Remarks

ON

ANAEMIA IN GENERAL PRACTICE*

BY

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About half the patients who are sent to me for anaemia have a normal blood count. They are not suffering from anaemia, but from debility, very often psychological in origin. An unhappy love affair does not require treatment with liver extract, but I have seen it prescribed in more than one such case on a mistaken interpretation of the symptoms as anaemia. On the other hand, anaemia is often overlooked, especially when it is complicated by the sallow complexion of the chronic abdominal invalid or the parchment skin of old age. If we remember that anaemia is likely to be present in long-standing cases of dyspepsia, and that pernicious anaemia is a disease of old age, we shall be forearmed and make fewer such mistakes. It is often difficult to be certain of the presence of anaemia from clinical inspection. The white face of the sedentary worker usually hides a normal blood, while the invalid who has been lying in the sunshine in the garden may have a sunburnt complexion along with a haemoglobin of 40 per cent. and anginal pain on exertion. The lips are not a much better guide than the skin. The conjunctivae and the palate best reflect the state of the blood.

Anaemia is one of the few diagnoses about which we can be absolutely certain. It is decided at once by the estimation of the haemoglobin, and I should like to lay down as my first axiom that *treatment should not be given for anaemia until the diagnosis has been confirmed by the haemoglobinometer*. Haemoglobinometry is a controversial subject, and the large number of apparatus which are on the market suggests that none is absolutely satisfactory. The Haldane apparatus is probably the most accurate for routine use, but it is a little too complicated for general practice, and not very handy at the bedside. The preliminary estimation of the haemoglobin can be rapidly and simply performed by the Tallqvist test, in which a drop of freshly drawn blood is taken on a slip of blotting paper and compared with a coloured scale. This test is quite as accurate as that made by many an expensive apparatus, and it far more sensitive than the unaided eye.

My second axiom is that *symptoms of anaemia rarely appear until the haemoglobin has fallen below 75 per cent.* There are certain exceptions to this axiom, more especially in pernicious anaemia, where glossitis and nervous changes may appear with a haemoglobin percentage little below the normal. It is nevertheless a good general rule, and if a patient has a haemoglobin of 75 per cent. or over, it is unlikely that weakness or dyspnoea is the result of anaemia. On the other hand, if the haemoglobin is below 75 per cent., the patient is truly suffering from anaemia, and the next step is to decide the exact nature of the anaemia. It is a short-sighted policy to begin treatment without further investigation. It is true that the anaemia may sometimes be relieved by a "grape-shot" prescription of iron, liver, arsenic, and hydrochloric acid, but in the absence of an accurate diagnosis it is impossible to foresee the future course of the illness or foretell the danger of relapses or complications. Moreover, the anaemia may be a symptom of some underlying

malady, which progresses unfavourably while time is lost during symptomatic treatment.

My third axiom, therefore, is that *if the haemoglobin is below 75 per cent., a complete blood count should be performed*. An accurate blood count may at once elucidate the diagnosis, showing perhaps leukaemia or frank pernicious anaemia. More commonly a banal anaemia of low colour index is found, and the diagnosis must be established by further clinical investigation. Anaemias may be roughly divided into:

1. Those which are essentially diseases of the blood-forming organs, and
2. Those which are secondary to some other disease.

