*ABC of Poisoning*MICHAEL NIELSEN
JOHN HENRYCARDIOVASCULAR, NEUROLOGICAL,
AND OTHER COMPLICATIONS

Cardiovascular complications

Major cardiovascular complications of
acute poisoning

- Cardiac arrest
- Hypotension
- Arrhythmias

Hypotension

Hypotension is the commonest cardiovascular complication of poisoning. Acute poisoning produces hypotension by direct effects on the circulation or indirectly through depressing the central nervous system or reducing blood volume. The major contributory factors are myocardial depression and peripheral vasodilatation (which on the arterial side diminishes peripheral resistance and on the venous side causes pooling and reduces venous return). Myocardial depression—for example, by β blocker, tricyclic antidepressant, and dextropropoxyphene poisoning—is an important cause of hypotension and is worsened by hypoxia or acidosis. Circulating blood volume may fall because of dehydration in prolonged coma, persistent vomiting, or fluid loss through abnormally permeable capillaries. Gross hyperventilation (as with severe salicylate poisoning) produces increased insensible fluid loss from the lungs.

Tissue oxygen delivery can be impaired at several levels. Apart from removal or inactivation of the poison, management must be directed at improving tissue oxygenation.

Assessment of hypotension—It is impossible to define rigidly the degree of hypotension that should be treated. A systolic blood pressure of 90 mm Hg is clearly more worrying in an elderly person with atherosclerotic disease than in an otherwise healthy young adult. The patient's age and any history or clinical or electrocardiographic signs of hypertension are therefore relevant. A 12 lead ECG must be done and will also provide a baseline should any further cardiac complications arise. Hypotension is less worrying if tissue perfusion seems adequate—as suggested by warm extremities (with a core to big toe temperature gradient of 5°C or less) and a good hourly urine output.

Management of hypotension—The first steps in severe hypotension are to restore the circulating volume and improve venous return. Raising the patient's legs may suffice as a temporary measure. A large bore intravenous cannula should be inserted and once raised jugular venous pressure and basal crepitations have been excluded, one litre of fluid (Hartmann's solution or isotonic saline) rapidly infused. If, despite this, the blood pressure remains low a central venous line should be inserted and further fluid given to restore the central venous pressure to between +10 and

Cardiac arrhythmias

+15 cm H₂O (measured from the midaxillary line). At this stage a colloid solution is preferable (ideally plasma protein fraction) as more of it will remain in the circulation, minimising any tendency to peripheral or pulmonary oedema. A central venous line should be established earlier in the elderly or in patients with known or suspected cardiac disease. If the central venous pressure is restored to +15 cm H₂O or more and hypotension persists inotropic support is indicated. Dopamine may be preferable, at least at low doses, if oliguria is present, or dobutamine, with its lesser effect on heart rate, if tachycardia or tachyarrhythmias are a problem. If the patient has bradycardia isoprenaline may be used, though the associated fall in peripheral resistance may be a disadvantage. Inotropic drugs should be used with extreme caution in patients treated or poisoned with monoamine oxidase inhibitors.

If, despite adequate volume replacement and inotropic support, the blood pressure does not improve, the central venous pressure may be failing to provide a reliable guide to the filling pressure of the left heart, and a balloon tipped pulmonary artery catheter should be used to measure pulmonary capillary wedge pressure. Other indications for a pulmonary arterial catheter are pulmonary oedema (particularly in the presence of hypotension), adult respiratory distress syndrome, or suspected pre-existing pulmonary vascular disease.

Hypoxia or acidosis will compromise myocardial function and must be corrected

Disturbances in heart rate or rhythm may complicate poisoning with many agents, either as a direct effect of the poison or secondary to hypoxia, hypercapnia, or electrolyte or other metabolic disturbances. These factors must be corrected as a priority. Many antiarrhythmic drugs are potent depressants of both cardiac contractility and conduction and are potentially arrhythmogenic, and so should not be used without careful thought. Because of the enormous potential for drug interactions consideration should be given to non-pharmacological treatment. Simple measures such as carotid sinus massage may suffice, though on occasions direct current cardioversion or temporary transvenous cardiac pacing may be needed.

Severe intoxication with tricyclic antidepressants is often associated with a variety of arrhythmias. Anticholinesterase drugs such as neostigmine or physostigmine have been used to treat tachyarrhythmias on the basis that they may be caused in part by the anticholinergic activity of the antidepressant. The effect of these drugs is, however, unpredictable and this probably reflects the fact that other factors, including quinidine-like activity, underlie the arrhythmias. It has also been suggested that drugs such as lignocaine, disopyramide, and β blockers may enhance cardiotoxicity induced by tricyclic antidepressants. Phenytoin is sometimes effective in managing the arrhythmias.

