IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 2 Ver. VIII (Feb. 2015), PP 51-58
www.iosrjournals.org

Anaemia in the Elderly - An Emerging Health Problem (A Neglectedproblem)

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Abstract:*Anaemia in the elderly is an extremely common problem associated with increased mortality and poor health related quality of life. It is easy to overlook in elderly because symptoms and signs of anaemia may be attributed to the ageing process itself.*
Keywords: *Anaemia; Elderly*

I. Background

Anaemia in the elderly is an extremely common problem associated with increased mortality and poor health related quality of life. It is easy to overlook in elderly because symptoms and signs of anaemia may be attributed to the ageing process itself [1]. It should never be considered as normal physiological response to ageing [2]. Multiple studies demonstrate that anaemia is an independent risk factor for increased morbidity, mortality and decreased quality of life. Increased functional deterioration is associated with decreasing heamoglobin concentration in an inverse and linear manner [3, 4].

Definition:

Anaemia is defined as a reduction in the number of circulating red blood cells or the heamoglobin concentration in the blood. World health organization defined it as a hemoglobin level <13gms/dl in men and <12gm/dl in women [5].

Prevalenceof anaemia in elderly:

The world population is ageing; in 2000 there were 600 million people aged 60 years and above, and it is estimated that this will be doubled by 2025 and more than tripled to 2 billion by 2050 [8]. The oldest old, often defined as those aged 85 years or older, are increasing in number.

The number of elderly individuals is expected to reach to an unpredicted level in the 21st century and anaemia represents an emerging global health problem having negative impact on quality of life of the elderly [9].A recent review of studies on anaemia in elderly patients confirm that reduced heamoglobin levels are seen 1 in every 7or8 persons over 65years living in the community; more common in hospitalized patients affecting almost 1 in every 2 patients [6].

Age related changes in haematopoietic system:

Haematopoesis is the production of blood elements occurring in an orderly, hierarchical fashion. Blood cell production requires stem cells, a functioning bone marrow, micro environment, nutrients, cytokines and haematopoetic factor.

Marrow shows haematopoetic changes due to ageing like decreasing in the number of committed stem cells and increasing in the fat content [13]. There is strong evidence that many markers of inflammation including Tumor Necrosis Factor –alfa, Interlukin-6 and Macrophage migratory inhibitory factor (MIF) are increased in elderly population regardless of health status [10, 11].

It is unclear that whether this chronic inflammatory state reflects primary age related immune dysfunction or a systemic response to the presence of co morbid conditions. Inflammatory markers are inducers of hepcidin secretion, implicated in mediating iron limited erythropoesis, thus contributing common path way for development of anaemia [12].

Epidemiology:

Many factors can affect a healthy person's measured heamoglobin levels including ethnic back ground, altitude of residence, smoking status and physiological fluctuations of plasma volume.

Of these anaemic patients, one third were identified to have nutritional deficiencies, one third were diagnosed having chronic diseases and in one third the cause remained unexplained [7].

Nutritional Deficiencies:

Approximately 34% of cases of anaemia in the elderly are nutritional deficiencies. Iron deficiency, either alone or in combination with vitamin B12, and or folate accounts for nearly 20% of all geriatric anaemias.

Most of these are attributed to iron deficiency including chronic blood loss (related to non-steroidal anti inflammatory drug induced gastritis, peptic ulcer, colonic ulcers, diverticulae, angiodysplasias, inadequate intake or absorption of iron). However folate deficiency (related to alcoholism and malnutrition), and vitamin B12 deficiency (primarily related to atrophic gastritis) also play a role. Without blood loss, anaemia takes several years to develop.

Causes of blood loss from the GIT are [14, 15]:

20%-40%	-	upper GIT disease
15%-30%	-	colon cancers, angiodysplasias, polyps, colitis.
1%-15%	-	upper and lower GIT disease
10%-40%	-	not known .

Vitamin B12 Deficiency:

While studies suggest that 5%-10%of elderly peoplewith anaemia are due to cobalamine deficiency, the actual prevalence of vitamin B12deficiency is likely to be much higher in elderly [16]. Only 60% of patients with B12 deficiency are anaemic. In addition neurological symptoms of B12 deficiency can develop before the patient become anaeamic. Deficiency is rarely due to inadequate intake except in pure vegans. Common causes are reduced intestinal absorption (lack of intrinsic factor), partial gastrectomy, small bowl disorders and bacterial over growth. These conditions may increases with age.

