Comment

These four case histories illustrate many of the features of this type of intestinal obstruction. Orange pith is a relatively common obstructing agent, and, while one case of obstruction due to almonds is already to be found in the literature (Latchmore, 1940), watercress (as in Case 4) has not previously been recorded as the obstructing foodstuff. In both Case 1 and Case 2 mastication was inadequate.

Summary

The great variety of foodstuffs reported to have caused acute intestinal obstruction are listed in order of frequency. In all, 178 cases were traced and obstruction was found to be due to 45 different agents. Of these, persimmons, peaches, oranges, mushrooms, bran, apples, figs, cherries, and grapes were the most frequent, in that order, and accounted for more than one-half the obstructions. Dried fruits accounted for almost one-third of the cases reported in recent years.

The geographical distribution, predisposing factors, clinical features, diagnosis, treatment, and prognosis of this condition are outlined. Oranges appear to be the most common obstructing agent in this country.

Four further cases are reported. Two of these were due to orange pith, one to almonds, and one to watercress: three impactions occurred in healthy lower ileum, and one at the site of an organic stenosis in the jejunum. The almond bolus was broken up and "milked" into the caecum, but enterotomy was necessary in the other three cases. All four patients recovered uneventfully.

I am indebted to Mr. D. A. Abernethy, Mr. A. Elliot-Smith, and Mr. A. J. Grace for permission to publish their cases.

APPENDIX

Alphabetical list of 44 authors not referred to by Fantus and Kopstein (1940), together with the obstructing foodstuff concerned.

- ¹Aird, I. (1949). *A Companion in Surgical Studies*. Livingstone, Edinburgh.—Beans, orange.
- ²Allen, A. E., and Smithwick, R. (1942). *New Engl. J. Med.*, **226**, 864.—Orange.
- ³Alsen, P. (1938). *Nord. med. Tidsskr.*, **16**, 1165.—Dried apple.
- ⁴Altman, G. G. (1931). *Kentucky med. J.*, **29**, 370.—Bone and peanuts.
- ⁵Anderson, A. L., and Anderson, C. W. (1930). *N. Orleans med. surg. J.*, **83**, 256.—Water-melons.
- ⁶Andrews, F. L., and Walker, T. F. (1937). *J. Amer. med. Ass.*, **109**, 431.—Dried peach.
- ⁷Baumeister, C. F., and Darling, D. D. (1947). *Ann. Surg.*, **126**, 251.—Orange.
- ⁸Benzadon, J. (1944). *Bol. Soc. Cir. Rosario*, **11**, 109.—Lettuce leaves. (Not verified.)
- ⁹Bombicino, J. A. (1945). *Rev. Sanid. mil., B. Aires*, **44**, 573.—Dried fruit.
- ¹⁰Canton, R. V. (1937). *Arch. urug. Med.*, **10**, 509.—Dried peach.
- ¹¹Caylor, H. D., and Nickel, A. C. (1936). *Ann. Surg.*, **104**, 151.—Apple and raw potato.
- ¹²Ciechanowski, S. (1938). *Zbl. allg. Path. path. Anat.*, **69**, 357.—Garlic bulb.
- ¹³Covaro, A. A., and Nunziata, A. (1939). *Rev. Med. Cienc. af.*, **1**, 11.—Dried peaches.
- ¹⁴Delrio, J. M. A., Paz, R., and Carpanelli, J. B. (1944). *Rev. Asoc. med. argent.*, **58**, 232.—Oranges, peaches.
- ¹⁵Desjardines and Bondet (1939). *Lyon méd.*, **163**, 708.—Fig.
- ¹⁶Dorling, G. C. (1945). *British Medical Journal*, **2**, 426.—Dried peach.
- ¹⁷Fleming, J. P., and Ward-McQuaid, J. N. (1950). *Aust. N.Z. J. Surg.* In press.—Orange.
- ¹⁸Griffith, F. W. (1936). *Ann. Surg.*, **103**, 769.—Orange (mentions collards).
- ¹⁹Herz (1931). Quoted by Griffith (1936).—Fig.
- ²⁰Roldan (1929). Quoted by Griffith (1936).—Dried peach.
- ²¹Zielke (1933). Quoted by Griffith (1936).—Poppy seeds. In discussion on Griffith's paper:
- ²²Bullock, W. O. (1936).—Persimmons.
- ²³Crisler, J. A. (1936).—Cantaloup.
- ²⁴Frank, L. W. (1936).—Insipissated food containing fibres.
- ²⁵Rhodes, R. L. (1936).—Bran.
- ²⁶Harless, M. S. (1937). *Ann. Surg.*, **105**, 295.—Peach.
- ²⁷Hart, W. E. (1923). *J. Amer. med. Ass.*, **81**, 1870.—Mentions celery.
- ²⁸Johnson, J. A. (1931). *Minn. Med.*, **14**, 635.—Apricot.

