The four patients whose case histories are presented above have certain features in common, apart from their site of origin. In all of them neoplastic change occurred after a long latent interval, which varied only between 26 and 30 years. They were all treated originally for benign conditions, and in three of them it is known that frequently repeated doses of x rays were given over a period of six months or more. In the three patients treated for thyrotoxicosis the tumours had arisen approximately 4 cm. deep to the centre of the irradiated area of skin, and these three patients had all suffered severe radiation damage to the skin, two of them requiring excision and plastic repair for either epitheliomatous change or necrosis. Case 4 alone failed to show any convincing evidence of skin damage, and for this reason it is doubtful whether the tumour can be attributed to irradiation. However, this is a comparatively uncommon site for cancer, and it is difficult to be persuaded that its appearance was purely coincidental. Radiation is only one of many known carcinogenic agents, and, although it cannot be held solely responsible, it may well have been a contributory factor in the genesis of this tumour.

The remaining three patients all seem to have developed tumours as a direct result of irradiation, and in two of them there are features which further support this aetiology. In Case 2 the tumour had the structure of a fibrosarcoma, and, although this tumour may rarely occur in the upper part of the oesophagus, it must be very rare in post-cricoid tumours. As Cade (1951) has pointed out, fibrosarcoma may develop on a basis of post-radiation scarring. In Case 1 the tumour arose in the pyriform fossa, which may be significant, as carcinoma in this site is predominantly a disease of men.

In conclusion it seems reasonable to speculate that, if the treatment of thyrotoxicosis by intense or prolonged irradiation was a common practice 25 to 30 years ago, further cases of radiation cancer in the laryngopharynx may occur, or have perhaps already occurred.

Summary

It is rare to find a tumour in any of the deep tissues following external irradiation, and the literature on this subject is briefly reviewed.

The case histories of four patients who developed tumours in the laryngopharynx after irradiation of the neck are presented. The criteria considered to be important in the diagnosis of radiation cancer are enumerated, and the reasons for regarding three of these tumours as examples of post-radiation cancer are given. In the fourth patient the aetiology of the tumour is open to doubt.

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FERROUS SULPHATE POISONING IN CHILDREN

BY

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Iron poisoning in children occurs through the temptation of attractive sugar-coated pills containing ferrous sulphate which, with good reason, are freely supplied to their mothers. The first comprehensive reports of this disaster in children were published in 1947, and, though it is difficult to believe that cases did not occur before, the first recorded case was that of a child of 16 months who died, in May, 1944, after swallowing 39 ferrous sulphate tablets (Thomson, 1947). Since this time there have been further case reports, and the clinical picture of the poisoning is becoming clear.

The daily press has recently given prominence to inquests on children who have died after swallowing ferrous sulphate tablets, and I have used this source of information to collect some details of four cases to add to the reports of four which I have seen myself. Brief reference has already been made to two of these coroners' reports (Cases 6 and 8) in a leading article in the *Lancet* (1949). The daily press has also made reference to the ignorance of parents and doctors alike concerning the effects and dangers of these tablets to small children.

It is the purpose of this paper to describe the clinical picture of iron poisoning in detail, to discuss the effects of large doses of iron, to propose a more positive therapeutic approach than has been given in previous medical articles, and to suggest a method of safeguarding children from these tablets.

The Tablets.—The most readily available tablets are green sugar-coated pills, and each of these contains ferrous sulphate, 3 gr. (0.2 g.), copper sulphate, 1/25 gr. (2.6 mg.), and manganese sulphate, 1/25 gr. (2.6 mg.). Forbes (1947) has shown by animal experiments that the effect of the copper and the manganese can be discounted, and that it is the ferrous sulphate which has the irritating and lethal effect.

The cases recorded below have, with the exception of the coroners' cases, all been treated in this department within the space of a year. In this period three other children were admitted with a diagnosis of ferrous sulphate poisoning, but they have been excluded because of lack of detail regarding what they had swallowed. One had the symptoms of poisoning, but the other two were not upset. The mother of one of the latter, aged 18 months, was quite sure he had swallowed 24 tablets, but only minute quantities of iron were recovered from the stools and stomach washings, and it was thought more probable that only a few pills had been taken than that 24 tablets had not made him ill.

