BLOOD DISORDERS IN THE ELDERLY

J. H. THOMAS

D. E. B. POWELL

BLOOD DISORDERS IN THE ELDERLY

By

J. H. THOMAS

M.R.C.P. (Lond.), D.C.H.

Consultant Physician (Geriatric Medicine), Bridgend General and Morgannwg Hospitals; Formerly Federal Adviser, British Caribbean Territory

AND

D. E. B. POWELL

M.D. (Edin.), M.R.C.P. (Lond.), M.R.C.Path.

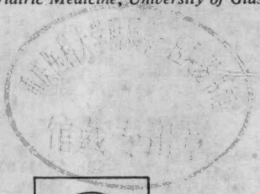
Consultant Pathologist, Bridgend General and Morgannwg Hospitals; Formerly Senior Registrar, United Bristol Hospitals

With a Foreword by

W. FERGUSON ANDERSON

M.D., F.R.C.P. (Glas.), F.R.F.P.S., F.R.C.P. (Lond.), F.R.C.P. (Edin.)

Professor of Geriatric Medicine, University of Glasgow



BRISTOL: JOHN WRIGHT & SONS LTD.

1971

Distribution by Sole Agents:
United States of America: The Williams & Wilkins Company, Baltimore
Canada: The Macmillan Company of Canada Ltd., Toronto

SBN 0 7236 0275 1

PRINTED IN GREAT BRITAIN BY JOHN WRIGHT & SONS LTD.,
AT THE STONEBRIDGE PRESS, BRISTOL BS4 5NU

PREFACE

THE number of elderly persons in the community is increasing, with the result that more attention is being given to prevention, rehabilitation, and to the social consequences of illness. Although the care of the elderly is a specialty in its own right, the boundaries between the specialties are artificial and increasingly difficult to maintain. This fact, together with the frequent association of diseases, made us consider the subject as part of general medicine. Blood disorders when present in the elderly are also best treated in this manner. However, the specialties of geriatrics and haematology are usually dealt with in separate departments and by different personnel, and because of this we decided to write a book that would, perhaps, help to bridge the gap.

The pattern of disease varies considerably with age, so that the medical practitioner, whether clinically or laboratory orientated, must take cognizance of this factor. We have found in the care of elderly patients the need for close co-operation between doctors and have endeavoured to incorporate this approach in the book. No attempt has been made to write a comprehensive textbook of haematology, but we hope that sufficient background is included to obviate the necessity for constant recourse to other sources. Both the subject-matter and bibliography are inevitably highly selective. Although conditions such as the haemoglobinopathies may be found in the elderly they are not discussed; other subjects, such as the congenital disorders, are not treated in any detail. Laboratory techniques are not described.

Case-history outlines have been included to illustrate or clarify certain features, although the majority are in no way exceptional. Several of them illustrate the more varied pattern of haematological disease seen in the elderly and underline the necessity of a multidisciplinary approach.

We hope that this basically practical rather than specialized treatment will make the book useful to senior students, membership candidates, and those dealing with sick elderly people, whether at home or in hospital. It could not have been written without the co-operation of colleagues, and we are particularly indebted to the following: Dr. A. G. Chappell, Dr. F. L. Dyson, Dr. R. Howell, Dr. F. W. Thomas, Dr. D. B. Richards, Mr. C. Havard, Mr. O. E. Owen, and Mr. A. W. Fowler. Dr. Alwyn Smith, the Senior Administrative Medical Officer of the Welsh Hospital Board, provided the South Wales cancer registration returns and Dr. Lewis Fanning the statistical evaluation. Dr. John Watkins and Dr. A. R. Mandal carried out surveys when registrars, and the nursing staff willingly co-operated. Mr. A. Dover, Mr. C. T. Dignam, Mr. D. H. Walters, and Mr. C. O. Rees did the bulk of the biochemical and haematological work, and Mr. W. T. Barr some

of the histological and photographic preparations. Mrs. Ann Robinson and Miss Glenys Philpotts were responsible for most of the typing. Finally, it is a pleasure to thank Professor Ferguson Anderson for the Foreword, and Mr. L. G. Owens, of the Publishers, for support and guidance.

J. H. T.
D. E. B. P.

FOREWORD

By Professor W. Ferguson Anderson

With more older people in the population of the developed countries of the world and with the expectation of even longer life in the future, doctors and medical students need more knowledge about illness in the elderly. This book is a comprehensive account of blood disorders in the upper age range.

