ABC of Poisoning

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ELIMINATING POISONS

Methods

- Forced diuresis
- Peritoneal dialysis
- Haemodialysis
- Haemoperfusion

Most poisoned patients recover with little more than nursing care, though about 10% will need intensive support to maintain vital functions. *In fewer than 5% of cases, however, are methods to increase poison elimination either feasible or appropriate.* Such techniques should as far as possible be undertaken only by those experienced in their use. Moreover, these methods are of little value in patients who have ingested drugs such as tricyclic antidepressants which are highly tissue bound.

Forced diuresis

Rationale

- 1 A substantial proportion of the poison is excreted in urine in unchanged — that is, non-metabolised — form or the metabolites are themselves toxic
- 2 The poison is distributed mainly in the extracellular fluid
- 3 The poison is minimally bound to protein
- 4 Elimination of the toxic substance is enhanced by manipulation of the urine pH so that the poison becomes maximally ionised and therefore excreted in the urine

Most drugs are weak electrolytes which, at physiological pH, exist partly as undissociated molecules. The extent of ionisation is a function of the ionisation constant (K_a) of the drug and the pH of the medium in which it is dissolved. (Ionisation constants are expressed in the form of their negative logarithm—pKa. Hence, the stronger an acid the lower its pKa and the stronger a base the higher the pKa.)

Indications

Forced diuresis should be considered, and may be indicated, in poisoning due to:

Alkaline diuresis

Phenobarbitone or barbitone
Salicylates
Phenoxyacetate herbicides

Acid diuresis

Phencyclidine
? Amphetamine*
? Fenfluramine*

Note: The excretion of quinine does not appear to be increased by acid diuresis

*Sedation alone is usually sufficient

Cell membranes are more permeable to substances that are lipid soluble and in the

non-ionised, rather than the ionised, form. Thus, the rate of diffusion from tubular urine back into the circulation is decreased when a drug is maximally ionised. Because ionisation of weak acids is increased in an alkaline environment, and that of basic drugs is increased in an acid solution, manipulation of the urinary pH enhances renal excretion. The elimination of weak acids by the kidney is increased in alkaline urine if the pKa of the drug is 3.0-7.5; elimination is increased in acid urine if the pKa of the drug is 7.5-10.5.

Contrary to popular belief the indications for forced diuresis are few. It should be considered only for those patients in whom laboratory analyses have confirmed that a toxic agent has been taken in sufficient amount to cause clinical evidence of severe poisoning. When the technique is used considerable clinical and analytical demands are placed on medical, nursing, and laboratory staff if the patient is to be managed without complications. Forced diuresis should be considered a metabolically invasive procedure and requires close supervision, preferably in an intensive care unit. It is particularly likely to be hazardous in the elderly, in patients with cardiac and renal impairment, and in those who are "shocked."

Potential complications

- 1 Fluid overload
- 2 Pulmonary oedema (non-cardiogenic pulmonary oedema may also occur in salicylate poisoning)
- 3 Cerebral oedema
- 4 Electrolyte and acid-base disturbances for example, raised Na^+ , lowered K^+ , Ca^{++} and Mg^{++} metabolic alkalosis

Procedures for forced diuresis in adults

Dialysis and haemoperfusion

Rationale

- 1 The drug or toxic substance should either diffuse easily through the peritoneum or dialysis membrane or be readily adsorbed to activated charcoal or uncharged resin
- 2 A significant proportion of the poison should be present in plasma water or capable of rapid equilibration with it
- 3 The pharmacological effect of the toxin should be directly related to the blood concentration
- 4 Dialysis or haemoperfusion should add significantly to other body mechanisms of elimination

Although the overall mortality from acute poisoning in those admitted to hospital is now less than 1%, the mortality remains high in those who have either ingested a hypnotic drug and are in grade IV coma or imbibed potent toxins such as methanol or ethylene glycol. While there can be no substitute for supportive measures, there is nevertheless a small group of severely poisoned patients who benefit from dialysis or haemoperfusion.

Following the use of dialysis in 1951 for the treatment of salicylate poisoning, both peritoneal dialysis and haemodialysis were widely used in the management of poisoned patients. As a result there are many published reports of the apparent value of dialysis in the treatment of acute poisoning. Yet most of these suffer from a dearth of analytical observations to support their conclusions.