AETIOLOGY OF ANAEMIAS

It is wise to remember that symptomatic anaemias are far more common than primary diseases of the blood-forming organs, and that they rarely respond to symptomatic treatment until the underlying disease has been corrected. The causes of symptomatic anaemia may be roughly classified as haemorrhage, infection, toxæmia, and new growth. Common causes of haemorrhagic anaemia are peptic ulcer, haemorrhoids, and menorrhagia. When infection produces anaemia the infection is usually obvious, and dominates the clinical picture, as in the anaemia associated with rheumatic heart disease, with subacute bacterial endocarditis, or with typhoid fever. Anaemia is often attributed to focal sepsis or to syphilis, but I have rarely seen anaemia much improved by the eradication of foci of sepsis or the treatment of a positive Wassermann reaction, and such findings are more often coincidences than aetiological factors. In respect to toxæmia I would emphasize the importance of chronic nephritis as a cause of anaemia, and I deprecate the attribution of anaemia to intestinal toxæmia. I have seen more than one patient who had been treated for months with bowel antiseptics, colon lavage, and vaccines of faecal organisms without any benefit, and who improved rapidly on the prescription of iron. Malignant disease should be considered in every case of obscure anaemia. Anaemia occurs more especially in malignant disease of the stomach and of the large bowel, in which it may be the presenting symptom. Such anaemia frequently responds well to iron² or to liver,³ the haemoglobin rising rapidly under treatment, but the growth progresses unchecked. Anaemia may be present in growths outside the gastro-intestinal tract, as in one of my patients who presented an obscure anaemia with a haemoglobin of only 24 per cent., and who ultimately proved to have carcinoma of the lung with widespread metastases. It is, however, rarely so severe as in gastro-intestinal carcinoma.

It is clear that the diagnosis of a case of anaemia requires a detailed history, a complete investigation, and a careful weighing of the data obtained. Particular attention should be devoted to the gastro-intestinal tract. Of special investigations one of the simplest and most informative is the examination of the stools for occult blood. I should never be content to treat a patient for anaemia when there was unexplained occult blood in the stools. But important as it is to exclude gross organic disease in the diagnosis of a case of anaemia, it is equally important not to attribute anaemia to trivial and unreasonable causes. The red blood cells and the marrow cells from which they arise constitute an organ larger than the liver. This organ is not only bulky but robust, as is shown by the sheep used in our bacteriological laboratories, which give 100 c.cm. of blood a week for years on end without developing anaemia, or by human transfusion donors who have given a litre of blood at short intervals

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without any serious fall in haemoglobin. When, therefore, severe anaemia develops in a patient who has only a moderate dental sepsis, or slight haemorrhoidal bleeding, or a normal pregnancy, it is much more likely that there is some underlying disorder of the blood than that the anaemia is due to such small causes.

CLASSIFICATION

I am accustomed to classify the primary or essential diseases of the blood into four main groups. I will dismiss the first three groups rather shortly, so that we may concentrate on the important fourth group, the treatment of which is so largely in the hands of the general practitioner.

1. *Leukaemia and Hodgkin's Disease*.—These diseases are characterized by changes in the white cells of the blood or enlargement of lymph glands. They are probably closely allied to the malignant growths, and are as invariably fatal. Treatment with x rays or with arsenic produces great symptomatic improvement, though life is probably but little prolonged.

2. *The Hepato-lienal Diseases*.—These are diseases of the blood in which the liver and spleen are also involved. Here I include acholuric familial jaundice and splenic anaemia. Treatment with liver and iron may produce transient improvement, but the only satisfactory treatment is splenectomy.

3. *The Haemorrhagic Diseases*.—This is an ill-defined assortment of diseases, some of which are of constitutional origin. Apart from the group of cases with reduction in the number of blood platelets which is benefited by splenectomy, treatment is empirical and unsatisfactory.

4. *The Anhaemopoietic Anaemias*.—This is the important group to which I wish to devote the remainder of this lecture. I am sorry that my classification compels me to use a rather unfamiliar title, but these anaemias can for practical purposes be regarded as conditions in which the nutrition of the bone marrow is impaired, and its ability to form blood cells correspondingly reduced. This malnutrition may be the result of defects in the diet, or in the digestion, or in the internal organism, more especially the endocrine glands. There are many conditions which give rise to anaemia in this way, but the two most important are: (1) iron deficiency, or idiopathic microcytic anaemia; (2) pernicious anaemia.