Diseases of the blood are not uncommon in older people, perhaps, as the authors state, because a long life gives opportunities for the body to acquire many diseases and for any defect that is present to be accentuated.

The normality of blood in old people is stressed and advancing age is found not to be associated with diminution of an erythrocyte life span or with compensatory failure.

Three aspects are noted to be of importance:—

1. Malabsorption—even of minor degree—especially when prolonged.
2. Antibody and enzyme level alterations and malignant change in cells.
3. Physiological recovery following illness which is incomplete, with diminished reserve power which may be further impaired by arterial disease.

Haemoglobin values, the present and main causes of anaemia, are described under the headings Blood Loss, Malabsorption, and Malnutrition. The importance of apathy, loneliness, impaired mobility, and financial stress is noted and attention is drawn to the compensatory mechanism whereby deficiency of a nutrient is associated with increased absorption. There is a most useful section on the investigation of anaemia with appropriate stress on clinical examination.

The chapter on general disease is complete, mentioning blood-pictures associated with tuberculosis, especially calling to mind the phenomenon of cryptic miliary tuberculosis. The completeness of the study is shown by reference to the anaemia in patients with bed-sores or trauma. Blood changes in rheumatoid arthritis are discussed in detail, while the effects of arterial disease are also considered.

As might be expected of the authors, an account of iron deficiency and metabolism with a practical and systematic approach to diagnosis is given. There is a most useful account of iron deficiency without anaemia, while the therapy of iron deficiency is fully discussed. The megaloblastic anaemias are considered in detail with a helpful account of the mental changes which may be found.

Deficiency of ordinary nutrients, prevention of anaemia, and a full account of other important blood diseases are given. This book thus contains a comprehensive and scholarly account of blood disorders with particular attention devoted to accurate diagnosis and adequate therapy. It is no bad thing that special attention is given to the elderly, where tiredness, depression, apathy, and weakness are so commonly ascribed to old age. This work will help innumerable old people as well as doctors and I commend it wholeheartedly. It is a combination of much study and research presented comprehensively by two well-informed physicians.

CONTENTS

BLOOD DISORDERS IN THE ELDERLY

1
INTRODUCTION

BIOLOGICAL ageing must not be confused with the pathological ageing that results from disease—although both may occur together. The life span of cells is not uniform. When old they are desquamated and replaced by young cells. Eventually the process becomes defective and biological ageing supervenes, although man does not live long enough for this to be the cause of death. Most of the cells in an old person are young, except those of the central nervous system. These persist from birth, but even in the brain the changes due to biological ageing are usually overshadowed by those caused by arterial and other disease.

The cellular components of the blood follow the usual pattern. When old and effete they are destroyed and replaced by young cells formed in the marrow. Erythrocytes live 110–120 days, though their survival is not uniform; granulocytes survive approximately 3 weeks and lymphocytes a widely varied period from a few days to months in a complicated recirculating path involving the marrow, spleen, lymph-nodes, and peripheral blood.

In the healthy person, blood formation keeps pace with blood destruction and when necessary the rate varies. Reduction of red blood-cell survival to 20 or 30 days is compensated for by a sixfold increase of erythropoiesis, but beyond this the marrow fails. Advancing age is not normally associated with diminution of erythrocyte life span or with compensatory failure.

There are several studies on red-cell longevity, including that of Woodford-Williams, Webster, Dixon, and MacKenzie (1962). They compared the findings in 22 healthy subjects over the age of 80 (10 males and 12 females) with those obtained in 9 students between the ages of 18 and 25 years and concluded that no significant changes occurred with ageing.

The cells appear the same as they do at a younger age, although an increase in mean corpuscular volume was noted by Olbrich (1947) and in red-cell diameter by Spriggs and Sladden (1958).

The biological function of the red cells is similar at all ages, although there may be minor differences in the elderly as manifested perhaps in a decreased ability to transport potassium and to resist osmotic changes.

Studies on leucocyte counts by Allen and Alexander (1968) did not show any change with age in men, but women between 50 and 65 years had significantly

lower total and polymorph leucocyte counts. This was present both in healthy blood donors and in hospital patients.

