ATYPICAL MEGALOCYTIC ANAEMIA

BY

G. D. KERSLEY, M.A., M.B., M.R.C.P.

ASSISTANT PHYSICIAN, ROYAL UNITED HOSPITAL, BATH

In view of the recent description by Wilkinson and Israëls¹ of a new group of megalocytic anaemias, the achresthic anaemias, a short series of cases of typical megalocytic anaemia with absence of achlorhydria recently investigated at the Royal United Hospital, Bath, seems worthy of record. The chief features recognized by Wilkinson and Israëls were: (1) megalocytosis in conjunction with normal gastric acidity; (2) the condition might occur at any age; (3) there were no associated digestive or central nervous system changes; and (4) the reaction to treatment and the prognosis were uncertain.

In the cases to be described most of these features were borne out, but in one there was a history of soreness of the tongue and there was slight denuding of the papillae, and in one case the gastric acidity was not estimated, owing to the gravity of the condition of the patient at the time of admission.

Case I

A boy, aged 11, was first admitted to hospital in 1932 suffering from anaemia, but from no symptoms not directly ascribable to the anaemia. The central nervous system appeared normal. On examination the tongue was normal; the spleen was just palpable, but the liver was not enlarged. The blood count was: haemoglobin, 24 per cent.; red cells, 1,200,000 per c.mm.; colour index, 1; white cells, 1,450 per c.mm.; polymorphonuclears, 730; lymphocytes, 590; and monocytes, 130. There was marked anisocytosis and poikilocytosis, and a few normoblasts were present. After treatment with liver and stomach preparations by the mouth the blood count rose to: haemoglobin, 56 per cent.; red cells, 3,700,000 per c.mm., and colour index, 0.77.

In 1934 the boy was readmitted with the same symptoms, and the blood count was: haemoglobin, 22 per cent.; red cells, 1,110,000 per c.mm.; and the colour index, 1. A stained film demonstrated definite megalocytosis. A test meal showed a rise in free hydrochloric acid from 0 to 65 c.cm. decinormal NaOH at the end of an hour and a half. After treatment with campolon injections and stomach preparations the blood count altered to: haemoglobin, 62 per cent.; red cells, 4,870,000 per c.mm.; and colour index, 0.6.

Case II

A woman, aged 46, was first admitted to hospital in 1933. She then gave a history of anaemia for twenty years, which had increased three years before, when she had suffered from an ulcerated mouth. She had been treated outside the hospital with liver, and had improved to some extent. On examination there was no sign of involvement of the central nervous system, of sore tongue, or of fever, and the weight was constant. The liver and spleen were not palpable. A blood count then showed the presence of a secondary anaemia: haemoglobin, 22 per cent.; red cells, 1,980,000 per c.mm.; colour index, 0.55; white cells, 3,800 per c.mm. This anaemia slowly improved under treatment with iron.

The patient was readmitted to the hospital a year later, when she had, in addition to her anaemia, some symptoms of tetany. The blood count was: serum calcium, 6.9 mg. per cent.; haemoglobin, 36 per cent.; red cells, 1,710,000 per c.mm.; colour index, 1; white cells, 1,400 per c.mm. The average size of the red cells was 8.2μ . Anisocytosis was present, and a few normoblasts, but no megaloblasts. Examination of the stomach contents revealed free hydrochloric acid. Under treatment with campolon injections and iron by the mouth there was at first no response, the haemoglobin remaining at 36 per cent. and the colour index rising to 1.2. A blood transfusion was given, followed by treatment with stomach preparations and iron, and the count then slowly rose to: haemoglobin, 62 per cent.; red cells, 3,130,000 per c.mm.; and colour index, 1.

Case III

A woman, aged 53, was admitted to hospital in 1933 with tiredness, soreness of the tongue, and pruritus. There were no digestive or central nervous system changes; the urine was normal, and the liver and spleen were not palpable. The blood count was: haemoglobin, 85 per cent.; red cells, 4,080,000 per c.mm.; colour index, 1.04; white cells, 3,500 per c.mm.; reticulocytes, 0.9 per cent. The van den Bergh reaction was negative. A test meal showed the presence of free hydrochloric acid, rising from 15 to 30 c.cm. decinormal NaOH at the end of an hour. Under treatment with campolon the reticulocyte response on the fifth day was 4.3 per cent., and the count rose to: haemoglobin, 86 per cent.; red cells, 4,890,000 per c.mm.; and colour index, 0.88.