In the seven preceding years during which this department has been in existence only one other such case has been admitted. This was a girl aged 2½ years who swallowed 60 tablets. Her mother thought she vomited back "nearly all the tablets," and, though she was pale and drowsy and had marked diarrhoea and vomiting, her recovery during the subsequent three days seems to

have aroused no special interest at the time. Her case has been excluded owing to the doubt about the number of tablets she retained.

Case 1

Between 5.30 and 6.10 p.m. on June 26, 1950, a girl aged 21 months swallowed 75 ferrous sulphate tablets. These made her sick, and her father, realizing what had happened, held her upside down over the kitchen sink, whereupon she vomited 21 tablets. After this a nurse gave her some salt and water to drink, and she was sick again. Later the family doctor washed her stomach out with normal saline, but on neither occasion were further tablets returned. From 6.15 p.m. the child was said to have been cold, pale, and semi-conscious.

At 8.35 p.m. she arrived in hospital, and her condition was that of a well-nourished but shocked child. She was cold and pale, with slightly cyanosed lips, and her pulse was rapid (150 a minute) and difficult to feel. She was semi-comatose in that she showed little resentment to painful stimuli, but she did open her eyes momentarily when roused. Further examination revealed no abnormality. Gastric lavage was carried out with normal saline, and 8 oz. (230 ml.) of sodium bicarbonate solution was left in the stomach. During this manipulation the returning fluid contained shreds of tissue and streaks of blood but no further tablets.

For the next 10 hours the child was unaware of her surroundings. She was very restless and frequently retched and vomited small quantities of dark red blood. Her respirations were irregular, shallow, and rapid (60-70 a minute) and her temperature rose to 102.8° F. (39.3° C.).

By 6.30 a.m. on June 27 she seemed a little better and was warm, though still pale and very restless. She was retching frequently but not vomiting quite so often, and for the remainder of the day her condition remained much the same. She occasionally showed a little interest in her surroundings and appeared to recognize her father. By evening she was drowsy and slept for short spells, but was very restless in the intervals. She was vomiting "coffee-ground" material but also taking drinks of water. Her bowels were opened three times, the stools being small, dark, and very offensive.

On June 28 she was taking a little more interest in her surroundings and tried to sit and stand up occasionally, but she was very "floppy" and seemed too weak to do so. She vomited "coffee-ground" material on two occasions, but was very drowsy and slept most of the time. Next day the improvement was maintained. She slept well through the night and was still drowsy during the day. No further vomiting occurred. On the 30th she was much more lively but still rather "floppy," and could not sit up on her own yet.

On July 3 her behaviour was normal, and she was discharged from hospital on July 7. A fortnight later her appetite was poor, and she had vomited at least once a day at home. Thereafter vomiting ceased, and on August 31 the mother said that her child "has really been back to her normal self for the past week."

Investigations.—June 26: 10.30 p.m., serum iron, 3.3 mg. per 100 ml. (normal, 0.035-0.22 mg. per 100 ml.). June 27: 1.30 a.m., serum iron, 2.25 mg. per 100 ml.; 9.30 a.m., serum iron, 1.12 mg. per 100 ml.; 10.15 a.m., B.P., 120/70; haemoglobin, 68%; 10.30 a.m., E.C.G., normal; 5 p.m., E.C.G., normal; 10.30 p.m., B.P., 105/60. June 28: 10 a.m., B.P., 135/70; haemoglobin, 60%; urinary iron content, nil; 3 p.m., urinary iron content, nil. June 29: 10 a.m., B.P., 120/65; haemoglobin, 62%; E.C.G. normal; 12.30 p.m., serum iron, 0.26 mg. per 100 ml.; urinary iron, 0.45 mg. per 24 hours. The urine contained a trace of albumin; microscopy showed nothing abnormal. August 31:—Liver-function tests: zinc sulphate, 9 units; thymol turbidity, 12 units; thymol flocculation, +++; cephalin-cholesterol, ++++; alkaline phosphatase, 23.8 units.

