PAPERS AND ORIGINALS

Acute Poisoning: Some Myths and Misconceptions

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Introduction

Poisoning accounts for a high proportion of acute medical admissions to hospitals in Britain. Estimates range from 50% of all female acute medical admissions in Oxford (Mills, 1970) to 19% of all acute medical admissions in Sunderland (Burston, 1969) and to 10% of all acute adult admissions (Matthew and Lawson, 1970). The incidence of acute poisoning increased by 80% between 1962 and 1966 (General Register Office, 1964, 1968). Nevertheless, the management of acutely poisoned patients is often shrouded in a haze of uncertainty and mysticism. Why this situation should obtain in such a common condition is difficult to determine. This paper attempts to assess the factors involved, to explode some myths, to draw attention to common misconceptions and mistakes, and to clarify some muddled thinking in the light of a personal experience of the clinical management of several thousands of acutely poisoned patients.

Authority on Acute Poisoning

Part of the problem is undoubtedly due to the fact that much of the available information on the features and management of poisoned patients is still presented with an air of authority by persons who seldom deal with live patients or by others who are not clinically involved to any depth. Pharmacologists and forensic pathologists have—*faute de mieux*—been accepted as authorities in clinical toxicology, and the literature remains rich in their folklore, as is shown below. The sections on acute poisoning in four popular textbooks of medicine were written by pharmacologists, neurologists, and others who rarely have clinical responsibility for poisoned patients. The proportion of pages devoted to acute poisoning in these textbooks is usually less than 1% despite the magnitude of the problem. Polson, the eminent forensic pathologist, and Tattersall (1969) entitled their book *Clinical Toxicology* and aimed to limit their scope to common poisons. Nevertheless, 29 pages are devoted to arsenical poisoning and only 13 to acute barbiturate poisoning, which is several thousand times more commonly encountered in *clinical* practice. Another textbook, also called *Clinical Toxicology* (Thienes and Haley, 1964) was written by an emeritus professor of pharmacology and toxicology and a research pharmacologist.

Nor can journals be exonerated from contributing to the increasing volume of misconceptions and the perpetuation of myths. A lack of expert refereeing of articles is often evident, particularly with regard to the merits of analytical methods. The publication of limited experience or isolated cases, often with inadequate laboratory data, allows the folklore of poisoning to increase. Unfortunately the flimsy evidence on which conclusions are based is often forgotten and the conclusions become accepted as standard practice. An outstanding example stems from the article by Cope (1961) on the place of oxygen therapy in cyanide poisoning. Experiments were undertaken on one man, one dog, and 12 goldfish, yet many articles on the treatment of this poisoning carry a favourable reference to this work.

Anonymity of leading articles is also to be deprecated; both readers and those whose work is reviewed are surely entitled to know the standing of the "expert" commentator.

To some extent therefore clinicians may be excused for their confusion in dealing with poisoned patients but the problem is now of such magnitude that indifference can no longer be condoned.

Carbon Monoxide Poisoning

Many medical textbooks state that the skin is pink in carbon monoxide poisoning. Indeed, Harrison (1970) states that "the most characteristic sign of carbon monoxide poisoning is the cherry colour of skin." There is no reason to doubt that this is true at necropsy, but it is exceptional in a living patient. It has not been observed once in 400 patients with CO poisoning admitted to this unit. Such patients are commonly cyanosed and pale.

It is often stated that breathing is depressed in carbon monoxide poisoning and that artificial respiration is required (*British National Formulary*, 1968a; Simpson, 1969). This is

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not so unless the patient is moribund. Breathing is in fact usually more than adequate. In our experience the arterial P_{CO_2} is usually low but hypoxia has induced such a fall in standard bicarbonate that the arterial pH is below normal. It would appear therefore that the hyperventilation which Leathart (1962) described as a rarity in CO poisoning is the rule for patients arriving alive at hospital. Nevertheless, since 1920 debate has centred on the desirability of administering oxygen with or without various percentages of carbon dioxide, usually 5 or 7%. Clearly the addition of carbon dioxide in any concentration is irrational as this will tend to reduce arterial pH even further.

The controversy regarding the addition of CO_2 arose from work on dogs which were poisoned to levels of carboxyhaemoglobin well above human tolerance. The findings were then extrapolated to humans, resulting in much debate and needless expense in the equipping of ambulances and casualty departments with special cylinders of oxygen and CO_2.