Case IV

A man, aged 59, was admitted to hospital complaining of tiredness and giddiness. There were no digestive or central nervous system symptoms, nor was there any soreness of the tongue. The spleen was not palpable, but the liver could just be felt. The blood count was: haemoglobin, 43 per cent.; red cells, 1,940,000 per c.mm.; colour index, 1.1; white cells, 5,300 per c.mm.; polymorphonuclears, 3,000; lymphocytes, 2,100; monocytes, 200. No nucleated red cells were present, but there was marked anisocytosis and poikilocytosis; reticulocytes, 0.8 per cent. Examination of the stomach contents showed a rise in the free hydrochloric acid of the fasting juice from 20 c.cm. to 65 c.cm. decinormal NaOH at the end of an hour. Under treatment with liver there was a reticulocyte response of 13.4 per cent. on the fifth day, and the amount rose to: haemoglobin, 62 per cent.; and red cells, 3,820,000 per c.mm.

Case V

A single woman, aged 50, was admitted to hospital with the following history. Since a child she had always been anaemic and rheumatic, and ten years before admission the anaemia had increased and there had been some menorrhagia. Both symptoms had been relieved by iron medication. Three months before admission the menorrhagia restarted, and there was then marked anaemia and tachycardia. Iron was given in large doses, but without success. A cough developed and an x-ray picture of the lungs showed a mottling suggestive of chronic fibrosis with superadded congestion.

One month before admission the menorrhagia increased, and a blood count then showed: haemoglobin, 32 per cent.; red cells, 1,400,000 per c.mm.; colour index, 1.1; and white cells, 11,000 per c.mm. A vaginal examination revealed no abnormality, and the heart appeared to have no valvular lesion. Treatment with campolon injections was immediately started. Just before the patient came into hospital there was a sudden flooding and she became maniacal.

When first seen in hospital she was very pale. The pulse rate was 110-140; the temperature ranged between 98° and 101° ; and the respiration rate was 28. The blood count was: haemoglobin, 10 per cent.; red cells, 760,000 per c.mm.; colour index, 0.68; and white blood cells, 9,600 per c.mm. A blood transfusion of one pint was given immediately, and this was repeated two days later. By this means and with energetic iron and liver therapy the blood count was gradually raised to: haemoglobin, 27 per cent.; red cells, 1,300,000 per c.mm.; colour index, 1.04; white cells, 16,900 per c.mm.; polymorphonuclears, 13,900; myelocytes, 100; myeloblasts, 100; lymphocytes, 2,000; and mononuclears, 500. The platelets were large but scanty (66,000). There was marked anisocytosis and poikilocytosis, and many normoblasts and megaloblasts were present: reticulocytes, 10.6 per cent. The blood fragility was normal.

On the seventeenth day the patient suddenly developed bronchopneumonia and died. Post-mortem examination showed extreme normoblastic activity of the marrow, which was greatly increased in amount. There was considerable fatty change with areas of congestion and haemorrhage in the liver and kidneys, and the spleen was enlarged and rather soft. The lungs revealed signs of bronchopneumonia, but the heart muscle was fairly good with no sign of valvular lesion. The uterus was normal, but the cervix contained two small polypi.

Summary

Five cases of atypical megalocytic anaemia are described. In the first, in a boy of 11, the stomach showed normal acidity and the condition reacted well to liver therapy.

The second case demonstrated the development of a megalocytic from a microcytic anaemia in a woman with normal gastric acidity. The condition failed to react to liver or iron therapy until after blood transfusion. The condition was associated with tetany.

Cases III and IV appeared typical of pernicious anaemia; in Case III the anaemia was associated with soreness of the tongue, but analysis of the gastric contents in both cases showed the presence of free hydrochloric acid.

Case V cannot be definitely classified as of achrestic anaemia, owing to the fact that on admission to the hospital the patient was too ill to have a test meal. An anaemia at first reacting to iron but later becoming definitely megalocytic, it showed no response to iron or liver therapy, and only reacted slowly to blood transfusion. The anaemia was accompanied by menorrhagia, and during the more severe stages with mania. The patient died of bronchopneumonia, and the post-mortem findings were those of intense normoblastic activity in conjunction with fatty degeneration of the vital organs.