- ²⁹Jones, A. S., and Davies, S. W. V. (1945). *British Medical Journal*, **1**, 734.—Orange.
- ³⁰Lambley, D. G. (1946). *Ibid.*, **1**, 684.—Dried peach.
- ³¹Latchmore, A. J. C. (1940). *Lancet*, **1**, 1153.—Almonds, apple, cherries, coconuts, monkey nuts, orange.
- ³²Linton, P. (1937). *Svenska Läkartidn.*, **34**, 593.—Dried apple (not verified).
- ³³Lyall, A. (1945). *British Medical Journal*, **1**, 734.—Dried fruit, dried apple.
- ³⁴McIver, M. A. (1932). *Arch. Surg.*, **25**, 1106.—Green corn, bran.
- ³⁵Mattson, H., and Larson, E. A. (1941). *Minn. Med.*, **24**, 559.—Coconut, chicken skins.
- ³⁶Newburger, B. (1941). *Rev. Gastroent.*, **8**, 293.—Persimmons.
- ³⁷Postel, H. J. (1939). *Ned. Tijdschr. Geneesk.*, **83**, 1959.—Dried apple.
- ³⁸Radcliffe, L. (1945). *British Medical Journal*, **1**, 135.—Orange.
- ³⁹Rambo, C. M., Lasky, L., and Iden, J. F. (1939). *Ohio St. med. J.*, **35**, 261.—Turtle eggs.
- ⁴⁰Ryan, T. F. J., and Nagle, J. (1945). *British Medical Journal*, **2**, 426.—Apricot.
- ⁴¹Santamarina, G. A. R., and Hours, R. D. (1939). *Sem. méd., B. Aires*, **2**, 856.—Banana.
- ⁴²Soothill, E. F. (1946). *Guy's Hosp. Gaz.*, **60**, 164.—Dried peach.
- ⁴³Storck, A., Rothschild, J. E., and Ochsner, A. (1939). *Ann. Surg.*, **109**, 844.—Water-melons, peanuts, raw butter bean, sweet potatoes.
- ⁴⁴Voncken, J. (1942). *Bull. Acad. roy. Méd. Belg.*, **7**, 368.—Carrots.

REFERENCES

(Authors not included in the Appendix)

- Ackman, F. D. (1939). *Canad. med. Ass. J.*, **21**, 710.
 Brunzel, H. F. (1918). *Dtsch. Z. Chir.*, **145**, 1.
 Calevaert (1933). *Pr. méd.*, **2**, 1976.
 Elliot, A. H. (1932). *Amer. J. med. Sci.*, **184**, 85.
 Fantus, B., and Kopstein, G. G. (1940). *Amer. J. digest. Dis.*, **7**, 60.
 Grieg, J. R. (1946). In *Special Pathology and Therapeutics of the Diseases of Domestic Animals*, by Franz Hutyrá, Joseph Marek, and Rudolf Maninger, 5th Engl. ed., **2**, 196. Baillière, Tindall and Cox, London.
 Handfield-Jones, R. M., and Porritt, A. E. (1948). *Essentials of Modern Surgery*, 3rd ed., p. 657. Livingstone, Edinburgh.
 Seifert, E. (1930). *Dtsch. Z. Chir.*, **224**, 96.
 Wooldridge, G. H. (1934). *Encyclopaedia of Veterinary Medicine, Surgery and Obstetrics*, 2nd ed., **1**, 460. Oxford Univ. Press, London.

