UNIT 4 ANAEMIA AND HEMATO-ONCOLOGY

Structure

4.0 OBJECTIVES

After reading this unit, you should be able to:

- define anaemia, enumerate its causes and type;
- diagnose; manage anaemia and
- refer the case to specialist in case it is difficult to treat.

4.1 INTRODUCTION

You have learned in Block 2 of this course about the gastrointestinal and respiratory problems, which effect the elderly more when their body resistance is low. Elderly at the same time loose the body resistance as a consequence of these problems. It, therefore, becomes a vicious circle. The suffering continues and more diseases come in. Anaemia is once such disease which, comes in as a consequence of repeated infections and sufferings. In this unit you will learn about anaemia in elderly. In addition, you will also learn about haemato-oncology in elderly with special emphasis on leukemias and multiple myeloma.

4.2 ANAEMIA

The exact incidence of anaemia in elderly population in India has not been worked out. The prevalence goes up as the age advances because there is a physiological decline in bone marrow functioning. There are areas, where hygienic conditions are not good,

e.g. worm infestations, other infections, poor sanitation, poor nutrition etc. There the haemoglobin levels are lower than at the places where elderly are health conscious. Hence the values vary from place to place and are equally effected by social, economical and cultural factors.

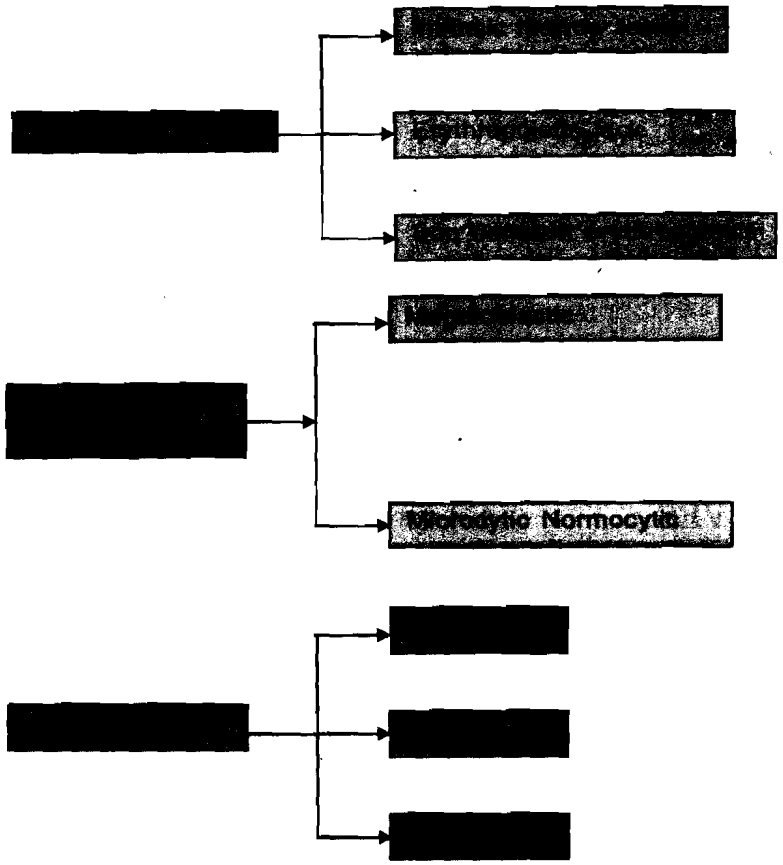
4.2.1 Classification

The physiological classification of anaemia can be as:

- Hypo-proliferative
- Ineffective Erythropoiesis
- Hemolytic

For the convenience of explanation we can put it in the chart as given below:

Chart 4.1: Types of Anaemia on the Basis of Aetiology



4.2.2 Aetiology

The following points may be kept in mind:

- The incidence of anaemia increases with age.
- Bone marrow reserves capacity decreases as the age advances.
- The response and recovery from various stress factors becomes slow and delayed as the age advances.

