one minute invariably provides adequate anaesthesia within the next half-minute. While the rate of equilibration can be expected to be most rapid early on, confirmation of an adequate approximation to equilibrium in the brain after one minute of nitrous oxide inhalation is nevertheless clearly desirable; for on it probably depends the whole future of nitrous oxide anaesthesia in dentistry and out-patient surgery.

It is certainly not necessary for equilibration of the whole body mass to be aimed at. Such a state inevitably occurs with anaesthetics of a high solubility resulting in prolonged induction and recovery, and Fink (1955) has shown this to result in one of the main hazards of prolonged nitrous oxide anaesthesia—the rapid elimination of some 28 litres of anaesthetic gas ensuing at the termination of anaesthesia, providing the necessity, once more, of oxygen therapy to remedy the “diffusion” or dilution variety of anoxic anoxia.

Technical Considerations

As a first step pure oxygen is administered at a flow rate of 10 litres or more per minute for two minutes. The patient is previously instructed to breathe normally via a tight-fitting nose- or face-piece. Pure nitrous oxide subsequently administered for one minute, at a flow rate similarly well in excess of the minute-volume and without rebreathing, will produce surgical anaesthesia in all healthy patients. Breath-holding is very rare with nitrous oxide as opposed to cyclopropane. At least 20% oxygen is then added as well as supplementary agents if the surgeon requires more than two to three minutes for the operation. If supplementary agents are not used anaesthesia will lighten during this period. It is interesting that Tom (1956) regards this stage, resulting after breathing 20% oxygen with nitrous oxide, still suitable for dental surgery in older children and adults. Certainly, less than 20% oxygen cannot safeguard against harmful anoxia if it is remembered that the average administrator of nitrous oxide is not an expert.

I have used this technique for over two years. Dental surgeons and casualty officers have appreciated the apparent lack of anoxia, nausea, and delirium. No premedication is used, but emptiness of stomach, bowel, and bladder is desirable.

The technique is useful in allowing time for patients to become accustomed to the apparatus while the anaesthetist carries on a monologue keeping the patient informed that he is not expected to feel any effect during the prelude of oxygen therapy. A few patients who had previous experience of nitrous oxide anaesthesia suggested that this technique removed the unpleasant sensations associated with increasing anoxia, and personal experimentation confirmed this admittedly biased impression.

My attention has been drawn to three facts which, if not mentioned, may allow the method to fall into disrepute. They are: (1) After administering pure nitrous oxide for one minute I habitually allow (except in obstetrics) merely 10–15% oxygen for 15–30 seconds, during which time the surgeon is generally able to embark on his operation without having to contend with a moving patient. Only then do I very carefully administer at least 20% of oxygen. (2) A single breath of air early on, such as during the switchover to anaesthetic gas, may vitiate the advantage gained by this method to a remarkable extent. This point cannot be overemphasized. (3) The astute may economize by using merely 4 litres of oxygen per minute for the purpose of nitrogen elimination. This will, however, result in some carbon dioxide accumulation.

Conclusions and Summary

A technique of nitrous oxide anaesthesia for brief operations in healthy subjects is described. It depends simply on routine nitrogen “washout” by administration of pure oxygen for two to two and a half minutes prior to the administration of pure nitrous oxide. Further reasons are advanced why this technique may avoid anoxia and, incidentally, nausea and delirium,

provided that the inherent limitations of nitrous oxide as a sole anaesthetic agent are observed. Except in expert hands, there must be strict limitation of the time spent on surgery, unless recourse is made to supplementary agents or a state of amnesia and analgesia such as results after the inhalation of 20% oxygen in nitrous oxide.

The idea of nitrogen elimination and its replacement by oxygen prior to nitrous oxide anaesthesia is not new (Neff *et al.*, 1950), but its overall importance appears to be overlooked in practice.

I am indebted to Dr. F. R. Gusterson for advice and encouragement.

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ACUTE RENAL FAILURE IN SALICYLATE POISONING

BY

E. J. M. CAMPBELL, M.D., M.R.C.P.

Assistant

AND

R. E. MACLAURIN, M.B., B.S.

Late House-physician

Medical Unit, the Middlesex Hospital, London

Salicylate poisoning causes complex acid-base and metabolic disturbances. If serious renal damage is present in addition, as in the following case, the management demands careful biochemical control.