There is reason to believe that some cases of aplastic anaemia come under this same heading, but aplastic anaemia is so rare that we need not discuss it now. Deficient supply of iron to the bone marrow results in a shortage of haemoglobin, and the anaemia which follows is characterized by the small size of the red cells and by their deficient complement of haemoglobin and consequent pallor. The anaemia is therefore described as microcytic and hypochromic, and it is of low colour index. This anaemia may occur when the iron and haemoglobin stores of the body are depleted by long-continued bleeding, as in haemorrhoids or in hookworm disease. The most typical examples, however, are found in infants, and in women of reproductive age. Chlorosis was probably a disease of the same type, but chlorosis has disappeared, and need not be considered to-day.

NUTRITIONAL ANAEMIA OF INFANCY

The investigations of Helen Mackay⁴ have shown that 40 per cent. of breast-fed babies and 70 per cent. of artificially fed babies in the hospital class are anaemic. Anaemia is perhaps less frequent in the wealthier classes. The anaemia, which is of low colour index, appears about the third month, reaches a maximum about the ninth month, and improves spontaneously on weaning. It is not a vitamin deficiency, as it develops on a high-vitamin

diet and is cured by iron alone. It is most severe in premature and small babies, which come into the world with a poor store of iron. It is almost certainly an iron deficiency, due to the low iron content of the milk, and it is more severe in artificially fed babies, because cow's milk contains less available iron than the mother's. Anaemia which is so general might have been regarded as physiological had not Helen Mackay shown that it leads to an increased susceptibility to infection. Colds, otorrhoea, bronchitis, and enteritis are twice as common in untreated babies as in those in which the anaemia is treated with iron. Iron should always be prescribed for small and premature babies, and there are few babies, breast-fed or artificially fed, who will not benefit from it. It is given as iron and ammonium citrate, $4\frac{1}{2}$ to 9 grains a day. A simple prescription is $1\frac{1}{2}$ grains of iron and ammonium citrate in 1 drachm of chloroform water, added to the feeds three times a day. Administration must be commenced very slowly, starting with only 2 or 3 drops of the mixture to a feed, and taking a week or ten days before the full dose is given. With this precaution it is unusual for the digestion to be upset. The mother should be warned that the stools will be black. Proprietary milks containing iron are now on the market. They are quite effective, but some little time should be taken in incorporating them in the diet to avoid dyspepsia. If a milk and cereal diet is prolonged after infancy so also is the anaemia. I am a firm believer in the importance of weaning babies early, and including eggs, meat, and green vegetables in the diet by the end of the first year. Many of the schemes of diet which are in use to-day and which are so strongly advocated in the health pages of the popular papers, underestimate the child's digestive powers, entail extra work and expense for the mother, and produce a flabby, anaemic baby. I have already mentioned that anaemia predisposes to infection. Such infection greatly aggravates the anaemia, which may be rapidly fatal unless a transfusion is performed.

ANAEMIA OF WOMEN

Just when we were congratulating ourselves that chlorosis had disappeared, we discovered that a rather different form of anaemia is very prevalent in women. This anaemia differs from chlorosis in having its highest incidence in the late thirties, and in being profoundly aggravated by pregnancy. Davidson and co-workers⁵ have shown that anaemia of this type with a haemoglobin below 70 per cent. is present in approximately 14 per cent. of women of the poorer classes in Aberdeen. It occurs also in the better classes, though with less frequency. The causes are:

1. The female reproductive cycle, with the loss of iron in menstruation and pregnancy.
2. A diet poor in iron.
3. Defective digestion of iron, 80 per cent. of cases having achlorhydria or extreme hypochlorhydria.

The sexual factor is paramount, while the importance of the dietetic and the digestive factors varies in different cases. Associated symptoms are glossitis, brittle or depressed finger-nails, and splenomegaly; in some cases the resemblance to pernicious anaemia is very striking. There is a great tendency to relapse, more especially during pregnancy, or at the menopause, when the menses become excessive. I have already commented on the feeding of infants, and I should like to make similar remarks on the feeding of pregnant women. The mother has to supply enough iron to her baby to last until it is weaned, or approximately 20 lb. in weight. She also loses blood at the confinement. If her diet is insufficient she develops anaemia and becomes more liable to puerperal infection, while her baby comes into the world with a poor store

of iron and develops nutritional anaemia.⁶ Anaemia is far more frequent than chronic nephritis or eclampsia, and the diet of the ordinary pregnant woman should be designed with this point in view; she should have red meat once a day, and abundance of green vegetables and fruit. In menorrhagia near the climacteric, severe anaemia will usually bias us in favour of an artificial menopause by x rays, radium, or operation, when we should have otherwise waited for the natural termination of the menses.

