EMERGENCIES IN GENERAL PRACTICE

BARBITURATE AND ASPIRIN POISONING

BY

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The summons, "Come at once: Mr. Smith has poisoned himself," may be the prelude to a medical emergency. How to deal with it depends to a large extent on circumstances of time and place. For example, Mr. Smith is, in fact, an employee of a general hospital, and, being on duty when the incident occurred, he is already on his way to a well-staffed and well-equipped medical ward. On the other hand, Mr. Smith may be a crofter 20 miles from the doctor's house and 100 miles from the nearest hospital. Most cases of poisoning, however, are seen in town practices, and it is against this background that the general practitioner is called upon to deal with the emergency.

The management of such a patient is likely to make excessive demands on the time and resources of the doctor who has innumerable commitments. It is therefore in the best interests of all concerned that steps should be taken to have the patient removed to hospital if the journey is not likely to prejudice his chance of recovery. However, even if transfer is practicable, *the immediate treatment given by the general practitioner is infinitely more important than anything that can be done some hours later.*

If the patient survives it will often be because the doctor or the relatives did the right thing at the outset; if, in the hospital ward, elaborate methods of resuscitation are needed it may well be because the simple forms of treatment were neglected while the patient was still at home. The general management is the same in nearly all the common types of drug poisoning, including acute intoxication by barbiturates and aspirin.

Removal of the Poison

The relative who telephones for the doctor must be told how to give first aid. This consists in making the patient vomit. If the patient is conscious—even though drowsiness is developing—vomiting can nearly always be induced by boldly thrusting a finger down the patient's throat. The vomitus should be collected in a clean pail for examination later. After vomiting has occurred the patient should be made to drink two cupfuls of warm water and then digital stimulation of the fauces should be repeated. This simple procedure carried out three or four times is invaluable. It is much more rapid and reliable than the use of reflex emetics; among these are common salt (a dessertspoonful in a tumblerful of tepid water) and mustard (a teaspoonful mixed into a thin paste with cold water and then diluted with tepid water to make a tumblerful); ipecacuanha wine (tinct. ipecac. B.P.—a tablespoonful) is even less reliable, and salts of the heavy metals (copper sulphate, zinc sulphate, etc.) should not be used because they are likely to damage the stomach and may even poison the patient, especially when they fail to cause vomiting.

The most reliable of all the drugs used as emetics is apomorphine hydrochloride. It acts centrally, but it is apt to fail if the brain is depressed by narcotics and other drugs such as barbiturates and salicylates, and for this reason the

administration of this drug to the comatose patient is a waste of time. On first seeing the patient the doctor will decide whether it is worth while to give apomorphine. If there is reasonable likelihood of success—as judged by the degree of consciousness and the state of the corneal reflex—a dose of 6 mg. (1/10 gr.) should be given intravenously at once. It usually acts within two minutes, but if given subcutaneously it may take five minutes. Emesis is more likely to occur if the patient is sitting or standing, rather than lying down (B. Isaacs, personal communication). Occasionally circulatory collapse occurs following the use of apomorphine. Further, when vomiting is induced in a patient already ill from poisoning, special care is needed to prevent aspiration of vomitus. These, however, are hazards which must be accepted when dealing with this kind of emergency.

No matter what may be the outcome of treatment with emetics the stomach must be washed out. And even when it seems virtually certain that the poison has passed into the intestine gastric lavage should not be omitted; experience shows that when suicide is attempted by rapidly swallowing a large number of tablets, many of them may become impacted at the lower end of the oesophagus and remain there until they are removed by the physician—or by the pathologist at necropsy.

Gastric Lavage

It is reasonable to assume that when the general practitioner accepts responsibility for the treatment of a patient suffering from poisoning he has had considerable experience of the routine procedure of washing out the stomach.

