CLINICAL TOXICOLOGY

CLINICAL TOXICOLOGY

C. J. POLSON

MD(Birm.), FRCP, FC Path, MRCS

of the Inner Temple, Barrister-at-Law,
Professor of Forensic Medicine, University of Leeds,
Honorary Consultant in Pathology to the Leeds
('A' Group) Hospital Management Committee

AND

R. N. TATTERSALL

OBE, MD(Lond.), FRCP

Consultant Physician to the United Leeds Regional Hospital Board
and to the Leeds Regional Hospital Board,
Senior Clinical Lecturer in Medicine, University of Leeds

London

Pitman Medical Publishing Company Ltd

First published 1959 by The English Universities Press Ltd
Second edition published 1969 by Pitman Medical Publishing Company Ltd

PITMAN MEDICAL PUBLISHING COMPANY LTD
46 Charlotte Street, London, W1

Associated Companies

SIR ISAAC PITMAN AND SONS LTD
Pitman House, Parker Street, Kingsway, London, W.C.2
P.O. Box 6038, Portal Street, Nairobi, Kenya

SIR ISAAC PITMAN (AUST.) PTY. LTD
Pitman House, Bouverie Street, Carlton, Victoria 3053, Australia

PITMAN PUBLISHING CORPORATION (S.A.) PTY. LTD
P.O. Box 7721, Johannesburg, Transvaal, S. Africa

PITMAN PUBLISHING CORPORATION
20 East 46th Street, New York, N.Y. 10017

SIR ISAAC PITMAN (CANADA) LTD
Pitman House, 381–383 Church Street, Toronto, 3

THE COPP CLARK PUBLISHING COMPANY
517 Wellington Street, Toronto, 2B

SBN: 272 79288 8

Printed in Great Britain at the Pitman Press, Bath
21 3029 11

Preface to Second Edition

We are grateful to all the reviewers of the first edition for their kind, and indeed generous, response to the first edition of this work. In the light of their constructively critical remarks, we have taken the opportunity in this second edition to rewrite several sections and have introduced new material to bring the text up-to-date. Coverage has also been extended to include a number of poisons omitted from the first edition, e.g. petroleum products, tetrachlorethane, Trilene, 'glue sniffing', and several other sources of poisoning (q.v.).

Our aim continues to be the consideration of poisoning in domestic as opposed to industrial circumstances; some slight overlap is unavoidable. In respect of each poison, therefore, we attempt to answer three main questions: In what ways can this poisoning occur in the home? What are its ill-effects, and what is the appropriate treatment? Additional 'background' information, e.g. the probable lethal dose, the post-mortem findings etc., is also given.

We have excluded iatrogenic poisoning because it has now attained a position of such importance that it merits separate treatment.

Those interested in the scientific aspects of toxicology and toxicological analysis must seek elsewhere for information. Fortunately, it is to be found in the well-known works of other authors.

Preface to First Edition

This book is intended primarily to describe the clinical features of poisoning in the home. Industrial poisoning and toxicological analysis are adequately described by others and trespass into their fields, therefore, has been avoided wherever possible.

A complete account of all known poisons has not been attempted because this would be impracticable in one volume of moderate size. The scope has been restricted to the common poisons, and those which, although uncommon, have practical importance; a few others have also been included because of personal interest in them.

No rigid plan has been followed since not all of the poisons described allow the same approach. In the main, however, the account of each is introduced by a general statement, and the relative importance of the poison is shown by reference to the incidence of cases. The possible sources of the poison are then discussed, followed by an account of circumstances in which the poisoning may occur. The lethal dose is given. Clinical manifestations, treatment and prognosis are considered in detail, and the post-mortem findings are also described.

The text is supported by illustrative cases and references, the prime purpose of which is to indicate the origin of facts and opinions, other than our own, stated in the text. The bibliography is selective but it includes most, if not all, of the principal references. The illustrative cases are drawn from our own practice—the serial numbers, e.g. FM 4114, relate to cases in the Department of Forensic Medicine, University of Leeds—but synopses of a number of excellent reports in the literature have also been prepared and used.

