excess dosing, give intravenous acetylcysteine if it is thought that > 60 mg/kg body weight paracetamol in 24 hours has been administered.
3. **Uncertain or unknown IV dose**: nomogram may be used to provide an assessment of risk based on a blood sample taken 4 hours after dosing, but a concentration of half the 100 line should be used to provide an adequate safeguard for initiating therapy (i.e. treat at above 50 mg/L at 4 hours post paracetamol in adults and children).

In all patients for whom treatment is being considered measure the plasma paracetamol concentration and U&Es, creatinine, bicarbonate, LFTs, glucose, FBC and INR 4 hours after the overdose (or immediately if more than 4 hours have already elapsed).

Calculating doses in pregnant patients – should be calculated using the pre-pregnancy weight and the NAC dose should be calculated using the patient's actual pregnant weight.

Calculating doses in obese adults – any adult patient >110 kg, the toxic dose and NAC dose should be calculated using a maximum of 110 kg rather than the actual weight.

Acute kidney injury may occur as part of acute hepatic injury (hepatorenal syndrome) or, rarely, in the absence of hepatic injury. Even a small rise may be clinically significant. NAC has not been tested as an antidote for this complication and there is uncertainty about its efficacy as a

treatment for isolated renal impairment. If creatinine has risen significantly, then recheck in 8-12 hours. Treat renal failure conventionally. Maximal abnormalities usually occur 3-7 days after exposure; recovery of renal function is the norm.

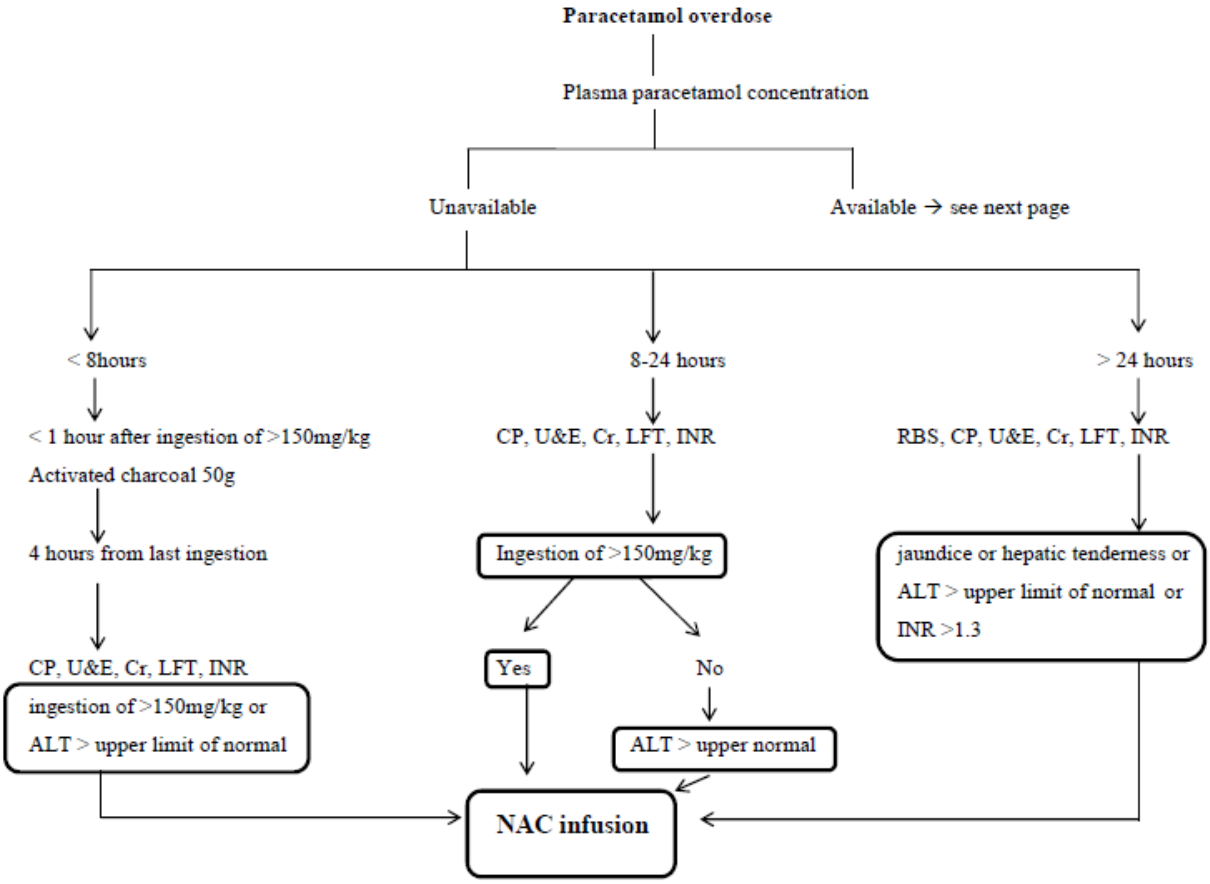
Haemodialysis may be indicated in addition to NAC if a patient has very high paracetamol concentrations (>700 mg/l) associated with coma and elevated blood lactate concentrations. For patients on haemodialysis, the dose of NAC should be doubled.

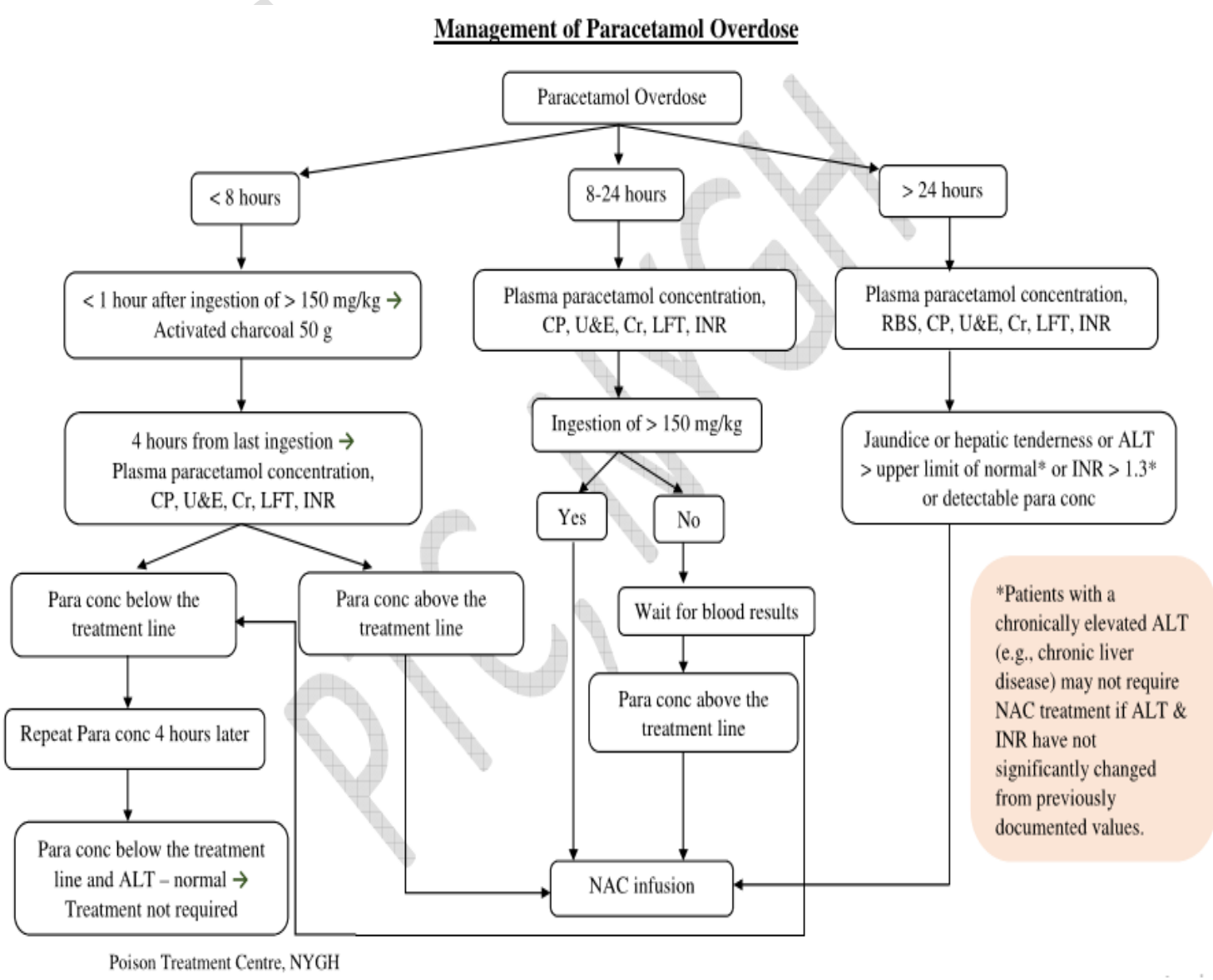
Advice to patients at discharged:

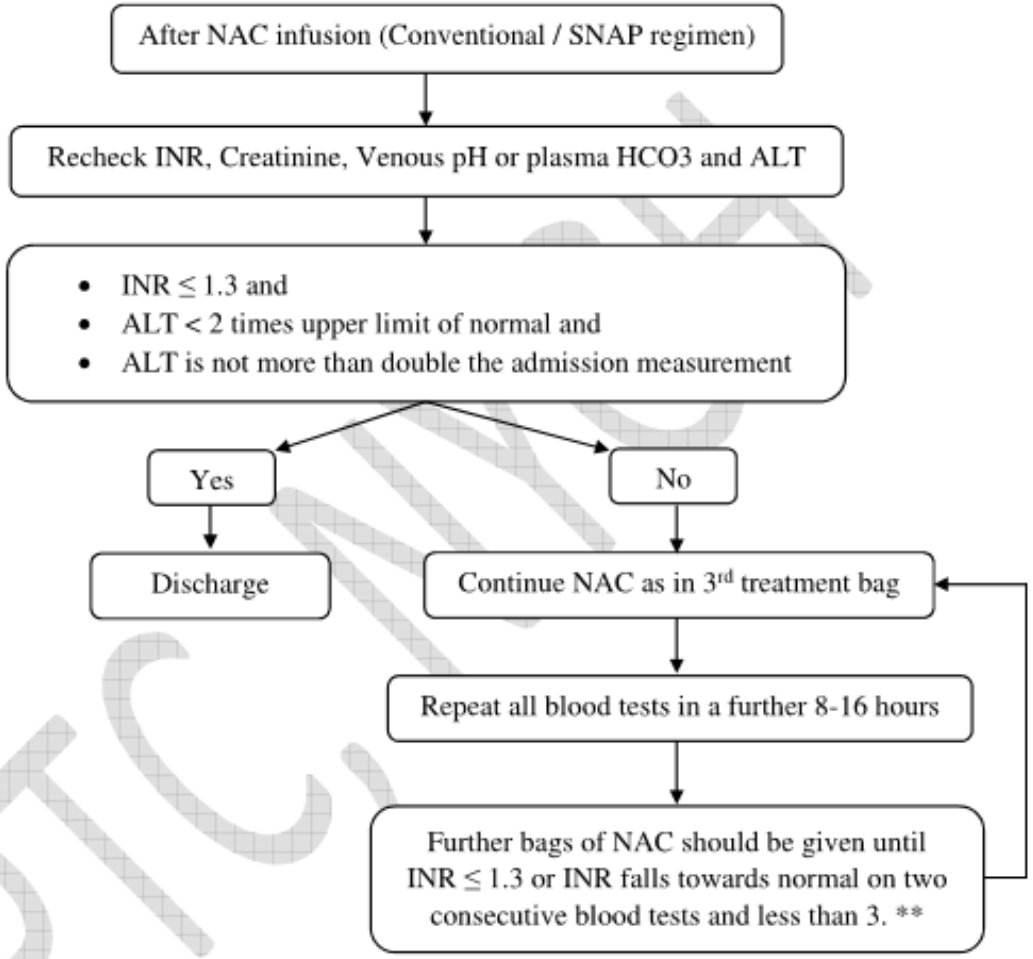
- All patients should be asked to return to hospital if they develop vomiting, abdominal pain or jaundice.
- Patients who do not meet the criteria for NAC treatment, but had an initial paracetamol concentration > 20mg/L, should be advised to avoid paracetamol for the next 12 hours.
- When NAC has been stopped according to the advice given above, but the patient has ongoing abnormality in liver function, the patient would be expected to have normal liver function within 2 weeks, and should therefore be advised to avoid paracetamol for this 2 week period.