A long life gives opportunity for the body to acquire many diseases and for any defect that is present to be accentuated. The following three aspects are of considerable importance:—

1. Malabsorption of a minor degree has a cumulative effect and can cause a deficiency anaemia. When investigated, the extent of the failure may be less than one expects unless its prolonged nature is realized. Minor blood-loss has to be assessed similarly.
2. There is considerable opportunity for antibodies to develop and wane, for enzyme levels to alter, and for cells to become malignant.
3. Physiological recovery following illness may be incomplete and reserve power insufficient to withstand stress. Arterial disease reduces the reserve still further. Both factors combine to make the clinical features of anaemia more protean than in younger patients.

Many diseases in the elderly are degenerative and incurable, but symptoms can often be ameliorated by attending to associated treatable conditions. The anaemias come into this category; not only do they produce symptoms, but their clinical features are often superimposed on those of other diseases. Consequently a blood examination is mandatory in every elderly patient and even minimal anaemia must be treated.

The belief that a mild degree of anaemia is to be expected in the aged because of physiological reasons, such as diminution of marrow function, is erroneous. The haemoglobin level should be the adult normal, even in centenarians.

HAEMOGLOBIN VALUES: PREVALENCE OF ANAEMIA

The earlier surveys were designed to ascertain the normal haemoglobin level at different ages. Miller (1939) presented a haematological study of 160 fit men who were inmates of a home for the aged. The literature was summarized as follows: Leichtenstern (1878) found a drop in the haemoglobin from 55 to 60 years and a rise in old age; Nascher (1914) considered the normal haemoglobin level to be between 90 and 110 per cent, and the red-cell count from 3 million to 5½ million; Williamson (1916) found the values to be fairly level between 16 and 60 years (16·9 g. per 100 ml. of blood in men), then a decline to 15·2 g. until the age of 75 years, and a rise to 15·6 g. beyond that age; Wintrobe (1930) concluded that there was no significant difference due to ageing. Miller's results averaged 14·3 g. per 100 ml.

The sex difference in haemoglobin levels was also studied. Olbrich (1947) found an average of 14·5 g. per 100 ml. in 23 males between 70 and 79 years and 13·4 g. in 20 women of the same age, but Hawkins (1954–6) stated that the sex difference in haemoglobin level diminished with advancing years.

Red-cell counts are slightly higher in males than in females. Olbrich (1947) indicated that 5·13 million red blood-cells per c.mm. was the normal in men at 70 years of age and 4·0 million in comparable women.

Kilpatrick (1961) reported the results of a survey carried out in a rural area of Yorkshire and compared them with those previously obtained in an industrial

community in South Wales (Kilpatrick and Hardisty, 1961). There were 40 men and 54 women over 65 years of age in the Yorkshire survey, and of these 80 per cent of the men and 86 per cent of the women were assessed. Anaemia was defined as being 85 per cent or less (12·5 g. per 100 ml.) for men, and 81 per cent or less (12 g. per 100 ml.) for women. By these criteria 20 per cent of the women between 65 and 74 years (25 per cent over 75) and 21 per cent of the men were anaemic. In general the incidence was higher than in South Wales, but comparison in the elderly was not possible as too few had been investigated. Miall, Milner, Lovell, and Standard (1967) in Jamaica found a similar higher prevalence in a rural sample, particularly in males (14·5 per cent rural; 5 per cent suburban at ages 55–64 years). Fry (1961) in a study of 'anaemia' (haemoglobin below 80 per cent) in a London general practice of 5000 patients indicated that the most vulnerable ages were: in males, children under 10 years and men over 60 years, and in females, all age-groups over 30 years with a peak at 50–59. Iron deficiency accounted for 92 per cent of the anaemias. He recommended that full facilities for investigation be given to all family doctors in at least one hospital of each local hospital group.

There are several surveys dealing with the incidence in hospital patients. Lawson (1960) reported on a study of 319 patients over the age of 60 years. Twenty-six per cent were anaemic when first seen, and a further 11 per cent developed anaemia (the criterion being a haemoglobin level below 80 per cent, 11·9 g. per 100 ml.). Bedford and Wollner (1958) found a final incidence of 41 per cent. Our own figures are similar. In 333 consecutive admissions to the hospital a haemoglobin level below 80 per cent was present in 29 per cent. There was no difference in incidence between the sexes (Powell, Thomas, and Mills, 1968).

Read, Gough, Pardoe, and Nicholas (1965), while investigating folic-acid deficiency in 51 consecutive admissions to a welfare home, noted that 12 per cent had a haemoglobin level of 70 per cent or less when first seen.

