of water, in the left 105 cm. Radiographs of the chest confirmed the lower position of the left clavicle (Fig. 3). A phlebogram carried out by injection into the antecubital veins showed a hold-up of the radio-opaque material at the outer edge of the first rib on the left, but not on the right. The arm was rested in a sling so adjusted as to elevate the

FIG. 2.—Photograph of Case 3 after radical amputation of the left breast with venous oedema of the left arm. Observe the dropping of the tip of the shoulder and clavicle on the left side.

FIG. 3.—Radiograph of Case 3, showing the different position of the shoulder girdle on the two sides.

tip of the elbow and thus the whole shoulder girdle. This resulted in a pronounced diminution in the oedema. The patient refused operative removal of a portion of the first rib.

Comment. — It seems that in some cases of post-operative oedema of the arm after radical mastectomy the condition is due to dropping of the shoulder girdle following the operation, leading to obstruction of the subclavian vein by pressure on the first rib. The obvious treatment of such cases would appear to be removal of that portion of the first rib causing the obstruction. Such observations suggest that, normally, in some subjects the shoulder girdle, contrary to common belief, may in part be held in position not only by suspension from structures above, but also by support below on the structures of the axilla, which are removed during radical mastectomy.

Summary

Two cases are described in which there occurred obstruction of the subclavian vein by the first rib as a result of tearing of structures supporting the clavicle. The injury resulted in gross pitting oedema of the arm, which was relieved by removal of a portion of the first rib. The significance of the observation in relation to some cases of post-operative oedema of the arm after radical mastectomy is discussed.

I wish to express my gratitude to Mr. A. D. Le Vay, who operated on Cases 1 and 2, and to the consultant staff of the Royal Cancer Hospital, for kind permission to publish this paper.

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PYLORIC STENOSIS AND FIBROUS STRICTURE OF THE STOMACH DUE TO FERROUS SULPHATE POISONING

BY

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During recent years several accounts of the effects of poisoning from compound ferrous sulphate tablets have been published, notably by Forbes (1947), Thomson (1947, 1950), and Spencer (1951). There has been an increasing awareness of the danger if these tablets are accidentally swallowed by children. The following case is thought worthy of record, as it exhibits certain features not noted in the cases so far reported.

Case Report

A previously healthy boy, aged 17 months, swallowed between six and twelve tablets of a proprietary preparation of compound ferrous sulphate at about 2 p.m. on July 21, 1951. He vomited shortly afterwards, and this was followed by haematemesis. On admission to hospital an hour later he was found to be restless and collapsed. Gastric lavage was performed and anti-shock treatment instituted. He continued to vomit small quantities of bright-red blood all that day. Next day he was quieter and vomited some dark-brown fluid only once, at 11 a.m. No further haematemesis occurred. He was discharged on August 3, by which time he was vomiting only occasionally and his stools were normal in colour. His weight at this time was 19 lb. 4 oz. (8,730 g.).

FIG. 1.—Barium meal August 28, 1951. Stricture of body of stomach.

After discharge from hospital he failed to improve. The vomiting gradually increased in severity, and he was readmitted to the same hospital on August 14. On examination he was found to be dehydrated and very restless. He weighed 17 lb. 12 oz. (8,050 g.). On August 17 and 20 he vomited large quantities of curds. On August 25 his weight was 16 lb. 12 oz. (7,600 g.). A barium meal examination done on August 28 was reported to show a stricture of the body of the stomach, through which the barium passed slowly, and some oesophageal dilatation (Fig. 1).

On August 31 he was transferred to Hammersmith Hospital. He was found to be a grossly wasted and dehydrated child, with depressed fontanelle; otherwise physical examination was negative. Intravenous saline and dextrose were given, and feeds by mouth of 1 oz. (28 ml.) of milk with casydol. He vomited five times on September 1, and seemed to have abdominal pain on taking feeds. Next day he was better and less dehydrated. It was thought that there was probably an obstruction at the lower end of the oesophagus. A gastrostomy was therefore performed on September 4, and from then on he was fed by this route. During the next week vomiting still occurred, but consisted mostly of mucus. A chest radiograph on September 11 showed the lungs to be clear. Next day stomach aspiration yielded 13 oz. (368 ml.) undigested milk and mucus.

On September 13 x-ray examination showed the tip of the gastrostomy tube in the oesophagus and some air in the large bowel. A barium meal was given by mouth. The oesophagus showed some dilatation, but no obstruction was noted at the lower end. The stomach contained excess resting fluid. A sharply demarcated constricting band was seen passing horizontally round the lower part of the body of the stomach. Distal to this the pyloric antrum was seen to be narrowed and its outline was slightly irregular. The

FIG. 2.—Barium meal September 13, 1951. Stricture of body of stomach, narrowing of pyloric antrum, and pyloric stenosis.

FIG. 3.—Barium meal 20 hours after Fig. 2. Air content of stomach demonstrates stricture and narrowing of pyloric antrum. Small amount of barium in transverse colon.

tally. There also appeared to be fibrosis and narrowing of the stomach distal to this stricture, with almost complete stenosis in the region of the pylorus.