Indications for liver transplantation

- Arterial pH <7.3
- Hepatic encephalopathy grade III or IV
- Serum creatinine > 300 μmol/L
- PT > 100 sec
- Lactate > 3.5 mmol/L on admission or > 3 mmol/L 24 hours post-paracetamol ingestion or after fluid resuscitation


Paracetamol overdose
Plasma paracetamol concentration
Unavailable
Available → see next page
< 8hours
8-24 hours
> 24 hours
< 1 hour after ingestion of >150mg/kg
Activated charcoal 50g
4 hours from last ingestion
CP, U&E, Cr, LFT, INR
ingestion of >150mg/kg or
ALT > upper limit of normal
CP, U&E, Cr, LFT, INR
Ingestion of >150mg/kg
Yes
No
ALT > upper normal
RBS, CP, U&E, Cr, LFT, INR
jaundice or hepatic tenderness or
ALT > upper limit of normal or
INR >1.3
NAC infusion


Management of Paracetamol Overdose
Paracetamol Overdose
< 8 hours
8-24 hours
> 24 hours
< 1 hour after ingestion of > 150 mg/kg → Activated charcoal 50 g
Plasma paracetamol concentration, CP, U&E, Cr, LFT, INR
Plasma paracetamol concentration, RBS, CP, U&E, Cr, LFT, INR
4 hours from last ingestion → Plasma paracetamol concentration, CP, U&E, Cr, LFT, INR
Ingestion of > 150 mg/kg
Jaundice or hepatic tenderness or ALT > upper limit of normal* or INR > 1.3* or detectable para conc
Yes
No
Para conc below the treatment line
Para conc above the treatment line
Wait for blood results
Repeat Para conc 4 hours later
Para conc above the treatment line
Para conc below the treatment line and ALT – normal → Treatment not required
NAC infusion
*Patients with a chronically elevated ALT (e.g., chronic liver disease) may not require NAC treatment if ALT & INR have not significantly changed from previously documented values.
Poison Treatment Centre, NYGH



Ref: TOXBASE®. Paracetamol overdose - features and management updated 11/2017; Available from: http://www.toxbase.org.

Methanol Poisoning
Management Guidelines
Poison Treatment Centre, New Yangon General Hospital

Methanol is present in some antifreeze products and commercially available industrial solvents (including Sterno cans and perfumes), and in low concentrations in some screen washes and methylated spirits. It may also be an adulterant of illicitly produced alcohol. It is less viscous than ethanol, with a strong alcohol odor. It is rapidly absorbed after ingestion.

Mechanism of Toxicity

Methanol is not of high intrinsic toxicity but is converted via alcohol dehydrogenase to toxic metabolites that are largely responsible for the clinical effects. The final product of methanol metabolism is formic acid. In addition to causing metabolic acidosis, formate (the conjugate base of formic acid) is an ocular toxin. Methanol poisoning causes a spectrum of vision changes from minimally hazy vision to "snowfield" vision and, most concerning of all, blindness.

Methanol is toxic by ingestion, inhalation and skin absorption. It is slowly and erratically metabolized in the liver and follows zero order kinetics. Approximately 3% of a methanol dose is excreted through the lungs or excreted unchanged in the urine. The half-life of methanol is prolonged to 30-50 hours during antidotal therapy.

Toxic Dose

- Ingestion of 10 mL of pure methanol has resulted in blindness.
- 30 mL has resulted in death.
- The UK workplace exposure limit (short-term) is 250 ppm (333 mg/m^3).

Features of Toxicity

Central Nervous System:	• Mild to moderate toxicity : Headache, confusion and vertigo • Severe toxicity : Convulsions, coma, extrapyramidal features
Visual:	• Common features : blurred vision, with the appearance of a "snow field", and photophobia • Optic disc and retinal oedema with diminished pupillary

	light response. • The extent of these features correlate with the severity of toxicity. • Persistent visual impairment including optic atrophy, diminished visual acuity, loss of colour vision, central scotoma or blindness (usually permanent, but in some cases a degree of recovery may occur over a period of months).
Gastrointestinal:	• Common features : nausea, vomiting and abdominal pain • Acute pancreatitis • Small, transient rise in liver transaminases
Metabolic:	• Severe metabolic acidosis with an increased anion and osmolar gap, tachypnoea • Hyperglycaemia • Renal failure in severe cases
Metabolic changes:	• Early presentation: High osmolar gap, a normal anion gap and a normal pH or hydrogen ion concentration over the first few hours • Later, osmolar gap will fall with increased anion gap with acidosis. • A high anion gap metabolic acidosis suggests that presentation is late and that a substantial amount of the toxic alcohol has been metabolised. • A high anion gap metabolic acidosis can occur after ingestion of any toxic alcohol (e.g. methanol; ethylene glycol; diethylene glycol) or with other clinical conditions (e.g. diabetic or alcoholic ketoacidosis, renal failure, multi-organ failure). If the lactate and ketones are not present and uremia is absent, **Ketoacidosis**, **Uremia**, and **Lactic acidosis** can be eliminated and the most likely cause of the metabolic acidosis is methanol or ethylene glycol poisoning.

Establishing the Diagnosis

The simplest way to establish the diagnosis of methanol poisoning is direct measurement of methanol concentration. Unfortunately, only qualitative assay is currently available in Occupational and Environmental Health Department, Yangon, Myanmar. There are two other approaches to establishing the diagnosis. The first relies on use of the “osmol gap” and the second focuses on the anion gap.

Osmol Gap

- The osmol gap is the difference between the measured laboratory osmolality and the calculated osmolarity, and represents unmeasured substances that are osmotically active, such as toxic alcohols.

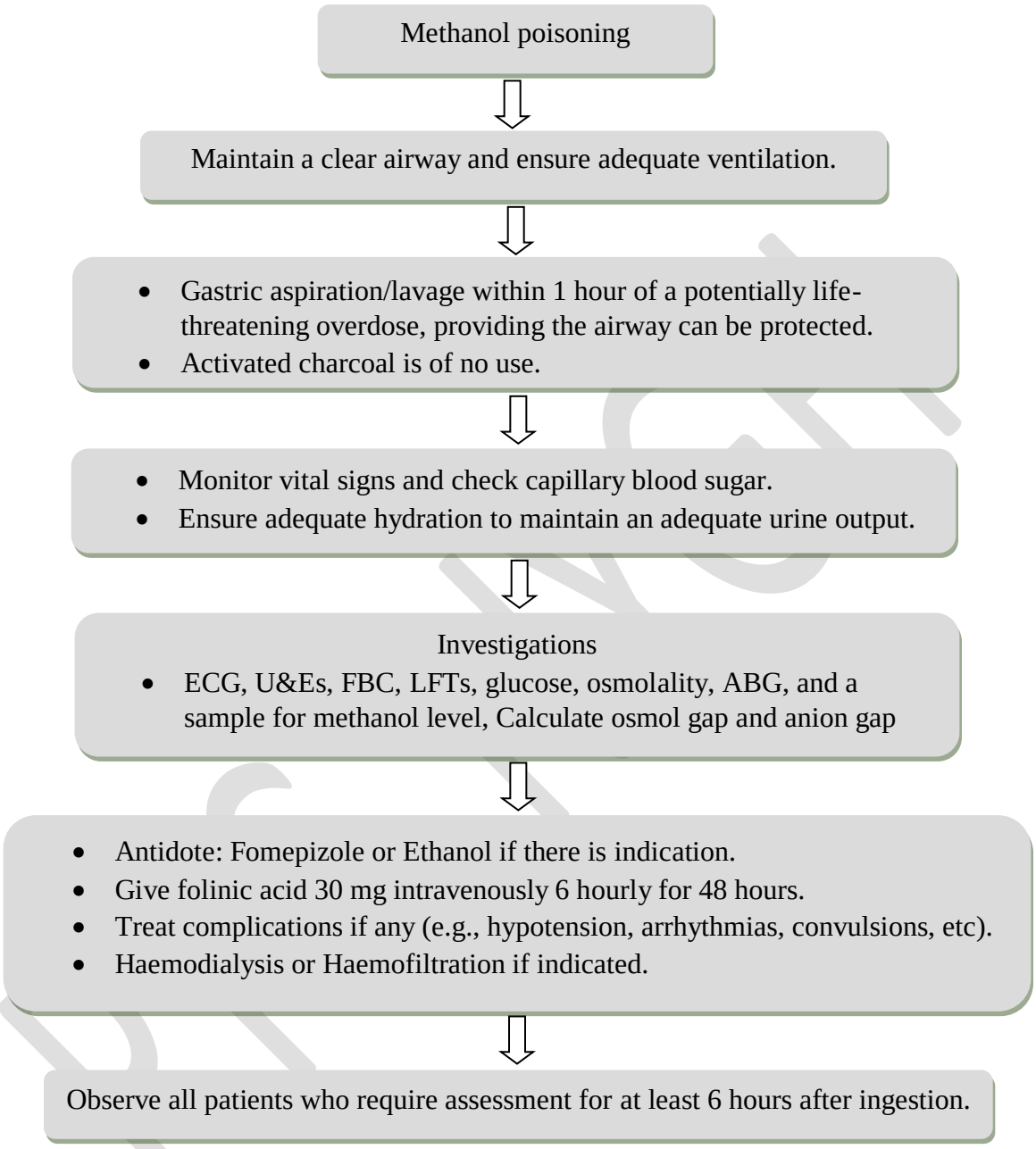
Calculation of Osmol Gap

Osmol gap = Measured osmolarity – Calculated osmolality

Measured osmolarity = 2 Na (mEq/L) + glucose (mg/dl) / 18 + BUN (mg/dl)/2.8

- If there were a large osmol gap, the diagnosis of toxic alcohol poisoning should be suspected.
- In practice, the osmol gap is not a sensitive screen for toxic alcohol poisoning.
- There is a very wide range of normal osmol gap across the population (-14 to 10) so significant changes in the patient's gap may not be apparent. Moreover, the osmol gap converts to an anion gap as poisoning progresses.

Management


Methanol poisoning
Maintain a clear airway and ensure adequate ventilation.
• Gastric aspiration/lavage within 1 hour of a potentially life-threatening overdose, providing the airway can be protected.
• Activated charcoal is of no use.
• Monitor vital signs and check capillary blood sugar.
• Ensure adequate hydration to maintain an adequate urine output.
Investigations
• ECG, U&Es, FBC, LFTs, glucose, osmolality, ABG, and a sample for methanol level, Calculate osmol gap and anion gap
• Antidote: Fomepizole or Ethanol if there is indication.
• Give folinic acid 30 mg intravenously 6 hourly for 48 hours.
• Treat complications if any (e.g., hypotension, arrhythmias, convulsions, etc).
• Haemodialysis or Haemofiltration if indicated.
Observe all patients who require assessment for at least 6 hours after ingestion.

Indications for antidotes

- There is a suspicion that more than 10 g (12.7 ml of 100%) of methanol has been ingested by an adult within the last 12 hours (or more than 0.1 g/kg in a child [equivalent to 0.127 ml/kg of 100%]). OR
- Any amount of methanol has been ingested and there is objective evidence of toxic alcohol exposure, e.g., high anion gap metabolic acidosis or osmol gap > 10 mosm/kg without there being another likely cause (e.g., ethanol intoxication).