Case 2

At 11 a.m. on February 2, 1951, a boy aged 23 months was found to have eaten 16 ferrous sulphate tablets and 10 iron plastules (the total iron content of tablets and plastules was 98 gr. (6.5 g.) of ferrous sulphate, or the equivalent of 33 ferrous sulphate tablets). He was immediately given salt and water to drink, and he vomited some "black liquid slime" containing some partly dissolved plastules and four tablets. In the next hour he vomited several times and then went to sleep. When he awoke at 1.45 p.m. he vomited about a tablespoonful of bright red blood, and at 2.15 p.m. he was admitted to hospital.

Examination showed a boy of average physique; he was pale and had cold extremities, and was retching frequently. His pulse rate was 140, his blood pressure 90/60, and his respiration rate 35. For the next 10 hours retching and vomiting continued, and about every half-hour he brought up a little blood and sometimes shreds of mucosa. He was restless and quiet in turns, but was co-operative and quite aware of his surroundings. At 11 p.m. both plantar responses were extensor.

For the next 24 hours he remained drowsy and slept fitfully, but when awake was still very restless. Vomiting was not so frequent and no longer contained blood, and after midday it ceased altogether. His general condition improved and his extremities were warm, but both plantar responses remained extensor.

On February 4 alternating drowsiness and restlessness continued, but he appeared brighter in himself and took more interest in his surroundings. His temperature had gradually risen to 101° F. (38.3° C.), but thereafter was normal. Next day his behaviour was normal, plantar responses were flexor, and his bowels were opened for the first time. He was discharged home on February 8, and two weeks later was "very well."

Investigations.—February 2: 3.30 p.m., serum iron, 3.42 mg. per 100 ml. February 8: serum iron, 0.33 mg. Liver-function tests: thymol turbidity, 3 units; thymol flocculation, nil; cephalin-cholesterol, +; zinc sulphate, 3 units; alkaline phosphatase, 5.8 units; serum bilirubin, absent.

Case 3

At 5.30 p.m. on November 25, 1950, a boy aged 11 months was found vomiting on the floor and beside him was a packet of ferrous sulphate tablets: 13 tablets were missing. He was put to bed but continued to vomit, and the parents estimated that he had returned bits of tablets amounting to four to six whole tablets. He thus retained seven to nine tablets. By 6 p.m. he had turned very pale and lay very still, crying only when he wanted to vomit. The vomit was a clear brown fluid and did not contain blood. On admission to hospital at 6.40 p.m. he appeared pale, quiet, and rather drowsy, and there was slight cyanosis of the lips. At 7 p.m. the stomach was washed out; at first he cried and struggled, but towards the end of the procedure he lay very still. Physical examination at this stage showed a well-nourished infant with no abnormal signs. The pulse rate was 150, the respiration rate 35, and all deep reflexes were present and brisk. For the next three hours he remained very quiet and pale, and he vomited once. Thereafter his colour improved and he slept through the night. The next day he appeared lively and quite normal. He passed two loose black motions; the pulse rate dropped to 100 and the respiration rate to 24. On November 27 he remained well, and next day was discharged home.

Case 4

At 3.30 p.m. on February 6, 1951, a boy aged 20 months was noticed by his mother to be rather quiet; she thought he looked drowsy and ill, and she became alarmed when she could not rouse him properly. His sister said he had been eating some tablets, and investigation showed that a maximum of five ferrous sulphate tablets were missing. At 4.30 p.m. his mother gave him some salt and water to drink,

and he vomited several times, two tablets being returned. At 6.30 p.m. he was admitted to hospital and kept under observation for 24 hours, but he was cheerful and lively on arrival, and at no time showed any ill effects from the three tablets which he had retained. Treatment was considered unnecessary.

"Coroners' Cases"

Case 5

At 12.30 p.m. on August 20, 1950, a boy aged 12 months, who had always been healthy, was put to sleep in his parents' bed. At 1.15 p.m. he was found playing with an unknown quantity of ferrous sulphate tablets, and four or five were removed from his mouth. He was made to drink salt and water and he vomited, but no tablets were returned. He was given some castor oil and then ate his dinner. He did not appear to be upset. At about 2.45 p.m. he vomited a brown-coloured liquid containing six tablets. The family doctor prescribed a further dose of castor oil, and said that if the child became worse he should be sent to hospital. The child went to sleep but woke up again and vomited. He was cold and clammy. At 5 p.m. he was found to be dead.

