Clinical Toxicology

THIRD EDITION

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Preface

Owing to the untimely death of Rex Tattersall I had to seek elsewhere for help in the preparation of this edition. I was indeed fortunate when Michael Green and Michael Lee agreed to be my co-authors.

The authorship of each of the chapters is indicated in the Table of Contents. I have retained the responsibility for those which I contributed to the earlier editions. Following scrutiny by my co-authors and the receipt of forthright but tactful comments severe pruning and a fair amount of rewriting was done.

My co-authors have rewritten and expanded pre-existing chapters and have added a good deal of new material. This has appreciably widened the scope of the book and improved its quality.

Throughout the preparation of this edition there has been complete harmony and I have enjoyed this collaboration.

We have tried to achieve a balance between the older literature on poisoning and the more modern information on analysis and biochemical mechanisms, while at the same time keeping in the forefront of our minds the practising physician and pathologist. Although not claiming to be comprehensive we hope that sufficient references to the original literature are contained to serve as a guide to the common and, indeed, to the uncommon poisons.

Several excellent pocket-size textbooks are now available. We hope that this work will bridge the gap between these and the large laboratory reference manuals.

Harrogate
April 1983

CYRIL POLSON

Acknowledgements

We are indebted to the various Coroners in the area served by our Department for permission to refer to cases and inquests. These Coroners include P S Gill, Esq, J A Turnbull, Esq, and A Morris, Esq. Their predecessors, notably J D Walker, Esq, OBE, have also been most helpful.

We would particularly thank Dr D MacKinnon, Pathologist at York District Hospital, for a copy of his autopsy report upon the carbon monoxide victim described by Dr King and Detective Chief Inspector Jobson; Professor W A Harland, MD, FRCPath, Regius Professor of Forensic Medicine, University of Glasgow, for information concerning the products of combustion in fires; and Ms Daphne Gloag, Staff Editor, *British Medical Journal*, for a copy of the Shipham Survey Committee's report on Soil Contamination.

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Mr R A Dalley, Public Analyst to West Yorkshire Metropolitan Council, and his colleagues, Mr L A Perkin and Mr F Henson, have given valuable help on innumerable occasions. Other colleagues, medical and scientific, have given generously of their time and skill. The Librarians in charge of the Medical Libraries at Leeds Medical School and St James's University Hospital have helped us in tracing references.

Finally, we thank Miss Pauline Whitaker and Mrs Julie Roger who have coped with our handwriting, and our frequent changes of mind; and

Katharine Watts and Howard Bailey of Pitman—they had a lot to put up with!

Publisher's Note

Many of the quantities given in older case references are quoted in Imperial and/or British apothecaries' measures.

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Note. The authorship of the various chapters is set out below. The numbers in italic indicate those chapters of which the author had a share of the writing.

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5, *6*, *12*, *14*, *15*, *20*, *21*, *28*
M R Lee: 1, 2, 3, 6, 22, 24
5, *12*, *20*, *28*

1 The Diagnosis of Poisoning

In the present clinical scene poisoning is usually self-inflicted; either as a deliberate suicidal attempt or as an attempt to gain sympathy or manipulate the environment, the so-called parasuicide. Murder by poisoning is now unusual and accidental exposure at work or at home is also rare. Poisoning in children, either accidental or deliberate, is a separate problem and will be dealt with in Chapter 3.

In acute poisoning the circumstances may arouse suspicion. A sudden illness occurs in a person previously in good health and the onset of symptoms is shortly after taking food, drink or medication. Other people may be affected or, more commonly, the patient is found alone and unconscious with empty tablet containers and even a suicide note. Alcoholic beverages are often found close to the body of the victim and they may have drugs dissolved in them. There might be a characteristic odour on the patient's body or breath: acetic acid; ammonia or phenol; the bitter almonds smell of cyanide; the irritant effect of formaldehyde. The skin and mouth should be inspected for signs of corrosive poisoning; and also for blistering. Blisters are most often seen with barbiturate overdose, but can be observed also in poisoning with other sedatives: the tricyclic antidepressants or carbon monoxide. They are seen most commonly where two surfaces of skin come into contact.

The body of the patient should also be inspected carefully for the marks of venepuncture in the antecubital fossae and on the backs of the hands. There may be bruising due to extravasation of blood, induration due to venous thrombosis and microabscess formation. The risks of pulmonary embolism and bacterial endocarditis should also be kept constantly in mind in the subject who 'mainlines' drugs intravenously. If opiate overdose is suspected then intravenous injection of naloxone can be both diagnostic and life-saving.