The book is intended for all, but in particular physicians, whose concern is clinical toxicology and it is hoped that it will increase interest in this subject.

Acknowledgements

We are indebted to the late R. E. Nutt, Esquire, LLB, HM Coroner for the City of Leeds, and to his immediate predecessor, Dr A. J. Swanton, for permission to consult and use the valuable records of their Court. We also thank a number of other Coroners for copies of depositions at Inquests held by them, and permission to use this material. These Coroners include: W. Blackhurst, Esquire, OBE, Stephen E. Brown, Esquire, LLM, E. T. Heap, Esquire, Norman Jennings, Esquire, H. Evans Jones, Esquire, R. Llewellyn Jones, Esquire, B. W. Little, Esquire, OBE, H. W. Rennison, Esquire, and Innes Ware, Esquire, OBE.

We owe a special debt to Dr F. G. Tryhorn, DSc, Dr A. S. Curry, MA, PhD, Dr M. R. R. Davies, LLM, PhD, DPA, Mr A. R. Taylor, MA, Professor Ester Killick, Dr Ian Dawson, Dr Gerald Evans and Dr T. K. Marshall for reading sections of the text and for their expert comments.

We thank Dr W. D. Buchanan, HM Medical Inspector of Factories, for supplying information concerning notifiable industrial diseases during 1932–53. Other material, in the form of autopsy records or toxicological reports, has been provided by: Dr Ian Dawson, Dr Gerald Evans, Dr Kenneth Frome and Dr William Goldie, pathologists, and Dr J. B. Firth, CBE, Mr L. C. Nickolls and Dr F. G. Tryhorn, Directors of Home Office Forensic Science laboratories. We are also indebted to Dr W. Fyffe Dorward, Dr E. W. Jackson, Dr B. A. Kilby, Dr G. A. Mogey and Professor Harald Gormsen for material.

The use of published work has been readily granted by Mr James Hodge, who allowed us to use the Notable British Trials series. Others include Messrs Christopher Johnson and Professor John Glaister, DSc, MD, FRS Ed, JP (the Merrifield case in *The Power of Poison*); Messrs George Harrap and Mr Douglas G. Browne and Mr E. V. Tullett (the Varenhorst case in *Bernard Spilsbury*); and the Editor of the *Practitioner* and Dr T. K. Marshall ('Bee and Wasp Stings'). We are also indebted to the Editor of *The Lancet* and the Editor of the *British Medical Journal*, together with those authors of case reports whom we have been able to

consult, for permission to cull illustrative cases from *The Lancet* and the *British Medical Journal*.

We thank the Controller of HM Stationery Office for permission to reproduce a substantial part of his publication *The Duties of Doctors and Dentists under the Dangerous Drugs Act and Regulations* (DD 101, 6th Ed, Home Office, March, 1956).

We thank Miss Eileen Read, BA, Sub-Librarian, in charge of the Medical Library, University of Leeds, for her assistance in tracing and checking references. We also thank those who have assisted us in proof-reading and, in particular, Miss Joy Bradley.

The tedious and arduous task of transcribing the manuscript has been in the capable hands of Miss Pamela Bradley and Miss Helen Bottomley, to whom we are also indebted for other secretarial assistance. In the preparation of the second edition we also had the assistance of Miss Lorraine Guy.

Contents

PART ONE

A General Consideration of Poisoning

PART ONE

A General Consideration of Poisoning

1

The Diagnosis of Poisoning

The symptoms of poisoning are so diverse that difficulties in diagnosis are usual unless a clear history is obtained of the administration of a particular substance. Fortunately poisoning is also comparatively rare, but for this reason the possibility of its occurrence may be overlooked. In acute poisoning the circumstances may arouse suspicion; a sudden illness in a person previously in good health and particularly if the onset is shortly after taking food, drink or medicine, and if other people are affected. In chronic poisoning the difficulties are much greater and indeterminate gastro-intestinal or neurological symptoms always merit full investigation and, if possible, the segregation of the patient from his domestic and working environments. Although most poisoning is suicidal or accidental there is always a possibility of homicide and occasionally of self-administration in psychotic individuals with the deliberate intention of producing an interesting or puzzling group of symptoms.