In spite of above factors if there are no pathological conditions or undue stress to the body the healthy elderly progresses well without being affected from anaemia.

The anaemia occurs either because of reduced function/hypoproliferation of the bone marrow or because of some depressive effect on bone marrow due to involvement of other organs like kidneys etc. Chronic inflammation any where in the body, lack of proper nutrition, endocrine factors etc. also act in the same way.

The anaemia also occurs if the blood formation (erythropoiesis) becomes ineffective due to certain deficiencies like folic acid and or vitamin B_{12}. Diseases like thalassemia may affect the erythropoiesis.

The anaemia may be caused by increased hemolysis. The hemolysis may occur without any reason or may occur due to diseases like metabolic disorders, cancerous conditions (lymphoma), because of autoimmune diseases or by the use of certain drugs.

4.2.3 Clinical Presentation

You must keep in mind anaemia and its causes while examining an elderly. The anaemia presents as pallor skin, general poor health, pedal oedema, and/or the presentation of other diseases, which are mentioned under aetiology.

On examination you may find lean, thin, emaciated patient, who might also have swelling over the feet/dependent area of the body. There may be puffiness around eyes. Tachycardia is a usual feature. There may be a short systolic murmur in heart (functional). Some times there may be signs and symptoms of congestive cardiac failure in the form of raised JVP, Basal crepitations, enlarged tender liver. The conjunctiva is usually pale. There may be signs and symptoms suggestive of deficiency of proteins and vitamins in the form of generalized swelling over the body, glossitis, sensory loss etc.

4.2.4 Investigations

Once you suspect anaemia and your suspicion is corroborated by physical examination you must try to confirm the diagnosis. You must try to find out the type of anaemia and if possible to know the exact aetiology of it.

The basic investigations include:

- A complete blood count (Hb, TLC, DLC, ESR, MCH, MCV, MCHC, and platelet count)
- Routine Urine Examination
- Stool Examination for Ova, Cyst and Occult Blood
- Serum Proteins and A:G ratio
- If facilities exist, an x-ray chest, liver function tests, kidney function tests

4.2.5 Treatment

Your treatment strategy should be based on the following lines to:

- treat the anaemia
- treat the aetiological factors responsible for causing anaemia

The treatment of aetiological factors will depend upon the aetiology itself. If you have facilities then treat otherwise it is good for you to refer the patient to the nearest proper centre. This centre may be a District Hospital, a Tertiary Care Centre, a Medical College Hospital or a Hematology Institute. This treatment might require a hospitalization needed for even chemotherapy or radiation sittings. At times the aetiological factor may be a simple worm infestation for which a tablet of Mebendazole/Albendazole or any other deworming agent might be needed.

The treatment of anaemia *per se* requires iron therapy, vitamins supplements, proteins supplements and mineral supplements. All the things may be given orally in the form of pills with a detailed advise about food and nutrition. It is essential that the advice about food has to be given not only to the patients but also to the members of family and care givers repeatedly. It is better to do it in many sittings and ask them whether they have followed it or not. Please keep in mind the local culture and customs as well as the crops and vegetables of the area.

At times you may have to opt for parental iron therapy. In emergencies or in severe anaemia you may give blood transfusions also.

4.2.6 Prevention

If you are actively involved with the local community, you will foresee the occurrence of anaemia in your patients. This is because you will be watching the hygienic conditions, their activities and their food habits. Your advice to the local administration (Gram panchayat, BDO or collector) regarding hygienic conditions in the area will always carry more value than a common man. The stagnant water, the use of unfiltered water by people at large, the proper disposal of sewerage and the care to avoid the contamination of eatables/drinking water are to be observed and intimated to the concerned authorities. Some general talks about healthy foods to patients, their relatives, general public or the people who interact and influence masses like teachers, social workers and leaders will help in long term management. At times the iron and vitamin tablets are advised prophylactically.