Further confusion regarding the proper management of carbon monoxide poisoning lies in the statement by an eminent professor of forensic medicine who in a recent book stated that blood transfusion may prove "vital" in severe carbon monoxide poisoning. One could not be other than deeply sympathetic towards the doctor in the witness box at a fatal accident inquiry who was asked why he had not used blood transfusion as advocated by the expert. Blood transfusion in a condition characterized by myocardial damage must be fraught with extreme danger.

Significance of the Dose

Case reports of poisoning often indicate that the patient took exactly *x* number of tablets of a particular drug. It is strange how doctors accept the patient's statement without question. In practice he will tend to understate the amount ingested if he feels guilty about indulging in self-poisoning; if he feels he must exaggerate his distress then he will overstate the number of tablets ingested. Tablets are usually ingested by the handful, and seldom therefore can reliance be placed on the patient's assessment of the number taken. It is far more important to give consideration to the possibility that another drug or alcohol may have been taken in addition.

Alcohol is frequently involved in episodes of self-poisoning (Kessel, 1965) and would be expected to speed the absorption of lipophilic drugs such as methaqualone or glutethimide and may through its own action increase the depth of coma. This is important in formulating a prognosis. A patient thought to be deeply unconscious from an overdose of amylobarbitone alone may be awake in a few hours if in fact the coma was very largely due to alcohol.

A further example of the uncritical acceptance of evidence is seen in the barbiturate automatism so beloved of coroners. The term "automatism" was "borrowed" by Richards (1934), a lecturer in forensic medicine, to explain the inability of three patients who had been unconscious following an overdose of a barbiturate to remember the ingestion of more than a therapeutic dose. He suggested that "the knowledge of the need for another tablet persists, while the memory is so affected by the drug that the patient does not realize that he has already satisfied the need, and automatically repeats the dose at intervals." This is an outstanding example of folklore which is deeply embedded in the literature on barbiturates. The myth of automatism, however, has been exploded by Aitken and Proudfoot (1969). It is perhaps charitable to retain such a description for the use of coroners, though this makes for inaccuracy of statistics on suicide. In patients who survive, however, it is no real kindness to accept such an explanation and deny them the benefit of an appropriate response to what has been a *crie de coeur*.

Clinical Signs in Sedative and Analgesic Poisoning

It is often considered that in unconscious patients fixed dilated pupils are an indication of irreversible brain damage and denote a serious prognosis. In poisoned patients this is not so, even after respiratory and/or cardiac arrest. Resuscitative measures should therefore never be abandoned simply on the evidence of such pupils. Further, it should be remembered that drugs with an atropine-like action in overdosage, such as the tricyclic antidepressants, antihistamines, and glutethimide, can produce coma with fixed dilated pupils from which full recovery can be made.

A further misconception regarding the pupil size in unconscious patients is that inequality with no other localizing neurological features indicates a vascular accident or other intracranial morbidity which might be surgically remediable. The pupils may, however, be unequal in hypnotic poisoning. In a patient between the ages of 15 and 50 who is unconscious and has no evidence of external damage to the head acute poisoning is the diagnosis until proved otherwise. Since barbiturates are still the most commonly abused drugs in respect of overdosage, a blood barbiturate estimation can be done more quickly and obviously with less inconvenience than shaving and preparing the unconscious victim of poisoning for a trephining operation.

Macewen's sign has become firmly embedded in the folklore of poisoning. Macewen stated in the differential diagnosis of coma that a painful stimulus would temporarily dilate the pupils in acute alcohol poisoning. While this is true, such a reaction occurs in many other types of hypnotic poisoning.

Bullae present on the skin of acutely poisoned patients are a helpful observation (Beveridge and Lawson, 1965). Their cause is disputed, but the theory that they are solely the result of pressure is open to question as they appear not on areas of maximum pressure such as the buttocks but commonly on contiguous surfaces of the fingers.

Though it is indicated in the *British National Formulary* (1968b) that adult patients poisoned by salicylate are unconscious, they are almost always conscious and may show considerable agitation. Coma in adults is uncommon and indicates a grave prognosis (Proudfoot and Brown, 1969).

Electroencephalogram

The aid of the electroencephalogram has been invoked in the current controversy over the definition of death, attention being paid to the value of a flat or isoelectric tracing. It was stated at the meeting of the World Medical Association in Australia in 1968 that the determination of the time of death "will be based on clinical judgement supplemented if necessary by a number of diagnostic aids, of which the electroencephalograph is currently the most helpful." Isoelectric tracings in hypnotic overdose, however, may persist for 23 hours, with eventual recovery (Bird and Plum, 1968).