The anaemia of women is of low colour index, and the specific treatment is iron. Liver is of no value. Iron must be given in large doses and preferably as a scale preparation, or as one of the ferrous salts. Minimum doses are: iron and ammonium citrate, 60 grains a day; and Bland's pill, 45 grains a day. Iron should always be given by mouth, as effective doses cannot be given by injection. Treatment in many cases will require to be continued till after the menopause; when the anaemia has been repaired, a generous diet and a maintenance dose of 10 grains of Bland's pill will usually be sufficient. Relapses must always be expected during pregnancy, and treated early, or the patient may become gravely ill. Once you are on the look-out for this anaemia of women, you will be surprised at its frequency. Both you and your patients will be impressed with the dramatic improvement in cases which you had formerly regarded as chronic abdominal invalidism or neurosis. But *you will only get satisfactory results by giving iron in large doses by mouth.*

PERNICIOUS ANAEMIA

In pernicious anaemia the malnutrition of the bone marrow is the result of achylia and defective gastric digestion. In the absence of the proteolytic ferments from the stomach, material which is essential for the normal function of the bone marrow and the spinal cord is not extracted from the food, and anaemia and degeneration of the spinal cord develop. The anaemia can be repaired by the use of liver or desiccated stomach—a substitution therapy. Pernicious anaemia can usually be diagnosed by the blood picture: the cells are larger than normal, the colour index is high, and there is excess of bile pigment in the serum. Owing to the insidious onset, the diagnosis is sometimes missed, the symptoms being attributed to the weakness of old age, debility after an influenzal attack, the change of life, carcinoma of the stomach, or a disordered liver.

I shall omit any clinical description of pernicious anaemia and devote myself to its treatment. The results are still unsatisfactory and in far too many cases the story is as follows. A patient is found to be suffering from pernicious anaemia, and he makes a good response to treatment with liver or allied substances. He is then told to eat 1/2 lb. of liver a day, and is lost sight of. Feeling himself better, he relaxes his treatment, perhaps taking liver only once or twice a week. As a result, he develops subacute combined degeneration of the spinal cord, and a general and quite unwarranted belief is fostered that treatment of pernicious anaemia is of little value in preventing the onset of spinal symptoms. The real conclusions from this history are: (1) that cases of pernicious anaemia should be kept under regular supervision to see that their haemoglobin is maintained above 90 per cent.; (2) that some less onerous treatment than 1/2 lb. of whole liver a day should be prescribed. Just as every patient with diabetes mellitus is under the threat of diabetic coma, so every patient with pernicious anaemia is under the threat of subacute combined degeneration. Treatment of pernicious anaemia is easier than that of diabetes mellitus, inasmuch as it is impossible to give an

overdose of effective substance. *The golden rule of treatment is to give enough effective substance to keep the blood count normal, and to increase the dose if any signs of spinal degeneration appear.* Alternatives to whole liver, adequate doses of which are intolerable to many patients, are extracts of liver, oral or intramuscular, and desiccated stomach. Liver extracts are too expensive for general use, but desiccated stomach is as cheap as, or cheaper than, whole liver.⁹ In the vast majority of cases of pernicious anaemia the anaemia is repaired and nerve changes are arrested by a daily dose of one ounce of desiccated stomach. Most of my patients take it in soda-water, half an ounce twice a day, and eat an ordinary diet with appetite and good digestion. They do not take liver regularly, and then only as an article of diet. They are warned that they must continue this treatment for the rest of their lives, and they are examined at monthly or bi-monthly intervals. My own observations are in complete agreement with the much larger experience of Wilkinson,⁷ that in patients treated in this way the blood remains perfectly normal, no nerve degeneration occurs, and any spinal symptoms present are usually alleviated.