In digitalis poisoning intravenous phenytoin may suppress ventricular arrhythmias as it accelerates the delayed conduction along Purkinje fibres, particularly in the presence of hypokalaemia. Amiodarone has also proved effective in the few cases treated.

Cardiac arrest

Cardiac arrest may result from direct cardiotoxicity of the agent itself or be secondary to hypoxia or electrolyte or other metabolic disturbances. The general principles of management apply, but two specific points are worth noting. Firstly, fixed, dilated pupils may be a direct manifestation of the poison (anticholinergic agents, glutethimide, or tricyclic antidepressants) or hypothermia and not carry the usual ominous prognostic significance. Secondly, it may be worth persisting with resuscitative measures for longer than usual. There are several reports of successful outcomes after several hours of external cardiac massage and artificial ventilation.

Neurological complications

Major neurological complications

- Central nervous system depression
- Convulsions
- Cerebral oedema

Correct nursing of the unconscious patient is essential.

Blisters, neuropathy, and rhabdomyolysis may occur as a result of pressure in comatose patients.

Central nervous system depression

Severe central nervous system depression leaves the patient unconscious, devoid of vital protective reflexes, and with depressed respiration. In patients found unconscious it is important to exclude a traumatic or metabolic cause (such as hypoglycaemia). Intravenous naloxone may be useful in both diagnosis and treatment, especially in comatose patients with small pupils. The depth of coma and any neurological signs should be recorded so that subsequent changes can be detected. A cerebral function monitor can be used to display continuously a processed electroencephalographic signal which, in the otherwise stable patient, may provide useful information on changes in the depth of coma. Correct nursing of the unconscious patient is essential in helping recovery and preventing further complications. This includes regular turning and attention to pressure areas, mouth and eye care, bladder catheterisation, physiotherapy, and careful, close observation. Adequate nutritional support must not be overlooked.

Blisters—Blisters may appear on the body of a patient who has been in prolonged coma. Common causes include barbiturates and other hypnotic drugs, narcotics, and carbon monoxide. They occur in the usual pressure areas but also in less obvious sites (such as the interdigital web). Erythema of the skin may lead to blister formation, often hours after the patient has arrived in hospital. Areas of blistering should be managed according to routine practice, with the aim of preventing infection.

Rhabdomyolysis—Rhabdomyolysis and myoglobinuria may follow uncontrolled convulsions, but they more often occur in comatose patients after prolonged tissue pressure and muscle ischaemia. This is most often seen with narcotic and hypnotic agents and ethanol and after carbon monoxide poisoning. Local swelling of muscles may be evident; creatine kinase, aspartate transaminase, and urate concentrations may be considerably raised; dangerous hyperkalaemia can occur; and myoglobin may be detected in the urine. Renal failure may result.

Causes of convulsions

Non-specific causes

- Hypoxia
- Hypoglycaemia
- Hypocalcaemia

Some specific causes

- Tricyclic antidepressants
- Theophylline

Convulsions:

- Have adverse cardiorespiratory effects
- Produce metabolic disturbances
- May cause cortical damage

Therefore control is essential

Cerebral function monitor in use.

The effect of 200mg thiopentone on intracranial pressure in a ventilated patient with generalised cerebral oedema

Neuropathy induced by pressure is an occasional complication in the deeply unconscious patient. The loss of response to pain may allow damage to a nerve if the patient remains in a position that results in pressure or traction. The most commonly affected nerves are the common peroneal and radial (producing foot drop and "Saturday night palsy").

Convulsions

Convulsions may be the presenting problem or may occur subsequently. They can be a sign of cerebral anoxia, a metabolic effect, or a direct drug effect on the brain, as, for example, with tricyclic antidepressants or theophylline. Control is essential because convulsions produce adverse cardiorespiratory and metabolic effects, and because of the damaging effect of continuing neuronal discharge on cortical and other neurones.

Treatment of convulsions—Priority must be given to maintaining the airway and oxygenation. Any treatable cause (hypoxia, hypoglycaemia, hypocalcaemia) should then be dealt with. Thereafter, the convulsions can usually be controlled using intravenous diazepam given slowly, in 2 mg increments, up to 20 mg. If this fails, a continuous infusion of diazepam may be considered, though intravenous clonazepam, phenytoin, chlormethiazole, or thiopentone may be needed to control repeated or continuous convulsions. All these agents may worsen respiratory depression. If so, or if the convulsions remain uncontrolled despite initial drug treatment, the patient will need to be anaesthetised, paralysed with neuromuscular blocking agents, and artificially ventilated. In this case the anticonvulsants should be continued and the patient watched carefully for evidence of continuing convulsive activity. This is clearly difficult when neuromuscular blocking drugs have been given, and a cerebral function monitor should be used if available. Failing this, sudden changes in pulse rate and blood pressure may indicate continuing convulsions.