INTRAVENOUS IRON IN THE TREATMENT OF ANAEMIA

BY

A. S. RAMSEY, M.B.E., M.D., M.R.C.P.

Principal Registrar, Royal Victoria Hospital, Belfast, and
 Musgrave Park Emergency Hospital, Belfast

It is not uncommon to see patients suffering from a microcytic hypochromic anaemia at hospital out-patient departments who have had oral iron therapy for months or years without benefit.

Excluding those cases in which diseases and deficiencies are present which could account for the continued anaemia, a considerable proportion of cases remain. These include: (1) those who have not tolerated iron in the dosage advised by the general practitioner, and who have failed to take any quantity of the preparations ordered; (2) those who seem unable to tolerate even the smallest doses of iron preparation given by mouth; and (3) those who seem unable to absorb adequate quantities of iron, the response to oral therapy falling far short of expectations. While many patients in Group 1 will tolerate a reduced dose of iron and obtain a satisfactory result, those in Groups 2 and 3 constitute a problem of introducing enough iron into the body to effect a cure.

Goodman and Gilman (1941) have shown that a healthy adult has 150 g. of circulatory haemoglobin containing 2.5 g. of iron. In an anaemic patient 25 mg. of iron must therefore become available to allow a rise of 1% haemoglobin.

Powell (1944) considers that one of the factors in iron absorption may be the permeability of the absorbing cells to iron. In her experience, resistance to treatment by iron in hypochromic anaemia is usually due to a failure of absorption, and it may be this factor of permeability of absorbing cells that is at fault. If that is so parenteral administration may be necessary to introduce sufficient iron into the body.

Parenteral Administration

It has long been known that the body can utilize preparations of iron when administered by injection. Stockman (1893), with subcutaneous injections of citrate of iron and sodium, recorded a pronounced rise in erythrocyte count and haemoglobin level in four cases of chlorosis. It has also been shown that injected iron is used almost quantitatively for the formation of haemoglobin (Heath *et al.*, 1932; Whipple and Robschey-Robbins, 1936; Hahn and Whipple, 1936; Goetsch *et al.*, 1946).

Unfortunately, even quite small doses of most preparations produce toxic effects. Goetsch *et al.* (1946) concluded that injecting colloidal ferric hydroxide or ferric oxide intravenously produced toxic effects too severe for this preparation to be of practical use. To avoid toxic effects the maximum dose of injectio ferri B.P. (intramuscular) is 2 ml., with an iron content of 7 mg. To raise the haemoglobin 50% would therefore require daily injections for six months.

Cappell (1930), in animals, had noticed that with saccharated oxide of iron there is no flocculation of the iron solution in contact with the blood plasma, and that mice and rats could be given repeated small injections to a total of seven to eight times the normal body content of iron without ill effects. A great advance in the problem of parenteral administration in man was made by Nissim (1947). He found that a practical dose of saccharated iron oxide could be administered without reactions, and that it was completely utilized in haemoglobin synthesis. Davidson and Girdwood (1948) confirmed the effectiveness of this preparation in one case, though they reported "marked reactions" with some of the injections as well as "severe reactions" in other cases. Slack and Wilkinson (1948) mentioned that they had been using saccharated iron in out-patients with "entirely satisfactory results."

Many cases of microcytic hypochromic anaemia have been treated at the Royal Victoria and Musgrave Park Emergency Hospitals, Belfast, with saccharated oxide of iron, using the proprietary preparation "ferrivenin," with most gratifying haematological results.

As it is intended to follow up these cases for some time full details are not being recorded at the moment. The reports of Slack and Wilkinson (1949) have been confirmed, the following case histories being typical of the responses obtained.