Folate Deficiency:

Unlike B12 deficiency, folate deficiency usually develops as a result of inadequate dietary intake. The body stores very little folate, only enough to last for 4 to 6 months. Like B12 deficiency, folate deficiency classically causes macrocytic anemia, although significant proportion of elderly with folate deficiency have normocytic anaemia. The symptoms are nearly indistinguishable from those of vitamin B12 deficiency.

Anaemia of Chronic Diseases (ACD):

As elderly persons often suffer from multiple chronic co-morbidities, it is not surprising that the ACD is a common cause of geriatric anaemia. ACD is primarily related to inflammation and usually develop in the presence of disorder like chronic infection, malignancy, autoimmune and inflammatory disorders.

Inflammation inhibits erythropoesis through a variety of mechanisms; by producing Inflammatory markers (Tumor necrosis factor –alfa, interlukin-6 and macrophage migratory inhibitory factor(MIF),interferon gama) and hepcidin. Recently it is suggested that hepcidin is a key regulator of iron balance in the ACD [17].

Chronic kidney disease is exceedingly common in the elderly, since renal function decline with age. There is a clear linier relation between the prevalence of anaemia and kidney function .The primary cause of anaemia in CKD is decreased production of erythropoetin, which is a stimulator of haematopoetic stem cells. Common diseases associated with ACD are tuberculosis, endocarditis, chronic UTI, chronic fungal infections, rheumatoid arthritis, collagen vascular diseases, polymyalgia rheumatica, chronic hepatitis, CKD, inflammatory bowel diseases and malignancies.

Un explained anaemia:

In one third of geriatric anaemias the cause is unexplained. Whether it represents a spectrum of undiagnosed etiologies or has a unifying pathogenesis remains unclear. Several theories postulated to explain this phenomenon, including decreased production of haematopoetic growth factor, presence of inflammatory cytokines, marrow abnormalities and androgen deficiency [18]. It is also thought that some of these cases actually may be unrecognized CKD or early stage of ACD or undiagnosed myelodyplasias [18]. Myelodysplastic syndrome, represents a pre-leukemia, is characterized by a defect in the development of one of the marrow cell lines, limiting the release of functioning cells. Anaemia result when the red cell lines are affected. Myelodysplastic syndrome should be a diagnostic consideration when white cell or platelet abnormalities accompany the anaemia.

Adverse outcomes of anaemia in elderly:

Morbidity and mortality is increased in these patients if their hemoglobin is decreased [19]. Geriatric anaemias has been associated withincreased frailty, poor exercise performance, diminished cognitive function,

risk of developing dementia, increased risk of recurrent falls, increased rate of major depression, cardiovascular diseases and increased hospitalization.

History and clinical features:
Careful elicitation of history can give the etiologies of anaemia in older individuals. Questions should address anaemia

- associated with blood loss
- chronic indigestion, malena, hematuria, hematocheazia, recent surgeries
- dietary history - inadequate diet, strict vegans, pica.
- heavy alcoholism - folate deficiency, peptic ulcers, bleeding varices
- long standing anemia - family disorders
- drug history - NSAIDS, warfarin,

Symptoms:
Symptoms are related to the rapidity of the development of anaemia , the percentage of fall in Hb, and concomitant medical conditions. The nonspecific nature of anaemia related symptoms poses a major challenge. General symptoms include:fatigue, weakness , dyspnoea on exertion , tinnitus, pre-syncope, palpitations, head ache, poor concentration, pale skin, worsening of pre existing cardiac disease like CAD,CCF. Neuropathy, ataxia, dementia are associated with B12 deficiency.

Signs: Physical examination may uncover etiology of anaemia, signs related to anaemia or both. Thus, the examination must be comprehensive. Special attention should be paid to the following:Pallor, icterus, edema feet, lymphadenopathy, tachycardia, hepatosplenomegaly, cardiac murmurs.

Investigations: Anaemia in the elderly is evaluated in a manner similar to that in younger individuals, including assessment of gastrointestinal blood loss, haemolysis, nutritional deficiencies, malignancy, chronic infection, renal and hepatic diseases and other chronic diseases.In patients without evidence of an underlying disease, the initial laboratory evaluation should include a complete blood count, RBC indices, reticulocyte count and peripheral smear.