Necropsy Report.—The body was that of a well-developed male infant. The nostrils, lips, and mouth were stained with a black liquid. The nasopharynx, trachea, and main bronchi contained much brownish-black semi-solid material, which was not frothy, and the lungs showed some mottling on their surfaces due to scattered areas of collapse. The stomach contained about 3 oz. (85 ml.) of thick black fluid and the mucous membrane was red and necrotic. A few scattered areas of congestion were present in the upper jejunum, and Peyer's patches of the entire small intestine were prominent. The large intestine contained black fluid but was otherwise normal. The liver was normal in size but rather pale. The heart, spleen, pancreas, kidneys, skull, and brain were normal macroscopically. The stomach contents gave a strongly positive dipyrindyl reaction for iron.

Histology.—The stomach showed necrosis of the superficial layers of the mucosa. Prussian-blue staining revealed a mass of iron in the necrotic portions of the mucous membrane and smaller amounts being absorbed into the blood stream. The liver showed cloudy swelling of the cells of the centrilobular zone and a slight increase of polymorphonuclear leucocytes in the liver sinusoids.

Case 6

At 8.15 a.m. on September 10, 1947, a girl aged 19 months was found vomiting after taking 15 or 16 ferrous sulphate tablets. She was taken to hospital and there given salt and water, and she vomited again. The mother was told that there were no beds available, and she was sent to another hospital. Here she was told that the tablets were not poisonous and would do the child no harm. The child was retching now but not vomiting, and the mother was told to take her home and give her plenty of milk to drink.

The mother was not satisfied and took the child to another doctor on the way home. He told her to give the child orange juice to drink and she would be all right. The mother then took the child home, put her in her cot, and went to make some orange juice. When she returned the child was dead. The time was 1 p.m., about four hours after the child had taken the tablets.

The necropsy showed intense congestion of the stomach, which contained blood and mucus, and the intestines were also congested. There was no vomit in the respiratory passages.

Case 7

At 9 a.m. on January 4, 1951, a boy aged 18 months started to cry and was given a cup of tea, whereupon he was violently sick and had diarrhoea. His mother found her box of ferrous sulphate tablets empty, and 44 tablets were missing. He was taken to hospital, where his stomach was washed out with 5 pints (2.8 litres) of fluid, flecks of blood and mucus being returned. Restoratives were administered, but he died. He was said to have been in a state of coma from 11 a.m., and he died at 2.30 p.m., five and a half hours after taking the tablets.

Necropsy showed acute dilatation of the right ventricle and congestion of the stomach and intestines, with, on analysis, substantial quantities of iron in the stomach contents. There was no vomit in the respiratory passages.

Case 8

One morning in September, 1949, a girl aged 14 months was found to have swallowed 44 ferrous sulphate tablets. The doctor was telephoned, but he said there was no danger. Later the child showed signs of distress and started to vomit, bringing up four tablets. The doctor was sent for and found a rapid pulse. He again said that there was no danger, but he called back later and prescribed castor-oil and kaolin. The child vomited and retched throughout the day, and in the evening was said to be semi-conscious and was put to sleep in her parents' room. During the early hours of the following morning the mother found her child to be dead, some 20 to 24 hours after taking the tablets.

At necropsy the stomach contained a quantity of black iron sulphide and showed intense congestion and oedema of its wall, with, in places, corrosion of the mucosa. There were "profound toxic changes in the liver."