Pincherle and Shanks (1967) gave the haemoglobin findings in 2000 business executives who included 262 males between 60 and 64 years and 44 males who were older. The level of 14·6 g. per 100 ml. did not drop with ageing and furthermore the incidence of even mild anaemia was negligible—0·32 per cent had a haemoglobin level between 80 and 85 per cent, and 0·1 per cent between 75 and 80 per cent. Lower levels were not found. They felt that the reason for this low incidence of anaemia compared with that in other surveys was the higher standard of nutrition and of medical care in the group studied.

Campbell and his colleagues (1968) gave the results of haemoglobin and plasma-urea concentration in a random sample of adults in Wales based on the electoral roll. Persons over 75 years of age were excluded as they probably needed a domiciliary visit. General practitioners co-operated by taking 2·5-ml. samples of venous blood. Patient refusal amounted to 6·5 per cent for males and 11·8 per cent for females. Four hundred and fifty-two blood samples were finally analysed. The mean haemoglobin level for men between 65 and 74 years of age was 15·2 g. per 100 ml., and for women 13·6 g. per 100 ml. No difference in haemoglobin concentration was noted in samples from different areas—whether rural or urban, agricultural or industrial. Ten per cent of the men had concentrations below 14·0 g. per 100 ml. and 11 per cent of the women below 12·0 g. per 100 ml. (14 per cent female in the age-group 65–75 years). They concluded that the haemoglobin

level in men remained steady up to 74 years and that in women there was an increase from 25 to 65 years and then a fall of about 0·5 g. per 100 ml.

Hobson and Blackburn (1953) carried out a home survey of a 1 in 30 random sample selected from the food office register in Sheffield. Only those living alone or with a spouse were included. Anaemia (80 per cent haemoglobin—11·7 g. per 100 ml.—or less) occurred in 5·1 per cent of 177 males aged 66–85 years and in 6·5 per cent of 246 females aged 61–87 years. Eight out of 9 males had iron deficiency and 13 of 16 females. None was receiving treatment for anaemia. The main contributory factors were poor diet (44 per cent) and rheumatoid arthritis (28 per cent). The mean haemoglobin level among 46 males living alone was 13·9 g. per 100 ml. which was considerably lower than the mean level of 14·5 g. per 100 ml. obtained in those living with their wives. These authors put forward the interesting suggestion that there could be a selective removal by death with advancing age of those with low haemoglobin levels.

Parsons, Withey, and Kilpatrick (1965), while undertaking a social survey of a 2 per cent sample of the whole population of the County Borough of Swansea, investigated the haematological indices of 208 persons, 65 years of age or over. Anaemia was defined as a haemoglobin level of 85 per cent (12·5 g. per 100 ml.) or less for men, and 81 per cent (12·0 g. per 100 ml.) or less in women. By these criteria 10·8 per cent of the men and 15·7 per cent of the women were found to be anaemic. Subdivision at the age of 75 years supplied further information. There were 7·2 per cent anaemic men in the age-group 65–74 years and 20·8 per cent in the 75– group, while in women the corresponding percentages were 11·1 and 23·3. Possible correlation with ingestion of aspirin was investigated but the result was negative. The anaemia was nearly always due to iron deficiency, only 3 having low serum vitamin-B_{12} levels.

From these and similar surveys it is apparent that the incidence of anaemia in the elderly is considerable and that its prevalence increases as age advances.

MORBIDITY AND MORTALITY

There are insufficient data on morbidity for worth-while comparisons to be made between those obtained in different countries. The incidence of pernicious anaemia and leukaemia varies, and iron-deficiency anaemia can be due to primary dietary deficiency in one country or to endemic hookworm disease in another. In this country the main cause of a macrocytic anaemia is vitamin-B_{12} deficiency whereas in India and the Far East it is folate deficiency. The age distribution of the population varies and in countries where the expectation of life is low the prevalence of pernicious anaemia, which is a disease of the elderly, is less than in those where the expectation of life is greater. Some anaemias are more easily treated than others, but the presence of concomitant disease—particularly in the very old—can still result in a high mortality. Moreover, anaemia can precipitate death when another disease is present, but death may not be attributed to it.

