

# ANAEMIA

Naresh Gupta, M.D.

Professor of Medicine and Head, Clinical haematology

Maulana Azad Medical College, and associated Hospitals, New Delhi-2

Email: [doctornaresh@bol.net.in](mailto:doctornaresh@bol.net.in)

Presence of blood is vital for survival, which explains the presence of haemoglobin in the human erythrocytes (Red Blood Cell, RBC). Haemoglobin is a metallo-protein with complex quaternary structure. It facilitates gas exchange for the cellular respiration, without which body cells would be deprived of their requisite energy requirements. A decrease in body haemoglobin i.e. anaemia will affect all organs, the greatest impact being on the organs with critical energy requirements.

Haemoglobin constitutes about 1% of total body weight. *Anaemia is a state of decrease in quantity or quality of haemoglobin in the body.*

## AETIOPATHOGENESIS

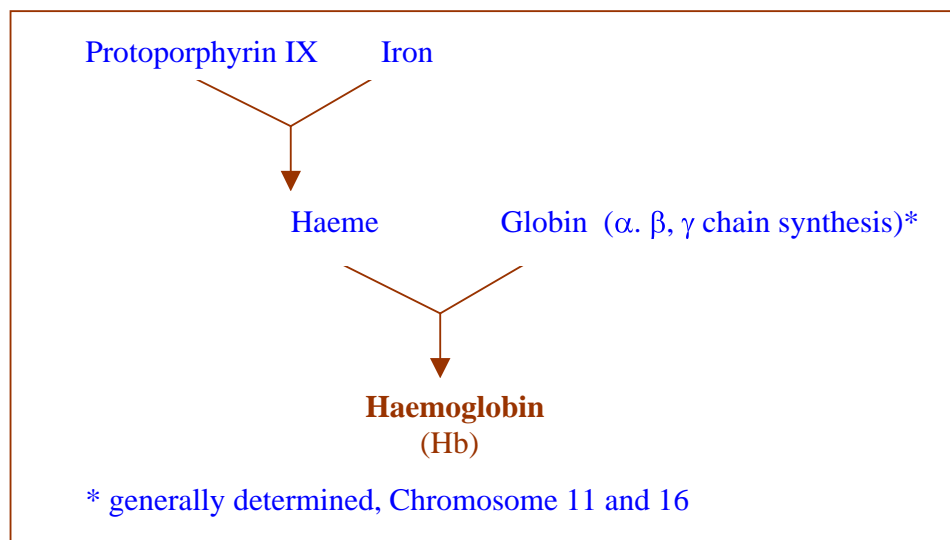
In order to thrive in blood, haemoglobin needs the protected environment of RBCs which have a limited life span of 100-120days. Hence the need for constant renewal.

Haemoglobin is synthesized within the nucleated red cells of bone-marrow. This bone marrow, incidentally, is also the source of all the other cellular components in blood. In adults, this function of erythropoiesis is restricted to the bones of axial skeleton and the flat bones. That is one of the determinants in choosing the site for diagnostic bone-marrow aspiration (BMA).

## HAEMOGLOBIN SYNTHESIS

Basic requirements for synthesis of adequate and appropriate Hb are:

1. Normal Globin synthesis (requires normal genes and their transcription)
2. Normal Porphyrin synthesis
3. Normal Iron metabolism



A deficiency at any of the levels of Hb synthesis may result in anaemia.

The synthetic pathways require the following vitamins as co-enzymes:

1. Folic acid
2. Vitamin B12 (cobalamins)
3. Pyridoxine

It is mandatory that the Hb thus synthesized be permanently cocooned within the shell of RBC for its full lifespan. The RBCs have their own structure and enzyme system. A defect in the production or survival of RBCs would also result in anaemia. Such defective RBCs are ineffective, not being able to carry on the assigned functions. Therefore they are removed from circulation by the macrophage-monocyte system of the body. **The end result is anaemia.**

Thus anaemia could be a result of:

1. RBC enzyme defects
2. RBC structure/ membrane defects, and
3. additionally, the Hb defects (as mentioned above)

### **CLINICAL**

Anaemia is a common problem in clinical practice, often unrecognized or overlooked. Its symptomatology is varied and depends upon, *inter alia*,