Blood Levels

It is often written that drug levels of hypnotics in the blood above a particular figure are potentially lethal (Hadden *et al.*, 1969; Maher and Schreiner, 1969). This does not take into account wide variations in individual rates of metabolism of the drug, nor does it consider tissue tolerance (Oswald, 1970). An epileptic may have a blood phenobarbitone level of 10 mg/100 ml and be slightly drowsy, whereas a person unaccustomed to this drug would be deeply unconscious at the same level. Blood or serum levels may, of course, confirm a diagnosis of poisoning and may be of medicolegal value, but

they are generally of little assistance in the management of unconscious poisoned patients.

Psychiatric Aspects

It must be reiterated that the actual dose of poison and the patient's resultant physical condition do not reflect the severity of the underlying psychiatric or sociological disorder (Central and Scottish Health Services Councils, 1968). But patients are still turned away from casualty departments because they have not rendered themselves sufficently physically ill to impress the admitting officer. The motive for taking an overdose requires to be understood. There can be no doubt that Kessel's (1965) definition of "self-poisoning" most accurately describes the act. It is misleading to call it "attempted suicide," "parasuicide," "pseudocide," or even "suicide." With such descriptions there is a strong chance that the real motive for taking the overdose may become obscured. The term "self-poisoning" does not invite this error.

Emesis or Gastric Lavage?

Controversy has raged over whether ipecac syrup should be used to provoke emesis. Its many advocates claim that it is effective (Robertson, 1962; Shirkey, 1966; Alpert *et al.*, 1967; Reid, 1969), but their criterion of effectiveness is simply that the poisoned patient has vomited, usually within an average of 18 minutes since ingestion of the ipecac. There can be no doubt that after ingestion of 20 ml of ipecac syrup and the motion of the vehicle taking the patient to hospital, vomiting will occur in the vast majority of poisoned patients. The fact that in most trials the vomitus was not analysed to determine if ingested poison had been effectively removed from the stomach does not seem to have been seriously considered by the ipecac syrup devotees. Corby *et al.* (1968) showed that the mean return of ingested substance after ipecac syrup administration in children was about 30%. A false sense of security therefore is likely to be engendered by this "effective" therapy. If there is any doubt that a potentially serious amount of poison still remains in the stomach then gastric aspiration and lavage should be undertaken. The risks of this latter procedure should not, however, be belittled in the semiconscious patient washed out by an inexperienced person.

Gastric aspiration and lavage has often been said to be ineffective (Harstad *et al.*, 1942; Shirkey, 1966; Victor *et al.*, 1968), but the critics, chiefly American, make this statement on ill-founded evidence. Gastric aspiration and lavage is often undertaken with a nasogastric tube by those who most strongly question its value. It is not surprising that the procedure is then thought to be ineffective. A 30 gauge Jacques stomach tube should be used in adults for gastric aspiration and lavage. By using a tube of such wide bore, tablets themselves, food with tablet particles adherent, and virtually all the stomach contents can be evacuated. This is not physically possible with a nasogastric tube.

Antidotes

Perhaps the most persistent myth of treatment of poisoning is that for each poison there is an appropriate antidote. Thus the first request of many doctors telephoning the Poisons Information Service is the name of the antidote to a particular poison. An antidote is a specific pharmacological antagonist and as such is a rarity in clinical toxicology. Even if the definition were extended to include the metal-chelating agents it would still be found that in clinical practice an "antidote" is available in less than 2% of episodes of acute poisoning. The obvious example is nalorphine, which antagonizes the toxic effects of opiates. Even with this poisoning folklore exists, for there is a stubborn resistance to depart from what has been stated to be the maximum dose. Most reference books advocate up to a total of 40 mg of nalorphine but how this mythical limit was established is lost in the mists of time. The dose to be used is that which will counteract the effects of the opiate; as much as 105 mg in one hour has been given in an adult patient (Wright and Syme, 1969).

It is also apposite to comment on the so-called "universal antidote"—a mixture of charcoal, magnesium oxide, and tannic acid—which has been used in the treatment of poisoning since 1904. This concoction has long been thought to have some power in reducing the effects of poisons. In fact its three constituents have a mutually inactivating effect. Universal antidote is thus neither an antidote nor is it universal (Henschler and Kreutzer, 1966); indeed it could itself give rise to poisoning.