Check Your Progress 1

1) Fill in the blanks.

   a) The incidence of anaemia.....with age.

   b) Bone marrow reserve capacity.....as age advances.

   c) Liver in anaemia may be associated with.....

2) Name the types of anaemias based on physiological classification.

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4.3 HEMATO-ONCOLOGY

Like anaemia the incidence of blood cancers also increase with age. There are lots of studies in European literature, which support this fact, but in our country this incidence has not been worked out in elderly population. A number of times, blood cancers are discovered during routine check-up or check-up for some other diseases. Chronic Lymphocytic Leukemia is by far the commonest leukemia that is seen in elderly. This is followed by Chronic Myeloid Leukemia. Other malignancies like lymphomas, Multiple Myeloma etc. are down in the list so far as malignancies are concerned.

You may classify hematological malignancies like this:

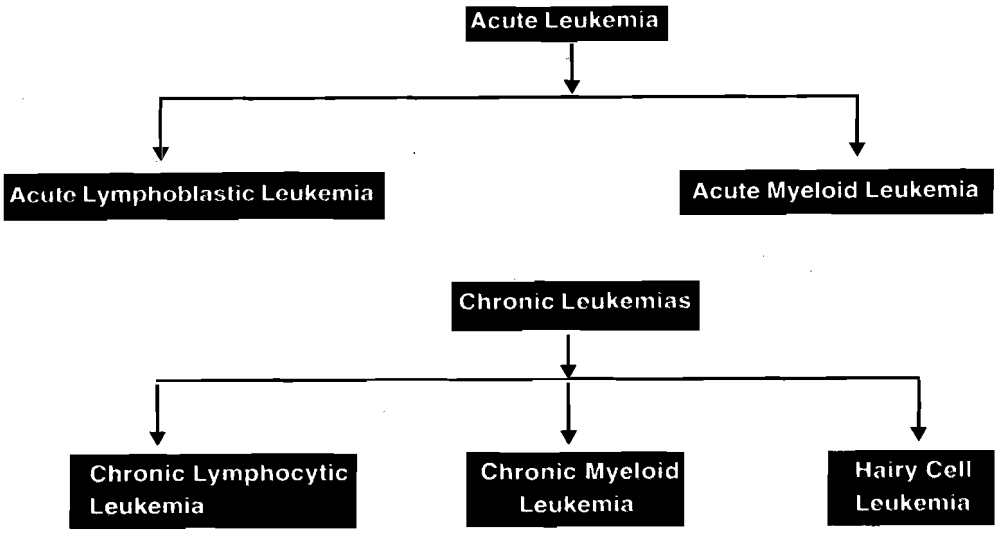
1) Leukemias

2) Lymphomas

3) Multiple Myeloma

Leukemias can be classified as per their occurrence, i.e. acute and chronic. You may also classify them as per the type of cells that undergo malignant change. From the point of view of convenience we would suggest you the following classification:

Chart 4.2: Classification of Leukemias



The Lymphomas may be classified as:

- Hodgkin's Lymphoma
- Non Hodgkin's Lymphoma

4.3.1 Clinical Presentation

Let us descuss the clinical presentations of different types of malignancies in the elderly.

1) **Leukemias in Elderly**

Leukemias can be classified as acute or chronic

Acute Leukemia

Acute leukaemia is primarily a disease of the elderly. Eighty per cent of elderly with acute leukemia have acute non-lymphocytic leukaemia. In spite of this, the incidence of Acute Lymphocytic Leukemia (ALL) is 4 times higher in the elderly than in children. Radiation exposure has been implicated as the cause in come cases, which is supported by a data on atomic bomb survivors from Hiroshima and Nagasaki, that shows a 10-20 per cent increased incidence of acute non lymphocytic leukaemia. Other aetiologies implicated are exposure to benzene, chemotherapeutic agents, chronic bone marrow disorders such as myelodysplastic syndrome, polycythemia vera aplastic anaemia viruses etc. In acute leukemias, primitive white blood cells accumulate rapidly in the bone marrow and invade may tissues including liver, spleen, lymph nodes and CNS. Normal bone marrow is replaced by these blasts, which results in severe anaemia and thrombocytopenia. Normal WBCs are replaced by these primitive cells, which results in the patient developing infections. The presentation of acute leukemia may be high fever, bleeding from the nose and mouth, GIT and genitourinary tracts. There is often lymphadenopathy and hepatosplenomegaly. The disease can also develop insidiously, with progressive weakness, pallor, a change in the sense of well-being and delirium.