- i) Severity of anaemia
- ii) Speed of its development
- iii) Primary disease causing anaemia
- iv) Presence of other co-morbid conditions

*Always identify these four variables in any patient with anaemia.*

The following **symptomatology** should alert the clinician to look for anaemia. It is listed in order of increasing severity of anaemia

- Often asymptomatic in mild anaemia
- Weakness, fatigue, lethargy
- Tiredness, decreased stamina up, dizziness
- Light headedness especially on standing up, headache, loss of concentration
- Breathlessness on exertion, palpitation, manifestations of congestive heart failure
- Coma, and death

In addition, there may be symptoms attributable to the primary disease responsible the anaemia.

The following **Clinical Signs** are helpful in a patient with anaemia. These patients often have a compensatory tachycardia, with a bounding pulse from high-volume circulation.

- *Skin and Mucosa* for
  - presence of pallor,
  - colour of palmar ridges,
  - petechiae/ ecchymosis, or

- dermatitis.
- *Eyes and oral cavity* for presence of
  - pallor,
  - icterus,
  - glossitis,
  - stomatitis,
  - cheilosis,
  - retinal haemorrhage or papilloedema
- *Nails* for presence of
  - pallor,
  - platynychia,
  - koilonychia,
  - clubbing, or
  - any discoloration.
- *Neck* for presence of
  - lymphadenopathy,
  - thyroid enlargement, or
  - jugular vein engorgement
- *Legs* to look for
  - local hygiene,
  - bare footedness,
  - pitting oedema,
  - leg ulcers (in haemoglobinopathies), or
  - peripheral neuropathy
- *Chest* for presence of
  - sternal tenderness,
  - functional or organic cardiac murmurs, or
  - any cardio-respiratory decompensation
- *Per Abdomen* to look for
  - liver span,
  - splenomegaly,
  - renal or other intra-abdominal lumps, and
  - presence of free fluid (ascites)
- *Per rectal & Proctoscopy* examination for
  - haemorrhoids,
  - fissures-in-ano, or
  - suspicious malignancy (prostate/colon)
- *Per vaginal* examination in women with an abnormal bleeding

**Remember Hb is not the sole determinant of clinical manifestations of anaemia.**

### **CLINICAL APPROACH TO A PATIENT WITH ANAEMIA**

Anaemia is not a disease by itself but only a manifestation of disease. Hence, it is imperative to look for the underlying disease responsible for anaemia.

**KEY ISSUES** to decide in a patient with anaemia are:

1. Is it a **TRUE** anaemia?
2. Is the anaemia **HEREDIATARY** or **ACQUIRED**?
3. Is there any **ABNORMAL BLEEDING**?
4. Is there exposure to **DRUGS, CHEMICALS, or TOXINS**?
5. Is there a co-existing **SYSTEMIC DISEASE**?
6. What is the nature of **DIET and ETHNICITY**?

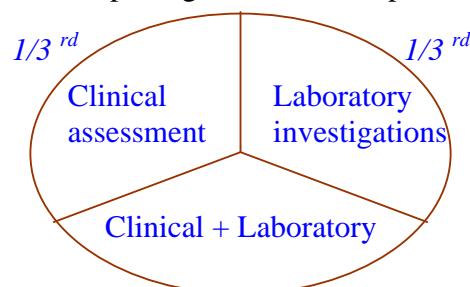
### **MAKING A DIAGNOSIS**

Ideally anaemia should be diagnosed when red cell mass (RBC mass) in the body decreases below the expected normal for a healthy population, which is a mean of 25ml/kg for women and 28ml/kg for men. However, measurement of RBC mass is difficult and not easily available. Hence a convenient and practical way to define anaemia is the measurement of *Hb concentration in blood*.

**Anaemia is said to be present when Hb concentration falls below 13gm/dl in men, or <12gm/dl in women. A lower threshold <11gm/dl defines presence of anaemia in small children.** This definition assumes a normal distribution of RBC mass and plasma volume. Problems may arise when this proportion is altered. For example, in normal pregnancy RBC mass increases by about 25% whereas the expansion in plasma volume is much greater, thereby bringing the *Hb concentration* down. And a Hb level of 11gm/dl may be a norm in pregnancy. One should be wary of such “**spurious anaemia**” or “**masked anaemia**” situations. These are physiological variations.