Clinical indications

Three of the following:

- 1 Severe clinical intoxication — for example, Grade 4 coma, hypotension, hypothermia, and hypoventilation in those who have ingested hypnotic drugs
- 2 Progressive clinical deterioration despite best supportive management
- 3 No evidence of improvement despite full resuscitative measures
- 4 Prolonged coma with complications — for example, pneumonia, "shock" lung — or underlying chronic respiratory disease
- 5 High plasma concentrations of the toxic agents. See below

Similarly, since haemoperfusion systems (in which blood passes through devices containing adsorbent particles such as activated charcoal or Amberlite XAD-4 resin) became available in 1973, there have been many reports extolling the virtues of this technique. Some equated recovery with efficacy even though subtoxic concentrations of drug were present. Furthermore, the technique was sometimes used when alternative treatments were both cheaper and more effective — for example, the use of naloxone in opiate poisoning or the use of pralidoxime in organophosphorus poisoning.

An impressive drug clearance by dialysis or haemoperfusion means nothing unless the plasma drug concentration is high enough to ensure that enough drug is removed to influence the clinical course favourably. In addition, dialysis and haemoperfusion are of little value for patients who have ingested overdoses of drugs which have a large volume of distribution, such as the tricyclic antidepressants, since the plasma contains only a small proportion of the total amount of drug in the body unless the rate of transfer from the tissues to plasma is rapid. Moreover, the amount removed would be negligible compared with hepatic elimination.

Specific indications

Peritoneal dialysis

Salicylates
Phenobarbitone
Barbitone
Methanol/ethanol
Ethylene glycol
Lithium
Isopropanol

Haemodialysis

Salicylates*
Phenobarbitone*
Barbitone*
Methanol/ethanol*
Ethylene glycol*
Lithium*
Isopropanol*

Haemoperfusion

Salicylates*
Phenobarbitone*
Barbitone*
Short and medium acting barbiturates
Ethchlorvynol
Glutethimide
Meprobamate
Methaqualone
Trichloroethanol derivatives
Disopyramide
Theophylline

*Haemodialysis and haemoperfusion are two to three times more efficient than peritoneal dialysis

Contraindications

- An antidote is available
- The toxic substance is a rapidly acting metabolic poison
- The substance is "irreversibly" acting — for example, an organophosphorus insecticide
- The drug ingested is relatively non-toxic — for example, a benzodiazepine
- The drug has a very large volume of distribution
- Cardiogenic "shock"
- Coagulopathy

Peritoneal dialysis has the advantage of being widely available but the disadvantage of being less effective than forced diuresis in the treatment of salicylate, phenobarbitone, and barbitone poisoning. Unless, therefore, the patient's condition is aggravated by concurrent renal impairment, forced alkaline diuresis is the treatment of first choice.

Haemodialysis is more efficient than peritoneal dialysis in increasing the elimination of lithium, methanol, isopropanol, and ethylene glycol. It is also effective in increasing the removal of phenobarbitone, barbitone, and salicylates, though patients poisoned by these drugs may be treated more simply by forced alkaline diuresis. Haemodialysis will not increase significantly the elimination of short and medium acting barbiturates and non-barbiturate hypnotics.

In contrast, haemoperfusion is very effective in increasing the elimination of all barbiturates, some non-barbiturate hypnotics, disopyramide, and theophylline. It may also have a role in the management of patients poisoned with paracetamol who present too late for protective agents to be used. Moreover, haemoperfusion will reduce the time taken for patients severely poisoned with hypnotic drugs to recover consciousness. As a result, complications such as pneumonia and shock lung develop less often, and not only the morbidity but also the mortality can be expected to fall in this small group of severely intoxicated patients.

Potential complications

Thrombocytopenia (about 30% reduction)
Leucopenia (about 10% reduction)
Loss of clotting factors
Lowered urea, creatinine, urate, calcium, glucose
Haemorrhage because of heparinisation
Patient may disconnect shunt lines
Air embolism
Infection

Summary of indications for elimination techniques

Elimination techniques should be considered in adults if plasma concentration:

Salicylates*

> 500 mg/l + metabolic acidosis	}	Alkaline diuresis
> 750 mg/l		
> 750 mg/l + renal failure	}	Haemodialysis or haemoperfusion
> 900 mg/l		

All barbiturates (except phenobarbitone and barbitone)

> 50 mg/l	}	Haemoperfusion
Ethchlorvynol > 150 mg/l		
Glutethimide > 40 mg/l		
Meprobamate > 100 mg/l		
Methaqualone > 40 mg/l		
Trichloroethanol derivatives > 50 mg/l		

Phenobarbitone/barbitone*

75-100 mg/l	Alkaline diuresis
> 100 mg/l	Alkaline diuresis, haemodialysis, haemoperfusion
> 150 mg/l	Haemodialysis, haemoperfusion