Acute leukaemia is diagnosed by routine blood examination which demonstrates the presence of blast cells. Bone-marrow shows an excess of blast cells with decreased or absent normal erythroid, granulocytic and megakaryocytic cells. Elderly patients with ALL have an overall poor long-term survival compared to children. Therapy usually consists of a combination of drugs including vincristine, prednisone, doxorubicin and L-asparaginase. Infections are the major cause of mortality and morbidity in acute leukemias. The choice of antibiotic depends upon predominant organisms causing infection in a given hospital.

Chronic Leukemia

In chronic leukemia, there is a neoplastic accumulation of mature lymphoid or myeloid elements of the blood. Chronic lymphocytic leukemia is primarily a disease of the elderly.

accounting for 25 or 40 per cent of all leukemias. Ionizing radiation plays no part in the aetiology of chronic lymphocytic leukemia. The presentation of CLL is highly variable. Over 25 per cent of patients have asymptomatic disease that is discovered on routine physical examination or blood analysis. The most common initial symptoms are fatigue, malaise and decreased exercise tolerance. In many older people, exacerbation of coronary artery or cerebrovascular disease may be the initial presentation. On examination, there will be lymphadenopathy and hepato splenomegaly. Fever is usually secondary to infection, but late in the disease the possibility of transformation into acute prolymphocytic leukemia or aggressive lymphoma should be considered. Diagnosis is by peripheral smear examination, routine blood analysis and bone marrow examination. CLL is treated with chlorambucil. The most common complications of CLL are bacterial infections with pneumonia and urinary tract infections.

2) Lymphomas in Elderly

Lymphomas may be Hodgkin's or non-Hodgkin's type (NHL). Hodgkin's disease usually has a predictable pattern of spread to contiguous lymph node area, while non-Hodgkin's lymphoma is usually widespread. NHL is more likely to have extra nodal involvement.

The diagnosis of Hodgkin's disease depends on histologic finding in the lymph node of the Reed-Sternberg cell. Histologically Hodgkin's type is classifed into lymphocyte predominant, mixed cellularity, lymphocyte depleted and nodular sclerosis types.

NHL are a heterogenous group of lymphoid malignancies which have common but many different features. Working classification of NHL is into low grade, intermediate grade and high grade.

Patients with Hodgkin's disease usually have enlarged lymph nodes in the neck at presentation. Although any nodal group can be involved, the cervical or axillary lymph nodes are the most common. Liver and spleen also may be enlarged depending upon the stage of the disease.

NHL appear to be multicentric in origin and have a tendency to spread widely during the course of the disease. Splenomegaly, bone marrow failure, autoimmune haemolytic anaemia and thrombocytopenia are occasional presenting features.

In Hodgkin's disease, limited radiation therapy is used for stage I and II and combination chemotherapy with or without radiation is recommended for stage III and IV. However, in elderly the regeneration of the bone marrow after radiation or chemotherapy is markedly diminished. Thus, one must consider limiting the usual medical field in elderly patients with early stage diseases. Similarly it may be impossible to give optimal chemotherapy to elderly patients, even though the benefits of aggressive chemotherapy out-weigh the risk. Many elderly patients can tolerate only 30-50 per cent of the optimal dose of chemotherapy. There is an increased incidence of a second malignancy in patients with Hodgkin's disease receiving therapy. The duration of chemotherapy is 6 to 12 months or at least 2 months following attainment of complete remission.