The stomach tube proper (not to be confused with Ryle's tube), the glass connexion, the main length of rubber tubing, and the funnel are shown in the diagram. The total length of tubing should be about 5 ft. (1.5 m.) and its diameter rather less than $\frac{1}{4}$ in. (1 cm.). There should be two or three apertures in the side of the tube near the tip to minimize the risk of blocking by debris in the stomach. A suitable funnel which is readily available has a diameter of $4\frac{1}{2}$ in. (11.5 cm.). If the stomach tube is first dipped into water no other lubrication will be needed. The rounded end of the

Gastric lavage. Note position of the head. A suitable funnel which is readily available has a diameter of $4\frac{1}{2}$ in. (11.5 cm.). If the stomach tube is first dipped into water no other lubrication will be needed. The rounded end of the

tube is guided to the back of the pharynx, taking care to avoid the trachea, and is passed down the oesophagus. It is convenient to mark the tube 20 in. (50 cm.) from the tip: when this mark passes the lips it may be assumed that the free end of the tube is lying in the stomach an inch or two beyond the cardiac orifice. The doctor's poisons bag should also contain a smaller stomach tube and accessories suitable for use in children. The prone position of the patient minimizes the risk of inhalation of gastric contents in the event of regurgitation of fluid alongside the tube. About one gallon (4.5 litres) of tepid water is needed for lavage. In cases of barbiturate poisoning sodium bicarbonate should *not* be used, as it promotes conversion of insoluble barbiturates to their soluble sodium salts. The stomach is emptied repeatedly by siphonage. Not more than half a pint (300 ml.) should be poured into the funnel at a time, because large volumes of fluid rapidly entering the stomach tend to drive the gastric contents through the pylorus. The washings should be set aside for analysis. The biochemist's problem is made easier if the *first few ounces* of the vomitus or stomach washings is kept separate for examination; the rest of the material—much more bulky and dilute—can be sent in a separate vessel.

Before withdrawing the tube a solution of magnesium sulphate (two tablespoonfuls of the crystals in half a pint (300 ml.) of warm water) should be run into the stomach and left there. This hinders the absorption of water from the intestine, and if the toxæmia has not resulted in intestinal stasis a liquid motion may be passed within a couple of hours; bowel activity can be further assisted by giving a simple enema. Drastic purgation is undesirable because it exposes the patient to the hazards of dehydration; and where easily absorbed drugs are concerned purgation is unlikely to be an important method of elimination after the first few hours have elapsed.

General Supportive Measures

Once the poison has entered the body tissues there is little or nothing to be done to prevent its characteristic action. Nevertheless, much remains to be done for the unconscious patient: he requires food and water, otherwise there will be serious metabolic complications; he must be protected from bacteria which are capable of invading many parts of the body; and he must be saved, if possible, from the dangers which threaten life when the vital centres in the medulla are depressed, with consequent respiratory failure and signs of anoxia, and cardiovascular paresis with falling blood pressure. The services of experienced nurses are indispensable: the hygiene of the mouth, the skin, and the bladder calls for special care, and charting of all treatment is highly desirable. Recognition of these requirements underlines the importance of early admission to hospital. When this is impossible, the general practitioner is obliged to make such arrangements as may be practicable to provide some of the amenities of a hospital. The problems are complex, and in trying to solve them the close collaboration of the district nurse, the medical officer of health, and the ambulance service will be invaluable.

Four or five pints (2.5 litres) of fluid may be required daily. The intragastric drip is the best method for giving fluid and nourishment. With the patient in the supine position a Ryle's tube, lubricated with water, is directed into one nostril, pointing the tip backwards but not upwards. If it passes down the oesophagus, then when the single mark on the tube reaches the nostril the free end should be in the stomach. A few drops of water are passed through the tube to exclude the possibility that it is lying in the respiratory tract. After administering milk or other fluids the tube should be occluded with a spring clip, pressure forceps, or spigot and fixed to the side of the face with adhesive tape. If, however, intra-gastric administration is impracticable, fluid should be given parenterally—glucose solution (5%) or 5% glucose in normal saline intravenously. Water can be given by rectal drip. This method, however, is not unreservedly recommended: trouble may arise from block-

ing of the tube, or it may be pulled out inadvertently while the patient is being moved in the course of routine nursing care.

The daily intake of fluid varies according to such factors as the degree of dehydration and the activity of the skin, but the amount should suffice to ensure an adequate daily output of urine (say 1.5 litres). The onset of infection, especially at the bases of the lungs, must be anticipated by giving soluble penicillin intramuscularly—500,000 units followed by 100,000 units six-hourly. Incontinence of urine is inevitable and calls for the insertion of a self-retaining catheter; infection of the urinary tract, which almost invariably supervenes, necessitates the prophylactic administration of small doses of a sulphonamide—sulphadimidine 0.5 g. four-hourly injected through gastric drip tube.