Cerebral oedema

An acute anoxic insult to the brain is the most likely cause of cerebral oedema. This may be directly related to the poison, as with carbon monoxide, or may follow a cardiorespiratory arrest, severe respiratory depression, or profound hypotension. The management is to treat the cause where possible, but is otherwise based on measures to reduce intracranial pressure. Paralysis with neuromuscular blocking agents and artificial ventilation to produce moderate hypocapnia (P_{aCO_2} 3.5–4.0 kPa, 26–30 mm Hg) are well established methods. By ensuring optimal chest wall compliance and by preventing coughing or straining, the paralysis keeps intrathoracic pressure as low as possible and so minimises any cerebral venous congestion. Moderate hyperventilation, by reducing cerebral blood flow, lowers intracranial blood volume and hence intracranial pressure. This effect, however, may last as little as six hours and the major advantage of artificial ventilation thereafter is in preventing coughing or straining and damaging fluctuations in blood gases. Intravenous opioid agents help to settle the patient on the ventilator and also minimise increases in intracranial pressure due to chest physiotherapy and other manoeuvres. Further measures aimed at controlling intracranial pressure include the use of osmotic diuretics or frusemide, positioning the patient with a head up tilt, and avoiding any pressure on the neck.

Continuous infusions of intravenous anaesthetic agents reduce cerebral oxygen requirements and further reduce cerebral blood volume, though any hypotension produced may outweigh this benefit. The value of cerebral protection with "high dose" intravenous barbiturates has yet to be established. Similarly, there is no evidence that steroids have any useful role in treating global anoxic cerebral damage. When possible the direct measurement of intracranial pressure may aid management, particularly in cases complicated by circulatory or respiratory problems.

Prompt attention to circulation and respiration may initially improve neurological signs. If the anoxic insult has been severe, however, then

- Persisting drug intoxication
- Hypothermia (35°C)
- Metabolic disturbances

May all occur in poisoning and exclude a diagnosis of brain stem death. If in doubt do not make the diagnosis

Renal complications

Oliguria

- Prerenal
 - clinical signs of hypovolaemia
 - urine sodium concentration ≤ 10 mmol/l
 - urine:plasma osmolality $>1.1:1$
 - a fluid challenge may provide confirmation
- Renal
 - urine sodium concentration ≥ 25 mmol/l
 - urine:plasma osmolality $<1.1:1$ (unless diuretics have been administered in last 24 hours)
- Postrenal
 - exclude obstruction / blocked catheter
 - drug crystals (eg acetazolamide), oxalate crystals (eg ethylene glycol), and urate crystals are rare causes

Hepatic and metabolic complications

Metabolic acidosis

Non-specific causes

- Hypoxia
- Circulatory failure
- Renal failure

Some specific causes

- Salicylates
- Methanol
- Ethylene glycol
- Ethanol
- Tricyclic antidepressants
- Paracetamol
- Carbon monoxide
- Isoniazid
- Iron

deterioration may occur, often on the second day. The delay presumably reflects the time taken for the progressive accumulation of cerebral oedema and rise in intracranial pressure. There seems little point therefore in providing ventilatory and other support for the usual, arbitrary 24 hours, and an initial period of 72 hours is probably more reasonable in cases where there has clearly been a severe anoxic insult.

After severe cerebral hypoxia brain stem death may result, although it is less common than a persistent vegetative state. The guidelines published by the Conference of Medical Royal Colleges and their Faculties in the UK clearly define the steps to be taken in diagnosing brain stem death. They emphasise the need for extreme caution if intoxication is suspected. If this is so then it is essential to consider the likely clearance rates of the relevant poisons and, if there is any doubt, to send blood samples for toxicological analysis.

While circulatory failure and hypotension of acute poisoning may alone produce renal failure, other factors may also contribute. Rhabdomyolysis with myoglobinuria is an important cause of acute renal failure. Acute haemolysis and haemoglobinuria can occur with arsine or stibine gas poisoning. Nephrotoxic effects may also be seen after poisoning with heavy metal salts. The renal failure which follows ethylene glycol is partly due to the deposition of calcium oxalate in the tubules, though other factors may be implicated. Paracetamol poisoning may also produce acute renal failure, sometimes in the absence of severe liver damage.