Response to therapy in iron-deficiency anaemia is satisfactory if the cause can be corrected, but the underlying disease, such as a carcinoma of the colon, may remain hidden or be inoperable. Diagnostic and therapeutic facilities differ within the same country and more so when several countries are compared. Nevertheless,

despite all these variable factors, considerable information can be obtained from a study of mortality statistics.

The death-rate per million population for the years 1964–6 in the United Kingdom are given in *Table I.*

Table I.—DEATH-RATE PER MILLION POPULATION (W.H.O. REPORT)

TYPES OF ANAEMIA	50–59 Years	60–69 Years	70–79 Years	80— Years
England and Wales				
Pernicious (other hyperchromic)	3·8	16·6	89·7	294·4
Iron deficiency	1·6	9·1	40·8	156·3
Other anaemia	8·4	23·1	51·7	93·6
Unspecified anaemia	1·4	9·0	30·9	99·7
Scotland				
Pernicious (other hyperchromic)	5·6	19·4	89·5	412·1
Iron deficiency	2·6	5·4	21·1	66·2
Other anaemia	8·7	26·1	62·1	139·8
Unspecified anaemia	5·6	14·0	79·5	179·9
N. Ireland				
Pernicious (other hyperchromic)	8·3	27·0	113·8	368·9
Iron deficiency	—	5·4	28·4	54·6
Other anaemia	10·3	24·3	66·4	68·3
Unspecified anaemia	2·1	21·6	71·1	327·9

The rate increases markedly beyond 60 years of age. The same trend occurs in other countries. Its incidence is similar in Australia and New Zealand, but is less evident elsewhere. Over the age of 70 the most common type is hyperchromic anaemia and this is more pronounced in those over 80, the percentage for England and Wales, Scotland, and Northern Ireland being 45·7, 52·1, and 45·0 respectively. Below the age of 70 death due to 'other anaemias' predominates.

The average death-rate for all types of anaemia rises from 5·8 per million persons in the 40–49 age-group to 409·4 in those aged 80 and over. Females predominate until the age of 70, and thereafter the mortality-rate is higher in males: 70–79 years: 146·6/135·9; 80+: 479/213·9.

The death-rate for hyperchromic and iron-deficiency anaemia remains higher in the female, the rate for hyperchromic anaemia at 80 and over being 130·5 per million in the female and 103·6 per million persons in the male, while for iron-deficiency anaemia the comparable rates are 37·2 and 20·4.

HAEMOPOIESIS AND AGEING

The various schemes of haemopoiesis have long been debated and are still subject to investigation, but we do not propose to recapitulate these arguments other than to summarize the important effects of ageing.

The anatomical effect can be seen in the extent and distribution of haemopoietic marrow. The normal adult has approximately 0·56 g. of marrow per gramme of blood, which constitutes 3·4–5·9 per cent of the body-weight (1600–3700 g.), i.e., it

approximates to the weight of the liver. The classic observations of Custer and Ahlfeldt (1932) established that the functioning haemopoietic marrow recedes from the periphery with ageing (*Fig.* 1).

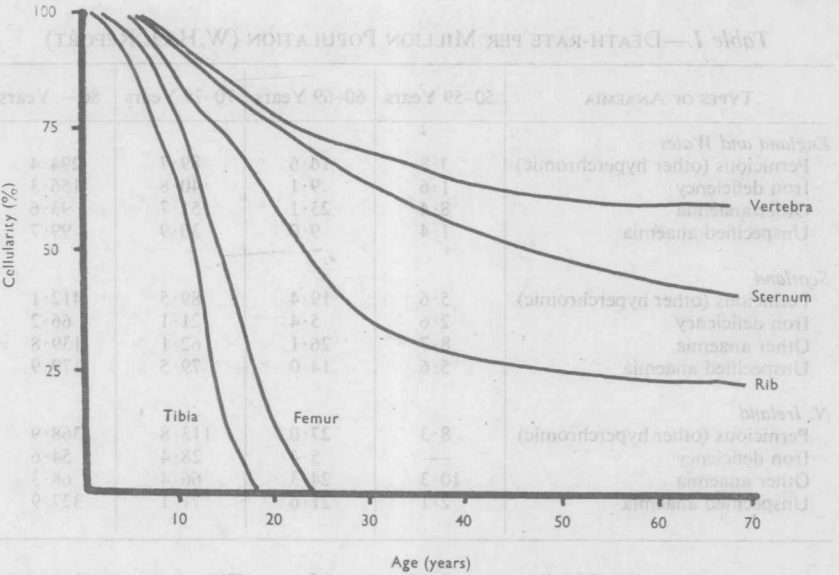


Fig. 1.—The cellularity of bone-marrow at different sites related to age.
(*After Custer and Ahlfedt*, 1932.)