Illustrative Cases

Case A.—A married woman aged 30 had had six months' treatment with oral preparations of iron by mouth, at the end of which her blood findings were: Hb, 6.64 g./100 ml. (45% Haldane); erythrocytes, 4,090,000; C.I., 0.56; slide—microcytosis, hypochromia, no primitive red cells. Two months later—still on oral iron—the blood findings were: Hb, 6.96 g./100 ml. (47% Haldane); erythrocytes, 4,040,000; C.I., 0.53. Two weeks later oral iron was discontinued and she was given iron intravenously. There was a pronounced clinical improvement, and the haemoglobin and erythrocyte count rose (Fig. 1). A fractional test meal had shown achlorhydria, not histamine-fast.

Case B.—A married woman aged 24 had a long history of anaemia. She was not able to tolerate ferri et ammon. cit., and

FIG. 1.—Case A. No response to oral iron; response to intravenous iron.

there was no response to tab. ferri sulph., which finally made her sick. At this stage blood examination showed: Hb, 5.9 g./100 ml. (40% Haldane); erythrocytes, 2,640,000; C.I., 0.73; haematocrit, 20%; M.C.V., $76 \mu^3$; M.C.H.C., 30%; slide—hypochromia, anisocytosis. Primitive red cells 1 per 100 white cells—normoblast type (c) 1. Oral preparations were discontinued and she was given iron intravenously. There was a pronounced clinical improvement, and the haemoglobin and erythrocyte count rose (Fig. 2).

FIG. 2.—Case B. Response to intravenous iron.

Case C.—A married woman aged 49 had a 14-years history of anaemia. She failed to respond to ordinary treatment. Blood examination showed: Hb, 4.14 g./100 ml. (28% Haldane); erythrocytes, 1,940,000; C.I., 0.73; haematocrit, 15%; M.C.V., $78 \mu^3$; M.C.H.C., 27%. Bone marrow showed maturation arrest of the late type of normoblasts (type C). These cells showed a pyknotic nucleus with rugged immature cytoplasm typical of an iron-deficiency anaemia. A fractional test meal had shown free acid. Iron intravenously produced a great clinical improvement and a rise in haemoglobin and the erythrocyte count (Fig. 3). Iron was not given by mouth from the time of the above blood and marrow examinations.

Massive Dosage

Nissim had shown in five cases that by increasing the dosage over a series of injections a 500-mg. dose of saccharated oxide of iron produced no reaction in three cases

FIG. 3.—Case C. Response to intravenous iron.

and only a very doubtful reaction in the fourth. The fifth patient had a slight reaction after the first of two 250-mg. doses and a moderate reaction after 500 mg. Five other patients were given initial dosage of 200 mg., 250 mg., 400 mg., 500 mg., and 500 mg. without reactions. A sixth patient, given an initial 1 g. of iron, developed a moderate reaction which responded quickly to treatment.

The material Nissim used was prepared in his own hospital, so that chemical characteristics of the solution might not have been constant. It was therefore decided to investigate the possibility of giving anaemic patients the total required amount of the standard preparation ferrivenin at a single injection. Such a procedure would have many

advantages—for example, (1) the avoidance of repeated attendances at out-patient departments; (2) defaulters due to fear of repeated injections would be eliminated; and (3) where veins were difficult to find, one successful venepuncture would avoid the possibility of future failures to enter a vein, etc.

After trying several methods of administration it was found most convenient to have a short narrow-bore rubber tube with adapters to fit the needle and a 5-ml. syringe, the adapter for the syringe incorporating a tap to allow replacement with filled syringes.

New cases of microcytic hypochromic anaemia due to pure iron deficiency were taken without selection as and when they were diagnosed at out-patient departments. Without preliminary test doses they were treated as under. (Haematological findings are shown in the accompanying table.)

Case Reports

Case 1.—A nurse aged 28 was given 300 mg. of metallic iron in 2% solution (15 ml. of ferrivenin) by slow intravenous injection. Severe pain developed along the course of the vein up to the shoulder; she became pale and felt faint, but quickly recovered. Four hours later she felt cold and had rigors, became dizzy, and had difficulty in standing upright. She developed headache and nausea, and vomited slightly. Next morning she felt somewhat weak for a few hours. One week later a further 300-mg. dose was given without any reaction.