Barbiturate Poisoning

In barbiturate poisoning respiratory failure is the chief danger. Serious prognostic signs are profound coma and the absence of poison in the gastric washings. Also, there may have been long delay in starting treatment. In such cases respiratory failure is almost certain to occur and this provides an urgent indication for transfer to hospital. The doctor should travel in the ambulance with the patient and be prepared to give artificial respiration *en route* if necessary. He should never leave the patient until his colleagues in the hospital have assumed responsibility; this is important, because in barbiturate poisoning respiratory failure often comes on *suddenly*.

In hospital the anaesthetist should be invited to supervise oxygen therapy and prepare appropriate apparatus to maintain a free airway and a satisfactory respiratory rhythm. Oxygen should be given without waiting for signs of anoxæmia, such as cyanosis of the extremities and the lobes of the ears. It is best administered by means of the B.L.B. mask or a special polythene bag at the rate of 6 to 8 litres a minute. If breathing becomes shallow artificial respiration must be started at once. The choice of method lies with the anaesthetist: bag ventilation of the lungs may be achieved manually or by a machine which ensures mechanical compression of the bag. The circumstances may warrant transferring the patient to the Drinker respirator and calling on a specially trained nursing staff. Artificial respiration and adequate oxygenation may maintain life until most of the barbiturate in the tissues has been either excreted or destroyed. The patient then gradually emerges from coma and normal breathing is resumed.

This phase of treatment, however, can often be shortened by giving analeptics. The two drugs most widely used are amphetamine sulphate and picrotoxin. *Amphetamine sulphate* is a safer drug than picrotoxin. The initial dose is 50 mg. intravenously, and this may be repeated after one hour if there is no obvious improvement—judged by recovery of the corneal reflex. If recovery is incomplete further doses of 25 mg. are given hourly. In severe cases a total dosage of 0.5 to 1 g. is not unusual. *Picrotoxin* is injected intravenously in 0.3% aqueous solution. The initial dose is 6 mg. (2 ml.), and this is followed by doses of 3 mg. (1 ml.) every three minutes until there is evidence of return of consciousness; but administration should not be pursued after *slight* twitching of the muscles occurs—for example, flickering of the eyelids. At this point caution is indicated: no more should be given for about 15 minutes, and then only if the twitching has ceased and the patient is relapsing into coma. If too much is injected there is a risk of causing convulsions, and these may be so persistent that intravenous injection of sodium thiopentone (0.1 to 0.5 g.) may be required to control them.

Interesting reports* have recently appeared on the actions of a new barbiturate antagonist called "NP 13" (β -methyl-ethylglutarimide), but it would be premature at the moment to offer an assessment of its value in general practice.

*Shaw, F. H., Simon, S. E., Cass, N., Shulman, A., Anstee, J. R., and Nelson, E. R. (1954). *Nature (Lond.)*, 174, 402. Harris, T. A. B. (1955). *Lancet*, 1, 181.

Aspirin Poisoning

The toxicity of aspirin is much less than that of the barbiturates. If the patient's stomach can be washed out within an hour of his swallowing the tablets the chances of serious constitutional upset are negligible. Absorption of a large quantity of aspirin usually produces an acidotic state with noisy hyperpnoea. This is easily identified as a sign of acute salicylism because of the other characteristic manifestations—tinnitus, deafness, congestion of the skin, sweating, mental confusion, and muscular twitchings.

The acidosis of aspirin poisoning is best treated by giving Ringer-lactate solution *B.P.* intravenously. One pint (570 ml.) can be given in the first hour, a second pint in the next two hours, and thereafter one pint every four hours. This relieves the acidosis without exposing the patient to the risk of developing alkalosis. At the same time, if the patient is co-operative and can tolerate fluids by mouth he should be encouraged to drink water, tea, and coffee. Two teaspoonfuls of baking soda, in divided doses, can be given during the first two or three hours of treatment.