Harstock, Smith, and Petty (1965) studied wedge biopsies of the iliac crest in 177 cases of sudden death where no disease likely to affect haemopoietic tissue had been found. They used a counting technique to assess the frequency of haemopoietic tissue in relation to fat and other structures. The mean percentage of haemopoietic tissue fell from 78·8 per cent under 10 years to 28·9 per cent at 70–79 years. There was a progressive decrease over the first three decades, followed by relative stability until a further decline took place after 60 years. The final stage could be related to an increase in fat subsequent to osteoporosis.

The physiological effects are difficult to evaluate because tests of haemopoietic function are either crude and imprecise or so artificial as to be of dubious relevance. Among the governing factors are erythropoietin, adrenocorticosteroids, thyroid and possibly other hormones, and many stimuli which provoke or depress haemopoiesis, such as oxygenation, body activity, fever, and toxins. There may be a considerable interplay of these factors.

Timaffy (1962) assessed the functional capacity of the leucopoietic system following stimulation by bacterial lipopolysaccharide (*Shigella sonnei*), and compared the responses of 25 healthy young adults (19–31 years) with those obtained in 25 elderly persons (70–83 years) the majority of whom were attending because of cataracts. The average rise in the leucocyte count was 108·07 per cent in the young

and 29·09 per cent in the elderly. The greatest difference occurred in the neutrophils and young granulocytes which rose ×25 in the young and ×3 in the elderly. Cream (1968) measured the neutrophil granulocyte peak with prednisolone stimulation and found an impaired response in the elderly.

Little is known of the direct effect of ageing on erythropoiesis. Old people show a diminished capacity for regeneration after haemorrhage, but this is difficult to distinguish from that due to coexistent chronic disease and other factors, such as renal failure. The capacity of the elderly to produce optimal reticulocyte responses to vitamin-B_{12} therapy in pernicious anaemia may be impaired, but, on the other hand, response to haemorrhage and to vitamin B_{12} or iron therapy is sometimes as satisfactory as in the young. Extramedullary haemopoiesis is seldom seen, but this is hardly a normal index of reserve capacity. To summarize, there is no clear evidence linking the morphological hypoplasia of erythropoietic marrow with functional impairment.

CAUSES OF ANAEMIA

The *main causes* of anaemia are:—

Blood-loss
Malabsorption
Malnutrition

Specific causes are considered separately in subsequent chapters.

Blood-loss

This is generally accepted as the most important single factor in the production of iron-deficiency anaemia. The mean daily blood-loss in the stools is about 3 ml., but Holt, Mayet, Warner, Callender, and Gunning (1968) found that the average blood-loss in 19 anaemic patients with a gastric hernia was 15 ml. Nearly half were losing the equivalent of 500 ml. a month (250 mg. elemental iron). In all, except 2, there was a fourfold compensatory increase of iron absorption, and the response to iron therapy was good. Many were free from gastric symptoms and 14 had negative occult blood tests.

The cause of gastro-intestinal bleeding is sometimes obscure although haemorrhoids, peptic ulceration, gastric herniation, and neoplastic lesions are fairly common. The diagnoses in 77 consecutive anaemic patients with gastro-intestinal blood-loss, other than from haemorrhoids, are given below:—

Carcinoma:	Colon, 8; Stomach, 9; Rectum, 8; Oesophagus, 1; Jejunum, 1
Hiatus hernia:	6
Ulceration:	Gastric, 10—2 giant; Duodenal, 6; Anastomotic, 1; Oesophageal, 1; Gastric and duodenal, 1; Gastric erosion, 2
Diverticula:	Colon, 5; Duodenal, 4; Oesophageal, 1; Jejunal, 1; Gastric, 1
Ulcerative colitis:	2
Thrombocytopenic purpura:	1
Uraemia:	1
Aspirin ingestion:	2
Unknown cause:	5

Occult blood testing is not an accurate method of detecting gastro-intestinal bleeding because the loss is often intermittent. Nevertheless, it is valuable in view of its simplicity and sensitivity, being positive when the loss is 5 ml. a day. However, undue reliance should not be placed on negative results. Bedford and Wollner (1958) found the Gregersen test positive in 55 per cent of admissions and in 78 per cent of those who were anaemic. Agate (1963) considered that hiatus hernia was probably the most commonly missed cause.