These days, electronic cell counters are widely available for estimating *Hb concentration*. These instruments automatically measure a lot many more parameters, apart from Hb concentration. Such parameters on RBC indices viz. the MCV, MCH, MCHC, RDW, RBC count, haematocrit and also the WBC and platelet counts are informative in patients with anaemia. Reticulocyte may be measured automatically, or manually.

Specific diagnosis in anaemia is a function of clinical assessment and laboratory investigations. The two must be put together for a comprehensive diagnosis.



## **INVESTIGATIONS IN A PATIENT WITH ANAEMIA**

1. Complete blood count is the single most important investigation in anaemia. It should include Hb, Hct, WBC, platelet count and RBC indices viz. RBC count, MCV, MCH, and RDW.
2. Peripheral blood smear examination, to look for abnormalities in RBC, WBC, and platelets
3. Reticulocyte count

The above triad comprises the primary investigations in anaemia and can be performed on a single EDTA blood sample.

Secondary investigations are guided by the results of the above tests in a given clinical context, and may include one or more from the following:

- Serum ferritin, vitamin B12, and RBC folate levels
- Hb electrophoresis and quantitation (Hb A2, Hb F etc)
- Blood biochemistry for hepatic and renal functions
- Bone-marrow aspiration
- Trepine biopsy from bone marrow
- Imaging studies may include X-ray chest/ skull/ other bones as warranted, ultrasound abdomen, radio-isotope studies
- RBC survival & kinetic studies (not available routinely)
- Other specialized tests include Coombs' test, osmotic fragility, Ham's test, erythropoietin level, immunocytochemistry, cytogenetics etc.

Another set of investigations may need be undertaken to unravel the primary causative disease. These would depend upon the clinical suspicion and the results of investigations as listed above.

Thus, a patient with diagnosis of **IRON DEFICIENCY ANAEMIA** (commonest type of anaemia in clinical practice) may warrant one or more of the following investigations:

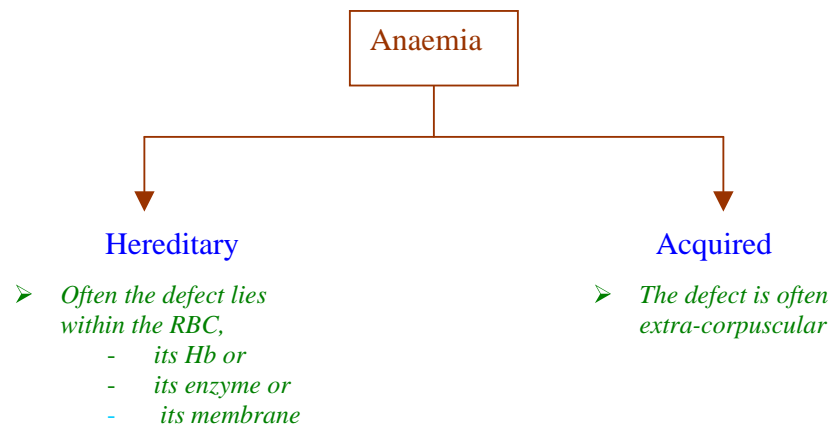
- Dietary history
- Stool for ova, cyst, and occult blood
- If stool shows occult blood positive, do GI endoscopy or Barium meal studies (Ba meal and Ba enema)
- Urine routine and for microscopic haematuria
- Gynaecological assessment in women
- X-ray chest PA
- ENT assessment
- Tests for a bleeding disorders (PR, APTT, BT etc)
- Tests of iron assimilation

Likewise, other types of anaemias may warrant a different set of investigations.