Analeptics

Recommendations regarding the use of analeptic drugs such as picrotoxin or bemegride should have disappeared from the textbooks following the clear demonstration by the Scandinavian experts Clemmesen and Nilsson (1961) and by Dobos *et al.* (1961) that they were not only ineffective but that the death rate in barbiturate poisoning could be greatly reduced by abandoning them. In a popular textbook on *applied* pharmacology published in 1968, however, it is stated that "One of the most effective pharmacological antagonists in barbiturate poisoning is picrotoxin, which can be given intravenously in repeated doses of 3 to 6 mg to the point of producing muscle twitchings. Amphetamine and methylamphetamine are often used in conjunction with picrotoxin." Furthermore, bemegride is said to be "an effective antagonist in barbiturate poisoning." However, having so written, a caveat is added to the effect that many physicians have ceased to use such stimulants. The reader, usually young, impressionable, without clinical experience, and overanxious to the point of feeling constrained to use active therapy, is thus left in a state of complete confusion.

Measures Purporting to Enhance Elimination of the Poison

It is often stated as a generality that forced diuresis, haemodialysis, or peritoneal dialysis shorten the period of unconsciousness (Myschetzky and Lassen, 1963; Hickson and Caridis, 1969; Maher and Schreiner, 1969). There is no doubt that within their individual limitations they are effective in the treatment of severe poisoning by long-acting barbiturates. As there is no way of determining how long a given patient will be unconscious it is impossible to say, except by means of an extensive and well-controlled prospective trial, that by using a particular procedure the period of unconsciousness has been shortened. Such claims, however, are frequent, and despite the total lack of evidence in support this "effective" form of treatment then enters the folklore of clinical toxicology. Hadden *et al.* (1969) demonstrated that in barbiturate poisoning, with the exception of long-acting barbiturates, there was no difference in the effectiveness of treatment with forced diuresis, peritoneal dialysis, or supportive treatment alone. They conclude by strongly advocating supportive treatment alone. Chazan and Cohen (1969) made a similar recommendation regarding glutethimide poisoning.

A further criticism of these procedures and their claimed value is that clinicians tend to draw conclusions from unsatisfactory analytical data. This occurred in the claims made for forced diuresis in barbiturate poisoning by Linton *et al.*

(1967). Their estimates of the urinary recovery of barbiturates included the contribution of water-soluble inactive barbiturate metabolites. The total "barbiturate" recovered thus included a quantity of the inactive metabolites. As so often happens the original paper making the claim received considerable attention while the subsequent letter in the correspondence columns by an expert such as Bloomer (1967) refuting the findings has been largely overlooked. It is interesting to show how misconceptions can then be translated into established fact, for Polson and Tattersall (1969), in their textbook, cite the article which Bloomer called to question as their sole reference in support of forced diuresis as an effective form of treatment of barbiturate poisoning.

Other errors which may result from the use of non-specific chemical methods of analysis of the dialysate or urine obtained by forced diuresis may be that the methods are so non-specific that they measure not only the original drug and its metabolites but also drugs given in treatment. All these substances are then regarded as the parent drug and a great achievement is claimed for the recovery of "poison." Such an example of this error recently appeared in a widely read journal. Patients poisoned by tricyclic antidepressant drugs were "treated" by peritoneal dialysis. The methyl orange method was used for quantitation of this group of drugs in the dialysate, but the assay would have included inactive metabolites, lignocaine given in therapy, and in one instance another drug also ingested. The authors, however, concluded, on the basis of this highly erroneous evidence, that peritoneal dialysis was an effective form of treatment of this poisoning and should be instituted without delay. As if this were not enough the paper went on to record that the finding of hyperglycaemia was an important and valuable sign in an unconscious patient and was strongly suggestive of tricyclic poisoning. In fact the blood glucose was almost certainly raised in their patients because of absorption of glucose from the standard peritoneal dialysing fluid used. There is no evidence that in tricyclic poisoning the blood glucose is other than normal. Subsequent to this article the Scottish Poisons Information Service was on occasions taken to task for not advocating peritoneal dialysis in tricyclic antidepressant drug poisoning, showing that this form of therapy had already been accepted without question.

The blame for such erroneous reporting as this does not entirely lie with the authors but also with the editor and his expert advisers. It is to be regretted that the editor concerned would not publish even a comment on a paper which was misleadingly inaccurate and even dangerous in the advice offered.

Conclusion

No man can be expert in every field, and the time has come for forensic pathologists and pharmacologists to cease writing about the clinical effects and treatment of acute poisoning in humans. Physicians themselves require to be far more critical of published work and of the methods they use to treat their patients. The editors of medical journals could help by being more discriminating in accepting articles on poisoning.

Acute poisoning is a major part of the work of general physicians, and the problem shows no sign of abating. Indeed the complexity of the problems increases daily with the advent of new drugs and different combinations. It is vital that clinical toxicology in all its aspects be founded on sound clinical observations and scientific measurements.

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