Symptoms and Signs of Poisoning

Certain constellations of symptoms produced by poisoning can cause considerable diagnostic confusion and these will be considered separately:

1 gastrointestinal irritation,
2 delirium,
3 coma,
4 convulsions,
5 polyneuritis.

Gastrointestinal Symptoms

The layman usually associates vomiting, diarrhoea and abdominal pain with poisoning but most commonly, rather than a chemical irritant, this turns out to be caused by a bacterium or virus. Several people may be affected at the same time and here it is valuable to preserve any remnants of food or drink that has been taken. In children Henoch-Schönlein anaphylactoid purpura may affect the gut and mimic exactly in its clinical presentation gastroenteritis caused by poison. The severe form of ulcerative colitis with a fulminating onset may also cause diagnostic difficulties in adults.

Delirium and Coma

Alcohol and cocaine may be associated with deprivation delirium. It may also complicate barbiturate addiction and be accompanied by major epileptic convulsions when drug addiction has been gross and prolonged. Signs of peripheral neuritis may be present as a result of deficiency of thiamine or other members of the B vitamin group. Metabolic disorders such as uraemia, hyper- and hypoglycaemic coma, myxoedema and thyrotoxicosis may closely imitate poisoning with delirium, and suitable clinical and biochemical investigation may need to be undertaken to exclude these disorders.

Coma may present great difficulty in diagnosis particularly if there is no history available. It is a wise general rule that anyone admitted to hospital in coma between the ages of 15 and 35 should be suspected of deliberate self-poisoning. Careful physical examination will usually exclude cerebrovascular accident, meningitis or head injury.

Psychiatric disorders such as depression and schizophrenia may present as stupor but usually there is little diagnostic difficulty here. Confusion sometimes arises between diabetic ketoacidosis and salicylate

poisoning, as a consequence of the forced Kussmaul respiration common to both conditions, but examination of blood and urine will usually resolve the problem without continued difficulty.

Convulsions

Many poisons taken by infants can produce serious convulsions, for example the H_1 antihistamine drugs, ferrous sulphate, amphetamines and other stimulant drugs. Fits are also a feature of lead encephalopathy, again particularly in young children, or when an organic lead compound is inhaled. In adults many drugs can cause convulsions, for example penicillin, insulin and amphetamine-like compounds. The distinction from idiopathic generalized epilepsy is usually made easily.

Polyneuritis

Wasting of the muscles of the limbs, together with weakness and depressed (or absent) tendon jerks is seen in many forms of acute or chronic poisoning such as that due to arsenic, thallium, alcohol, carbon disulphide and the organic phosphorus compounds. These toxic polyneuritides must be separated from other varieties such as post-infectious (Guillain Barré syndrome), diabetic, intermittent porphyric, carcinomatous, and that due to polyarteritis nodosa.

In lead poisoning the extensors of the wrist are usually weak. Glycosuria can occur in thallium poisoning, and increased excretion of porphyrins in lead poisoning. This may result in misdiagnosis as diabetic and porphyric polyneuritis respectively. Chemical detection of the metal in blood, urine or hair will aid the diagnosis.

Finally, three conditions must be mentioned that can mimic chronic poisoning exactly. Polyarteritis, with its polyneuritis, abdominal pain and renal damage, can imitate heavy metal poisoning closely, as can disseminated lupus erythematosus with polyneuritis, hair loss, delirium and convulsions. Acute intermittent porphyria can cause a motor polyneuritis together with abdominal pain and convulsions. The diagnostic situation may be further clouded in porphyria by the provocation of attacks by barbiturate or other sedative drugs. Here the situation may be clarified by a positive family history and by the passing of a dark red urine, going darker on standing and containing an excessive amount of porphobilinogen.

Further Reading

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2 The Treatment of Poisoning

The treatment of poisoning can be divided into a number of headings:

1 the general management of poisoning;
2 the management of shock;
3 the management of respiratory complications;
4 the administration of specific antidotes;
5 accelerated elimination of the poison by forced diuresis, dialysis, or charcoal haemoperfusion.

The General Management of Poisoning

The first decision to be made by the attending physician is whether to admit the poisoned patient. This decision is often not as straightforward as it might appear. The tablets taken may be unknown; the patient may be unwilling or unable to give a clear account of his actions. Some drugs may have a delayed effect, for example paracetamol or ferrous sulphate. The coincidental taking of alcohol may also blur the clinical picture.

It is often wise to admit the patient, at least overnight, to an acute holding ward where the extent of the overdose can be evaluated; information can be obtained on the toxicological hazards of the particular compound and psychiatric advice can be obtained.