Antidotes

- There are two antidotes that can prevent the production of toxic metabolites: Fomepizole and Ethanol.

Antidote	**Dose**
Fomepizole	15 mg/kg IV followed in 12 hours by 10 mg/kg q 12 hours x 4 doses
Ethanol	Loading dose: 0.6 g/kg IV Titrate to concentration of 100 mg/dL

- Fomepizole is the preferred antidote since it does not require regular monitoring of blood concentrations or cause inebriation. It is particularly useful in children, patients who are at risk of coma, those who have liver dysfunction or have recently been exposed to disulfiram or metronidazole and pregnant women. However, it is currently unavailable in Myanmar.
- Ethanol is an effective antidote but is associated with more complications. **If there is any delay in obtaining fomepizole, administer ethanol urgently initially, followed by fomepizole when available.**
- The **target ethanol concentration in toxic alcohol poisoning is 100 mg/dl**. In order to achieve this concentration, the dose will need to be titrated. At lower concentrations, ethanol is less effective and at higher concentrations, intoxication and respiratory depression will ensue.
- Treatment with an antidote decreases the rate at which methanol is metabolised. Treatment may be required for several days whilst methanol is eliminated from the body.

Intensive monitoring may be required during this period, particularly for patients treated with ethanol. The decision to discontinue an antidote should be guided by measurement of the methanol concentration.

- Once initiated, an antidote should be continued until the plasma methanol concentration is less than 50 mg/L (0.05 g/L; 1.56 mmol/L).
- Serum half-life of methanol is 30-54 hours but, during haemodialysis, is reduced to around 4 hours with intermittent haemodialysis and 8 hours with continuous veno-venous haemodialysis or haemofiltration.

Indications for Haemodialysis (Haemofiltration)

- methanol concentration greater than 500 mg/L (0.5 g/L; 16 mmol/L)
- visual disturbance
- features of CNS toxicity
- severe metabolic acidosis
- renal failure
- deteriorating condition despite supportive measures
- severe electrolyte imbalance
- a desire to shorten the duration of the poisoning.

Dialysis should be continued until:

- plasma methanol concentration is undetectable **AND**
- acidosis and signs of systemic toxicity have resolved.

Poor Prognostic factors

- Convulsions
- Coma
- Shock
- Persistent acidosis
- Bradycardia
- Renal failure

References

4. TOXBASE®. Methanol - features and management updated 12/2016; Available from: http://www.toxbase.org.
5. Hoffman RS, Smilkstein MJ, Howland MA, Goldfrank LR: Osmol gaps revisited: Normal values and limitations. J Toxicol Clin Toxicol 1993; 31: 81-93.
6. Nelson LS, Hoffman RS. Howland MA, Goldfrank LR. An intensive review course in clinical toxicology, 2009.
7. Thomas SHL. Methanol and ethylene glycol in Poisoning: Davidson's Principles and Practice of Medicine 23rd Ed (2018): 147.

Narcotic overdose

Drug	Estimated toxic dose
Alfentanil	Refer all for medical assessment
Buprenorphine	0.01 mg/kg
Codeine phosphate	2.5 mg/kg
Diamorphine (Heroin)	0.2 mg/kg
Dihydrocodeine	1.5 mg/kg
Fentanyl	0.04 mg/kg
Methadone	0.4 mg/kg
Morphine salts	0.4 mg/kg
Pethidine	6 mg/kg
Tramadol	4 mg/kg

Management

1. Maintain a clear airway and ensure adequate ventilation.
2. Cardiac arrest

   CPR should be continued for at least 1 hour and only stopped after discussion with a senior clinician. Prolonged resuscitation, even for several hours, may be appropriate following poisoning as recovery with good neurological outcome may occur.
3. Patients exposed to high-potency preparation should be given naloxone urgently if: consciousness is impaired or exposure occurred within the last 10 minutes even if asymptomatic.
4. If the patient has been exposed to any opioid drug and develops respiratory depression, airway obstruction or vomiting with impaired consciousness, give naloxone urgently and consider referral for intensive care.

   Naloxone

   The dose of naloxone depends on the circumstances of exposure.

   For opiate-induced respiratory depression following acute overdose, rapid titration of naloxone is necessary to reverse potentially life-threatening effects.

Severe opiate-induced respiratory depression (For adults)

- Give an initial dose of 0.4mg
- 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. Larger doses 4mg may be required in a seriously poisoned patient.
- Aim for reversal of respiratory depression and maintenance of airway protective reflexes, not full reversal of unconsciousness.

Once an adequate response has occurred, monitor ABG, oxygen saturation and respiratory rate.

IM naloxone is an alternative in the event that IV access is not possible or is delayed. Observe the patient for recurrence as the duration of action of naloxone is shorter than that of all opioid analgesics – repeated doses of naloxone may be required.

IV infusion following resuscitation

IVI of naloxone are often useful where repeated doses are likely to be required.

Start with an hourly infusion rate equal to around 60% if the doses required to adequately reverse respiratory depression. The infusion will then require to be titrated to the desired clinical effect.

For adults, 2mg of naloxone + Normal saline 100ml (5ml/hour) and dose adjusted to clinical response

Infusions are not a substitute for frequent review of the patient's clinical state.

Patients at risk of acute withdrawal (chronic opioid use or when there is a need for therapeutic effect)

- Give an initial dose of 0.1-0.2mg
- If there is no response after 60 seconds, give a further 0.1 mg.
- If there is still no response after another 60 seconds, give another 0.1 mg.
- Continue titrating up the dose to a maximum of 2mg until an adequate response is achieved.

- If still no response (after a total of 2 mg), give a further 2 mg dose. Larger doses 4mg may be required in a seriously poisoned patient.
- Aim for reversal of respiratory depression, not full reversal of unconsciousness.

Failure of a definite opioid overdose to respond to large doses of naloxone suggests that another CNS depressant drug or brain damage is present.

5. Consider oral activated charcoal (50g in adults or 1g/kg in children) if a toxic amount or more has been ingested, provided the patient is not vomiting and their airway can be protected. It should be given as soon as possible after ingestion. It is reasonable to assume that administration of activated charcoal later than 1 hour post ingestion may be beneficial for sustained release preparation.
6. For asymptomatic patients, monitor PR, BP, RR, Oxygen saturation and conscious level at least hourly for at least 6 hours after exposure (12 hours if modified release preparation). Observe for 24 hours if hydromorphone SR, transdermal patches or taken a very large overdose.

   Consider ABG to exclude respiratory depression even if respiratory rate is normal.
7. For all symptomatic patients:

   Monitor closely for the need for naloxone until all the following conditions are met:

   1) Features of opioid toxicity have resolved fully.
   2) The patient has maintained adequate ventilation without naloxone for at least 6 hours, or 12 hours if the patient has ingested a patch or a MR preparation.
   3) Exclude ongoing respiratory depression even in patients with normal respiratory rate before discharge, if necessary with ABG analysis.

   Monitor BP, PR, RR and GCS every 15 minutes initially. Monitor O2 saturation continuously in patients with a reduced level of consciousness. Consider ABG to test for hypercapnia or hypoxia in patients with reduced respiration.

   Check U&E, Cr and CK in patients at risk of rhabdomyolysis (eg. History of prolonged unconsciousness).
8. Perform a 12 lead ECG in all patients who require assessment (repeat ECG in symptomatic patients or in those who have ingested sustained release preparations).
9. Hypotension and bradycardia

   Ensure adequate fluid intake to maintain urine output.

Hypotension and bradycardia in sedated opioid-toxic patients may be responsive to naloxone therapy.

10. Agitation and delirium

    The primary goal of management is to keep patient and staff safe while allowing continued evaluation. Exclude hypoxia, infection, hypoglycemia and raised ICP.

    For pharmacotherapy in adults:

    Give an initial dose of oral or IV diazepam 10-20 mg. Further boluses, given IV, may be administered if the patient remains agitated, provided there is no impairment of respiratory function. Patients with severe agitation (may need IV DZ total dose in excess of 100 mg) need urgent referral to critical care.

    Haloperidol (5-10 mg IM) may be an adjunct when agitation remains resistant to two or more DZ doses.

11. Treat urticaria and pruritus (Chlorpheniramine PO 4-8mg or IV 10 mg).
12. Check for infection at sites of injection and for clinical signs of endocarditis, pneumonia and pulmonary oedema.

Narcotic overdose

Airway, breathing, circulation

↓

oral activated charcoal 50g if within 1 hour and if later than 1 hour for SR preparation

↓

Cardiac arrest → CPR

↓

Treatment for hypotension, bradycardia, agitation and delirium, pruritus and infection

↓

Asymptomatic patients → monitor PR, BP, RR, sPO2 and GCS at least hourly for at least 6 hours after exposure / 12 hours if modified release preparation / 24 hours if hydromorphone SR, transdermal patches or taken a very large overdose and ABG analysis

Symptomatic patients →Monitor BP, PR, RR and GCS every 15 minutes initially. Monitor O2 saturation continuously in patients with a reduced level of consciousness. Check ABG, U&E, Cr and CK

↓

Monitor closely for the need for naloxone until

- Features of opioid toxicity have resolved fully
- adequate ventilation without naloxone for at least 6 hours, or 12 hours if the patient has ingested a patch or a MR preparation
- Exclude ongoing respiratory depression even in patients with normal respiratory rate before discharge, if necessary with ABG analysis

Give Naloxone urgently if

- impaired consciousness or
- exposure within the last 10 minutes even if asymptomatic

Give Naloxone urgently and consider referral for intensive care

- respiratory depression
- airway obstruction or
- vomiting with impaired consciousness

Severe opiate-induced respiratory depression (For adults)

IV Naloxone 0.4mg

↓ no response after 60 seconds

IV Naloxone 0.8 mg

↓ no response after 60 seconds

IV Naloxone 0.8 mg

↓ no response after a total of 2 mg

Give a further 2 mg dose (Larger doses 4mg in a seriously poisoned patient)

↓

When adequate response occurred → monitor ABG, O2 saturation and respiratory rate Observe the patient for recurrence

IV infusion following resuscitation (where repeated doses are likely to be required)

Hourly IV infusion of 60% of total dose required to reverse respiratory depression **OR**

2mg of naloxone + 100ml of Normal saline (5 ml/hour) and titrate according to response

Patients at risk of acute withdrawal (chronic opioid use or when there is a need for therapeutic effect)

IV Naloxone 0.1-0.2mg

↓ no response after 60 seconds

IV Naloxone 0.1 mg

↓ no response after another 60 seconds

IV Naloxone 0.1 mg

↓ no response after a total of 2 mg

Give a further 2 mg dose (Larger doses 4mg in a seriously poisoned patient)

↓

When adequate response occurred → monitor ABG, O2 saturation and respiratory rate Observe the patient for recurrence

Benzodiazepine overdose

Toxicity

Suggested toxic doses for adults who are not daily users / adults who are daily users if more than their usual dose

Drug	Suggested toxic dose
Alprazolam	0.05mg/kg
Bromazepam	0.7mg/kg
Clonazepam	0.6mg/kg
Diazepam	0.7mg/kg
Lorazepam	0.2mg/kg
Midazolam	1mg/kg

Management

1. Maintain a clear airway and ensure adequate ventilation
2. The benefit of gastric decontamination is uncertain. Consider activated charcoal 50 g for adults; 1g/kg for children if the patient presents within 1 hour of ingestion of a toxic dose or more, provided the airway can be protected.
3. Monitor vital signs, cardiac rhythm and check RBS.
4. Perform a 12-lead ECG in all patients who require assessment. Check cardiac rhythm, QRS duration and QT interval.
5. In all patients who require assessment, check FBC, U&E and LFT. Check CK activity if features of toxicity are present.
6. All patients who require assessment should be observed for at least 4 hours after exposure. Asymptomatic patients can then be considered for discharge with advice to return if symptoms develop.
7. Consider ABG in patients who have - GCS < 8, AVPU scale P or U, Reduced oxygen saturation on pulse oximetry
8. Indications for Flumazenil (benzodiazepine antagonist)
    - Reversal of sedative effects of benzodiazepines in anaesthetic procedures.