On September 15 jejunostomy was performed, and three hours later hourly feeds were started through the tube. In the next three days he gained 11 oz. (312 g.) in weight, and his general condition was somewhat improved. However, subsequent to this the child's condition gradually deteriorated, and he died on September 20.

Necropsy (Dr. Keith Simpson).—Forty hours after death. Body in a poor physical state, with considerable loss of flesh and marked dehydration. Recent operations for both gastrostomy and jejunostomy completed successfully and without operative mishap—but with suppurative peritonitis ensuing after the second of these procedures. No residual corrosive change at the lips or in the glottis and no mechanical obstruction to the cardiac orifice. Liver showed

barium shadow ended distally in a smooth convexity directed backwards and to the right (Fig. 2). Every effort was made to identify the pylorus and duodenum. However, this was not possible. No peristalsis was observed in the stomach. The gastric mobility appeared normal. At four hours no barium had left the stomach, and it was decided to remove most of it via the gastrostomy tube to avoid the danger of aspiration into the lung. Re-examination next day, at approximately 20 hours, showed there was a small amount of barium in the transverse colon, and some still remaining in the stomach. The stricture was seen at this time, as the stomach was filled with air (Fig. 3). From these investigations it was thought that there was a well-defined constricting fibrous band passing round the body of the stomach horizontally.

mild toxic change only. Some excess mucus and oedema fluid was found in the bronchial tree, but no pneumonitis nor pulmonary collapse was seen. There was early extension of infection into the right pleural sac from the peritoneum. In the stomach there was remarkable thickening of the wall by scar tissue extending distally from the lower third of the body. A broad band of scar tissue contracted the pyloric antrum transversely, and thickening of the wall extended into the pyloric sphincter. In the scarred area there was distortion and narrowing of the gastric lumen.

The cause of death was acute suppurative peritonitis following jejunostomy for obstruction to the stomach by scarring due to poisoning with compound ferrous sulphate tablets.

Discussion

Very few cases of pyloric stenosis and fibrous stricture of the stomach due to the ingestion of poisons, without producing concomitant fibrous stricture of the oesophagus, can be found in the English literature, but apparently such cases are more common in foreign countries. Cases have been reported due to the following causative agents: sulphuric acid (Halstead, 1919); hydrochloric acid (Schulenburg, 1941; Joll, 1941); formaldehyde (Vinson and Harrington, 1929); tincture of iodine (Wilensky and Kaufman, 1939); and lysol (Grey Turner, quoted by Schulenburg, 1941). Very recently a case has been reported of pyloric stenosis arising in a 3-year-old boy about one month after swallowing 67 compound ferrous sulphate tablets (Crosskey, 1952).

Compound ferrous sulphate tablets consist of ferrous sulphate 3 gr. (0.2 g.), copper sulphate 1/25 gr. (2.6 mg.), and manganese sulphate 1/25 gr. (2.6 mg.), usually coated with sugar and coloured bright green. Somers (1947) and Forbes (1947) have shown that the ferrous sulphate is the lethal agent, the small amounts of copper and manganese making no difference to the toxicity of the tablets. Forbes (1947) and Spencer (1951) have independently suggested that the ferrous sulphate is converted in the stomach into ferric chloride, the latter producing the main local lesions.

Twenty cases of poisoning with compound ferrous sulphate tablets in children have been reported in the literature so far. Of these, 10 (50%) have recovered, all apparently remaining symptom-free after discharge from hospital, and 9 (45%) have died within two and a half days. One case (5%) recovered, but subsequently developed pyloric stenosis. Nearly all these patients vomited after taking the tablets, but 66.7% of those that died had haematemesis or blood in the stomach washings, compared with only 30% of those that recovered without sequelae.

Experimental work by Somers (1947) and Forbes (1947) in animals has demonstrated that the gastric changes are roughly proportional to the size of the dose for each species. In children the gastric appearances at necropsy have been consistent and similar to those found in the experimental animal. In children there is an area of haemorrhagic gastritis with oedema (Prain, 1949) situated in the middle third of the stomach near the greater-curve side and involving both walls. A less degree of similar reaction extends over the rest of the stomach. Microscopy shows oedema of the submucosa, necrosis of the mucous membrane, vascular thrombosis, and impregnation of the mucosa and vessel walls with iron. Forbes (1947) and Spencer (1951) emphasize the haemorrhages that occur into the stomach wall.

It is unfortunate that the stomach in the present case was not examined histologically. It is evident, however, from the accounts given of similar cases and experimental work in animals that the process of repair following the intense haemorrhagic gastritis, if given time, would lead to fibrous contracture of the pyloric antrum and pyloric stenosis. This fibrosis may also be increased by superficial peptic ulceration and subsequent scarring following the shedding of the gastric mucosa. In fact, the development of the fibrous reaction in the submucosa and muscular coat of the pylorus was noted in the biopsy specimen in Crosskey's case (1952).

