ANAEMIA IN THE ELDERLY

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The recognition of anaemia in elderly patients is of profound importance. Anaemia is frequently not obvious at clinical examination; it always has a cause, which may or may not be serious (that is to say, anaemia can never be attributed to old age, *per se*) and its presence may gravely affect the course of such diseases as myocardial and cerebral arteriosclerosis, which may co-exist in the same subject.

Several factors contribute to the difficulty of recognizing anaemia in the aged. The symptoms produced by anaemia are frequently explained away by the patient as due to weakness inherent upon age. Disabilities which, in earlier life would lead to early medical examination, are often ignored when the wage-earning period is passed. Inability to walk a mile because of dyspnoea cannot be neglected during the wage-earning years. After retirement the disability is ascribed to age, and the swollen ankles which the anaemia produces attributed to the same cause. The result is that the patient takes to his chair and leads a life of semi-invalidism. The appearance of the skin is of little help in the aged. 'The ageing skin becomes yellow, thin and less elastic. There is a waste of subcutaneous fat and roughness, flaccidity and dryness. The lumina of the arteries being considerably narrowed in senescence, the skin is poorly supplied with blood, and becomes atrophied' (Thewlis, 1946). All these appearances obscure anaemia, while the colouring of the tongue and the conjunctivae can be quite misleading. It is not, therefore, surprising, that in old people anaemia frequently goes unrecognized. A third obstacle to diagnosis is the faulty orientation of many medical men towards the subject. Anaemia is neither rare nor, when it exists, is it inherent upon age. It is, on the contrary, a frequent condition and one which, when present, is always due to disease. The idea, widely accepted until recently, that with advancing years the level of the blood haemoglobin and red cells falls has been disproved (Howell, 1950). Stieglitz (1949) writes: 'In the

entire blood system, in both cell count and cell character, in plasma volume and plasma composition, there is a greater constancy and uniformity in this tissue throughout the entire span of life than in the other organs of the body.'

Anaemia is, however, not only frequent but its effects on the body are serious; these effects are, in fact, more serious than at any other time of life. The first effect is to produce a condition of severe weakness and malaise, leading to a state of invalidism which is, however, remediable if detected and properly treated. Much invalidism that accompanies old age is irremediable. How anxious should we be, therefore, to detect and cure cases of remediable invalidism. Left untreated, the anaemic old person, perhaps already more or less senile, retires to bed and becomes a burden to the community until he is finally sent, labelled 'senility,' to hospital, where he will occupy a bed for weeks or months until death or correct treatment sets him free.

Mrs. E.H., aged 79, was admitted to Belmont Hospital on July 15, 1949, as a case of senility. She was weak and apathetic, but apart from a certain degree of pallor showed no physical sign of organic disease. An immediate blood haemoglobin estimation was 54 per cent. (Sahli). Full blood count showed R.B.C. 2,200,000, colour index 1.2, fair degree of macrocytosis. Treatment with liver extract produced a rapid multiplication of the red cells, 10 per cent. of reticulocytes being present on the tenth day. Her general condition improved, she became sprightly and humorous and her blood count rose to 4,860,000 red blood cells. By September 24, 1949, she was fit to return home on maintenance doses of liver.

The second result of anaemia is to produce a train of symptoms which, though insufficient to warrant hospitalization, is nevertheless a cause of anxiety both to the patient and his relatives. These symptoms, which are mainly cerebral in nature, comprise dizziness, true vertigo and sensations of faintness. They are, no doubt, due to

cerebral anaemia and can, of course, be seen when the blood count is normal in cases where cerebral arteriosclerosis diminishes the blood flow to the higher centres of the brain.

A third and most important result of anaemia is its effect of exaggerating the ill effects of other illnesses. These ill effects are mainly seen in the cardiovascular and genito-urinary systems.

Mrs. F.D., aged 77, was admitted to Belmont Hospital on December 4, 1948, on account of cardiac asthma, the result of congestive heart failure. There was marked skin pallor, ascites and gross dropsy of legs and sacrum. The liver was enlarged and the spleen could be felt as low as the umbilicus. The cervical veins were fully distended and the lung bases oedematous. Blood count showed R.B.C. 2,000,000, Hb. 40 per cent., W.B.C. 161,000, neutrophils 42.5 per cent.; the remaining white cells being mainly myelocytes and metamyelocytes. The patient died on December 27, 1948.