- Patients who develop reduced ventilation and coma and who otherwise would require mechanical ventilation.

Contraindications –

1) co-ingested medicines that may cause convulsions (eg TCA)
2) in the presence of features suggestive of TCA ingestion, including a wide QRS interval with large pupils
3) use in a patient post-cardiac arrest
4) flumazenil should not be used as a diagnostic test

Dose of Flumazenil

Adult dose

- It is not necessary or appropriate in cases to fully reverse CNS depression; adequate ventilation is the aim.
- IV over 15 seconds
- First dose: 0.5 mg, wait 30 seconds if unsuccessful or only partially successful, give
- Second dose: 0.5 mg, wait 30 seconds if unsuccessful or only partially successful, give
- Third dose: 1mg
- If there is no response after 2mg within a few minutes it is unlikely that flumazenil will reverse CNS/respiratory depression.
- Not more than 3 mg as a bolus loading dose should be given within one hour.
- If drowsiness recurs, or there is inadequate airway protection and reduced ventilation, bolus doses (0.5–1mg) can be given and repeated at 20 minutes intervals. Alternatively, an IV infusion 0.5-2mg/hour, adjusted to individual response, can be instituted.

Paediatric dose

- Flumazenil should only be given to children if ventilation is seriously compromised.
- IV over 15 seconds, Not more than 2 mg
- First dose: 0.01 mg/kg, wait 30 seconds if unsuccessful or only partially successful, give
- Second dose: 0.01 mg/kg, wait 30 seconds if unsuccessful or only partially successful, give
- Third dose: 0.02 mg/kg
- If there is no response, it is unlikely that flumazenil will reverse CNS/respiratory depression.

- If drowsiness recurs, or there is inadequate airway protection and reduced ventilation, bolus doses (0.02 mg/kg) can be given and repeated at 20 minutes intervals. Alternatively, an IV infusion 0.002-0.01mg/kg/hour, adjusted to individual response, can be instituted.

Warning

1) The duration of action of flumazenil (half-life 52 minutes, duration of action 1-2 hours). Patients must be kept under observation for 4 hours in case toxicity recurs.
2) Flumazenil may precipitate a withdrawal syndrome in benzodiazepine-dependent patients, convulsions in epileptics and arrhythmias in patients who have taken cardiotoxic drugs.
3) Flumazenil should be used with caution in mixed overdoses where the drugs involved are not known and in patients with a history of convulsions, head injury or chronic benzodiazepine use.

9. Hypotension
    - Ensure adequate fluid resuscitation. Treat brady and tachyarrhythmias appropriately.
    - Consider early referral to critical care for patients with fluid-resistant hypotension.
    - Vasopressors and inotropes can be initiated in an emergency.
    - The first line vasopressor in poisoned patients is usually noradrenaline but this generally requires central access.
    - Inotropes –

      adrenaline (1mg of adrenaline in 500ml of NS – run at 100 ml/hour initially, titrate up or down to effect)

      dopamine (200mg of dopamine in 500ml of NS – run at 50ml/hour initially, titrate up or down to effect. For children, make up (3 x weight in kg) mg of dopamine to 50ml of NS – 1ml/hour (1mcg/kg/min), dose range is 5-15ml/hour (5-15 mcg/kg/min).

Benzodiazepine Overdose

ABC, clear airway

↓

Activated charcoal 50 g if within 1 hour of ingestion

↓

ECG, RBS, FBC, U&E, CK and LFT

↓

Observe for at least 4 hours after exposure → Asymptomatic → Discharge

↓

GCS < 8, AVPU scale - P or U, Reduced oxygen saturation → ABG

Indications for Flumazenil

1. Reversal of sedative effects in anaesthetic procedures
2. Reduced ventilation and coma

(see contraindications)

0.5 mg Flumazenil (IV over 15 seconds) (first dose)

↓ Wait 30 sec

If unsuccessful or only partially successful

0.5 mg Flumazenil (second dose)

↓ Wait 30 sec

If unsuccessful or only partially successful

1 mg Flumazenil (third dose)

↓

No response after 2mg within a few minutes → consider other causes

(Not > 3 mg within 1 hour)

↓

Drowsiness recurs, inadequate airway protection and reduced ventilation

↓

Bolus doses (0.5–1mg) and repeated at 20 minutes intervals (OR) IV infusion 0.5-2mg/hour

Corrosive Poisoning
Management Guidelines
Poison Treatment Centre, New Yangon General Hospital

A corrosive is a substance that causes functional and histologic damage on contact with tissue surfaces. Common corrosive substances include drain decloggers, toilet bowl cleaners and dishwasher detergents which contain acids and alkalis. Button batteries contain alkali such as sodium and potassium hydroxide.

Type of Corrosives

Acids (Compounds with pH < 7)	**Alkalis** (Compounds with pH > 7)
• Hydrochloric acid • Sulphuric acid • Sulphamic acid • Phosphoric acid • Acetic acid • Hydrofluoric acid	• Sodium hydroxide • Potassium hydroxide • Calcium carbonate

Mechanism of Toxicity

Acids	**Alkalis**
• Hydrogen (H+) ions in acid desiccate epithelial cells, produce eschar resulting in what is histologically called **coagulative necrosis**. • In most series, acid ingestion caused both gastric and esophageal injury, with whitish discoloration of esophageal mucosa and smooth muscle spasms.	• Hydroxide ions in alkaline xenobiotics penetrate tissue surface producing what is histologically described as **liquefaction necrosis**. • The process includes protein dissolution, collagen destruction, fat saponification, cell membrane emulsification, transmural thrombosis, and necrosis.

Features of Poisoning

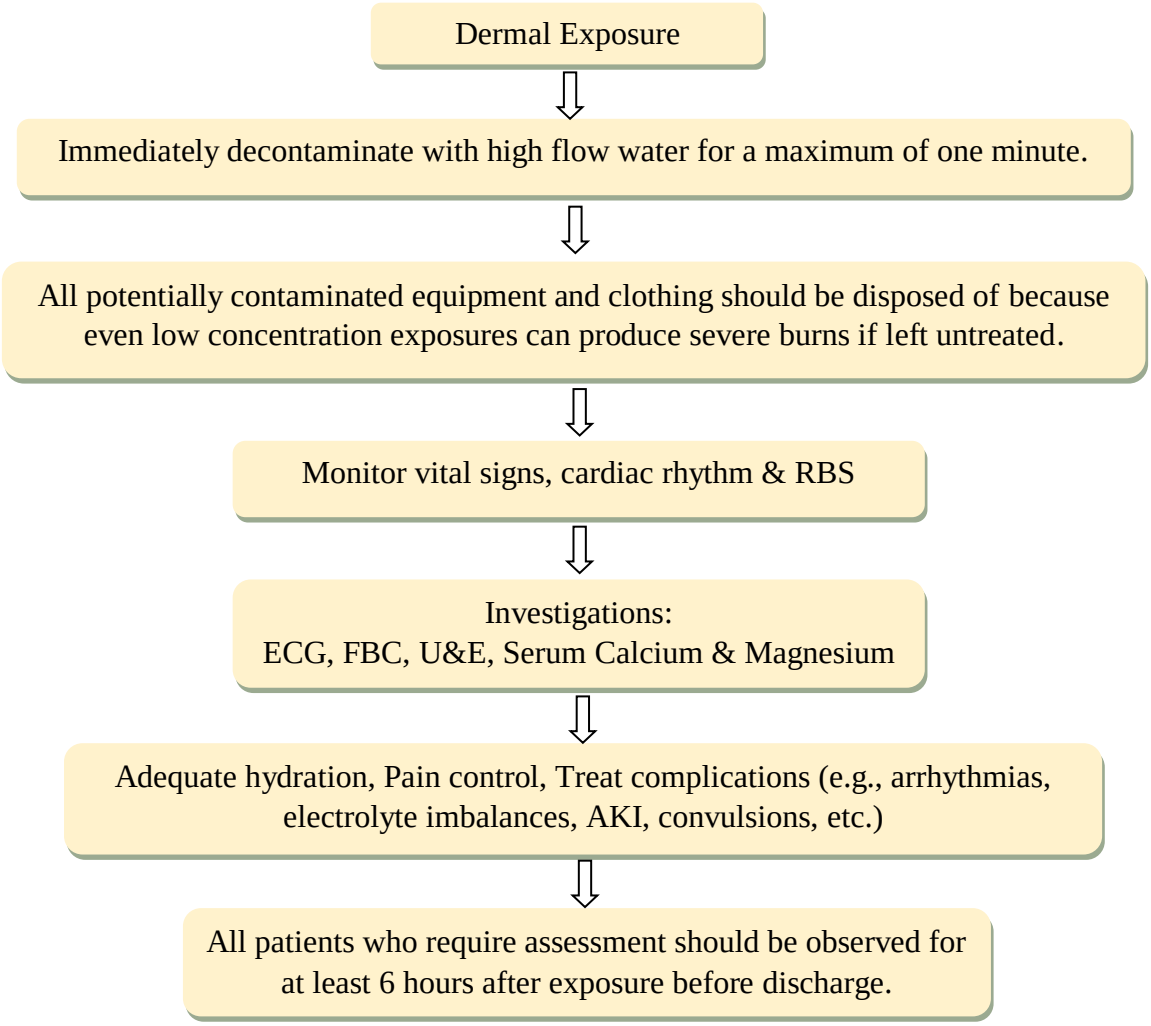
- The extent of injury is determined by duration of contact, ability of substance to penetrate tissue, volume, pH, concentration, presence of food in the stomach and titratable acid or alkali reserve (TAR).
- The TAR is the amount of neutralizing substance (tissue or another neutralizing xenobiotic) required to bring the pH of the corrosives to physiologic pH. TAR may be the most important predictor of potency.
- Neutralization of corrosives occurs at expense of tissues, resulting in release of thermal energy and burns.

Route of exposure	Features
Eye exposure	Conjunctivitis, chemosis (conjunctival oedema), corneal epithelial coagulation and necrosis
Dermal exposure	Pain, ulceration and necrosis.
Inhalation	Irritation of eyes and nose with sore throat, cough, chest tightness, headache, ataxia and confusion. Dyspnoea and stridor due to laryngeal oedema may follow. Haemorrhagic pulmonary oedema with increasing breathlessness, wheeze, hypoxia and cyanosis may take up to 36 hours to develop.
Ingestion	Ingestion can lead to tissue injury from both the direct corrosive effects of the acid and an exothermic reaction causing thermal injury. **Immediate local features:** Burning of the mouth and throat with retrosternal and abdominal pain. The larynx may also be affected causing oedema, airway obstruction and difficulty in clearing bronchial secretions. There is often hypersalivation, vomiting, dysphagia, odynophagia, haematemesis and hypotension. Oesophageal or gastric perforation may occur. **Long-term complications:** Oesophageal or gastric stricture may develop over weeks or months.