Interpretation of test results in initial evaluation:

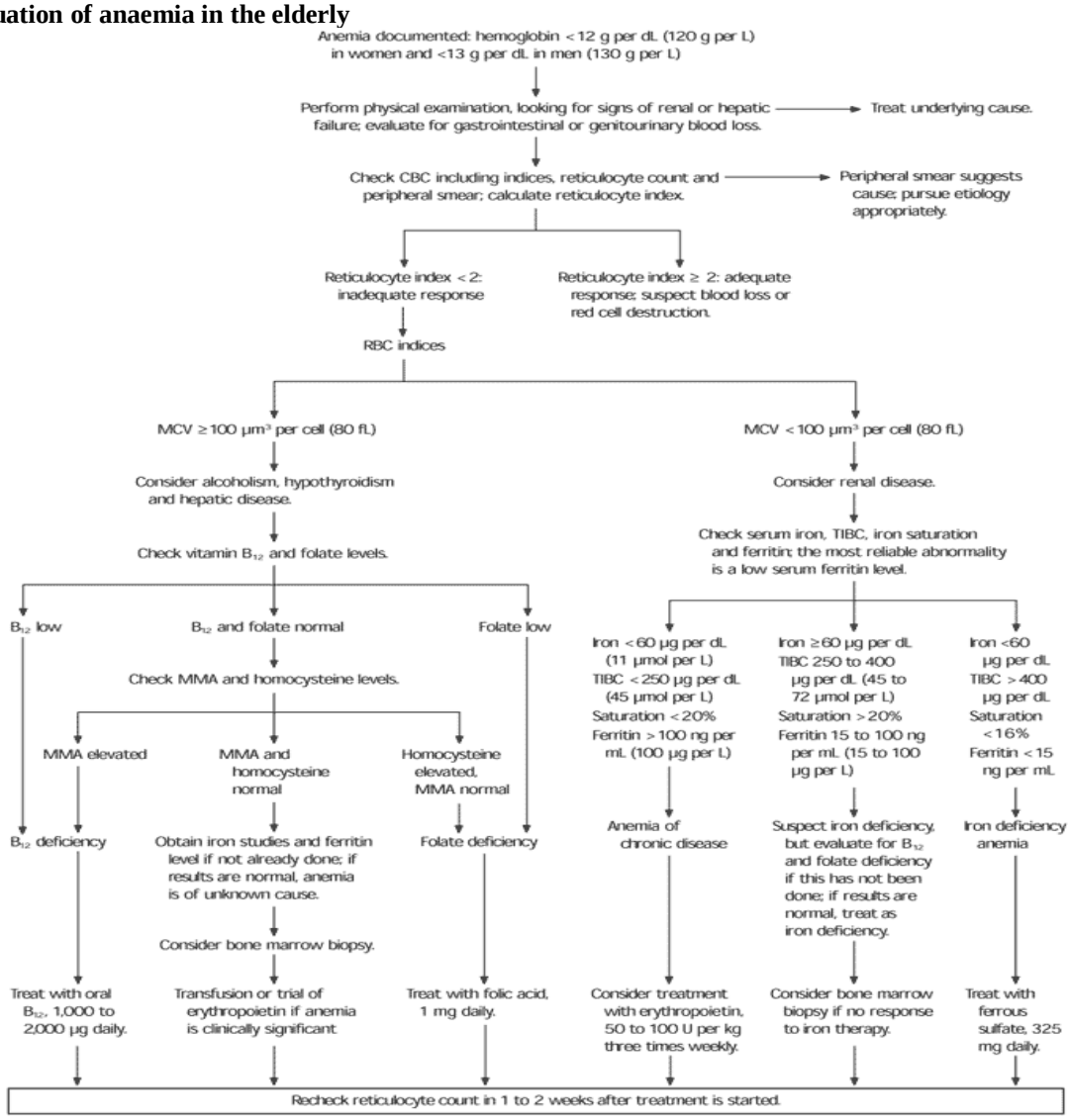
Test	Finding	Possible etiology
RBC indices	MCV<80	IDA, ACD.
	MCV>100	Vit.B12,folate deficiency
	MCV-normal	Renal, liver, thyroid disorders
WBC, platelet counts	Abnormal	Marrow production problem
Peripheral smear	Burr cells	CRF
	Spherocytes, fragments	Haemolyticanaemia
	Dysplastic changes	Myelodysplasias
Reticulocyte count	<1%	Inadequate production
	>1%	Increased production but unclear appropriate magnitude or not
Reticulocyte index	>2	Reticulocyte release appropriate for anaemia
	<2	Inadequate response to anaemia

Anaemia algorithm used for evaluation of younger adults are based on mean corpuscular volume (MCV) but such algorithm may be less helpful in the elderly because the classic changes in erythrocyte size do not often accompany anaemia in this age group. In most elderly patients with anaemia red cell indices disclose normocytic normochromic anaemia [20,1].