No physician can be familiar with the poisonous hazards of all the drugs available to the patient intent on suicide. Here mention must be made of local poisons information centres usually sited in teaching hospital pharmacies. There is also the National Poisons Information Service, sited at strategic centres within the United Kingdom.

Most patients who are poisoned will recover with simple supportive treatment. A minority will require full intensive care which may include dialysis and even charcoal haemoperfusion.

The first priority in an overdose is to maintain the airway by means of an oropharyngeal airway if there is any risk of respiratory depression. This will enable the administration of oxygen and prevent the tongue falling back and obstructing the pharynx. The semiprone head down position should be maintained as this minimizes the risk of inhaled vomit. Gastric lavage increases the risk of aspiration of vomit and, if the patient is deeply unconscious, a cuffed endotracheal tube should be passed to prevent this complication.

Two measures are available to reduce or prevent the absorption of ingested poison. They are gastric lavage and therapeutic emesis. The former is the usual method in hospital, whereas the latter is often employed as a first aid measure.

Gastric lavage is usually carried out with a wide bore tube lubricated with Vaseline or glycerine. It is essential to make sure that the tube is not in the trachea and this can be done by injecting a small volume of air down the tube and listening over the stomach with a stethoscope. The stomach is then washed out three to four times with 300 to 400 ml of water and aliquots of the washings saved for subsequent analysis. Gastric lavage should only be employed with caution when corrosives have been taken as there is a risk of perforation of the oesophagus or stomach. It should be avoided altogether when petroleum spirit has been swallowed as there is a serious risk of aspiration pneumonia.

An alternative method of emptying the stomach, particularly in children, is to use emetic drugs or procedures. Stimulation of the pharynx is often unsuccessful and the most widely adopted method is that of the oral administration of syrup of ipecacuanha. The usual dose is 10 ml for children from 6 to 18 months of age; 15 ml for older children and 30 ml for adults. The preparation employed should be Paediatric Emetic Draught BPC. Ipecac contains several emetic alkaloids including emetine and cephaeline and was once widely used for the treatment of amoebic dysentery. It has now been abandoned due to its cardiotoxicity.

The alkaloids act both by direct irritation of the stomach (and upper gut) and also by stimulation of the vomiting centre in the medulla oblongata. Ipecac is contraindicated in poisoning with petroleum products; where there is marked sedation; and if antiemetic drugs such as phenothiazines or H_1-antihistamines have been taken.

Other emetics, such as sodium chloride or copper sulphate by mouth, or apomorphine by injection are now obsolete. Oral salt is particularly dangerous as it can lead to dangerous hypernatraemia due either to a failure to induce vomiting, or to the administration of an excessive dose. The author has personal experience of a fatal case of mesenteric arterial

thrombosis in an elderly lady associated with a plasma sodium of 175 mmol/l where death from the overdose was unlikely to have occurred. Other workers have reported similar findings [1].

Some attention has been paid to the use of oral adsorbents to further limit the uptake of poison by the stomach or gut. Recently, Medicoal has become available which is an effervescent form of activated charcoal. This preparation is in a fine particulate form with a large surface area for adsorption. It should be remembered that it is an adjunct to stomach wash-out (or emesis) and not a substitute. The usual dose of charcoal is 5 to 10 g in a glass of water and this adsorbent may be particularly useful in poisoning with drugs such as the tricyclic antidepressants.

Management of Respiratory Depression and the Lung Complications of Poisoning

In the severely poisoned patient with respiratory depression it is essential to assess the adequacy of ventilation. Minute volume, respiratory rate and arterial blood gases should be measured simultaneously. Minute volume is measured with a Wright meter attached by a face mask, or by direct connection to the expiratory valve of the endotracheal tube. A minute volume of less than 4 l/min is usually associated with significant depression of respiration.

A high respiratory rate caused by drugs, or an associated metabolic acidosis, may be associated with inadequate overall ventilation as only the dead space is being aerated. In these circumstances it is essential to measure PaO_2 and $PaCO_2$ in the arterial blood gases. Several points about the blood gases should be borne in mind. If the patient has had chronic obstructive airways disease PaO_2 may have been low to start with and also poisonous compounds can artificially lower $PaCO_2$ initially, either by direct stimulation of the respiratory centre (e.g. salicylates) or by depression of metabolism (e.g. barbiturates, phenothiazines). If the patient is thought, or even suspected, to have taken opiates then naloxone should be given intravenously and repeated regularly. The improvement in minute ventilation and blood gases with naloxone should be measured.