The Clinical Picture

Excessive amounts of ferrous sulphate have a fairly constant effect on small children. Within the first hour even the mildest cases make their mothers apprehensive, for they look pale and ill and they generally vomit. At first the vomitus may contain unaltered tablets, and in the more severe cases it often contains small amounts of bright red blood by the third hour, and by this time the child presents the fully developed and characteristic

Summary of Case Records

Case No.	Age (Mths)	Sex	No. of Tablets Taken	No. of Tablets Returned and After How Long	No. of Tablets Retained	Treatment Before Admission	Time Before Admission	Treatment After Admission	Tachycardia	Early Pallor	Drowsiness	Vomiting	Haematemesis	Result	Time Before Death
1	21	F	75	21. 30 mins.	54	Salt water; gastric lavage	3 hours	Gastric lavage; bismuth carb.; vitamin mixture	+	+	+	+	+	Recovered	—
2	23	M	33	4+. Few mins.	Less than 29	Salt water	3½ "	Bismuth carb.; I.V. glucose-saline; vitamin mixture	+	+	+	+	+	"	—
3	11	M	13	4-6. Few mins.	7-9	Nil	70 mins.	Gastric lavage; bismuth carb.; vitamin mixture	+	+	+	+	—	"	—
4	20	M	5	2. 1 hour	3	Salt water	3 hours	Nil	—	—	+	—	—	"	—
5	12	M	?	6. 1½ hours	?	Salt water; castor oil	—	"	?	?	+	+	—	Died	4 hours
6	19	F	15-16	None	15-16	Salt water	—	"	?	?	?	+	—	"	4 "
7	18	M	44	4. "	44	Nil	?	Gastric lavage	?	?	?	+	—	"	5½ "
8	14	F	44	4. "	40	Castor oil; kaolin	—	Nil	+	?	?	+	—	"	20-24 hours

This table is similar to that used by Thomson, but has been slightly amended.

picture. Pallor, coldness, tachycardia, retching, vomiting, and drowsiness, together with restlessness, are almost constant. Of these vomiting and drowsy restlessness are the predominant features of the illness, and the length of time they continue depends on the number of tablets taken. Thus Case 4 was drowsy and looked ill for an hour or two after only three tablets, whereas Case 1, who retained 54 tablets, was semi-comatose for 24 hours and drowsy for four days, and it was eight days before she behaved normally.

Haematemesis in the first 12–24 hours is frequent, and, though it is an alarming symptom, it does not usually lead to an excessive loss of blood. Diarrhoea is uncommon, which is surprising when one considers the irritating effect of the tablets on the stomach. However, the small bowel escapes gross damage, and this may be due to the reaction of the alkaline intestinal juices converting the ferrous sulphate into insoluble iron compounds.

Increase in the respiratory rate was noticed in the first three cases, and in Case 1 the alteration was pronounced, the excursions were very shallow, and the rhythm was also irregular. These features have not been reported in other cases, though Somers (1947) noticed shallow breathing and an increased rate in experiments on rabbits. Two other cases have been reported with abnormal physical signs in the chest, but, in these, aspiration pneumonia was the probable cause.

Detailed physical examination adds little to what has been noted already. Abdominal distension is not present and tenderness is only infrequently found, and then is of slight degree. The central nervous system, apart from the altered mental state, has shown abnormal signs only in Case 2, in which bilateral extensor plantar responses were noticed on the first evening, and these reverted to normal on the fourth day as the child recovered.

A further feature that must be mentioned is a misleading period of clinical improvement preceding collapse which has been observed in some fatal cases during the second and third 12-hour periods. Thus Thomson's (1950) fourth case (reported fully by Prain, 1949) appeared quite well on the second day, but collapsed quite suddenly and died after 39 hours, whilst the other death in Thomson's series and Forbes's first case also followed this pattern.

Study of the case records of the eight deaths so far reported (including those in this series) reveal two critical periods in the illness. The first is after four to six hours, when three of the children died; the second is from 20–53 hours, and it includes the remaining five deaths. The significance of these periods is discussed later.

Mode of Action

It is clear from the necropsy findings in all cases that the stomach bears the brunt of the initial damage. It is reported as being oedematous and congested, with haemorrhagic and necrotic areas of variable extent which mainly involve the crests of the rugae. The small intestine is generally affected only in its proximal part, and then to a less degree than the stomach, and it shows congestion and perhaps oedema of the mucous membrane. The liver also shows gross changes, which vary from cloudy swelling to areas of necrosis, but the only other abnormalities that have been detected are cloudy swelling of the kidneys, heart, and pancreas, congestion of the spleen with necrosis of the Malpighian corpuscles, and congestion and patchy collapse of the lungs with aspiration pneumonia.