Other tests: Serum ferritin level is considered the best single test for diagnosing IDA (proportional to the body stores). However in elderly serum ferritin test is not reliable test, because ferritin levels increase with age. But transferrin receptor-ferritin index have high specificity and sensitivity in diagnosing IDA. It is a simple, noninvasive test. It may eliminate the need for bone marrow examination.
Bone marrow examination needed in[30].

- Pancytopenia
- monoclonal gammapathy
- suspicion of myelodysplastic syndrome
- smear showing immature cells, nucleated cells
- undetermined status of iron stores
- unexplained progressive or unresponsive anaemia

Evaluation of anaemia in the elderly



Management: Once the cause is determined, the approach is to implement the appropriate treatment to correct anaemia. Treatment of underlying cause should prevent further iron loss.

Iron deficiency anaemia:

All patients with IDA should have iron supplementation both to correct anaemia and replenish body stores [22].

Oral therapy: simple and effective.

- Ferrous sulphate - 200mg three times a day; other alternatives are ferrous fumerate and ferrous gluconate.
- Ferrous sulphate 325mg once a day for prolonged periods to minimize the side effects and improve compliance [23].
- Enteric coated or slow released preparations may fail to produce the desired therapeutic benefits because of their reduced availability at the iron absorption site in the duodenum and upper jejunum.
- Reticulocyte count increases 3 to 4 days after the initiation of therapy [24].
- Haemoglobin concentration should rise by 2gms/dl after 3 to 4 weeks [25].
- To replenish the body iron stores, iron supplementation should be continued for at least 3 months after correction of anaemia [25].

Parentaraltherapy should be considered when there is intolerance to at least two oral preparations, non-compliance and severe iron malabsorption [26].

Preparations:
- Iron dextran - slow intravenous or intravenous infusion
- Iron sorbitol - deep intramuscular injection
- Anaphylactic shock is a potentially serious side effect, pre treatment test dose should be given [25].
- Inj. .methyl prednisolone 125mg intravenously before infusion should prevent delayed complications of total dose infusion [27].
- Parenteral forms are very expensive and the rise in Hb level is no faster than with oral iron.

Red cell transfusion:
The erythrocyte transfusion is justified in elderly if the [22, 28]
- anaemia is symptomatic
- unlikely to respond promptly with treatment
- symptomatic cardiovascular deterioration
- symptomatic functional deterioration
- pre operatively
- before chemotherapy
- end stage renal diseases

Erythropoietin stimulating agents:
It is approved for the treatment of anaemia of chronic diseases with limited value.
Preparations: epoetin - alfa, epoetin - beta, epoetin - omega.50- 100U /kg body weight, three times in a week, subcutaneously.