Case 2.—A woman aged 39 took 400 mg. of iron and within a few minutes developed pain in both lumbar areas and in the front of her thighs. She broke out in a sweat, but quickly recovered. Several hours later nausea, vomiting, and weakness developed, which lasted several hours. One week later a further 400 mg. was quickly followed by nausea, coldness, and weakness. This reaction responded quickly to brandy and warmth. One week later 200 mg. (remainder of calculated requirement) was given without reaction.

Case 3.—A woman aged 27 received 400 mg. of iron. Several hours later she felt weak, developed nausea, and vomited for several hours. She had anorexia and remained in bed for two days. Three weeks later a further 400 mg. was given, and one and a half hours later she had a rigor, developed a headache and nausea, and vomited for half an hour. She remained in bed for 24 hours.

Case 4.—A woman aged 44 was given 400 mg. of iron which caused a pain along the course of the vein up to the shoulder while the injection was in progress. This was followed by a feeling of heat all over the body, an irritation in the throat which made her cough, and slight pain in both thighs. She recovered quickly. One week later she had another 400 mg., and three further weekly injections of 200 mg. were given, all without reaction.

Case 5.—A woman aged 49 took 400 mg. of iron and one hour later had nausea, vomiting, and diarrhoea, and developed a generalized urticaria which lasted for 12 hours. One week later she was given 600 mg. of iron, and later a further 200 mg., with no ill effects.

Case 6.—A woman aged 52 took 500 mg. of iron without any immediate or late toxic reactions.

Case 7.—A girl aged 16 was given 500 mg. of iron, which caused severe pain along the vein up to the shoulder while the injection was in progress. One hour later pains developed all over the stomach and in both lumbar regions. She had rigors, nausea, and vomiting for two and a half hours and felt light-headed, but five hours after injection she was perfectly well. The vein thrombosed at the site of injection. The remaining iron in smaller doses caused no reaction.

Case 8.—A youth aged 19 was given 600 mg. of iron. Five hours later he developed tightness in the chest, sweated, had nausea, and felt weak for several hours. Later he took 400 mg. without reaction.

Case 9.—A woman aged 33 took 700 mg. of iron and one hour later developed nausea and vomiting. She had rigors and

Haematological Findings Before and After Massive Intravenous Injections of Ferrivenin

Case No.	Ferrivenin (mg. Metallic Iron) and Day of Injection	Day from First Injection*	Hb mg./100 ml. (% Haldane)	R.B.C. (Millions)	P.C.V.	M.C.V. μ^3	M.C.H.C.
1	Day 1-300	0	11.18 (75%)	4.19	38%	90	30%
	" 8-300	22	13.74 (93%)	4.44			
	" 36	36	13.59 (92%)	4.49			
2	Day 1-400	0	8.88 (60%)	3.99	30%	77	30%
	" 8-400	43	14.04 (95%)	4.52			
	" 15-200	127	14.7 (99%)	5.02			
3	Day 1-400	0	7.99 (54%)	3.85	29%	78	27%
	" 22-400	43	12.28 (83%)	4.67			
	Refused further injections						
4	Day 1-400	0	7.69 (52%)	4.02	30%	75	26%
	" 8-400	36	12.13 (82%)	3.75			
	" 15-200	120	13.44 (91%)	4.6			
	" 22-200						
	" 29-200						
5	Day 1-400	0	8.44 (57%)	3.76	28%	76	30%
	" 38-600	21	10.65 (72%)	4.36			
	" 91-200	91	12.3 (83%)	4.2			
	" 141	141	13.74 (93%)	4.16			
6	Day 1-500	0	11.55 (78%)	4.42	44%	100	25%
	" 53	53	15.39 (104%)	4.74			
	" 196	196	14.8 (100%)	5.0			
7	Day 1-500	0	7.69 (52%)	3.56	31%	88	24%
	" 8-100	15	10.5 (71%)	4.6			
	" 15-100	36	12.3 (83%)	4.54			
	" 22-200	43	15.24 (103%)	5.25			
	" 29-300						
8	Day 1-600	0	9.02 (61%)	4.3	34%	80	27%
	" 49-400	22	9.47 (64%)	4.46			
	" 155	155	10.4 (70%)	5.25			
9†	Day 1-700	0	10.95 (74%)	4.18	36%	87	32%
	" 57	57	12.73 (86%)	4.26			
10	Day 1-800	0	4.4 (30%)	2.96	19%	66	22%
	" 6-100	14	9.62 (65%)	3.6			
	" 7-100	35	10.9 (74%)	4.55			
	" 12-300	42	15.39 (104%)	4.77			
	" 15-300						
	" 22-100						
11	Day 1-900	0	9.47 (64%)	4.02	32%	80	30%
	" 36	36	13.9 (94%)	4.8			