Methods.—The plasma sodium and potassium concentrations were measured by flame photometry, the chloride by the method of Van Slyke and Hiller (1947), the bicarbonate by the method of Van Slyke and Neill (1924), and the salicylate by the method of Smith and Talbot (1950). The arterial carbon dioxide and oxygen tensions were measured by the Riley method (Riley, Campbell, and Shepard, 1957) and the pH calculated from the nomogram of Singer and Hastings (1948).

Case History

On February 13, 1957, a spinster of 52 swallowed 75 aspirin tablets—total dose approximately 375 gr. (25 g.). Throughout February 13 and 14 she became increasingly drowsy, but remained rousable and was drinking adequately but passing little or no urine. She did not vomit. She was referred to hospital at midday on February 15. There was no previous history suggestive of renal disease.

On admission she was drowsy and confused but responded to simple questions. Her oral temperature was 98° F. (36.6° C.), pulse 105. She was breathing deeply at a rate of 32 a minute. The blood pressure was 100/70; all her extremities were warm and she was sweating. There were bilateral subconjunctival haemorrhages and a purpuric rash on the trunk and arms. During the first six hours in hospital she passed 26 oz. (740 ml.) of urine which was acid and contained protein, hyaline and granular casts, and large amounts of salicylates. Gastric washings contained no salicylates. The blood Hb concentration was 13.9 g./100 ml. Results of other measurements are given in the

Table. The prothrombin "concentration" (Quick) was 28% of normal, to correct which 20 mg. of vitamin K₁ was given intramuscularly.

Results of Investigations

	February						
	15	16	17	18	19	20	21
Weight (lb.)		136	126	136	136	135	135
Blood urea (mg./100 ml.)	255	325	255	183	100	66	39
Plasma sodium (mEq/l.)		142	140	150	152	150	145
Plasma potassium (mEq/l.)		3.6	3.0	2.9	5.8	5.0	4.2
Plasma chloride (mEq/l.)	108	110	122	110	112	108	112
Plasma bicarbonate (mEq/l.)	13	12	13	23	33	28	25
Plasma salicylate (mg./100 ml.)	55			< 5			
Plasma salicylate (mEq/l.)	3.5			< 0.3			
Arterial pH	7.46		7.44				
" pCO ₂ (mm.Hg)	17		18				
" PO ₂ (mm.Hg)	87.5		95				

During the first 12 hours sodium chloride solution (0.45%) and dextrose (2.5%) was given, to a total of 6 pints (3.4 litres) intravenously, together with glucose drinks (4 pints—2.3 litres) by mouth. During this period she passed 2½ pints (1.4 litres) of urine, but her blood urea rose from 255 to 325 mg./100 ml. (see Table).

February 16.—She appeared much brighter and was drinking freely. Intravenous fluids were therefore discontinued and glucose drinks in 0.45% sodium chloride were given. However, later in the day and during the night she became less co-operative, refused to drink, and developed diarrhoea and urinary incontinence.

February 17.—In view of the loss of weight and clinical evidence of further dehydration intravenous therapy was restarted, again with 0.45% sodium chloride and 2.5% dextrose. Ten pints (5.6 litres) were given in the next 24 hours—this volume being based on the weight loss in the preceding 24 hours. She was also given 125 mEq of potassium (as citrate) by mouth.

February 18.—The patient was clinically much improved. She had gained 10 lb. (4.5 kg.) in weight. There was little clinical evidence of dehydration and the hyperpnoea had ceased. The haemorrhages were absorbing and her mental state was improving. She was, however, weak, and, in spite of the potassium supplement, the plasma potassium concentration had fallen well below the lower limit of normal. The other striking abnormality in the blood chemistry was the persistently raised chloride concentration. As the blood urea had fallen, indicating some return of selective tubular function, and she was now drinking freely, intravenous therapy was discontinued. Glucose drinks in 0.45% sodium chloride were again given. During the next 24 hours she also received 200 mEq of potassium (as citrate) and 400 mEq of sodium bicarbonate.