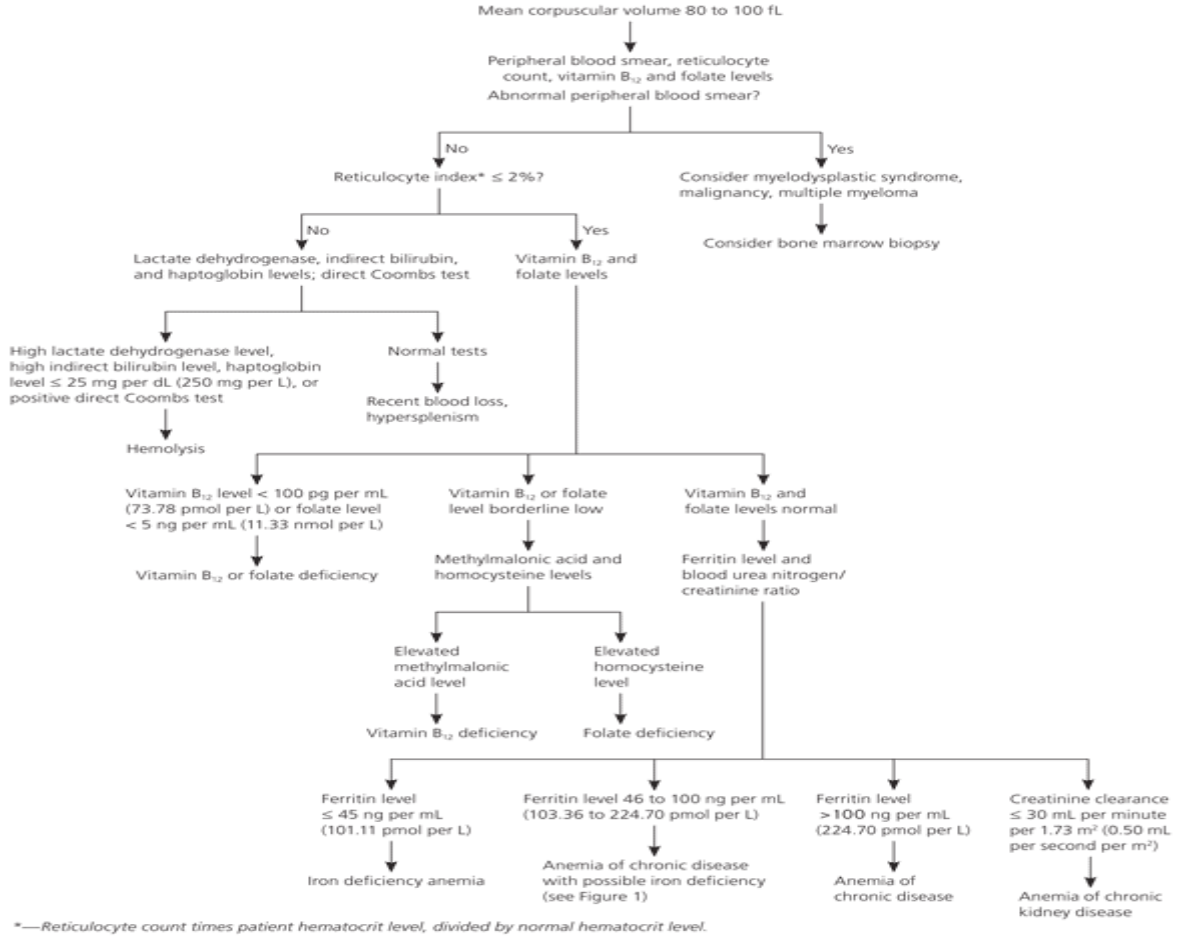
Treatment of Vit B 12 deficiency:
Treated by oral or parentaral therapy.

Parentaral therapy: Inj.methylcobalamine 1mg, intramuscularly,daily for one week, followed by weekly once for one month and monthly once thereafter.

Oral therapy: 1 to 2 mg daily has been shown to be as effective as parentaral preparations [29].