Those in whom no reason for the bleeding is found form an interesting group. They amounted to 14 per cent of patients with iron-deficiency anaemia described by Bannerman, Beveridge, and Witts (1964). The follow-up was negative in 75 per cent and they concluded that although gastric erosions perhaps accounted for some, in the majority the cause remained obscure. Anaemia tended to recur but responded to therapy. In the elderly, more so perhaps than in the young, it is difficult to decide how thoroughly one should pursue the investigation when radiological examination of the gastro-intestinal tract is negative. Intestinal polypi, erosions, ischaemic colitis, and vascular anomalies may remain undetected. Laparotomy is not justified, but in view of the frequency of neoplastic lesions at this age barium studies should be repeated in 3–4 months. Despite these precautions it is not unusual for a neoplasm to be obvious a year or two later.

Other sources of bleeding, such as haematuria, vaginal bleeding, and epistaxis, are fairly common reasons for admission to hospital. Obvious loss may be intermittent, with less in between. This may not be noted, with the result that the anaemia may seem excessive. Bleeding from the urogenital tract, as in carcinoma of the prostate, bladder, and kidney, is a common cause of this phenomenon, as the urine may contain excess red blood-cells when haematuria is not evident. The amount of iron normally lost in the urine is about 0·5 mg. a day, but this is probably exceeded in many elderly persons, especially males. Oesophageal varices have occasionally to be considered because cirrhosis of the liver is not unusual. McKeown (1965) gave an incidence of 1·5 per cent in necropsy material.

Malabsorption

Iron and folates are absorbed in the upper part of the small intestine, and vitamin B_{12} in the lower ileum. The incidence of atrophic gastritis increases as age advances, with the result that the production of 'intrinsic factor' may diminish and consequently fail to participate in the absorption of the dietary vitamin B_{12}. Normal gastric function also has a complex role in iron metabolism. Jejunal diverticula sometimes develop and interfere with the normal absorption of folate. Steatorrhoea is not an uncommon finding, although gluten enteropathy is rare. Patients who have undergone surgery of the gastro-intestinal tract may present several years later with anaemia due to malabsorption. Of 85 consecutive patients who were anaemic from a gastro-intestinal cause 5 had had a previous partial gastrectomy.

Malnutrition

The normal diet contains 10–12 mg. of iron, 10 μg. vitamin B_{12}, and 100 μg. folate per day, which is sufficient to supply the 1 mg. of iron, 2 μg. vitamin B_{12}, and 50 μg. folate that are necessary to maintain erythropoiesis. A diet devoid of all meat, fish, fowl, dairy produce, and grain products still contains about 0·4 μg.

vitamin B_{12} per day and would have to be taken continuously for about 2 years before vitamin-B_{12} deficiency developed, provided absorption was satisfactory and the stores full when the diet commenced. Such limitation of food intake is unlikely to be encountered except in vegans and even in them few symptoms develop. Smith (1962) investigated 12 such subjects and found that apart from 2 who had subacute combined degeneration of the cord, they were healthy. Four were over 50 years of age, and 1, a female of 71, had been a vegan for 30 years. Her haemoglobin was 83 per cent, serum vitamin B_{12} 80 pg. per ml., and serum iron 25 μg. per 100 ml. None had a haemoglobin below 80 per cent and in 7 it was 90 per cent or above. The serum vitamin-B_{12} level was below 150 pg. per ml. in 8, and in 5 it was 90 pg. per ml. or less, the lowest being 48 pg. per ml. This was in a female aged 48, who had been a vegan for 18 years. He contrasted their lack of physical signs, despite the low serum vitamin-B_{12} levels, from that seen in patients with tobacco amblyopia, where the levels of serum vitamin B_{12} could be normal, and yet the condition responds to cytamen injections. However, as the amblyopia is probably due to failure of cyanide detoxication by vitamin B_{12} it is more likely to develop when vitamin B_{12} is deficient than when dietary intake and absorption are satisfactory. The oldest patient among the 65 reported on by Foulds, Chisholm, Bronte-Stewart, and Wilson (1969) was aged 84 years.