February 19.—Clinically she was further improved. Her weight was steady and the blood urea had fallen further. It is clear from the other biochemical findings that she had been given too much potassium and probably too much sodium bicarbonate. Unfortunately, the potassium and bicarbonate concentrations were not known at the time and full acid-base studies were not repeated. The raised bicarbonate concentration was probably due to a

metabolic alkalosis, but it is not known whether there was an alkalaemia or what respiratory changes there were. The subsequent clinical course was uneventful. Her blood urea returned to normal levels and protein disappeared from the urine. A psychiatrist confirmed a diagnosis of endogenous depression, and she was transferred for psychiatric treatment.

Renal Damage in Salicylate Poisoning

Although at the time of admission the patient was passing large volumes of urine, the rising blood urea and its subsequent fall to normal make the diagnosis of acute tubular failure very probable. An unusual feature was the very high blood urea only 48 hours after taking the salicylate. However, the profound metabolic stimulation produced by salicylates probably accelerated the rate of tissue breakdown to levels much greater than those usually seen in acute tubular necrosis. We were unable to obtain from the patient, her relatives, or her family doctor evidence that would incriminate any agent other than the salicylates as the cause of her renal condition.

Several reports of salicylate intoxication mention the presence of protein and casts in the urine. We were, however, able to find only three cases in which descriptions are compatible with the diagnosis of acute tubular necrosis (Bywaters and Joekes, 1948; Bracey, 1951; Miller, 1955). It would seem possible that some degree of renal damage is commoner than is at present recognized and may play a part in the acid-base disturbance. The possibility should be borne in mind in dealing with patients with salicylate poisoning because the presence of renal damage leads to the retention of salicylate, complicates the acid-base and electrolyte disturbances, and makes treatment more difficult.

The Acid-base Disturbance in Salicylate Poisoning

This subject has been reviewed by Singer (1954). The first effect of salicylate is to cause hyperventilation and a respiratory alkalosis. Some hours later a metabolic acidosis develops, part at least of which is probably due to the accumulation of organic acids. Our patient apparently had entered this stage of combined disturbance when she was admitted to hospital. In the Chart we have plotted her acid-base structure on admission and two days later on a bicarbonate-pH diagram (Davenport, 1950) to show the

The acid-base disturbance plotted on a bicarbonate-pH diagram. The findings on February 15 and 17 are indicated by $\times$. The displacement below the normal buffer line represents the metabolic acidosis. The low CO₂ tension represents the respiratory alkalosis. The position on the horizontal scale shows the alkalaemia. The circle indicates the probable conditions if the pulmonary ventilation had been controlled to maintain a normal CO₂ tension.

coexistence of these two defects. It is, of course, not possible on the data available to distinguish between a secondary or compensatory component of the metabolic acidosis and a primary component.

This method of plotting the acid-base disturbance shows that the simple estimation of bicarbonate concentration or alkali reserve in conditions such as these gives insufficient information for proper management. In the present case, the combination of a low bicarbonate concentration and overbreathing could easily have been misinterpreted as indicating a primary metabolic acidosis with acidaemia and have led to the administration of alkali with possibly harmful results.

Treatment

After the first few hours in hospital it was clear that the patient, in addition to having salicylate intoxication, was also in the early diuretic phase of acute renal failure probably due to tubular necrosis. The latter condition required water and electrolyte replenishment, which was given as described above. Attempts to collect full balance data were unfortunately frustrated by the diarrhoea and urinary incontinence. Correction of the acid-base disturbance would have required the administration of alkali to combat the metabolic acidosis, and the reduction of pulmonary ventilation to correct the respiratory alkalosis. Alkali is often recommended because, in addition to combating the metabolic acidosis, it hastens the excretion of salicylates. We withheld alkali in the early stages of treatment because there was an alkalaemia and because the severe renal damage would probably have prevented the rate of salicylate excretion from being significantly increased. It is of interest that in the most authoritative review of the subject Harvie and Singer (1955) doubt the value of alkali administration even in the presence of adequate renal function.