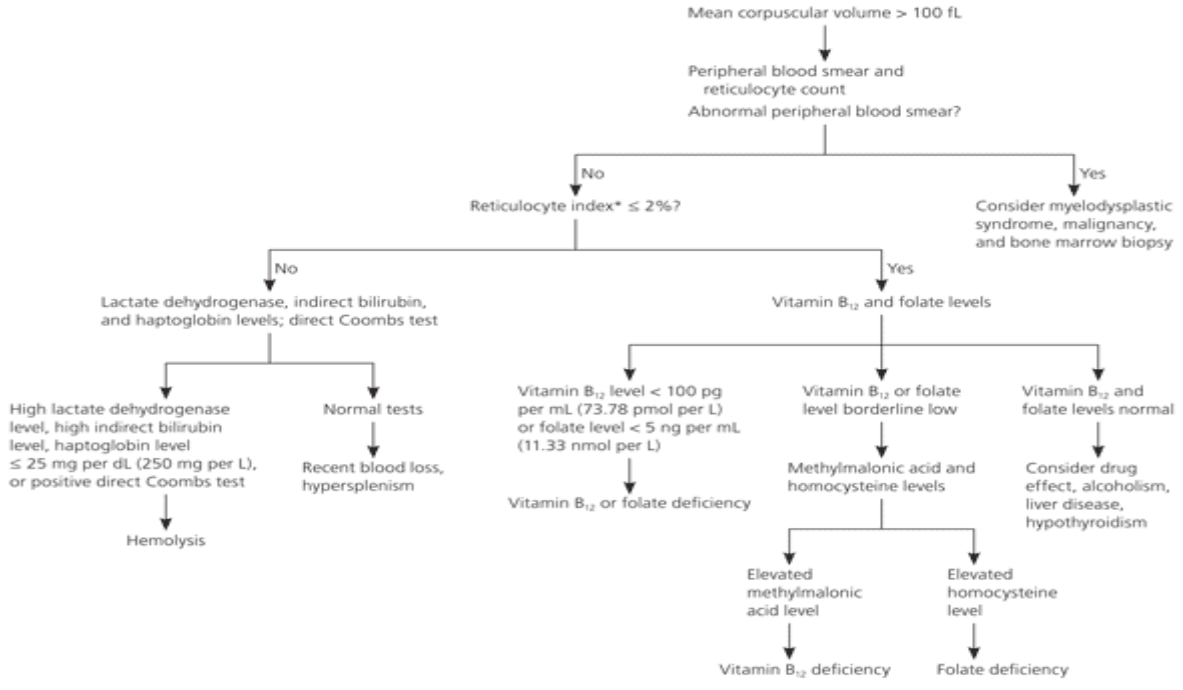
Treatment of folate deficiency:
Oral therapy: folic acid 1 mg daily.

Diagnosis of normocytic anemia [32]:



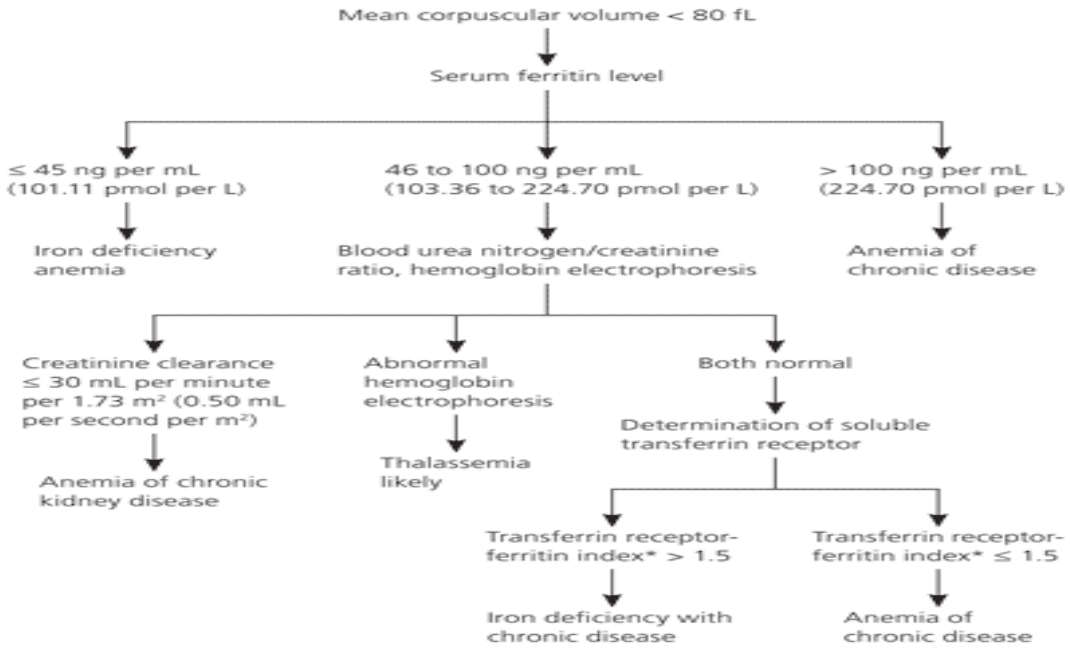
*—Reticulocyte count times patient hematocrit level, divided by normal hematocrit level.

Diagnosis of macrocytic anemia[32]:



*— Reticulocyte count times patient hematocrit level, divided by normal hematocrit level.

Diagnosis of microcytic anemia [32**]**



*—Transferrin receptor-ferritin index is calculated by dividing the soluble transferrin receptor level (mg per L) by the log of the ferritin level (ng per mL).

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