Methanol, ethylene glycol

> 0.5 g/l	Peritoneal dialysis, or haemodialysis	Dialysis is indicated if more than 30 g has been ingested or there is metabolic acidosis, mental, visual, or funduscopic abnormalities. Many antifreeze solutions now contain methanol as well as ethylene glycol
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Isopropanol

> 0.4 g/l	Haemodialysis	Significant hypotension is an important clinical indication for haemodialysis
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Lithium

> 5 mmol/l	Peritoneal dialysis or haemodialysis	Forced diuresis is ineffective and an infusion of sodium chloride dangerous
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Theophylline

> 60 mg/l	Haemoperfusion	Correction of hypokalaemia is most important and may obviate the need for haemoperfusion
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* NB: Haemodialysis or haemoperfusion are two to three times more efficient than forced diuresis or peritoneal dialysis.

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What are the hazards of mammography and how often may a woman be safely subjected to it?

The hazards of mammography should now be small in a good mammography unit. The main one is that of exposure to ionising radiation. Trauma secondary to excessive compression has been reported in women with silicone prostheses but this should not occur with good technique. Women exposed to large doses of ionising radiation have been observed to have an incidence of breast cancer that is higher than that in the normal population after a latent period of over 10 years. One series studied were Japanese women exposed to the atomic bomb effects.¹ This showed a possible excessive incidence in women aged under 20 who were receiving more than 100 rads, but this was a whole body dose of neutrons as well as x rays. The increased risk at the lower levels of irradiation is difficult to calculate and is taken as a linear extrapolation from higher doses. This has been expressed as an incidence of 7.5 excess cancers per million women per year per rad,² but as the sensitivity is age related and this estimate was derived from an essentially young population it is thought to be a substantial overestimate and may almost certainly be halved for women over 30. Measured doses in a recent series give a range of 0.06 to 0.15 centi Gray (rads) per film. Zerotography gave doses of two to three times as much. These estimates were made on apparatus specifically designed for mammography with good compression and reasonable focus film distance.

The risk has to be evaluated against the benefits of mammography. In the patient with symptoms the benefits far outweigh the risks. Suitable operations may be planned and segmental resections undertaken in selected cases of malignancy with much more confidence even in very young women. Occult carcinoma is not infrequently found in patients presenting with pain but no mass. A primary examination and a follow up examination after three or six months on equivocal cases would not be considered excessive in any woman over 20. Screening for occult cancer presents another problem. In this case the age limit should not be less than 35 unless there is a very high risk—such as a family history of mother or sister developing

cancer before the age of 40. After the age of 35 examinations at yearly intervals using two projections per breast as a base line and possibly using one oblique view in the follow up years is generally acknowledged to give benefits that outweigh the risks. Fifty per cent of cancers would be detected by mammography alone, and detection rates of 4.8 per thousand in women of over 35, rising to eight per thousand in women of over 50 have been reported in a recent series.³—AUDREY TUCKER, consultant radiologist, London.

¹ McGregor DH, Land CE, Choi K, *et al.* Breast cancer incidence among atomic bomb survivors, Hiroshima and Nagasaki, 1950-69. *JNCI* 1977;59:799-811.

² Committee for the Biological Effects of Ionizing Radiation. *The effects of population exposure to low levels of ionizing radiation*. Washington DC: National Academy of Science. National Research Council, 1980.

³ Hutchison J, Tucker AK. Breast screening in a healthy population. *Clin Oncol* (in press).

What advice would you give to a man whose skin itches when wearing garments made of polyester? No rash occurs.

Polyester fibres include the trademarks Terylene and Dacron. They confer wash and wear properties on clothing and have not themselves been shown to be skin sensitisers or irritants.¹ The dyes and finishes applied to polyester fabrics are rare causes of allergic contact dermatitis.² In the absence of a rash this complaint is probably due to one of two properties of polyester. The more likely reason is that polyester fibres are not so absorbent and permeable as natural fibres; sweat therefore tends to remain longer on the surface of the skin and is a mild irritant. There is a wide individual variation in the itch threshold for mild irritants such as sweat, and this man probably has a lower threshold than average. The second, and less likely possibility, is mechanical irritation by the fibre itself. This happens with wool and is commoner in atopic individuals than non-atopics.³—R J G RYCROFT, consultant dermatologist, London.

¹ Fisher AA. *Contact dermatitis*. 2nd ed. Philadelphia: Lea and Febiger, 1973:138.

² Cronin E. *Contact dermatitis*. Edinburgh: Churchill Livingstone, 1980:36-92.

³ Rajka G. *Atopic dermatitis*. London: Saunders, 1975:86.