Prain suggested that liver failure is the cause of death in iron poisoning, but he admits that "the extent and degree of change in the liver seem scarcely sufficient to explain the fatal issue." It seems clear, too, that if liver failure is to be blamed for death then the histological changes are hardly comparable to those found in, for example, acute yellow atrophy, and in iron poisoning death occurs much quicker than is usual in that disease. For these reasons I would suggest that one must look elsewhere for the cause of death.

Serum iron estimations in Cases 1 and 2, between four and five hours after the tablets had been swallowed, showed levels of 3.3 and 3.4 mg. of iron per 100 ml., compared with the normal of 0.035–0.22 mg. per 100 ml. (Sven Dahl, 1948). These figures approximate almost exactly to the level, quoted by Slack and Wilkinson (1949), of 3.6 mg. per 100 ml. which is attained after an intravenous injection in adults of 200–300 mg. of an iron sucrose preparation. The symptoms reported to follow intravenous injections of iron include pallor, headache, vomiting, weakness, and collapse (Ramsey, 1950), and encephalopathy (Birch and Till, 1951), while Hurst (1931) and Napier (1936) recorded cases of presumed iron encephalopathy in adults after iron medication by mouth. There would seem to be a similarity here between the effects of iron given intravenously in adults and poisoning by ferrous sulphate in children, and I feel that iron poisoning results in a widespread interference with cell function, and that probably the most important organ involved is the brain. Histological proof of this is unfortunately lacking, for the available necropsy reports do not mention detailed examination of the brain.

I would suggest that the genesis of the illness is as follows. The initial vomiting, haematemesis, tachycardia, and collapse are due to the direct corrosive effect of the iron on the stomach. This causes considerable shock (as in other corrosive poisons), and it is this, together with the rising serum iron, which is the main cause of death in the first period (four to six hours). This stage of shock lasts for some 12–24 hours and then passes off, and it is its passing which causes the misleading improvement seen in some fatal cases during the second and third 12-hour periods. Concomitant with this process, and starting very soon after swallowing the tablets, iron is absorbed into the general circulation, and the serum iron may reach 15–100 times the normal level. The necropsy findings, though incomplete, make it reasonable to suppose that this amount of iron can cause profound cell dysfunction and that its effect will be general, though some tissues will be damaged more than others. The occasional untoward sequelae of intravenous injections of iron in adults and the not dissimilar type of illness observed in severe iron poisoning in children suggest that the central nervous system is deeply involved, and I feel that iron probably exerts its most important effect on the cells of this system and through this action causes death.

Treatment

Hitherto all reported cases have been treated "on general principles." That is to say, the stomach has been emptied either by an emetic, such as salt and water, or by lavage, and bicarbonate of soda or bismuth carbonate, or both, have been utilized to convert the soluble ferrous sulphate into insoluble iron compounds. These measures are both rational and simple, and were carried out on the cases in this series. In Case 5 six undissolved

tablets were vomited one and a half hours after the child had taken them, so, clearly, every effort should be made to empty the stomach in the first few hours; and it should be remembered that whole tablets will not pass through a stomach tube.

Dimercaprol ("B.A.L.") has been used on two occasions (Thomson, 1950; Roxburgh, 1949), but no claim of its efficacy has been made, and Edge and Somers (1948) have shown in experimental work on mice that when used either orally or intravenously it increases, rather than decreases, the toxic effects of ferrous sulphate. It was not used in this series.

Shortly after the admission of Case 1 to hospital Dr. A. L. Latner, of the Department of Biochemistry of this hospital, was called in consultation, and he made the following suggestions: (1) As iron might act as a heavy metal and combine with SH groupings and thereby interfere with oxidation, tocopherol, which acts as an antioxidant and appears to cut down cell oxidative requirements, should be prescribed. (2) Methionine should be given (a) as a source of SH groupings and (b) in an attempt to prevent the development of the fatty changes in the liver seen in some previous cases. (3) That the drowsiness and sudden death of previous cases might be due to some interference with the oxidative enzymes and with the utilization of the vitamin B complex. Also, as deficiency of certain members of this group is associated with fatty change in the liver, then members of the vitamin B complex should be given as well.