In this case of chronic myeloid leukaemia a severe anaemia led to the production of congestive failure in a heart already damaged by arteriosclerosis. The effect of anaemia in maintaining renal insufficiency is shown by the following case:—

Mr. O.M., aged 69, was admitted under the author's care on December 22, 1948, as a convalescent transfer from another hospital, following a first-stage prostatectomy, a raised blood urea having precluded the completion of surgical treatment. Although a blood examination at an earlier date had revealed anaemia, no recent blood count had been made nor anti-anaemic treatment given. His general condition was poor and his mucosae pallid. Blood urea on transfer was 128 mgm. per cent., blood count 2,750,000 red cells, Hb 7.72 gm. per cent. The urine was heavily infected by an acid-splitting *B. Proteus*. Treatment of the anaemia with oral and intravenous iron, produced a fall of the blood urea with an improving blood count. On March 9, 1949, the blood count had passed the four million level and the blood urea was 79 mgm. per cent. During the same time the infected bladder had been treated vigorously. With further improvement of blood count and blood urea, the second stage of the prostatectomy was subsequently completed with success.

To prove the presence of anaemia is as simple as establishing the presence of diabetes mellitus by a urine examination. The possibility of its presence in every geriatric case should be considered, and the haemoglobin estimated as a routine precisely as the urine is examined. To send blood from every case to the laboratory for this simple examination is a cumbersome and

time-wasting procedure; haemoglobin estimation is a bedside procedure which should be done by the physician personally. The apparatus required is inexpensive and small enough to be carried in a diagnostic case, the technique is simple and the result quickly obtained with a reasonable degree of accuracy. So valuable is the information gained that it is the author's opinion that a haemoglobinometer should be part of every general practitioner's outfit; in hospital practice the estimation should be made by the house physician as part of his clinical examination and not be left to laboratory technicians. Any one of the three common 'dilution methods' will be found satisfactory though Haldane's method utilizing coal gas is impractical in rural areas while Gower's method of simple dilution is less accurate and can be utilized only in daylight. Sahli's method is easy, reliable and can be used with natural or artificial light. The author considers it the method of choice. Details of all these methods will be found in any textbook on clinical pathology. The Talqvist method, using blotting paper, is not only grossly inaccurate but may be fallacious. Dameshek (1945) goes so far as to describe 'Talqvist Anaemia' which he defines as a non-existent anaemia given prolonged anti-anaemic treatment following upon an incorrect diagnosis.

A haemoglobin level found to be less than 75 per cent. should be taken as an indication for full blood count. While the pathologist is making this examination the physician himself should begin to examine a series of stools for the presence of occult blood.

Some justification for this departure from normal medical routine would appear to be necessary. This justification is found in the frequency of gastro-intestinal haemorrhage as a cause of, or associated with, anaemia in the elderly. So common is this association that a bowel origin for any anaemia in old age should be thought of before other causes are considered. Even if the pathologist should report a macrocytic anaemia of the pernicious type, gastric carcinoma may still be present as the cause of the condition. Careful and repeated examination of the stools for occult blood should therefore be made. So important indeed is this examination and so simple to carry out in the clinical side room, that it should be done by the physician himself. The sending of specimens to the laboratory is time consuming and results in delay in obtaining information essential for the patient's management.

Details of the test, as given by Hutchison and Hunter (1950), are as follows:—

A suspension of a powder containing 0.2 gm. of barium peroxide and 0.025 gm. of pure benzidine in 5 cc. of freshly prepared 50 per cent.

glacial acetic acid, is run on to a smear of faeces on a clean microscope slide. A blue or blue-green colour developing within a minute indicates the presence of blood.

If it is borne in mind that a blue or blue-green reaction appearing *within 30 seconds* indicates bleeding whatever the diet may have contained, the usual custom of excluding red meat and green vegetables will be found unnecessary. Contrary to frequently-repeated statements in textbooks, the administration of iron salts has no effect whatever on this examination. Repeatedly positive occult blood tests are strongly indicative of bowel haemorrhage and warrant thorough radiological search for the point of origin. Similarly occult blood tests which are repeatedly negative are strong evidence against the presence of gastro-intestinal bleeding and may make radiological examination unnecessary. The combination of the bedside haemoglobin estimation with the examination of the stool (or a faecal fragment removed from the bowel at rectal examination) for occult blood, is a vital measure giving, as it often does, a strong presumption of the cause of the anaemia within five minutes of the conclusion of the initial clinical examination. This information, so easily and swiftly obtained, may even be of more diagnostic significance than the result of gastro-intestinal radiography.