When a patient is seen in relapse it is wise to accelerate recovery by injecting intramuscular extracts of liver. Patients with subacute combined degeneration should also be given intramuscular extracts of liver until the blood is normal, in addition to treatment by mouth, to arrest the progress of the disease. For maintenance treatment I rely on desiccated stomach, but advise the patient to take as much marmite and bemax as possible. In isolated cases iron and thyroid gland may be indicated. I am not convinced of the value of massive doses of iron in subacute combined degeneration, as I have seen subacute combined degeneration develop in a woman who was having massive doses of iron for a microcytic anaemia. Nor do I often prescribe hydrochloric acid in pernicious anaemia, as desiccated stomach overcomes any tendency to dyspepsia, and it is desirable that treatment should be as simple as possible.

Subacute Combined Degeneration

While it should always be possible to prevent the development of subacute combined degeneration, it is more difficult to treat the established disease. Nevertheless it is surprising how much improvement is sometimes made. The victims of subacute combined degeneration are usually elderly people, who regard paralytic symptoms as omens of an impending dissolution which they are powerless to avert. They take to their beds and give up hope of ever walking again. This attitude is often encouraged by over-solicitous relatives, and it must be vigorously opposed. Every effort should be made to get the patient up on a couch or a wheel chair, and to encourage him, by massage and re-education, to stand and walk. I have been much more vigorous in my treatment of subacute combined degeneration since I had the following experience.

Mrs. C. L. R., aged 40, came to see me supported by two sticks and a devoted husband. She had been anaemic all her life, had had sprue in China at the age of 34, and pernicious anaemia in Jerusalem at age 39. From this last attack she had recovered as regards her blood, but had much weakness of her legs, which she attributed to a fall and a sprained ankle. In actual fact she had subacute combined degeneration, with spastic paresis of both legs and a bilateral extensor plantar response. She was not pleased with my diagnosis, and on some excuse did not pay a fee then—or later. A chiropractor agreed with her own diagnosis of a sprain, and manipulated her, telling her he had replaced an artery which had been twisted. She promptly gave up her sticks and boarded a ship back to Jerusalem without assistance.

When a patient has organic disease we are too apt to take symptoms at their face value and to accept a degree of disability which is out of proportion to the anatomical damage. Hurst has emphasized this point in his lecture on "The Hysterical Element in Organic Disease,"³ and elsewhere, and we can hardly be too often reminded about it. In subacute combined degeneration the nerve lesions can be arrested by adequate dosage of effective substance, except in the terminal stage of bladder infection and transverse myelitis. It is doubtful whether the lesions are entirely spinal in situation or irreparable in nature; some of the sensory change is probably due to degeneration of peripheral nerves, which can recover completely. But quite apart from the possibility of the regeneration of damaged nerve tissue, there is no doubt about the gain in bodily vigour under adequate treatment of the anaemia, and the ability of many of these crippled patients to regain the use of their hands and feet if they are properly encouraged and carefully re-educated.

Mr. M., aged 60, developed symptoms of subacute combined degeneration in September, 1929, though he had been failing in health for some time before. He was rather remiss about attending his doctor, and took only the equivalent of 1/4 lb. of liver a day in liver extract. During 1930 and 1931 the red cells remained between $3\frac{1}{2}$ and 4 millions, and the haemoglobin about 80 per cent. The nervous symptoms were unchanged, and paraesthesia was always present. In the summer of 1932 he suddenly lost the use of his legs. The blood count was now: red cells 3,630,000, white cells 7,000, haemoglobin 80 per cent. He was confined to his bed for about four months. Joint sense was practically absent in the toes, the tendon reflexes were depressed, and both plantar reflexes were extensor. He had much flatulent dyspepsia, and developed a venous thrombosis in the left leg. Suspicion of a carcinoma was aroused, and the patient himself took so gloomy a view of his future that he gave away his valuable car to a friend. He was taken into hospital and treated with intramuscular injections of liver and desiccated stomach by mouth. His blood count improved to: red cells 4,880,000, white cells 7,800, haemoglobin 96 per cent., colour index 1. With massage and re-education he learnt to walk with two sticks. He continued the desiccated stomach on discharge, and six months later the blood count was practically identical. Joint sense was still grossly impaired and Romberg's sign positive; the tendon reflexes were exaggerated, and the plantar reflexes were both extensor. Nevertheless he was able to work in the garden without a stick, and had bought a new car, in which he had recently driven over 100 miles in one day. His handwriting, which had previously been almost illegible on account of the numbness of the hands, had also much improved.