A urinary catheter should be inserted in any severely poisoned patients, particularly if they are comatose or hypotensive. Urine output should be closely monitored. In the oliguric patient (urine output less than 0.5 ml/kg/hour) the clinician must attempt to make the distinction between prerenal causes, intrinsic renal damage, and postrenal causes. Having established this, treatment follows conventional lines. In some cases acute renal failure may develop without oliguria. The principles underlying the management of established renal failure are the same regardless of the cause. If haemodialysis is indicated for acute renal failure, it may also remove any remaining poison and correct any other related metabolic disturbances.

Hepatic complications

Occasionally poisoning may be followed by fulminant hepatic failure (as, for example, after paracetamol, carbon tetrachloride, or *Amanita phalloides*). The extraordinary capacity of the liver for regeneration means that the patient who survives has every chance of regaining normal liver function. These patients develop multiple problems and should be treated in an intensive care unit. The best results are obtained in specialist liver units, though patients with fully developed hepatic failure with established cerebral, respiratory, circulatory and metabolic problems travel poorly. If there is any suspicion, therefore, that specialist treatment may be needed, early discussion and, if appropriate, transfer, should be undertaken without delay.

Metabolic complications

Metabolic complications may take almost any form. Biochemical abnormalities such as hypoglycaemia or hypokalaemia can be easily detected and treated if present. Disturbances in body temperature, especially hypothermia, may also occur.

Metabolic acidosis—Tissue hypoxia, renal failure, and the direct biochemical effects of many toxins can lead to a severe metabolic acidosis, which must be corrected by treating the cause when possible. Sodium bicarbonate may be necessary to restore the arterial pH in the most severe cases, in which there is evidence of disturbed myocardial function.

Hypothermia will be missed unless a low reading thermometer is used

ECG showing bradycardia with J waves in a patient with hypothermia

Hypothermia—Hypothermia is a common complication of poisoning, particularly if the ambient temperature is low or there has been a long delay before the patient was found. Hypothermia in comatose patients results from diminished heat production (through lack of muscle activity and general depression of metabolic rate) and increased heat loss (through cutaneous vasodilatation). The major danger in hypothermia lies in the increasing likelihood of ventricular arrhythmias and ultimately ventricular fibrillation as the core temperature falls below 30°C. The rectal temperature should be taken with a low reading thermometer or the condition may be missed. In severe hypothermia the pupils are fixed and dilated and tendon reflexes may be depressed. The electrocardiogram usually shows sinus bradycardia and, occasionally, J waves. The safest treatment is to rewarm the patient passively by covering him with a "space blanket." Oesophageal (ideally) or rectal temperature and the electrocardiogram should be monitored continuously. In severe hypothermia (core temperature of less than 30°C) active rewarming may be considered. Active surface warming in this condition can be dangerous. It may produce peripheral vasodilatation at a time when the core, and hence cardiac, temperature is still depressed, and consequently the heart may be unable to cope with the additional demand. Various methods of active central rewarming have been used, including artificial ventilation with warmed gases, peritoneal lavage, or gastric irrigation with warm fluids and even extracorporeal circulation. Such methods are rarely necessary. Should the patient require intravenous fluids these must be warmed. There is good evidence that if blood gas and acid-base measurements are made with the sample at 37°C correction of the result for the patient's temperature is unnecessary. If cardiac arrest occurs, it is worth persisting with cardiopulmonary resuscitation for long periods.

Hyperthermia is uncommon but is most often seen in anticholinergic poisoning in children, in whom the associated hallucinations, tachycardia, and dilated pupils are characteristic. Surface cooling is usually all that is needed. Hyperthermia may be associated with antidepressant overdose; mild degrees are sometimes seen with tricyclic antidepressants (though hypothermia is more common), but a more malignant form is associated with severe poisoning by monoamine oxidase inhibitors. With the latter it seems to be related to gross overactivity in skeletal muscle, and the core temperature may rise rapidly to above 41°C. The basis of temperature control in such cases is the early use of muscle relaxants such as pancuronium (and therefore artificial ventilation), and dantrolene may have a role.

Other complications

Complications should be foreseen and prevented

Acute poisoning may be complicated by many other conditions. These include disseminated intravascular coagulation, deep vein thrombosis and pulmonary embolism, bleeding from oesophageal or gastric erosions, and the complications of the various treatments that may be used. Limited space precludes consideration of all the possibilities, but the principle that prevention should, where possible, be the aim, will bear repeating.

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