In the present case the rapid development of the fibrous stricture of the pyloric antrum and the pyloric stenosis can be seen by comparison of the two barium-meal examinations done 16 days apart. This clearly excludes a congenital abnormality.

Summary

A case of pyloric stenosis and fibrous stricture of the pyloric antrum developing in under two months in a child after swallowing compound ferrous sulphate tablets is described. Death was due to acute suppurative peritonitis following jejunostomy.

The literature on ferrous sulphate poisoning and fibrous stricture of the stomach due to the ingestion of corrosive poisons is briefly reviewed.

My thanks are due to the physicians and surgeons under whose care the patient was at Hammersmith and Margate Hospitals for permission to publish the case, to Dr. J. Duncan White and Dr. J. P. Thierens for permission to use the radiographs, to Dr. Keith Simpson for his necropsy report, and to Mr. Basden for the reproductions of the radiographs.

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METHOD OF PREVENTING INSULIN ATROPHY

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Many theories have been put forward to explain the development of fat atrophy occurring at the site of injection of insulin in some diabetic patients, and in our opinion no better summary of these views has been given than that of Marble and Smith (1942).

During an extensive survey of 57 cases of insulin atrophy occurring in this clinic it occurred to us that, whatever the exact mechanism of its production, the high local concentration of insulin at the site of injection is probably a significant factor. Dispersal of this concentration seemed to be a logical step towards lessening or preventing such atrophy.

The use of hyaluronidase as a spreading agent suggested itself. The obvious danger was too rapid absorption of insulin into the blood stream, with consequent hypoglycaemia. Several stabilized diabetics in hospital, not showing insulin atrophy, were therefore given their usual doses of insulin with added hyaluronidase. No appreciable change was found to occur in their diabetic control. No hypoglycaemia was observed, whilst, on the other hand, there was no evidence that the insulin was rendered ineffective. In studying the control of

diabetics by the inunction of an insulin hyaluronidase mixture, Bresgen and Heinlein (1951) also found that the insulin was not inactivated.

Accordingly, in 1951 three children who showed marked atrophy at whatever site insulin had been given were chosen for a trial. They lived in a home for diabetic children attached to the National Children's Home at Frodsham, Cheshire, and their diabetic condition was under constant supervision by trained nursing staff. Areas in which insulin had not been previously given were chosen in each child for regular injections of an insulin-hyaluronidase mixture, and injections have since been confined to these new sites.

The insulin-hyaluronidase mixture was made daily by dissolving 3 mg. of hyaluronidase in 400 units of soluble insulin (80 units per ml.). From this mixture the individual doses were drawn up. This addition of hyaluronidase to insulin did not produce any alteration in their diabetic control, and injections of the mixture caused no more discomfort than had injections of insulin alone.

Case Reports

Case 1.—A girl born on December 3, 1938, had been a diabetic since 1944. She was first seen by us in September, 1950, when she showed insulin atrophy in both arms and both thighs. Her parents stated that the atrophy developed in the arms in about six months and in the thighs in about four and a half months after beginning insulin injections. Her diet contained 250 g. of carbohydrate daily up to May, 1952, since when she has had a "free diet." Injections of soluble insulin twice daily from September, 1950, to February, 1951, in the arms and thighs greatly increased the atrophy already present. Though she has had no more injections in the arms and thighs since February, 1951, the atrophy remains unchanged. From March 1, 1951, to January 27, 1953, the insulin-hyaluronidase mixture was given into the buttocks only. The total daily dose varied during this period from 72 to 88 units. No subcutaneous atrophy of the buttocks has developed from the use of this mixture.

Case 2.—A girl (born September 15, 1943) had been a diabetic since 1948, and was first seen by us in August, 1950, when she showed marked insulin atrophy of both arms and both buttocks. We were informed by her parents that insulin atrophy was "very bad" in the arms within about nine months of starting insulin injections. Her diet contained 160 g. of carbohydrate daily at first; it being increased to 235 g. at present. From March 1, 1951, to October 28, 1952, the insulin-hyaluronidase mixture was given into the anterior abdominal wall only. The total daily dose varied during this period from 64 to 68 units. No subcutaneous atrophy of the anterior abdominal wall has developed.

Case 3.—A boy (born September 4, 1941) developed diabetes mellitus in 1949, and was first seen by us in May, 1951, when insulin atrophy was present in both arms. At that time his diet contained 190 g. of carbohydrate daily, and this has gradually been increased to 250 g. daily. Injections of soluble insulin were given twice daily, into the left thigh only, from May 26 to November 20, 1951, the total daily dose varying between 84 and 45 units. Atrophy was then observed to have developed at this site. Since November 21, the insulin-hyaluronidase mixture has been given into the right thigh only. The total daily dose has varied between 48 and 56 units. The mixture has been used for 16 months up to March 20, 1953, and has produced no atrophy in the right thigh.

Discussion

It would seem from our observations in these three cases that the addition of hyaluronidase to insulin has prevented atrophy developing, whereas, with insulin alone, atrophy