Despite the adequacy of haematinic factors in normal diets malnutrition still occurs. Apathy, loneliness, impaired mobility, and financial stress are potent causes. Moreover, the body stores may already be low and when combined with occult blood-loss and decreased absorption, deficiency may become severe.

The body normally compensates for a deficiency by increasing absorption so that when this mechanism is defective or the dietary intake insufficient, anaemia results.

ERYTHROCYTE SEDIMENTATION RATE (E.S.R.)

Although Westergren (1957) indicated that the upper limit of normality was 5 mm. in the first hour in men, and 10–15 mm. in women, higher values are frequently obtained in 'healthy' elderly persons.

The rate of red-cell sedimentation is governed by factors affecting both cell and plasma. Increased viscosity retards sedimentation, while a decrease in red-cell volume accelerates it. When these factors are allowed for, the rate is mainly dependent on the concentration in the plasma of fibrinogen, alpha-2, and gamma-globulin, the most important being fibrinogen. Elevation of this fraction, as may occur with ageing (Steinman, 1964), perhaps accounts for the unexpected high values that are sometimes obtained. An increased serum lipid concentration is another possibility.

Women have higher normal values than men, but the explanation is obscure because the greater incidence of anaemia that occurs among women in the younger age-group is not a feature in the elderly. Perhaps hormonal influences are in some way responsible.

Bottiger and Svedberg (1967) analysed the E.S.R. in 1457 men and 1021 women between the ages of 20 and 70. They were all physically healthy. Those whose parents suffered from, or had died from, ischaemic heart disease or cerebrovascular accidents were excluded. The results indicated that above the age of 50 the

upper normal limit for men was 20 mm. and for women 30 mm. in the first hour.

Boyd and Hoffbrand (1966) studied the E.S.R. in 303 patients admitted to a geriatric unit, and concluded that in nearly a third there was no apparent cause for values above 20 mm. in the first hour, and that in some instances this was so when the value was as high as 40 mm. They decided that occult urinary tract infection was not the explanation.

The presence of such a wide range in the E.S.R. of healthy elderly persons diminishes the value of the test as a diagnostic aid. In exceptional circumstances similar values may be obtained, for example, in a patient with early myelomatosis or temporal arteritis as in another who is healthy. Serial readings help clinically, but they are seldom available.

The enormous variety of pathological states associated with a raised E.S.R. is not surprising, as most infections, whether acute or chronic, can produce an altered serum protein pattern. When a grossly elevated reading is obtained, collagen disease, arteritis, and myelomatosis have to be considered although the elderly are also subject to the same diseases as affect younger people. Their presentation, however, is often different so that well-recognized entities such as pyometra, bacterial endocarditis, septicaemia, abscesses, and purulent arthritis may be overlooked. Occasionally a high E.S.R. is obtained for which there is no apparent explanation.

PLASMA PROTEINS

There is wide variation in the levels of protein fractions. Reduction of albumin and elevation of gamma-globulin are often noted, but this could be physiological.

Haferkamp, Schlettwein-Gsell, Schwick, and Störiko (1966) measured the protein fractions of 145 inhabitants of a village in Switzerland, ranging in age from 15 to 91 years (55 over 61 years). There was no significant difference in the total protein content between the different age-groups, but electrophoresis and quantitative immunological tests showed an increase in gamma-globulin and a decrease of albumin as age advanced. This change appeared in the fifties and was maintained.

Other authors have been less definite. Some have shown that protein patterns are unchanged with ageing in healthy individuals, while others regard a fall in serum albumin and high values of gamma-globulin to be normal in the elderly. The difficulty in differentiating between health and disease in these persons is often semantic, owing to the frequent occurrence of occult disorders in the apparently healthy. The distinction is largely theoretical because for practical purposes it is only in ill people that serum proteins need be assessed.

Chesrow, Turner, Shaffner, and Musci (1957) showed that gamma-globulins increased and ascribed it to intercurrent infection and malnutrition. Eckerström (1958) investigated 30 persons between 70 and 90 years of age. They had normal blood-pictures, erythrocyte sedimentation rate, renal and hepatic function, and were all well nourished. There was an elevation of gamma-globulin and this was considered to be primarily due to infection or tumour. Woodford-Williams, Alvarez, Webster, Landless, and Dixon (1964) concluded that the changes seen were probably the result of numerous factors, with underlying disease, immobility, and malnutrition being the most important. Chronological ageing as a cause