Freier *et al.* (1957) described the case of a patient with salicylate intoxication in whom the respiratory alkalosis was treated by the use of muscular relaxants and artificial respiration to decrease the ventilation. Although they did not estimate the pH or pCO₂ the severe tetany of this patient makes it very probable that there was in fact an alkalaemia. It might be inadvisable, however, to use this method simply on the evidence of a high pulmonary ventilation in the absence of good evidence of an alkalaemia. The Chart suggests that if we had acutely reduced the alveolar ventilation to restore the arterial pCO₂ to normal levels (40 mm. Hg) a mild alkalaemia (pH 7.46) would have been converted into a more severe acidaemia (pH about 7.26).

Fortunately, the clinical progress of our patient and the mild degree of alkalaemia did not demand any specific treatment for the respiratory alkalosis.

Summary

A case of acute renal failure probably due to tubular necrosis following salicylate poisoning is described. A review of the literature suggests that renal damage in salicylate poisoning may be commoner than is generally appreciated and may play a part in the acid-base disturbance. The acid-base disturbance and its bearing on treatment are discussed.

We thank Professor A. Kekwick, under whose care the patient was admitted, for his permission to report this case, and Dr. R. B. Singer for his helpful comments. Many of the investigations were performed by the staff of the routine laboratory of the Courtauld Institute.

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Medical Memorandum

Retroperitoneal Duodenal Rupture

Cohn *et al.* (1952), in a review of 25 cases, estimated that the mortality of retroperitoneal rupture of the duodenum due to blunt force is 20%. Johnson (1944), in a review of the world literature from 1916 to 1944, found only 52 bona-fide cases of retroperitoneal rupture, with a mortality of 50%. Schumacher (1910) and Guibé (1910) gave a mortality of over 90%. The mortality has been falling steadily, no doubt due to more recent methods. When it is considered that the lesion is sometimes discovered only at necropsy and that several series record that it has been missed at laparotomy, there need be no surprise that the mortality remains as it is.

It has been estimated that 10% of all gastro-intestinal ruptures are duodenal and that a quarter of those are retroperitoneal, 90% of the latter affecting the second and third part.

AETIOLOGY

The second part of the duodenum is fixed relatively rigidly by its peritoneal attachments and the third part is vulnerable because it can be compressed against the lumbar spine. Another more theoretical factor in the mechanism of rupture is the blow-out effect: when the pylorus is closed and the duodeno-jejunal angle acute an air trap is formed. The causative forces are many—crush and blast injuries, kicks, traffic accidents, sudden deceleration causing steering-wheel impingement in the epigastrium, etc. The force may be minimal and the causative accident ignored because it was so trivial.

Associated injuries include damage to the liver, spleen, kidney, pancreas, stomach, intestines, omentum, and biliary passages. The lower ribs and transverse processes are often involved and there may be thoracic or more distant skeletal injuries. All these, especially the intraperitoneal lesions, serve to distract the surgeon's attention at the time of operation, and unless signs are fairly gross the duodenal injury may be overlooked.

DIAGNOSIS

The mode of presentation is by no means constant. There is often a paucity of symptoms, and the early course may be benign and insidious. To await overt signs like generalized rigidity may mean the optimum time for intervention has passed. Shock is not usually present, and indeed until the duodenal leak in the retroperitoneum has reached significant proportions symptoms and signs are minimal.

The commonest symptom is abdominal pain, constant and of steadily increasing severity, usually in the right half of the abdomen and often going through to the back. Testicular pain has been described from irritation of the testicular nerves accompanying the spermatic arteries by the retroperitoneal exudate (Butler and Carlson, 1931). Vomiting may come late, and some cases have a minor haematemesis. A rise in temperature and pulse rate may not be evident early. Tenderness and guarding in the right hypochondrium are constant, and, later, rigidity and absent bowel sounds in a larger area indicate peritoneal involvement. Occasionally the crepitation of surgical emphysema in the abdominal or thoracic wall may be felt and pelvic crepitation on rectal examination has been described. There is no constant clinical picture, and only a vigilant awareness and a high "index of suspicion" of the condition enable an early diagnosis to be made. Ancillary investigations provide a useful guide, radiological examination being the most helpful. A plain x-ray film of the abdomen can be of the utmost value. This may reveal nothing abnormal, but more often shows free air in the retroperitoneum which may outline the right kidney or present a characteristic "bubble" effect. The retroperitoneal exudate usually obscures the right psoas shadow.