Poisoning by the corrosive group of substances is not likely to be overlooked; in most cases there is some obvious damage to the mucous membranes of the mouth, but if the substance has been swallowed rapidly this may be minimal on the lips and face and only apparent on a full oral examination. Some of the corrosives have also a characteristic odour, for example acetic acid, ammonia or phenol, and others, such as potassium permanganate and nitric acid, a striking colour. Certain other groups of symptoms produced by poison are much more puzzling and present considerable diagnostic difficulties, and these will be considered under separate headings.

Gastro-intestinal irritation

Vomiting, abdominal colic and diarrhoea are considered by the layman to be the cardinal signs of poisoning and it is most often in this group that the patient's relatives consider poisoning to be a likely diagnosis. When several people have been affected within a few hours it may be possible to incriminate a particular food as the vehicle of the irritant and if any of this remains it should be preserved for chemical and bacteriological

examination. In the vast majority of instances a bacterial toxin is responsible for the symptoms if they develop suddenly, and a bacterial or virus infection if they develop after twelve to forty-eight hours. The latter group commonly have some febrile reaction. Chemical irritation of the gastro-intestinal tract often produces vomiting as an initial symptom, whereas this is much less common in the dysenteric group of infections, though it may be prominent in cholera. In children the onset of any febrile condition may be preceded by vomiting and bowel disturbance, and this also applies in peritoneal irritation and Henoch–Schönlein disease. Obstructive lesions of the small intestine frequently present with abdominal pain, vomiting and diarrhoea, and vomiting may be a prominent feature of meningeal irritation from any cause.

Chronic bowel looseness, with or without colic, and wasting may be due to chemical irritants, but is more often due to mechanical irritation from colonic neoplasm, Crohn's disease, ulcerative colitis, diverticulitis, gastro-colic fistula, steatorrhoea, or simply a nervous over-activity of the gastro-colic reflex and colonic motility. Clinical experience during the past ten years suggests that this last form of neurogenic colic and diarrhoea is an increasing problem, particularly in women. If chronic chemical irritants are suspected the patient should be admitted to hospital for investigation under controlled surroundings, though the daily visiting which is now customary makes this control more difficult than in the past.

Delirium

By tradition, toxaemia due to chemical poisons or metabolic disturbance, and pyrexia are regarded as the causes of delirium and to these we must add certain deficiencies of the 'B' group of vitamins, anoxia, traumatic, vascular or inflammatory brain lesions, rarely acute psychoses and the deprivation symptoms produced by lack of barbiturates, alcohol and narcotic drugs.

Generalised systemic infections are unlikely to present great difficulty, but on occasion occult infection may produce minimal febrile response, but quite severe toxic delirium, particularly in elderly people. Urinary tract infections and chronic bacterial endocarditis should always be considered in this context. Tuberculous and meningococcal meningitis and cerebral abscess should be excluded in most cases by examination of the cerebrospinal fluid and focal brain lesions by the presence of specific neurological changes. Head injury may be difficult to exclude in the absence of any specific history.

Cerebral anaemia may result from cardiac or respiratory failure with the corresponding physical findings, but also from anaemia of any type and from carbon monoxide poisoning. The sudden cerebral changes which may accompany severe gastro-intestinal bleeding may be very puzzling, but a

rectal examination will usually reveal the presence of melaena. Deprivation delirium usually occurs in addicts who have had their supply of drugs restricted. Alcohol and cocaine may be associated with this type of delirium and it may complicate barbiturate addiction and be accompanied by major epileptic convulsions when addiction has been gross and prolonged.