The outcome of these suggestions, later known as the "vitamin mixture," was prescribed, and the ultimate recovery of Case 1, who had taken a larger dose of iron than any other case previously described, encouraged us to use a similar regime in Cases 2 and 3, with equally satisfactory results. In Case 1 this treatment was started 22 hours after the tablets had been swallowed, and in Cases 2 and 3 it was started within a few hours of the child's arrival in hospital.

When Case 2 arrived in hospital, also having taken a very large dose of ferrous sulphate—98 gr. (6.5 g.)—though in this instance not all in tablet form, it was argued that if the 20–53-hour period was a critical one then it was important to see that the child entered it in as good general condition as possible. This child had haematemesis and was vomiting and thirsty, but he was not clinically dehydrated; however, he was given a slow intravenous infusion of 5% glucose-saline in order to maintain rather than correct the fluid balance. After this was carried out his condition improved, he had no further vomiting, and he made a rapid recovery.

The cases in this series and those described by Thomson (1947, 1950), Forbes (1947), and Roxburgh (1949), with a total mortality of 47% (17 cases, 8 deaths), give a more depressing view of ferrous sulphate poisoning than is justified, for there must be many mild cases which require little or no attention and, because they arouse no particular interest, are not reported. However, while these tablets remain in such common use it seems only too certain that there will be further cases, and for these I would suggest the following treatment:

1. Efforts to make the child vomit should be carried out immediately in the home, either by giving him salt and water to drink or by placing the fingers in his throat.

2. Gastric lavage with sodium bicarbonate solution as soon as possible: 10 oz. (285 ml.) of the solution should be left in the stomach.

3. Bismuth carbonate, 3 gr. (0.2 g.) should be given four-hourly.

4. Precautions should be taken against the inhalation of vomit.

5. Intravenous infusion of fluids should be considered. If shock is severe plasma should probably be used initially, otherwise 5% glucose-saline should be given to maintain fluid balance in severe cases.

6. The following vitamin mixture should be given:

Aneurin hydrochloride	..	..	..	..	10 mg.
Nicotinamide	..	..	..	..	30 "
Riboflavin	..	..	..	..	10 "
Tocopherol	..	..	..	..	15 "
Methionine	..	..	..	..	500 "

These amounts should be multiplied by the child's age in years and then divided into three daily doses.

With the exception of methionine all these substances can be given intramuscularly until vomiting stops; thereafter they can be given by mouth and often in tablet form, for these children have already shown an aptitude for swallowing tablets.

Prevention

Following, perhaps, on the suggestions of others who have written on this subject, the leading manufacturers of ferrous sulphate tablets have now printed in large letters on their packets that these tablets are dangerous to young children. This is the first step in prevention, but so far it is the only one that has been taken. Now, it seems irrational that some things which children are expected to take, such as cod-liver oil, remain unpalatable, whereas ferrous sulphate tablets, which are intended mainly for adult use, are made both attractive and sweet. Possibly adults would not take them if they were otherwise, and no suggestion would be acceptable which had this result; for these tablets play a vital part in maintaining the health of large numbers of the population, including the pregnant woman. For this reason I feel that the tablets should remain in their present form, but that some obstacle should be placed between the tablet and the child, and I would like to suggest that this could be done as follows:

The daily dose of three tablets should be wrapped separately and securely in small packets in the same way that sugar is sometimes supplied in hotels in packets containing two lumps. In the German Army Medical Service nearly all tablets were supplied in packets of five, and 10 of these units were fixed together, making bundles of 50. This was done presumably for ease in handling, but if it could be carried out as a general measure it should also be practicable in this instance. A glance at the case histories shows that almost all the children poisoned are under 2 years of age, and I feel that if members of this age group accidentally obtained tablets wrapped in the manner suggested they might play with them for a long time without opening the packet, and, even if they did free some of the pills, the speed at which they could swallow them in quantity would be very effectively reduced.

Summary

The clinical picture of iron poisoning in children is described in detail.