REFERENCE

¹ Wilkinson, J. F., and Israëls, M. C. G.: *British Medical Journal*, 1935, i, 139 and 194.

A CONTRIBUTION TO THE TREATMENT OF BURNS

BY

ALFRED C. TURNER, M.B., B.Ch.Belf.,
F.R.C.S.Ed.

SURGEON, THE ANGLO-IRANIAN OIL COMPANY

Ten years ago E. C. Davidson of Detroit introduced a new method of treatment of burns by means of tannic acid solution. The surgeon has thus been armed with a weapon completely replacing modes of treatment which were clumsy, unsatisfactory, and expensive, while mortality has been very considerably lowered and suffering greatly reduced. There will be no doubt in the minds of those experienced in the treatment of extensive burns of the first three degrees that the coagulating method is the ideal one. Certain aspects of the tannic acid technique are, however, unsatisfactory. An attempt has been made to overcome the worst of these by modifying the treatment while still retaining the basic ideal—the "coagulated" and desiccated surface.

The advantages and disadvantages of any particular line of treatment can only be ascertained by careful examination and analysis of a large series of cases. The observations which follow were made over a period of five years, during which the tannic acid method was used, and a one-year period in which modifications of this technique were adopted. The total number of cases of burns in this series, inclusive of all degrees sufficiently serious to render the patient unfit for work, was 2,696.

Disadvantages of Tannic Acid

1. *The Coagulum.*—In the case of tannic acid this is coarse, tough, and not transparent. Any pus formation beneath it is difficult to diagnose, and may spread over a large area rather than perforate an unyielding scab. In this way much of the young epithelium may be destroyed before any signs of damage are manifest. When the scab, floating on a bed of pus, is removed later a very coarse type of granulation tissue will be found beneath, which is difficult to control and ultimately tends to produce extensive scarring. These observations suggested to us that certain definite advantages could be claimed for a thin, transparent scab.

2. *Destructive Action.*—Tannic acid may well be described as "dirty," and is, in addition, most destructive to clothing and bed linen. This necessitates the use of a mackintosh to protect the bed. The mackintosh acts on the burnt area like jaconet used in a fomentation. Delay in evaporation takes place to such an extent as seriously to interfere with one of the main essentials of the treatment. The choice, therefore, lies between sacri-

ficing the bed linen or restricting the evaporation from the surface of the coagulum, which is so essential for its well-being.

3. *Instability in Solution.*—A further very important objection to tannic acid is that it rapidly becomes unstable in the aqueous solution required for use. This makes its employment most cumbersome both as a first-aid measure and also in hospital practice.

The above disadvantages suggested a search for an equally satisfactory coagulant which would not destroy linen and could be kept indefinitely in solution.

Process of Repair of a Burn

In the process of repair the exudate from the surface does not coagulate, or does so only in a very slight degree. Fibrin strands may be demonstrated, but are usually insufficient in quantity to form a firm coagulum. Many drugs are found to have the property of assisting in the formation of a coagulum. Our contention is that the ideal drug to employ is one with strong antiseptic and bactericidal properties, which will at the same time help to bind the crust. After a trial with several drugs, mercurochrome (di-sodium-dibromo-oxymercury fluorescein) was selected, as it appeared to possess the necessary qualities. It was given an extensive trial over a period of one year, and the following observations were made.

1. Mercurochrome does not precipitate protein, and can therefore be claimed as an effective antiseptic in the presence of protein.

2. In cases treated with this drug the crust formed is thin and transparent.

3. Bed linen is not in any way destroyed.

4. It is non-irritating to the tissues.

5. A 2 per cent. aqueous solution is stable for an indefinite period.

6. Epithelialization under the scab takes place rapidly. It was noteworthy in using some other drugs, particularly trypanflavine, that though the crust formed was excellent little or no epithelialization took place beneath it, and aseptic necrosis of the superficial living tissues occurred.

Technique and Results of Mercurochrome Treatment

The treatment of shock and exhaustion are dealt with on generally accepted lines and will not be further discussed here. With reference to the preliminary local treatment there are certain points of importance.

1. No general anaesthetic—not even nitrous oxide and oxygen—is given. Many cases of extensive burns require hours of preliminary work, which can only be accomplished by dealing with small areas at a time. Large doses of morphine or other opiates are recommended, and are usually quite effective.

2. All dead tissue is stripped from the burnt area and foreign material removed. The greater the care taken in this the better will be the end-result.