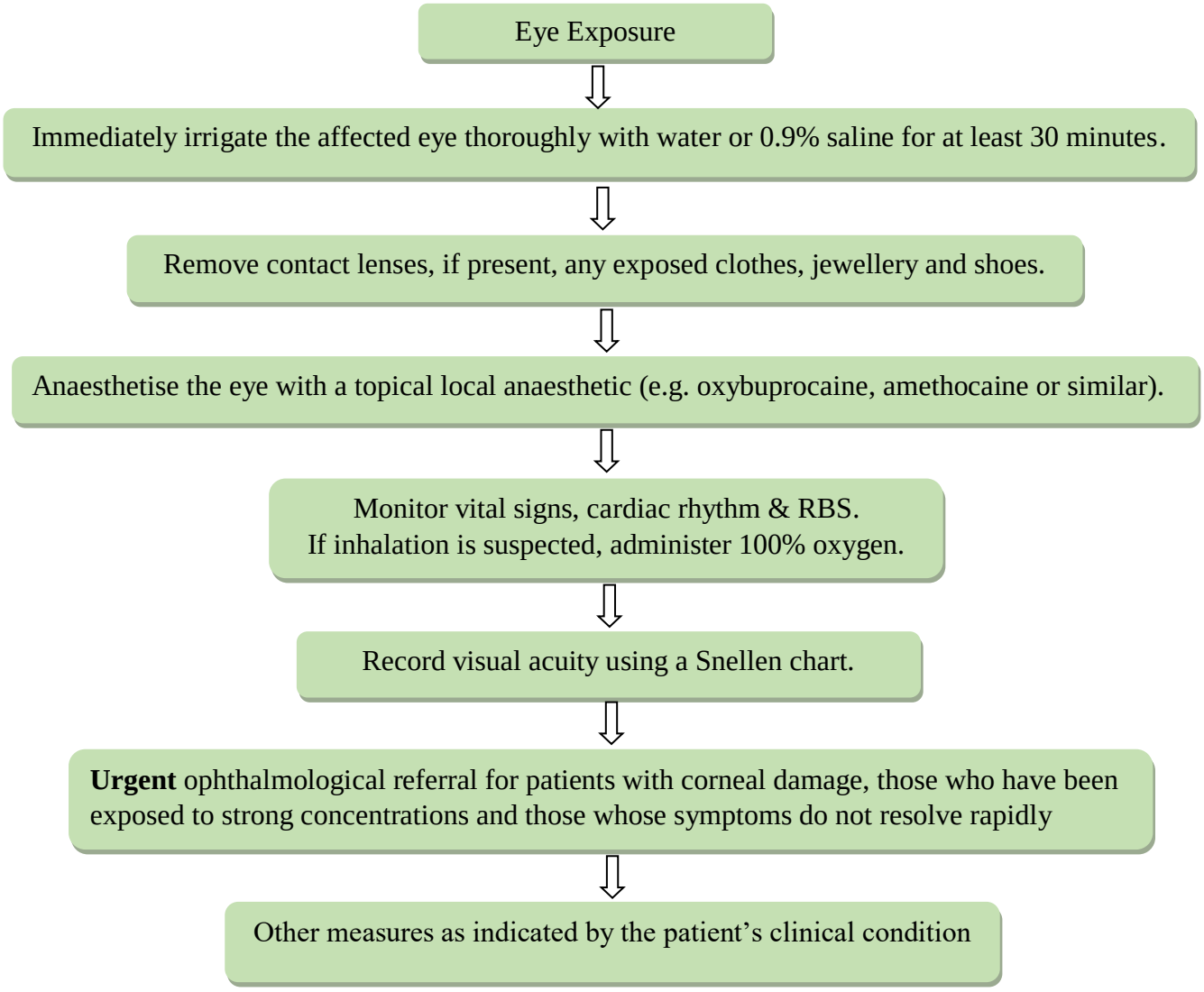
	Systemic toxicity: In addition to local tissue damage, acids can be systemically absorbed, leading to multiorgan damage, metabolic acidosis and hemolysis. Hypocalcaemia, hypomagnesaemia and metabolic acidosis. Hyperkalaemia is also common. Myoclonus, tetany, convulsions, CNS depression, cardiac conduction disturbances and arrhythmias (prolonged QT interval, ventricular tachycardia and ventricular fibrillation) may occur secondary to hypocalcaemia and other electrolyte disturbances.

Acute Management of Corrosive Poisoning

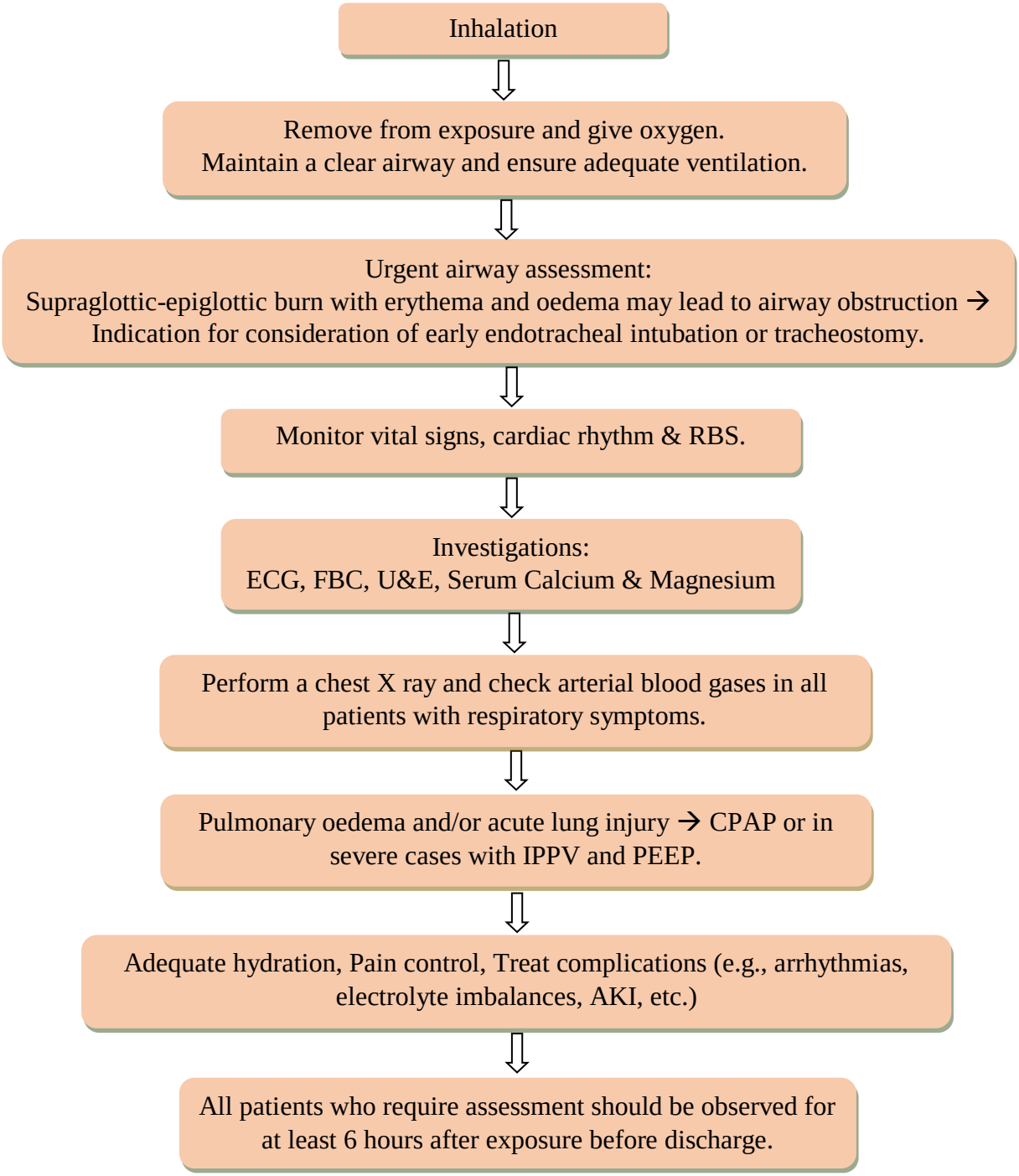
Dermal exposure



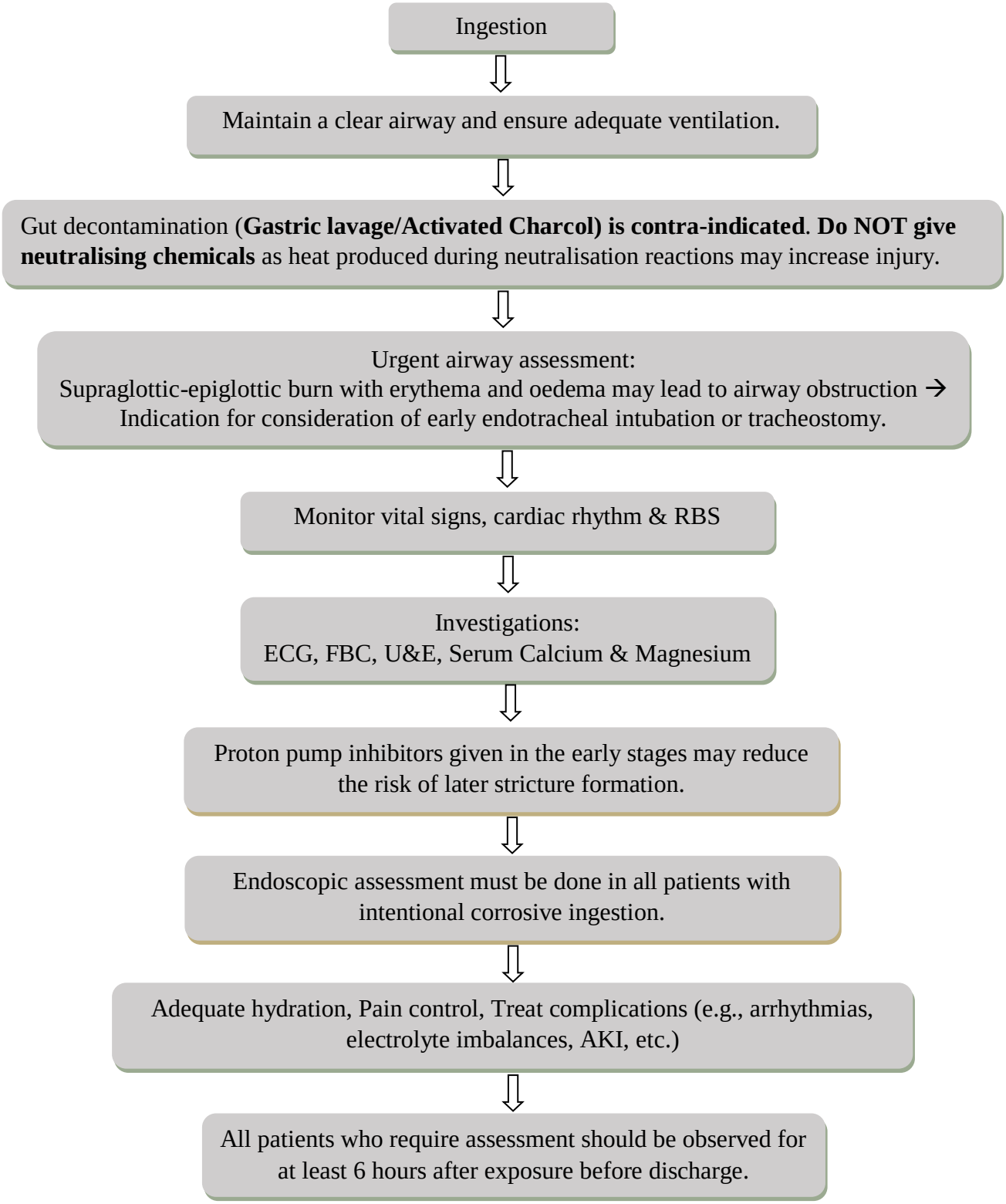
Eye exposure



Inhalation


Inhalation
Remove from exposure and give oxygen.
Maintain a clear airway and ensure adequate ventilation.
Urgent airway assessment:
Supraglottic-epiglottic burn with erythema and oedema may lead to airway obstruction →
Indication for consideration of early endotracheal intubation or tracheostomy.
Monitor vital signs, cardiac rhythm & RBS.
Investigations:
ECG, FBC, U&E, Serum Calcium & Magnesium
Perform a chest X ray and check arterial blood gases in all patients with respiratory symptoms.
Pulmonary oedema and/or acute lung injury → CPAP or in severe cases with IPPV and PEEP.
Adequate hydration, Pain control, Treat complications (e.g., arrhythmias, electrolyte imbalances, AKI, etc.)
All patients who require assessment should be observed for at least 6 hours after exposure before discharge.