In cases of NHL, most patients have advanced stage disease and require chemotherapy. Chemotherapeutic cures in NHL paradoxically tend to occur only in patients with intermediate and unfavourable prognosis histologies.

3) Multiple Myeloma

Multiple myeloma is characterized by neoplastic proliferation of immature plasma cells in the bone marrow. The consequences of abnormal plasma cell growth cell tumour include osteolysis, haematopoietic suppression, hypogammaglobulinemia, paraproteinemia, paraproteinuria and renal disase. Anaemia is most common but neutropenia and thrombocytopenia also occur. About one half of patients with multiple myeloma have renal disease. Urinary tract infections, glomerular deposits of amyloid stones from hypercalcemia and hyperuricemia and plasma cell infiltration of the kidney all may occur. The most frequent symptom of multiple myeloma is bone pain which occurs in about 70 per cent of patients. Pain is often in the lower back or ribs and gradually increases in intensity. Systemic signs and symptoms include pallor, weakness, fatigue, dyspnea and palpitation. Signs of thrombocytopenia are common. Signs of

infection also occur frequently as a result of neutropenia and immunoglobulin deficiency. Hyercalcemia is very common in patients with destructive bone lesions and may result in anorexia, nausea, vomiting, polyuria, poydipsia, constipation and dehydration. Particularly in the elderly, drowsiness, confusion and coma can result from hypercalcemia. Hyperviscosity syndrome occurs if the monoclonal immunoglobulin is IgM. Purpura, ecchymoses, epistaxis, GIT bleeding, blurred vision and ischem neurologic symptoms are common features of hyperviscosity. Diagnosis is by x-ray of the skull which shows lytic lesions. The absence of lytic lesions and plasma cell infiltration makes a diagnosis of benign monoclona gammopathy likely. Urine examination for Bence-Jones protein and presence of serum monoclonal protein is diagnostic of multiple myeloma. Regarding management, radiation is reserved for localized lesions and is most helpful in back pain. Commonly used chemotherapeutic agents are melphalan and prednisone. The two drugs are given daily for 4 days and treatment is repeated at intervals of 4 to 6 weeks for at least three courses before remission is confirmed. Hyperviscosity can be treated effectively in the short term by plasmapheresis.

4.3.2 Investigations—Baseline

The complete blood count may give a clue about the disease. Low haemoglobin, a very high total leukocyte count and a normal or reduced number of platelets are the hallmark of the leukemias. For further diagnosis one may require a bone marrow examination which may be done from the sternum or the iliac crest. For evaluation of the patient, if possible one should also do a routine urine examination, stool examination (to see the microscopic bleeding), x-ray chest, x-ray of the abdomen and ultrasound to detect organomegaly.

4.3.3 Referral

When you clinically suspect a malignancy and the baseline investigation support your diagnosis please refer the case immediately to a tertiary care centre or a hospital, which is well equipped to treat this problem. The referral centre will of course, first do, a detailed clinical examination and baseline investigations to confirm the diagnosis. Later on they will do more investigation to do the staging of the disease from the point of view of treatment and prognosis.

The bone marrow examination and the CD count in case of chronic lymphocytic leukemia and leukocyte alkaline phosphatase and Philadelphia Chromosome in chronic myeloid leukemia are done at the referral centres. Tartaric acid, Phosphatase activity and ribosome lamella complex in hairy cell leukemia etc. are also routinely done in reference centres.

The bone marrow, lymphnode biopsy, CT scan abdomen are done in case of lymphomas.

Serum Protein Electrophoresis, Urine for Bence-Jones proteins, skeletal survey etc. are done for multiple myeloma.