The proof of the presence of anaemia, so fully discussed above, is, however, only the first of three steps in the diagnosis of a case which presents this feature. The second step is the elucidation of the type of anaemia, while the final step is the discovery of the underlying cause. The two last features have already been touched on. The elucidation of type is largely the matter of the pathologist, who will answer the question as to whether the picture is that of a hyperchromic macrocytic anaemia or that of a hypochromic or normochromic one. This does not, however, settle the diagnosis even when the blood picture is that of pernicious anaemia. Once firmly diagnosed this form of anaemia requires life-long treatment with liver extracts given not less than once in three weeks. For this reason full confirmation of the diagnosis should, whenever possible, be made by means of a fractional test meal (employing histamine), observation of reticulocyte response to liver therapy at, or soon after, the fifth day and, lastly, if at all possible, a sternal marrow puncture. While a histamine-fast achlorhydria is persistent the other features on which the diagnosis depends are immediately banished by liver therapy and remain absent for several weeks after treatment is discontinued. The discovery of the underlying cause if the anaemia is other than primary in nature depends on routine clinical in-

vestigation, beginning with a full history followed by complete physical examination, including examination of the rectum and proceeding to special investigations beginning with testing of stools for occult blood. This investigation will follow the lines pursued in investigating anaemia at any age and need not be discussed further here.

Classification of Anaemia

For the classification of anaemias at any time of life standard textbooks of medicine should be consulted. A convenient, if somewhat 'rough and ready' classification, is based on the colour index of the blood. Anaemia is thus sub-divided into hyperchromic, normochromic and hypochromic according to the colour index being above, at or below unity. These groups can be sub-divided, taking into consideration the size of the red cells. The hypochromic group thus gives rise, for example, to normocytic hypochromic anaemia and microcytic normochromic anaemia. Working on this basis we can list the common anaemias of old age as follows:—

1. Hyperchromic. Pernicious anaemia.
2. Normochromic. (a) From acute haemorrhage; (b) cachectic conditions, malignant and nutritional; (c) febrile conditions; (d) primary blood diseases.
3. Hypochromic. (a) Prolonged or repeated haemorrhage, with depletion of iron reserves; (b) deficiency anaemia from malnutrition; (c) microcytic hypochromic anaemia of women (Witts).

That some of the cachectic cases may be entirely nutritional in origin, that they may occur in males as well as females and that the anaemia produced may be normocytic in type and not microcytic is shown by the following case:—

L.P., a male aged 77, was admitted to the Belmont Hospital on December 4, 1948, complaining of weakness, anorexia and weight loss. He was emaciated and anaemic, but there were no signs of visceral disease or of haemorrhage. Blood count showed R.B.C. 2,100,000, Hb 40 per cent., C.I. 0.95, W.B.C. 5,000. Some degree of microcytosis was present. With full diet and iron, orally and intravenously, the blood picture returned rapidly to normal, since when he has remained well. A social history showed much undernutrition due to self-neglect and inadequate food.

Microcytic hypochromic (nutritional) anaemia, while most frequent in middle-aged women is also found in later age groups. The symptoms, which are indefinite, usually include fatigue, dyspnoea and often minor degrees of dyspepsia. Brittle spoon-shaped nails, a dry red tongue and a sallow complexion are found on examination. These

signs may be accompanied by the dysphagia of the Plummer Vinson Syndrome. The outstanding feature of the blood count is the remarkable reduction in the colour index, which may be as low as 0.4. Iron is curative if given over a period of months, progress being checked by regular haemoglobin estimations.

Severe anaemia from repeated blood loss, which may occur from the nose or from the bowel, is a common finding in geriatric practice and a not uncommon cause of congestive heart failure. In such cases considerable depletion of the body's iron stores ensues. In such cases not only must the cause of the anaemia be treated (e.g. injection of haemorrhoids or cauterization of varicose venules in the nasal septum), but the anaemia itself be given prolonged and thorough treatment so that iron stores are returned to normal. If this iron depletion is not borne in mind the slow response of the blood count to iron therapy will cause anxiety.

Treatment of Anaemia

In view of the associated arteriosclerosis of the brain and myocardium so frequent in age, speed of treatment is even of greater urgency in anaemias of the aged than in younger subjects. The slowness of convalescence in the elderly is another urgent reason for shortening the duration of the acute stage of the original illness.

The first step in treatment is the prescription of the correct remedy, which depends on accurate haematological diagnosis supported by careful clinical examination. As a general rule neither iron nor liver should be administered until the type of anaemia has been discovered. This is particularly important as regards liver, as this preparation will cause alteration in the blood picture, obscuring the diagnosis. It must furthermore be borne in mind that some anaemias change in character. A hypochromic anaemia, responsive to iron, may later relapse and show itself as iron resistant. These cases are found to be now macrocytic and to present a true pernicious anaemia picture.

Although cases of pernicious anaemia undergoing rapid blood regeneration on liver therapy sometimes need iron in addition, the converse (that hypochromic anaemias also require liver) does not hold true. Hypochromic anaemias are helped by iron but not by liver; the use of liver in such cases is unnecessary, inconvenient and wasteful. Iron by mouth, best given as tab. ferr. sulph. gr. 3, three times a day, is usually well tolerated and satisfactory. If iron salts cause bowel upset, constipation (which may lead, in old age, to faecal impaction), nausea or, if the anaemia be severe, recourse should be had to intravenous iron.