Ingestion


Ingestion
Maintain a clear airway and ensure adequate ventilation.
Gut decontamination (**Gastric lavage/Activated Charcol) is contra-indicated**. **Do NOT give neutralising chemicals** as heat produced during neutralisation reactions may increase injury.
Urgent airway assessment:
Supraglottic-epiglottic burn with erythema and oedema may lead to airway obstruction →
Indication for consideration of early endotracheal intubation or tracheostomy.
Monitor vital signs, cardiac rhythm & RBS
Investigations:
ECG, FBC, U&E, Serum Calcium & Magnesium
Proton pump inhibitors given in the early stages may reduce the risk of later stricture formation.
Endoscopic assessment must be done in all patients with intentional corrosive ingestion.
Adequate hydration, Pain control, Treat complications (e.g., arrhythmias, electrolyte imbalances, AKI, etc.)
All patients who require assessment should be observed for at least 6 hours after exposure before discharge.

Diagnostic Testing

Laboratory	• Complete blood count • Chemistry • Coagulation studies • Grouping and Matching
Imaging	• CXR & Abdominal XR (not sensitive but may identify esophageal or gastric perforation) • CT scan of chest and abdomen
Endoscopy	• Endoscopy should be **performed within 12 hrs and not later than 24 hrs post ingestion.** • Early endoscopy provides prognostic information and facilitates discharge of patients with no evidence of injury. • Use of endoscope at should be **avoided between 5 days and 2 weeks post-ingestion** as risk of perforation is the greatest during this time period.

Classification of Esophageal burns by endoscopic visualization & Management

Classification	Appearance	Risk	Management
Grade I	Hyperemia or edema without ulceration	No risk of stricture	PO Challenge
Grade IIa	Noncircumferential lesions, ulcers, exudates		PO Challenge
Grade IIb	Near-circumferential, lesions, ulcers, exudates	Strictures in 75%	Early feeding, Long term surveillance for strictures and carcinoma.
Grade III	Deep ulcers, necrosis	Almost always lead to strictures and high risk of perforation.	Early feeding, Long term surveillance for strictures and carcinoma. Surgery indicated if perforation present.

Esophageal burns may require 8 weeks to heal. For deep burns, healing is followed by esophageal shortening, progressive narrowing of lumen, and scar formation or strictures.

References

8. TOXBASE®. Corrosive Poisons (Acids and Alkalis) - features and management updated 9/2018; Available from: http://www.toxbase.org.
9. Ashcraft KW, Padula RT: The effect of dilute corrosives on the esophagus. Pediatrics 1974; 53: 226-232.
10. Crain EF, Gershel JC, Mezey AP. Caustic ingestions-Symptoms as predictors of esophageal injury. Am J Dis Child 1984; 138: 863-865.

Rodenticide Poisoning
Management Guidelines
Poison Treatment Centre, New Yangon General Hospital

Rodenticides commonly contain anticoagulants, and less frequently other ingredients. Some products may contain solvents such as propylene glycol. Products are usually formulated as bait blocks/sachets, or as additives to grain or cereal. Occasionally as a paste or powder.

Ingredients

Anticoagulants		**Others**
Short-acting	**Longer-acting**	
• Warfarin • Coumatetralyl	• Brodifacoum • Difenacoum • Chlorophacinone • Bromadiolone • Difethialone	• Alphachloralose (CNS depressant) • Calciferol (Vitamin D) • Thallium • Fluoride salts • Norbormide • Phosphorus

Short-acting anticoagulant rodenticides (e.g., warfarin, coumatetralyl)

Toxicity

Rodenticide preparations containing warfarin (0.025-1.2%) or coumatetralyl are unlikely to be serious in a single acute accidental ingestion as the concentration of anticoagulant is low. However, intentional consumption of large quantities may result in significant anticoagulation.

Overdosage with warfarin for human anticoagulation (0.5 mg, 1 mg, 3 mg, 4 mg, 5 mg tablets; 1 mg/mL suspension) is potentially more serious. Some products may contain other toxic ingredients, including propylene glycol, large doses of which may cause CNS depression, cardiac effects, convulsions and metabolic acidosis.

Mechanism of toxicity

Anticoagulant rodenticides inhibit vitamin K1 2,3-epoxide reductase. This prevents synthesis of vitamin K dependent clotting factors II, VII, IX and X. The onset of anticoagulant effects is likely to be delayed due to the presence of active clotting factors in the circulation.

Features of Poisoning

Ingestion / Systemic Toxicity

Features are unlikely to arise in children who have ingested a small amount of rodenticide baits. After ingestion, prolongation of the prothrombin time (PT) or raised INR is usually evident within 48 hours and patients may remain profoundly anticoagulated for several days after ingestion of large amounts or after chronic ingestion.

Large overdoses may cause epistaxis, gingival bleeding, spontaneous bruising, haematomas, haematuria, bilateral flank pain, haemoperitoneum, rectal bleeding, melaena and menorrhagia. Haemorrhage into virtually any organ may occur.

Inhalation

Inhalation may cause irritation of the respiratory tract. May be absorbed via the respiratory tract and systemic features may ensue.

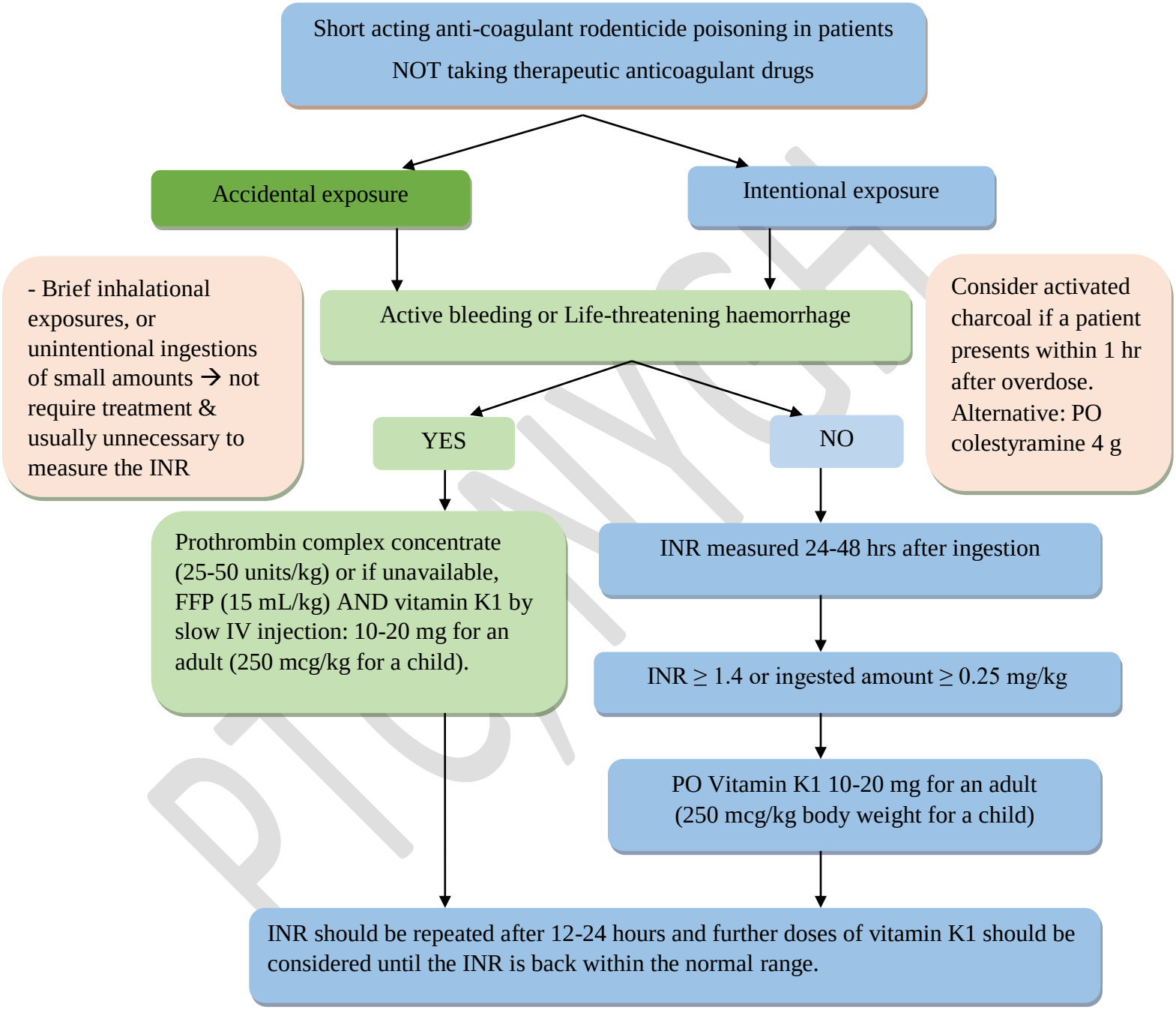
Dermal Exposure

May be irritating to the skin. Dermal contact with liquid concentrates may lead to significant absorption and to the development of systemic features.

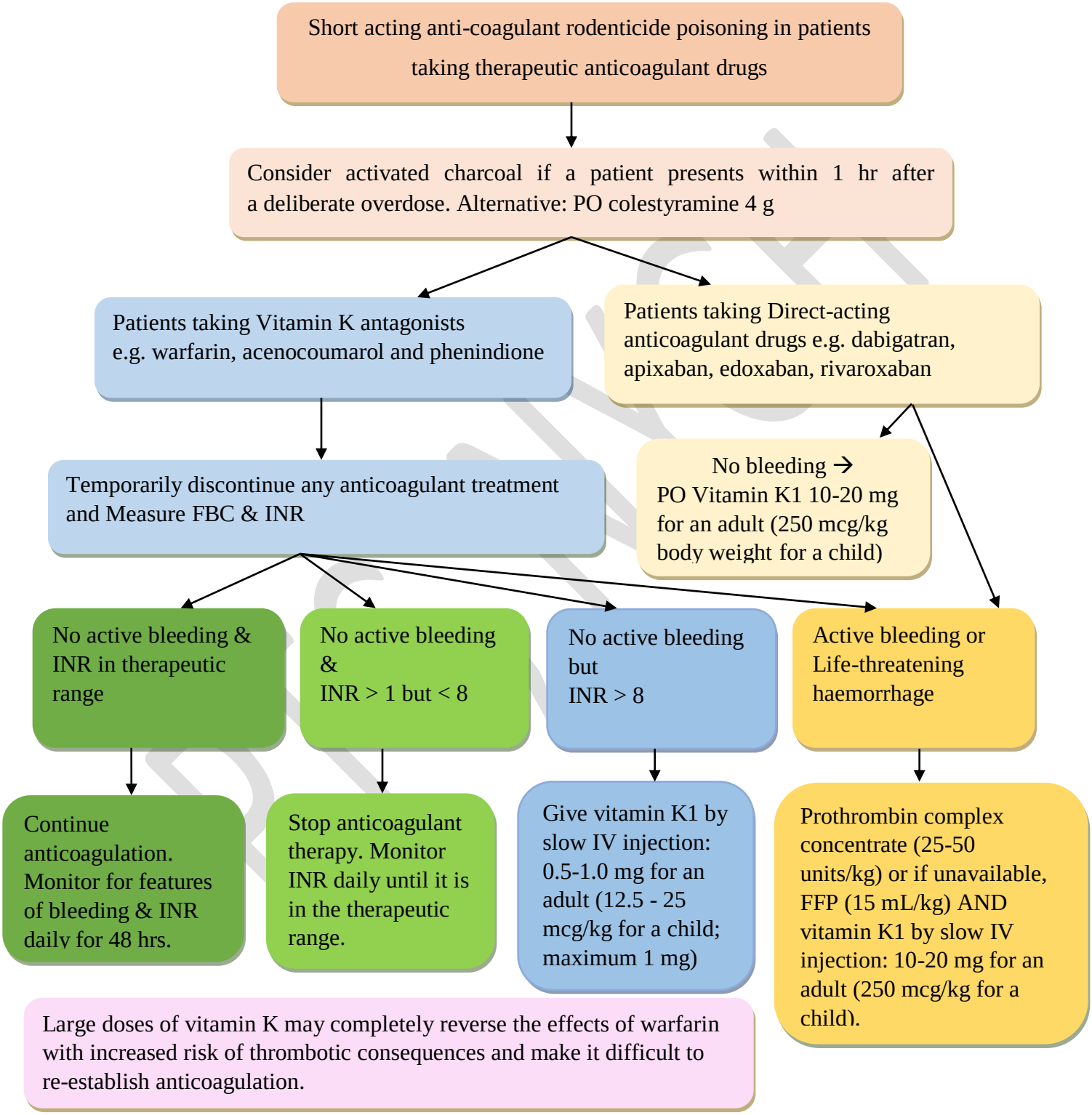
Eye Exposure

May be irritating to the eyes.