* Day 0 = Few days before first injection, Day 1 = Day of first injection.
† Menorrhagia undisclosed at first examination probably reduced haematological response.

her skin felt tight all over her body. The reaction lasted 12 hours, but she remained in bed for 48 hours.

Case 10.—A woman aged 41 took 800 mg. of iron and one and a half hours later she felt dizzy and developed nausea, epigastric pain, and vomiting. She had rigors and her temperature rose to 103° F. (39.4° C.). Five hours after the injection she felt well again, and her temperature returned to normal. The vein later thrombosed at the site of injection, causing a localized discomfort for a few days. The remaining iron was given in smaller dosage without reaction.

Case 11.—A nurse aged 21 received 900 mg. of iron without any immediate reaction. One hour later she suddenly developed severe pain in her arms, legs, feet, back, and abdomen, and developed severe nausea and vomiting. She was admitted to hospital in a collapsed condition, grey-coloured. Her pulse could not be felt at the wrist, and there was pronounced tenderness over all areas of the abdomen, with rigidity and a positive rebound reaction. Auscultation of the abdomen revealed normal peristalsis. Rectal examination was painless. The condition in many ways resembled a perforation. She was treated with warmth, brandy (which was vomited), and "omnupon" intravenously. Two hours later her pulse could be felt at the wrist, her B.P. was 90/50, and there was much less vomiting. The following day she was very much better, and at the end of 24 hours had no symptoms.

Discussion

Patients suffering from a microcytic hypochromic anaemia without any other clinically demonstrable pathological feature who fail to respond to oral preparations of iron supplemented with vitamins, liver, thyroid, etc., have in the past remained in a state of chronic ill-health or required repeated blood transfusions to become symptomless.

These patients will respond dramatically to intravenous saccharated oxide of iron. After several doses of 100 mg. daily, or at any longer interval if more convenient, the dosage can gradually be increased to 200 mg. and 300 mg. if desired, with very little danger of any toxic side-effects. Unfortunately the total amount of iron required will not be tolerated by patients without prohibitive toxic reactions if given by single injection. Antihistamine drugs were used for some patients without preventing or reducing the toxic reactions.

However, a full course always consists of fewer than 10 injections and is the treatment of choice in refractory iron-deficiency anaemia. It is the most convenient method of treating patients who are unable to tolerate oral preparations of iron and is especially useful in pregnancy and the puerperium when gastric upsets are common and a rapid response is desirable (French, 1948; Govan and Scott, 1949). It has been found useful in chronic ulcerative colitis, idiopathic steatorrhoea, and rheumatoid arthritis (Sinclair and Duthie, 1949) associated with iron deficiency. As the iron cannot be replaced by a single injection, oral administration still remains the best method in the majority of cases of secondary iron-deficiency anaemia.

Cappell (1930) studied the fate of saccharated oxide of iron injected into mice. Like other insoluble suspensions, iron oxide is taken up by the reticulo-endothelial cells lining vascular channels, mainly in the liver and spleen, being completely removed from the plasma within 24 hours.

Vannotti (1946) and Greenberg *et al.* (1947), using radio-iron, found that in anaemic animals and patients most of the iron is removed from the plasma within a few hours. Cappell showed that the reticulo-endothelial cells, by their metabolic activity, converted the finely particulate nature of the iron into a soluble iron which was released into the blood plasma. This soluble iron is in loose combination with the plasma proteins and is capable of passing through

capillary walls to be stored in the lymphatic nodes and the parenchyma cells of the liver and kidney.