The effects of large doses of iron on children, and the genesis of the resulting illness, are discussed.

A new method of treatment is proposed.

A suggestion is made whereby further cases might be prevented.

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CHILDHOOD FACTORS IN DUODENAL ULCER*

BY

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At the present time it is a commonplace to regard duodenal ulcer as a "psychosomatic" illness. By this most authors imply that it is a disease which is caused, in part at least, by psychological stresses to which, according to many, a number of people are predisposed by a specific type of personality.

While there is a certain amount of agreement on the nature of this personality among the various authors who believe in a psychosomatic aetiology of the disease, very few attempts have been made to demonstrate that patients with duodenal ulcer differ significantly from the general population. The difficulties of making such a comparison are great, as "personality" is an intangible quality and not easily measured. Moreover, the work of those who have endeavoured to overcome these difficulties—for example, Davies and Wilson (1937) and Brown *et al.* (1950)—is open to the objection that any difference shown between a group of ulcer patients and a group of controls may be due to the effects of the disease rather than be an indication of its cause: it is conceivable that chronic pain in itself may affect the personality, or at any rate the performance of psychological tests.

It is therefore surprising that the childhood of patients with duodenal ulcer has not been more extensively studied, as any difference between the childhood of these people and others could not be the result of the disease. All psychologists are emphatic on the importance of the childhood in the genesis of the adult personality. Moreover, there are a number of clear-cut factors in childhood of importance in the development of personality which can be assessed accurately and used for a numerical comparison between groups.

A few authors have investigated the problem of duodenal ulcers from this aspect. Draper and Touraine (1932) found more males than females among the sib-

lings of duodenal ulcer patients in the proportion of 138 males to 100 females, in contrast with a group of cases of gall-bladder disease, in which the female siblings outnumbered the males in the proportion of 130 to 100. This was based on an investigation of 32 cases of peptic ulcer and 32 of gall-bladder disease. They use this observation to support their theory of a masculine-feminine conflict in ulcer patients.

Mittelman and Wolff (1942), in a review of 30 cases of duodenal ulcer, conclude: "The failure of the home in every instance to lend a stable background resulted from a variety of causes—unhappy married life of parents, separation or loss of father during the child's development, early remarriage of mother after separation from father."

Kapp, Rosenbaum, and Romano (1947) also state: "In each patient the origin of such strong dependent wishes was traced either to rejection in childhood or to spoiling during the same period."

Moses (1946) also considered the childhood important. He writes: "This marked basic insecurity was the most prominent feature common to the entire group. It was related to the concrete frustrating economic and emotional environment in which they were reared. The majority of these individuals came from broken homes and from a marginal economic level with its limited social and educational opportunities."

Ruesch (1948), comparing duodenal ulcers in 42 naval personnel and 20 civilians, makes the following statements: "Ulcer bearers were generally the youngest or the younger-born children in the family. In terms of years they were separated from their older and younger siblings. . . . Our patients were on the average between 3 and 6 years old at the birth of a subsequent child. . . . The naval patients were characterized by a preponderance of brothers and the civilian patients by a greater frequency of sisters."

Thus it will be seen that there is little agreement among those who have investigated this problem, and most of them have considered small series of cases. Therefore it seemed worthwhile to compare a fairly large group of patients suffering from duodenal ulcer with a similar group suffering from other diseases. Gastric ulcers were excluded in order to reduce the number of variable factors, and because most authors in the past have considered psychological factors to be of more importance in duodenal ulcer than in gastric ulcer.

Present Investigation

The points chosen for investigation were those factors in childhood which might be of importance in affecting the personality and which could be ascertained with accuracy—for example, size and composition of family, age at death of parents, illness in childhood, etc.

Factors believed to affect the incidence of duodenal ulcer are sex, age, occupation, geographical situation, and time. To eliminate errors due to these factors the investigation was limited to males, and the patients in the control group were chosen to match the ulcer group in five-year age groups.

Occupational differences can only have been slight, as all were hospital patients in a regional hospital in North-west London, and, as is shown later, there was no difference between the two groups in social class. Temporal differences can be ignored, as both the ulcer patients and the control group were interviewed in 1950.

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