Management of Short acting anti-coagulant rodenticide poisoning in patients NOT taking therapeutic anticoagulant drugs



Management of Short acting anti-coagulant rodenticide poisoning in patients taking therapeutic anticoagulant drugs



Long-acting anticoagulant rodenticides (e.g., bromadiolone, brodifacoum, chlorophacinone, coumatetralyl, difenacoum, difethialone, diphacinone, flocoumafen)

Toxicity

Long-acting anticoagulant rodenticides are up to 100 times more potent than warfarin. However, preparations of rodenticides available for domestic and professional use tend to have a low concentration of the active anticoagulant (e.g. 0.005%).

Significant toxicity usually only occurs via ingestion. However toxicity has been reported rarely after skin exposure to a liquid preparation or inhalation. The onset of bleeding may be delayed for several days and the intentional consumption of large quantities can cause profound anticoagulation for weeks or months.

Mechanism of toxicity

Long-acting anticoagulant rodenticides inhibit vitamin K1-2,3-epoxide reductase. This prevents synthesis of vitamin K dependent clotting factors II, VII, IX and X. The onset of anticoagulant effects is likely to be delayed due to the presence of active clotting factors in the circulation.

Features of Poisoning

Ingestion/ Systemic Toxicity

Features are unlikely to arise in children who have ingested a small amount of rodenticide baits. After ingestion, prolongation of the prothrombin time (PT) or raised INR is usually evident within 48 hours; however, the onset of bleeding may be delayed for several days or weeks. Patients may remain anticoagulated for weeks or months after ingestion of large amounts or after chronic ingestion.

Epistaxis, gingival bleeding, spontaneous bruising, haematomas, haematuria, bilateral flank pain, haemoperitoneum, rectal bleeding, melaena, menorrhagia, and haemorrhage into virtually any organ may occur following significant anticoagulant exposure. Many, if not most, patients with haemorrhage will have evidence of bleeding into more than one organ. Compartment syndrome from bleeding into a muscle compartment has been reported. Severe

blood loss may result in hypovolaemic shock, coma and death. Most deaths are due to intracranial bleeding. Paradoxical thrombosis has also been reported.

Inhalation

Inhalation may cause irritation of the respiratory tract. May be absorbed via the respiratory tract and systemic features may ensue.

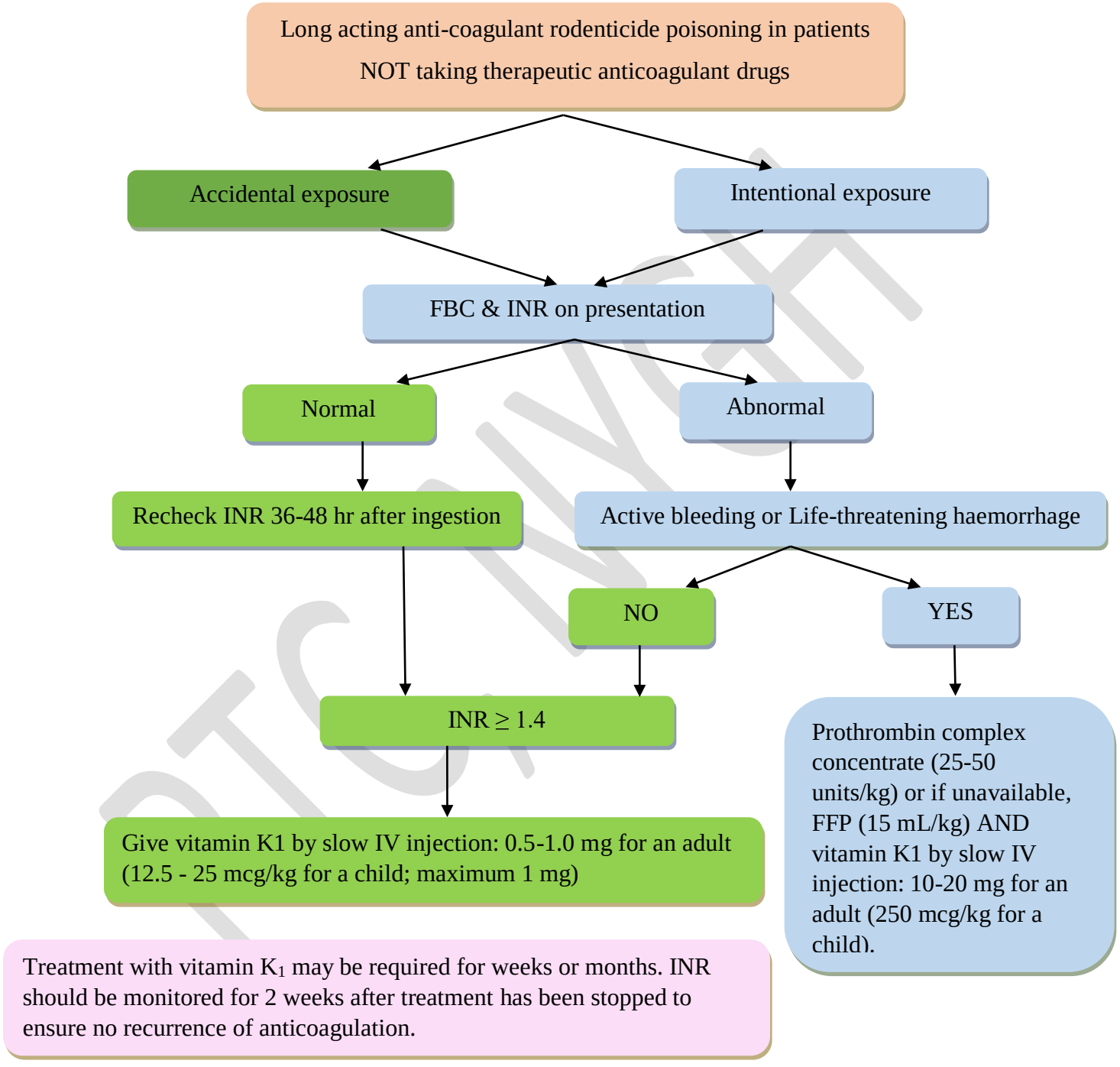
Dermal Exposure

May be irritating to the skin. Dermal contact with liquid concentrates may lead to significant absorption and to the development of systemic features.

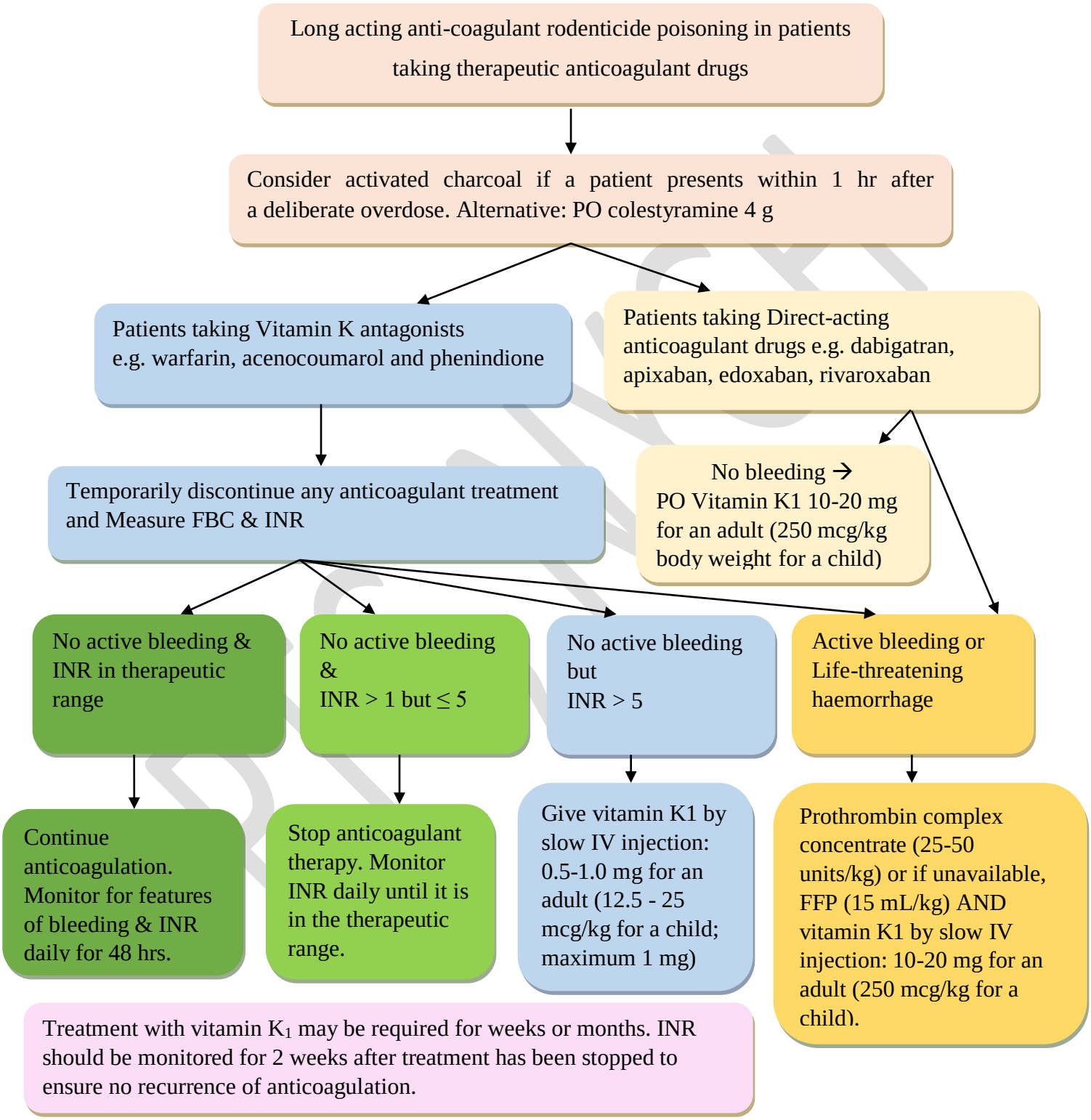
Eye Exposure

May be irritating to the eyes.

Management of Long acting anti-coagulant rodenticide poisoning in patients NOT taking therapeutic anticoagulant drugs



Management of Long acting anti-coagulant rodenticide poisoning in patients taking therapeutic anticoagulant drugs



References

11. TOXBASE®. Rodenticides - features and management updated 10/2019; Available from: http://www.toxbase.org.

Petroleum poisoning

Features

Respiratory

Aspiration into the lungs may cause pneumonitis or lipoid pneumonia. Initial features include choking, gasping, coughing and haemoptysis. Signs and symptoms may progress over 24 - 48 hours with wheeze, breathlessness, bronchospasm, hypoxia, fever and leukocytosis. Chest x-ray changes include patchy shadowing and pulmonary oedema (may be delayed for 24 - 72 hours). In severe cases shock and cardiorespiratory arrest can occur.