It would be easy for me to multiply instances of this kind, for unfortunately about half the cases of pernicious anaemia I see are patients who have relapsed from inadequate treatment and developed subacute combined degeneration. And while I have seen several paralysed patients improve so much as to be able to return to normal life, others have been too far advanced to respond, the bladder has been involved, and necropsy has revealed cystitis and ascending nephritis. It is lamentable that in so many cases to-day the life of a patient with pernicious anaemia is merely extended long enough for him to develop subacute combined degeneration. There is no more reason for patients with pernicious anaemia to succumb to subacute combined degeneration than for diabetics to die in coma. Both complications are preventable by careful treatment.

I would repeat that the treatment of pernicious anaemia is easier and cheaper than that of diabetes mellitus. It is impossible to give an overdose of effective substance, and the treatment need in no way interfere with the enjoyment of a normal diet and an active life. There is no excuse for relaxation of treatment, and every patient should be frankly told the danger of such a course.

Occasional estimations of the haemoglobin should be as much a routine as tests of the urine and blood in diabetes mellitus. We have had ten years to learn the modern treatment of pernicious anaemia, and it is time we took its lessons to heart.

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THE HEALTH OF ANTIMONY OXIDE WORKERS

BY

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The smelting of antimony ores, and the production of antimony metal, has been practised in England for at least two centuries, but the commercial production of pure grades of antimony oxide for pigmentary and similar purposes has been in operation only since the war. Antimony trioxide (Sb_2O_3) is now manufactured in large quantities, and this material, which is in the form of an extremely finely divided white powder, is much used.

The smelting of antimony ores has never been regarded as a dangerous occupation, and the only malady from which antimony smelters suffer (and then only occasionally) is an irritation of the skin, which results in blotches or minute pustules—sometimes extremely unpleasant owing to itchiness. The parts of the body most affected are the front and back of the forearms, the front of the chest, and the epigastrium. The irritation appears to be caused when dust falls on a skin damp with perspiration, but it is noteworthy that many workers are not affected, and that in this connexion personal cleanliness is an important factor. It is found that the irritation invariably disappears completely in the course of a few days if the worker ceases to have contact with antimony dust. In view of the increasing use of antimony oxide in industry, it was felt desirable in the interest of the worker to ascertain whether or not the handling of this material demands special hygienic precaution. Feeling that the conditions of exposure of workers engaged in the manufacture of the material are likely to be more severe than those involved in its use, I made an inquiry into the health of some workers who had been engaged in its manufacture for a period of thirteen years—which period covers the production of this material on a commercial scale in England. Shortly after its manufacture was commenced the question was raised as to the possible toxic character of antimony trioxide, and at that time medical opinion could only be based on experience of the processes of antimony smelting, in which the production of antimony fumes, oxide, etc., is inevitable. The view then expressed was that there was no evidence to indicate that there were any dangers in the production or use of antimony trioxide; indeed, evidence to the contrary was available. The late Sir Thomas Legge, in evidence before the Home Office Departmental Committee on Paints, stated that antimony oxide was only a mild irritant and could not be described as a poison at all.

THE SURVEY

The following recent investigation, which affords confirmation of earlier medical opinion, has been made possible through the courtesy of the Cookson Lead