Deficiency of the 'B' group of vitamins is likely to occur in the elderly, the psychotic or the alcoholic and in those who have some major gastro-intestinal defect, resulting in inadequate absorption. The signs of peripheral neuritis, other vitamin deficiencies and of the loss of the filiform papillae from the tongue usually help in the diagnosis, but a therapeutic test using a massive dose of the 'B' complex intravenously may be necessary before this cause can be excluded. Metabolic disturbances include uraemia and cholaemia, hyperinsulinism, ketosis, myxoedema and thyrotoxicosis, but in all these conditions there are likely to be specific physical and biochemical findings. The chemical poisons most frequently associated with delirium are the barbiturates in small doses, chronic bromide intoxication, alcohol, hyoscine, atropine, cannabis indica, amphetamine and cocaine. The first three of these are the common ones and delirium is usually indicative of a fairly minor degree of intoxication. If the patient is separated from his source of intoxication recovery is quite rapid in the case of barbiturates and alcohol, but a high bromide level in the blood and tissues may persist for some time. In poisoning by atropine and hyoscine dilated pupils and excitation are usual and excitation is the most prominent feature in amphetamine poisoning and in the earlier stages of cannabis indica intoxication. Excitation and convulsions occur if cocaine poisoning is at all severe.

Coma

Most of the conditions considered under the heading of delirium will produce coma if the cerebral damage is more severe. Here any history which may be obtained is of great value. If loss of consciousness is known to have followed a prolonged episode of progressive cerebral deterioration or emotional disturbance, it will be most important to exclude the metabolic and endocrine diseases as well as cerebro-vascular disease and space-occupying lesions of the brain. On the other hand circumstantial evidence of this type can be most misleading, for instance mental disturbance may be a prodromal feature in suicidal poisoning or the mental changes may represent an early phase of barbiturate poisoning before a lethal overdose has been taken.

A history of the sudden onset of loss of consciousness is similarly valuable and suggests cerebro-vascular damage or some similar sudden catastrophe. Convulsions in association with the onset of coma may be due to epilepsy, hypertensive or lead encephalopathy, cerebro-vascular

disease, meningeal irritation and various forms of poisoning, in particular the antihistamine group of drugs and cocaine.

It frequently happens in hospital practice that a patient is admitted in coma without any history being available and it is in this group that the greatest diagnostic difficulties arise. In these patients one should first consider the most likely causes of coma in the particular age group concerned and then proceed to a careful physical examination. Cerebro-vascular lesions are likely to be associated with focal neurological signs, hypertension and arteriosclerosis or cardiac lesions, the older age groups and sometimes neck rigidity. Meningeal irritation by infection, trauma or subarachnoid haemorrhage is usually associated with neck stiffness, a positive Kernig's sign, and sometimes fever or vomiting. Electric shock and head injury usually have associated burns or external injury. Carbon monoxide poisoning is usually apparent from the circumstances in which the patient has been found, but may be complicated by barbiturates or alcohol. The metabolic and endocrine comas have characteristic physical findings, but in this group the coma of severe myxoedema with its associated hypothermia may be overlooked. Psychiatric conditions such as severe depression, schizophrenia and hysteria may present as severe stupor, but there is no true loss of consciousness, examination is usually resisted and physical findings are absent. The barbiturates and alcohol are the two common poisons presenting in this way and both may be present in the same patient. Methyl alcohol, the narcotic drugs and aspirin are less common and exhibit more definite physical signs. Confusion sometimes arises between diabetic acidosis and aspirin poisoning, but this can be resolved by a careful examination of the urine and a blood sugar estimation.

Convulsions

A clear distinction must be made between spinal or tetanic convulsions, usually related to minor external stimulation, tonic in character and without disturbance of consciousness and cerebral or epileptic convulsions with loss of consciousness and alternating phases of tonic and clonic spasm. Spinal convulsions are characteristic of tetanus and of strychnine poisoning, but may be simulated by hysteria. Cerebral convulsions may be produced by many poisons in infancy, particularly the antihistamine drugs, camphor, ferrous sulphate and amphetamine. In adults picrotoxin, cocaine, barbiturate deprivation, camphor, and lead may be considered. The differentiation from idiopathic or symptomatic epilepsy may present considerable difficulty, but the treatment by cerebral depressants of the barbiturate group is the same irrespective of the underlying cause.