Rarer complications include pleural effusions or pneumatoceles, lipoid pneumonia, emphysema, pneumothorax and pneumomediastinum.

Gastrointestinal

Nausea, vomiting and abdominal pain. Rarely: diarrhoea, haematemesis and melaena, corrosive damage and perforation.

Systemic

Drowsiness leading to coma, ataxia, convulsions, cardiac arrhythmias, and respiratory collapse. Rarely: abnormal LFTs, acute kidney injury, myocarditis, intravascular haemolysis and disseminated intravascular coagulation.

Management

1. Maintain a clear airway and ensure adequate ventilation. Give oxygen if indicated.
2. Gastric lavage should **NOT** be undertaken due to the increased risk of aspiration.
3. Monitor vital signs and cardiac rhythm; check RBS.
4. All patients who require assessment should be observed for at least 8 hours after ingestion. Perform a chest x-ray in all patients, preferably 6-8 hours after exposure (or earlier if clinically indicated).
5. Perform a 12-lead ECG in all patients who require assessment. Repeat 12-lead ECGs are recommended, especially in symptomatic patients.
6. In symptomatic patients check FBC, U&Es, LFTs and consider arterial blood gases.
7. **Convulsions**

Give oxygen, check blood glucose, U&Es and ABG. Correct acid base and metabolic disturbances as required.

Single brief convulsions do not require treatment.

Control convulsions that are frequent or prolonged with IV diazepam (10-20 mg in adults; 0.1-0.3 mg/kg body weight in children).

Further doses of benzodiazepines may be needed in adults; refer to intensive care. In children seek consultant paediatric input.

If unresponsive to the above measures, the patient should be referred urgently to critical care.

8. **Bronchospasm**

   Treat conventionally with nebulised bronchodilators and steroids.

9. **Pulmonary oedema and/or acute lung injury**

   Treat with continuous positive airway pressure (CPAP) or in severe cases with IPPV and PEEP.

10. There is no good evidence that prophylactic corticosteroids (inhaled or systemic) and antibiotics are of benefit.

11. Antibiotics may be required if pneumonia or sepsis develops.

12. Other measures as indicated by the patient's clinical condition.

    Patients should be advised on discharge to seek medical attention if symptoms subsequently develop.

    On discharge, patients and their carers should be advised to present immediately to the Emergency Department if symptoms develop, especially those suggestive of aspiration e.g. cough, even if mild or transient, choking, fever, breathlessness, vomiting or drowsiness. These features may occasionally develop up to 48 hours after exposure.

Petroleum poisoning

Airway, breathing, circulation

↓

*Gastric lavage should **NOT** be undertaken*

↓

Monitor vital signs and ECG, RBS, FBC, U&Es, LFTs and ABG

↓

observed for at least 8 hours after ingestion → discharge if asymptomatic

↓

chest x-ray in all patients, preferably 6-8 hours after exposure

↓

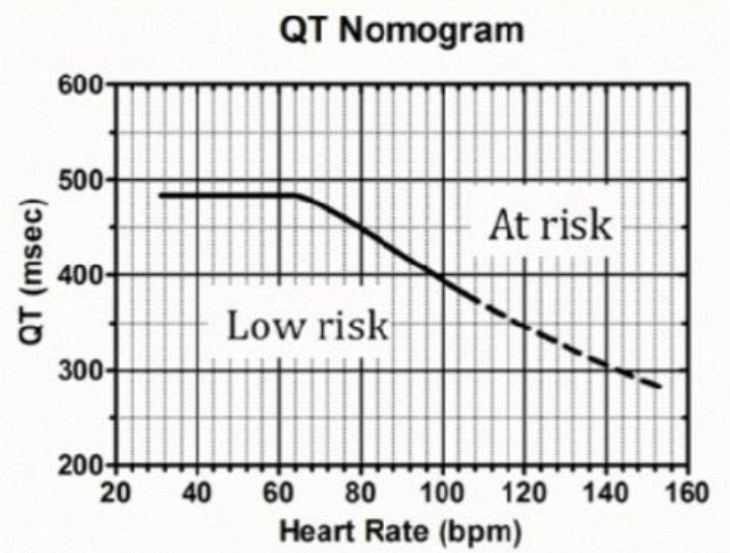
Treatment for convulsion, bronchospasm

If Pulmonary oedema and/or acute lung injury → Refer to intensivist for CPAP, IPPV, PEEP

Management of Prolonged QT interval

If the QT interval is prolonged, check serum potassium, magnesium and calcium and replace as necessary to keep within the high normal range. Check ABG and correct any hypoxia or acidosis. Review all medications that may prolong QT interval.

Risk of torsade de pointes also depends on factors other than QT prolongation, with increases in risk associated with bradycardia (especially heart block), frequent pauses associated with ectopics or atrial fibrillation, underlying structural heart disease, digoxin or diuretic therapy, female sex and increased age. Assess risk of torsade de pointes using QT-HR nomogram (a combination of heart rate and uncorrected QT interval, do not use the QT interval calculated by some ECG machines)



Consider magnesium sulphate if high risk - IV Magnesium sulphate over 10-15 minutes: adult 2 g (8mmol of Mg2+), children 25-50 mg/kg (max – 2 g).

Torsade de pointes and VT/VF preceded by a prolonged QT interval should be treated urgently with magnesium sulphate IV 2 g (8mmol, or 4ml of 2 mmol/ml solution) in adults and 25-50 mg/kg (max 2 g) in children over 30-120 seconds. This may be repeated twice at intervals of 5-15 minutes if necessary. Magnesium concentration should be measured after administration.

New Yangon General Hospital

Standard Operating Procedure

of

Acute Poisoning

New Yangon General Hospital

Standard Operating Procedure of Acute Poisoning

Purpose

A standard operating procedure is a document which describes the regularly recurring operations to ensure that the operations are carried out correctly (quality) and always in the same manner (consistency).

This SOP (Standard Operating Procedure) is intended to provide overall management procedures for acute poisoning patients.

Procedures

1. Triage

At emergency department, quick assess the patient and give immediate necessary treatments. (According to Poison Management Guidelines, NYGH)

2. History taking

To obtain detailed information about acute poisoning and identify the poison, the following should be asked thoroughly.

(1) What type of poison – herbicide, insecticide, medicine, traditional medicine, narcotic drug

(2) Route– (Contact/Absorption), Inhalation, Ingestion)

(3) Amount – spoon, cup, bottle

(4) When– exposure started time

(5) By who – accident or suicide or homicide

(6) Duration– contact time, inhalation time

(7) Place of occurrence– (Home, Residential institution, School, other institution and public administrative area, Sports and athletics area, Street and highway, Trade and service area, Industrial and construction area, Farm, Other specified places, Unspecified place)

(8) Activity at the time of poisoning– (While engaged in sports activity, While engaged in leisure activity, While working for income, While engaged in other types of work, While resting, sleeping,

eating or engaging in other vital activities, While engaged in other specified activities, During unspecified activity)

(9) Occupation– occupational hazard or not

(10) History of previous suicidal attempt and psychological problem

(11) Past medical history, social and family history

3. Physical examination

Proper examination of the patient should be done to assess the toxidromes. (According to Poison Management Guidelines, NYGH)

4. Medico–legal report

Duty Medical Officer has to fill the Medico–legal report and record in police case register book. Need to stamp Medico–legal marking on the OPD booklet, admission chart, admission register book and investigation request forms.

5. Decision for care

Decide whether the patient needs to be admitted or not, based on the patient conditions. If the patient does not need to admit, give appropriate treatment for outpatient care and counseling.

If the patient needs to be admitted, the following procedures should be continued.

6. Take samples and send to respective departments to identify the poison

Sr.	Type of poisoning	Available test	Types of samples	Amount required	Department where to send samples
1.	Methanol Poisoning	Methanol Level	Blood	20 ml	O&E Health Dept:
2.	Carbonmonoxide Poisoning	Carboxyhaemoglobin level	Blood	20 ml	O&E Health Dept:
3.	Cyanide Poisoning	Methaemoglobin level	Blood	20 ml	O&E Health Dept:
4.	Lead Poisoning	Lead level	Blood	20 ml	O&E Health Dept:

Sr.	Type of poisoning	Available test	Types of samples	Amount required	Department where to send samples
5.	Drug Overdose	Acetaminophen (Paracetamol level)	Blood	20 ml	DMR
6.		Acetyl salicylic acid	Urine	30ml	DMR
7.		Amitriptyline	Urine	30ml	DMR
8.		Atropine	Urine	30ml	DMR
9.		Benzodiazepines	Urine	30ml	DMR
10.		Chlorpheniramine maleate	Urine	30ml	DMR
11.		Carbamazepine	Urine	30ml	DMR
12.		Ferrous sulphate	Urine	30ml	DMR
13.		Haloperidol	Urine	30ml	DMR
14.		Phenothiazine	Urine	30ml	DMR
15.		Propranolol	Urine	30ml	DMR
16.		Phenytoin	Urine	30ml	DMR
17.	Narcotic Overdose	Alfentanil, Buprenorphine, Codeine, Diamorphine(Heroin) Dihydrocodeine, Fentanyl Methadone, Morphine, Pethidine, Tramadol	Urine	30 ml	CEO
18.	Stimulus Overdose	Amphetamine	Urine	30 ml	CEO
19.	All Poisons	All Poisons	Blood	20 ml	CEO
			Urine	30ml	

Abbreviation

O&E Health Dept: – Occupational and Environmental Health Department

DMR– Pharmaceutical Toxicology Research Division, National Poison Control Centre, Department of Medical Research, Yangon

CEO (Yangon) – Chemical Examiner Office (Yangon)

Write down all results of chemical analysis in Police case register book and Medico–legal report.

7. Inform to Occupational Health, Yangon Regional Public Health Department

If poisoning occurs in a group of workers, it may be related to occupational hazards. So it should be informed to Occupational Health, Yangon Regional Public Health Department and cooperate with them to detect source of poisoning and prevent further occurrence.

8. Non– specific and specific treatment

Give non–specific and specific treatments, based on patient's signs and symptoms and type of poison. (According to Poison Management Guidelines, NYGH)

Provision of ICU care for critically poisoned patients and refer to specialist hospital when specialist care is needed. (e.g. for renal dialysis)

9. Investigations

Necessary laboratory tests and imaging studies are done according to Poison Management Guidelines, NYGH.

10.Medical social counseling (Roles of Medical social workers)

Assess the social condition of the patient and provide appropriate counseling.

Arrange to obtain financial assistance, food assistance and other assistance for carrying out patient's treatment.

Make the patient and family understand the nature of illness and help the patient to deal with complications of illness.

Help to solve the problems and find the way to go back home especially picked up patients.

11. Psychological support

Proper referral of the poisoned patient who need psychological assessment to psychiatrist.

Refer and admit the patient to Mental Health Hospital if the patient needs further treatments.

12. Rehabilitation

Physiatrist and physiotherapist treat the poisoned patient with chest physiotherapy , swallowing rehabilitation and neuro rehabilitation if necessary.

13. Post mortem examination

When the poisoned patient expires, post mortem examination must be done for medico–legal purpose. During post mortem examination, take cardiac blood (20 ml) and gastric juice (30–50 ml) and send to Chemical Examiner Office (Yangon) for second time examination.

Write down all PM findings in PM findings record books (Mortuary and ERC), Poison case PM findings record book, Police case register book and Medico–legal report clearly and precisely.

14. Medico–legal issue

When Court of Law summon for the case, first seen doctor should answer about the case before the Court of Law. And also need to submit Medico–legal report, results of chemical analysis and detail PM findings (if patient expires) to the Court of Law.

15. Follow up care for discharge patients

Improved and recovered patients are discharged from hospital and closely follow up to detect and treat the complications of poisoning. Also follow up in rehabilitation and psychiatrist OPD to provide rehabilitation and psychological assistance for being disabled life.