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THE FUNCTION OF HISTAMINE

REPORT OF A SYMPOSIUM IN LONDON

On April 6 and 7 the Ciba Foundation held a symposium on histamine in honour of Sir Henry Dale, O.M., F.R.S., whose work with Laidlaw, and later Richards, laid the foundations of our knowledge of this substance. In conjunction with this symposium, on the preceding two days, April 4 and 5, the Physiological Society and the British Pharmacological Society held another symposium on histamine. This was at the Wellcome Foundation, London, and our correspondent's impressions of it are given below.

[FROM A SPECIAL CORRESPONDENT]

What is the function of histamine in man? No doubt the desire to find this out was one of the main reasons for the large attendance of scientists of different disciplines and from various countries at the recent symposium in London, arranged by the Physiological Society and the British Pharmacological Society.

Gastric Secretion

However, it is likely that most of the scientists were disappointed in their quest, for only C. F. CODE (Rochester) had sufficient of both knowledge and courage to claim for histamine a definite role in normal bodily function and to defend his claim against considerable criticism. Code holds that histamine is the normal direct stimulus for the secretion of gastric juice, and that all other stimuli—nervous or humoral—exert their effect by activating this histamine mechanism. His case is based on the local high concentrations of histamine found in the stomach and duodenum, on the presence of histamine in gastric juice in amounts closely correlated to the volume and acidity of the juice itself, and, of course, on the fact that injected histamine provokes gastric secretion. Support

for Code's conclusions was also to be found in the comments of R. A. GREGORY (Liverpool), who has shown that histamine potentiators will increase gastric secretion in response to a number of different stimuli.

Nerve Transmission and Vasomotor Control

No other definite claim for a physiological function of histamine was put forward. There was, on the other hand, quite a lot of evidence about what histamine does not do. U. S. VON EULER (Stockholm) drew attention to the large amounts of histamine found in some peripheral nerves, especially in post-ganglionic sympathetic nerves (adrenergic), but no explanation for its presence there was offered. Section of such nerves is followed sometimes, though not always, by a reduction in the histamine content of the organ they supply; but no experiments on the effect of tetanic stimulation of these nerves on their histamine content have been carried out. One is consequently unable to judge whether the histamine is actually present in the nerve fibres themselves or not, and, if it is, so located, whether it plays a part in nervous transmission. R. F. WHELAN (Belfast), from studies of blood-flow under a variety of experimental conditions, came to the conclusion—based solely on evidence of resistance to block by antihistamines (always a doubtful criterion)—that there is no evidence that histamine plays any part in vasomotor control.

Allergy and Anaphylaxis

W. L. M. PERRY (London) discussed the role of histamine in skin allergies and thought that histamine was not involved in the direct pathway leading from the antigen-antibody reaction to the skin lesion. He suggested, however, that the fraction of skin histamine located in mast cells might have a defensive action in causing oedema and thus diluting and washing out foreign materials; and that the fact that large amounts of histamine in mast cells are found in the skins of only those animal species which do not easily form fixed-tissue antibodies in the skin might be because this histamine is a substitute for the antibody defence mechanism.

H. O. SCHILD (London) reviewed the role of histamine in anaphylaxis. Large amounts of histamine are known to be released during an anaphylactic reaction, both *in vivo* and *in vitro*; but Schild pointed out that other substances are also formed. This point was taken up by several others, notably by D. F. HAWKINS (London), who showed that, in anaphylaxis in the isolated smooth muscle of bronchi, a slow-reacting substance is released as well as histamine; and by W. E. BROCKLEHURST (London), whose demonstration of the release by the specific antigen of a similar substance from both sensitized guinea-pig lung and from human asthmatic lung was coupled with evidence of its power to contract human bronchial muscle. All these contributions suggest that histamine may not be the most important or the most direct cause of the symptoms of anaphylaxis and allergy in man; and Brocklehurst's work especially may have considerable importance in our understanding of the nature of asthma and the well-known failure of antihistamines in the treatment and prevention of asthmatic attacks.

Thus, on balance, there was a general concurrence of opinion that histamine is of less importance than previously thought in anaphylaxis and in allergies of various kinds; and that there is as yet no evidence that it has any physiological function in the peripheral nervous or vascular systems—a depressingly negative series of conclusions.

Patterns of Histamine Distribution

We may not have much idea why histamine is present in the body; we may know only an increasing number of things with which it appears to have little to do; we do know, however, a very considerable amount about where it is, how it gets there, and how it is released and excreted,