Polyneuritis

Peripheral muscular weakness often associated with wasting and, sometimes gastro-intestinal disturbance, may be due to poisoning by lead,

arsenic, thallium, carbon disulphide, alcohol, orthocresyl phosphates, acrylamine, thalidomide, and possibly gold, and mercury. These forms of poisoning have to be distinguished from infective and diabetic polyneuritis, intermittent porphyria, polyarteritis nodosa, deficiency of aneurin, cyanocobalmin and pyridoxine, and the neurological changes which may be associated with malignant disease, particularly bronchial neoplasm. This differentiation may present considerable difficulties and it may only be possible to exclude metallic poisoning by chemical analysis and this may be misleading in view of the rapid excretion of thallium.

In lead poisoning, the extensors of the wrist are usually weak, while in the other metallic poisonings, and with orthocresyl phosphates, the lower limbs are more often affected. Transient glycosuria may occur in lead poisoning, but this is a much more marked feature of thallium poisoning. The loss of hair in thallium poisoning helps to distinguish it from diabetic polyneuritis and also the increased blood and urinary porphyrin levels in the former, though this may in itself lead to confusion with idiopathic or paroxysmal porphyria. In both conditions there may be episodes of abdominal pain and the differentiation may depend on the hair loss and the detection of thallium in the urine.

Some hair loss may occur in chronic arsenical poisoning, but pigmentation of the skin is usual and arsenic can be demonstrated in the skin, nails, hair, and excreta, also there is no disturbance of porphyrin or sugar metabolism.

Polyarteritis nodosa is a condition in which such diverse and bizarre symptoms occur that it always presents a diagnostic problem, often not solved even by repeated muscle biopsy, and the diagnosis may have to rest on the exclusion of the other possible causes of the particular symptom pattern concerned.

Carbon disulphide poisoning usually arises as an industrial disease and presents with gastro-intestinal disturbance, combined with central and peripheral nervous symptoms. The work history will usually provide the lead to a correct diagnosis.

Orthocresyl phosphate poisoning has usually occurred in massive outbreaks in association with the adulteration of cooking fats by lubricating oil. Sporadic cases present much more difficulty, but there will usually be a history of contact with chemicals. Acute intermittent porphyria, though rare, is a cause of polyneuritis, usually motor in type, and also of attacks of abdominal colic associated with constipation. There may be a family history of similar troubles and attacks may be precipitated by taking barbiturates and particularly by intravenous barbiturates used in general anaesthesia. The urine is red in colour, darkening on standing and contains porphobilinogen.

2

The Treatment of Poisoning

The treatment of poisoning falls naturally into three phases. First, the separation of the patient from the source of poisoning and all possible measures to prevent absorption and to expedite excretion; second, any symptomatic treatment necessary to keep the patient alive, and finally, once a definite diagnosis has been made, any known specific antidote should be administered. With the exception of carbon monoxide most of the common poisons are swallowed and speed is the essential factor in successful treatment. If the poison has been swallowed by accident the mistake is usually discovered at once and help sought. *The early production of vomiting is of much greater value in avoiding absorption than the most extensive gastric lavage carried out after a delay of half an hour.* Emesis is most easily induced by digital stimulation of the fauces which can be carried out by a co-operative patient or by a sensible relative or neighbour. A cupful of strong solution of salt in hot water will produce the same result or may be used in combination with digital stimulation. Simple instructions of this nature can be given by telephone and success may be achieved before the doctor can arrive at the home, or before an ambulance can be obtained to take the patient to hospital. In urban practice it is usual for all patients with known or suspected poisoning to be taken to the nearest casualty department, and this is probably the wisest course even when apparently satisfactory emesis has been achieved. In children who have swallowed poisonous tablets or medicine, removal to hospital for gastric lavage is particularly important, as certain drugs such as ferrous sulphate may be lethal even after a period of apparent recovery from the initial symptoms.

Apomorphine hydrochloride 8 mg by subcutaneous injection, will sometimes induce vomiting when other methods have failed, but it does have a definite depressive action and may add to the degree of respiratory failure which develops in some forms of poisoning.

Gastric lavage should be carried out as early as possible when any non-corrosive poison has been swallowed. This may not be immediately possible when the poison has a convulsant action, e.g. strychnine, and