Intravenous iron is best given as ferrous saccharate ('Ferrivenin'—Benger) made up in 5 ml. ampoules (each containing 100 mgm. of iron), one ampoule being given daily. To test tolerance on the first two days 1.5 and 3.5 ml. are given. Intolerance, which is very rarely shown with the above-mentioned dosage, is indicated by chills, backache and faintness. Care must be taken that the fluid, which is highly irritating, does not escape into the perivenous connective tissue as severe pain and a marked tissue reaction, leading perhaps to a sterile abscess, may occur. Difficulty in injection is increased by the dark brown colour of the preparation. As venous thrombosis occasionally occurs, the patient should present at least two good veins before intravenous therapy is decided upon. Provided the body iron stores are not depleted 5 cc. of Ferrivenin should raise the haemoglobin level by 4 per cent. A daily injection will thus give a weekly haemoglobin increase of 28 per cent. in addition to any help given by oral iron. The great advantage of such rapid therapy is of immense value in dealing with debilitated aged people.

The treatment of pernicious anaemia requires either an active preparation of liver or desiccated hog's stomach presented to the patient in a manner which preserves its activity. The use of folic acid alone or in combination with other haematinics is unjustifiable in this condition as it restores the blood picture without, however, protecting the body from spinal cord degeneration, the dread disease it may even predispose the patient (Wilkinson, 1949). Liver preparations are best given parenterally as this assures that the patient is periodically observed and allows treatment to be checked by regular blood counts.

At the present time in the United Kingdom, the choice of a liver preparation is difficult. With the great shortage of liver first grade organs are reserved for consumption as food, and only less suitable livers are made available for pharmaceutical use. For this reason the therapeutic effect of any liver preparation should be carefully watched, however high the reputation of the product being used. If it is suspected that the batch of extract in use is inactive the product should be immediately changed.

As a matter of routine, six or seven days after treatment has been initiated, the red blood cells should be recounted and a reticulocyte count carried out. (For the practitioner living at a distance from a laboratory this examination should present no great difficulty; 2 ml. of blood taken into an oxalated tube or Wintrobe bottle should be posted to a laboratory.) Further counts of red cells should be made at intervals of seven to ten days until the blood count has reached normal

level, after which examinations of haemoglobin monthly should be adequate. A satisfactory response to anti-anaemic therapy is indicated by (a) clinical improvement; (b) an adequate reticulocyte response in eight to ten days; (c) a steady rise in the red cell count after this period has elapsed. The aim of treatment, which should always be capable of realization, in every correctly-diagnosed case should be five million red cells and a haemoglobin level of 100 per cent.

The scarcity of raw liver and the uncertainty of action of liver extracts in this country at the present time makes the isolation of crystalline vitamin B₁₂ (the anti-anaemic factor to which liver owes its therapeutic activity) a valuable advance in treatment (Ungley, 1949). Its precise position is at present being worked out. The advantages of its use include:—

1. The certainty of its chemical composition and consequent reliability in use.
2. The absence of all side reactions.
3. Availability and comparative cheapness.

It has a further beneficent effect on spinal cord function (unlike folic acid) and can be expected to reverse the neurological changes in subacute combined degeneration if given before the axis cylinders are destroyed. After restoration of the blood picture an intramuscular maintenance dose of 50 mgm. (given as 1 ml. Cytamen '50,' Glaxo) once in three weeks should be adequate.

During maintenance therapy the following points should be borne in mind:—

1. Considerably larger maintenance doses of liver and vitamin B₁₂ preparations are required in old age than with younger subjects.
2. The often accepted monthly interval between

injections is excessive. 'No patient should go more than two or three weeks without a liver injection of any type' (Wilkinson, 1949).

3. Especially in the aged, a careful haematological check should be had over treatment, whether the patient is being treated by liver or iron. Haemoglobin should be estimated every two or three weeks and the red cells counted every other month.

The problem of whether to give or to withhold blood transfusion in cases of pernicious anaemia in relapse in elderly subjects has been purposely left till last. Unfortunately severe relapses in the aged are frequently accompanied by more or less severe congestive heart failure, so that there is a grave danger of overloading an already embarrassed circulation. Each case must be judged on its merits. If transfusion is decided upon 'packed cells' will generally be preferred to whole blood.

Summary

Difficulties inherent in the recognition of anaemia in the aged are outlined and discussed.

The severe ill-effects on the elderly constitution are stressed.

Estimation of haemoglobin and examination of stools for occult blood should be part of the physician's personal clinical investigation of the case. These two examinations, taken together, will frequently make a short cut to the true diagnosis and save much time and expensive investigation. A plea for the exclusion of anaemia by routine bedside haemoglobin estimation of all cases is made.

The classification and treatment of anaemia, with special reference to variations found in the aged, is set out.

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