Oxygen should be given in incremental steps in an attempt to raise PaO_2 to 10.7 kPa (80 mmHg); first with 24%, then 28%, and still higher concentrations when necessary. If this partial pressure of oxygen cannot be maintained or the $PaCO_2$ rises above 6.6 kPa (50 mmHg), particularly

if minute volume remains below 4 l/min, then the patient will probably require positive pressure ventilation. Pressures of 5 to 10 cm of water are usually required and will often give rise to a maintained improvement in PaO_2. Airflow obstruction may be produced by the inhalation of gastric contents; by pulmonary oedema or pneumonia and will necessitate a rise in input pressure, an ominous sign of patient deterioration.

Pulmonary oedema is a serious consequence of poisoning with irrespirable gases (q.v.) and with certain other poisons such as salicylate. The pulmonary capillaries leak plasma into the interstitial space and this is usually associated with an increased respiratory rate and parallel deterioration in the blood gases. Diuretics such as intravenous frusemide will reduce the fluid overload component but will not reverse the damage to the pulmonary capillaries. Inhalation pneumonia is usually a complication of acid gastric contents entering the trachea and bronchial system. The material finds its way to the lowest part of the lung and may manifest itself as an area of pneumonia on the chest X-ray. Severe airflow obstruction may develop, due probably to the effect of acid on 'irritation' receptors in the bronchial tree. Chemical pneumonia is often followed by the secondary development of lung abscesses.

Bronchospasm should be treated as for severe asthma, with salbutamol, theophylline derivatives (including aminophylline) and large doses of intravenous hydrocortisone. Antibiotics, for example ampicillin, should be given. If a lung abscess develops then metronidazole should be added to deal with the element of Gram-negative infection.

In some patients who are unconscious for a prolonged period basal atelectasis may develop with sputum retention and secondary infection. Broad spectrum antibiotics should be given, sputum and blood culture specimens taken, and regular turning of the patient together with physiotherapy continued.

Progressive respiratory failure may be caused by the adult respiratory distress syndrome [2]. This is usually seen within 12 to 24 hours of a major injury, or overdose, and is associated with hypotension. There seems to be a marked rise in pulmonary venous pressure with increased pulmonary capillary leak. Platelet aggregation may take place in the pulmonary circulation with the release of vasoactive substances.

Positive pressure ventilation is usually effective but may lead to a reduced cardiac output. It is then essential to measure central venous pressure and left atrial wedge pressure (by Swann Ganz catheter) to ensure careful balancing of the greater and lesser circulations. Whereas the complication of respiratory distress syndrome was usually uniformly fatal, recent series show only a 10 to 30% mortality.

Cardiovascular Collapse (Drug-induced Shock)

Shock has been defined as peripheral circulatory failure which results in an inadequate bood supply to vital organs. As a result of this inadequate blood supply, arterial PaO_2 falls; there is a rise in arterial lactate levels, accompanied by a fall in pH, signalling acidosis.

The clinical signs include a blood pressure less than 80 mmHg systolic, together with tachycardia, a cold pale skin, collapsed peripheral veins and oliguria. The main feature of shock due to drugs seems to be a relative dilatation in the venous bed with a somewhat diminished plasma volume. Venous return to the heart is reduced with a resulting fall in cardiac output and arterial pressure. As a result of the reduced venous tone there may also be an escape of fluid into the extravascular space increasing tissue turgor and further compromising blood supply to the organ.

Certain drugs are particularly associated with a serious fall of blood pressure and shock. They include the phenothiazines, barbiturates and opiates. Each group of drugs has specific properties which may induce or aggravate shock. The phenothiazines (e.g. chlorpromazine) have a powerful alpha-adrenergic blocking effect dilating peripheral arterioles and veins. The barbiturates have both peripheral vascular and myocardial depressant effects. Opiates, on the other hand, depress respiration and can also produce significant peripheral vasodilation, perhaps partially due to histamine release. In prolonged shock of any kind it is likely that enkephalins may be released into the bloodstream, perhaps from the adrenal medulla, and naloxone may therefore have a non-specific effect in raising the blood pressure, not confined to its pressor effect in opiate overdose.

The Management of Shock in Drug Overdose

There are three main methods of combating shock in the drug-induced syndrome:

1 expansion of intravascular volume by transfusion;
2 vasoactive drugs;
3 correction of metabolic acidosis.

1 Infusion of colloid substances

Generally crystalloids, such as normal saline, are of little value in this form of shock as they simply add to the volume of the extravascular space by diffusion through the capillary walls. Colloids such as high molecular