Wintrobe *et al.* (1947) showed that this soluble iron could be converted into haemoglobin, appearing as early as 48 hours after the administration of iron.

The cause of the toxic reactions that occurred in the cases described in this paper is still in doubt. Goetsch *et al.* (1946) found similar reactions with different preparations and thought them to be due to a heavy-metal effect. The pain felt along the course of the vein while the injection is in progress is probably due to venospasm. It occurred in one patient on the needle entering the vein and lasted for several minutes until the needle was withdrawn, although nothing was injected. Govan and Scott had somewhat similar experiences. The immediate reactions occasionally seen were all mild, and occurred only in apprehensive patients. Of the late reactions, the resemblance of the symptoms to those that occur in patients with paroxysmal haemoglobinuria from cold (Whitby and Britton, 1946) is very striking, and may well be caused by sudden increased activity of the cells of the reticulo-endothelial system. If this is the cause of the symptoms in both conditions—even though the nature of the injected iron is probably different from the iron released from haemoglobin breakdown—it is unlikely that any preparation of iron will be found which would allow treatment of anaemic patients by single rapid injection.

Summary

Intravenous iron therapy is now a practical method of treating microcytic hypochromic anaemia and is the method of choice for patients unable to tolerate iron given orally or in cases of refractory iron-deficiency anaemia.

Toxic reactions are avoided when the dosage begins with 100 mg. of saccharated iron oxide and is increased slowly to 200 or 300 mg.

Severe toxic reactions occur when attempts are made to replace the requirements of iron by a single intravenous injection. These reactions are described in detail.

The toxic effects closely resemble the symptoms of paroxysmal haemoglobinuria caused by cold. A possible explanation of these reactions is postulated.

I wish to thank Dr. M. G. Nelson, who carried out most of the haematological examinations.

REFERENCES

- Cappell, D. F. (1930). *J. Path. Bact.*, **33**, 175.
 Davidson, L. S. P., and Girdwood, R. H. (1948). *British Medical Journal*, **1**, 733.
 French, D. G. (1948). *Ibid.*, **1**, 901.
 Goetsch, A. T., Moore, C. V., and Minnich, V. (1946). *Blood*, **1**, 129.
 Goodman, L., and Gilman, A. (1941). *The Pharmacological Basis of Therapeutics*, p. 1110. New York.
 Govan, A. D. T., and Scott, J. M. (1949). *Lancet*, **1**, 14.
 Greenberg, G. R., Ashenbrucker, H., Lauritsen, M., and Wintrobe, M. M. (1947). *J. clin. Invest.*, **26**, 114.
 Hahn, P. F., and Whipple, G. H. (1936). *Amer. J. med. Sci.*, **191**, 24.
 Heath, C. W., Strauss, M. B., and Castle, W. B. (1932). *J. clin. Invest.*, **11**, 1293.
 Nissim, J. A. (1947). *Lancet*, **2**, 49.
 Powell, J. F. (1944). *Quart. J. Med.*, **13**, 19.
 Sinclair, R. J. G., and Duthie, J. J. R. (1949). *Lancet*, **2**, 646.
 Slack, H. G. B., and Wilkinson, J. F. (1948). *British Medical Journal*, **1**, 753.
 ——— (1949). *Lancet*, **1**, 11.
 Stockman, R. (1893). *British Medical Journal*, **1**, 881, 942.
 Vannotti, A. (1946). *Bull. schweiz. Akad. med. Wiss.*, **2**, 90.
 Whipple, G. H., and Robschey-Robbins, F. S. (1936). *Amer. J. med. Sci.*, **191**, 11.
 Whitby, Sir Lionel E. H., and Britton, C. J. C. (1946). *Disorders of the Blood*, 5th ed., p. 281. Churchill, London.
 Wintrobe, M. M., Greenberg, G. R., Humphreys, S. R., Ashenbrucker, H., Worth, W., and Kramer, R. (1947). *J. clin. Invest.*, **26**, 103.