4.3.4 Follow Up

You must follow the following drug regimens according to type of leukemia as outlined below:

Drug Regimen

a) Acute Lymphoblastic Leukemia

   Cytosine Arbinoside and Daunomycin

b) Chronic Myeloid Leukemia

   Busulphan, Hydroxyurea, Interferon and Bone Marrow Transplant

c) Chronic Lymphocytic Leukemia

   Chlorambucil, Deoxycofarmycin and Spleenectomy

d) Hodgkin's Lymphoma

Radio Therapy and/or Chemotherapy which includes Vincristine, Procarbazine, Mustine Hydrochloride and Prednisolone

e) Non Hodgkin's Lymphoma

Chlorambucil, Endoxan etc.

f) Multiple Myeloma

Melphalan or Regimens like VMHC or VAD

VHMC – Vincristine, Malphalan, Endoxan and Prednisolone.

VAD – Vincristine, Doxorubicin, Dexamethasone.

Side Effects

Loss of hair, severe anaemia, secondary infections are very common during above treatment. One should keep vigil for the same and do repeated blood counts. At times one may loose the patient because of the side effects of therapy rather than the disease itself. Proper antibiotics/antifungals for infections and blood transfusions for anaemia may be required.

Complications

Upper and lower respiratory infections are by far the commonest complications. Haemorrhages are also very common and sometimes they may be massive. Fungus infections also complicate the disease because of low body resistance/broad-spectrum antibiotic therapy. Vitamin deficiencies specially that of B-complex are generally seen.

4.3.5 Supportive Therapy

These patients usually require supplementation of proteins and vitamins in their diet. You may be required to give blood transfusion if the haemoglobin falls below eight grams. When platelets come down platelet concentrates transfusion may be required. When uric acid levels rise, than to prevent the kidney damage allopurinol may be given. Suitable antibiotics to control infections may be needed. Administration of immunoglobins may be done when their levels are low and spleenectomy may be done if hyperspleenism becomes evident.

Check Your Progress 2

1) How do patients with Hodgkin's disease present?

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2) Fill in the blanks.

a) The commonest leukaemia seen is elderly is .....

b) The commonest symptom of multiple myeloma is .....

4.4 LET US SUM UP

Have an high index of suspicion of anaemia while examining an elderly, which helps to clinch the diagnosis faster. After diagnosing anaemia, try to look out for the aetiological factors that cause anaemia. Treatement strategy should be aimed not only at treating anaemia but also to treat the aetiological factor causing anaemia.

Suspect leukaemia in an elderly who presents with malaise, ill health, bleeding from nose, in the urine or stool and inter current infection in the upper respiratory mucosa.

Complete haematological profile including peripheral smear and bone marrow examination helps in arriving at a diagnosis of haematological disorder.

Early diagnosis and early treatment of complication reduces the morbidity of both anaemia and leukaemia. In case of leukaemia presenting in advanced stage in the elderly, therapy should be aimed at reducing pain rather than to treat the primary disorder, as quality of life is more important.

4.5 KEY WORDS

Anaemia	:	Where haemglobin is less than 10 gm/dl.
Erythropoisis	:	Formation of blood in the body.
Leukaemia	:	Abnormal proliferation of blood cells both myolid and lymphoid.
Lymphoma	:	Neoplastic proliferation of lymphoid tissue of gland.
Multiple myeloma	:	Neoplastic proliferation of immature plasma cell in the bone marrow.

4.6 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) a) increases

   b) decreases

   c) enlarged tender liver

2) The three types of anaemia based on physiological classification are:

   — Hypoproliferative

   — Ineffective erythropoesis

   — Hemolytic

Check Your Progress 2

1) Patients with Hodgkin's disease usually have enlarged lymphnodes most commonly of the cervical or axillary group. Depending upon the stage of the disease the liver and spleen may also be enlarged.

2) a) CLL

   b) bone pain.

4.7 FURTHER READINGS

Fauci, Braunvald, Issel bacher *et al., Harrison's Principle of Internal Medicine,* 15th edn., McGraw Hill, 2001.

Tallis, Raymond, Howard Fillit and J.C. Brocklehurst, *Brocklehurst's Textbook of Geriatric Medicine and Gerontology*, Churchill Livingstone, London, 5th edn., 1998.