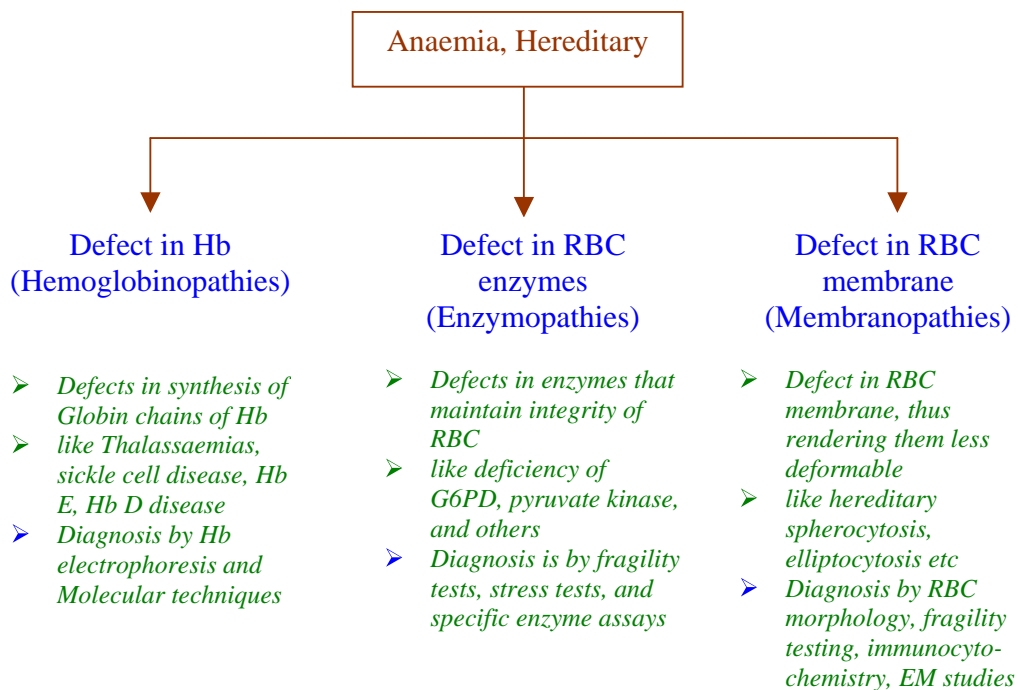
## **DIAGNOSTIC PARADIGMS IN ANAEMIA**

Diagnosis in a patient with anaemia can be approached from several angles. It is dictated by the available clinical and laboratory information. Accordingly, numerous

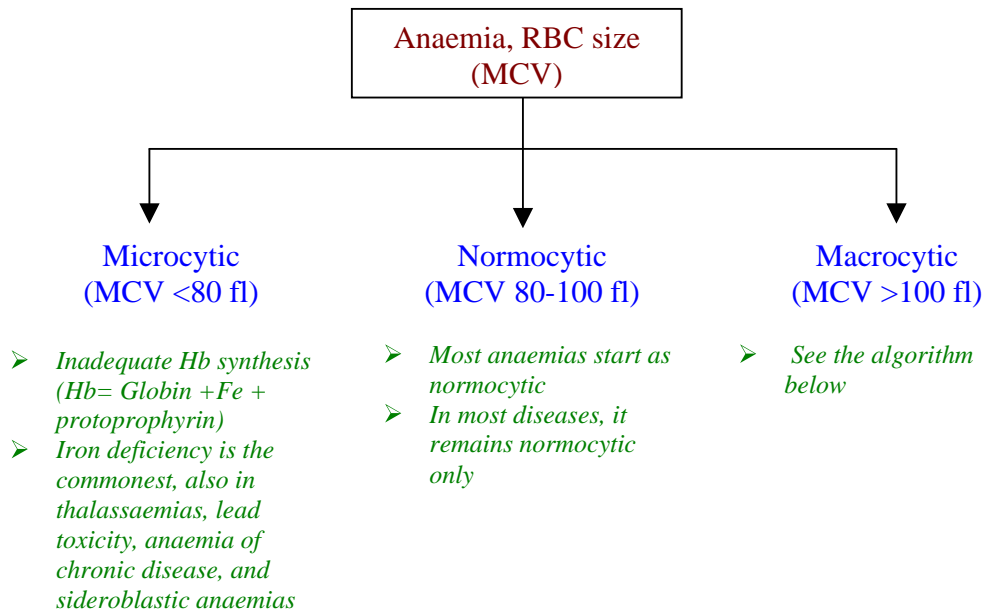
classifications exist for the diseases causing anaemia. The following SET OF ALGORITHMS is helpful in diagnosis of anaemia in a given patient.



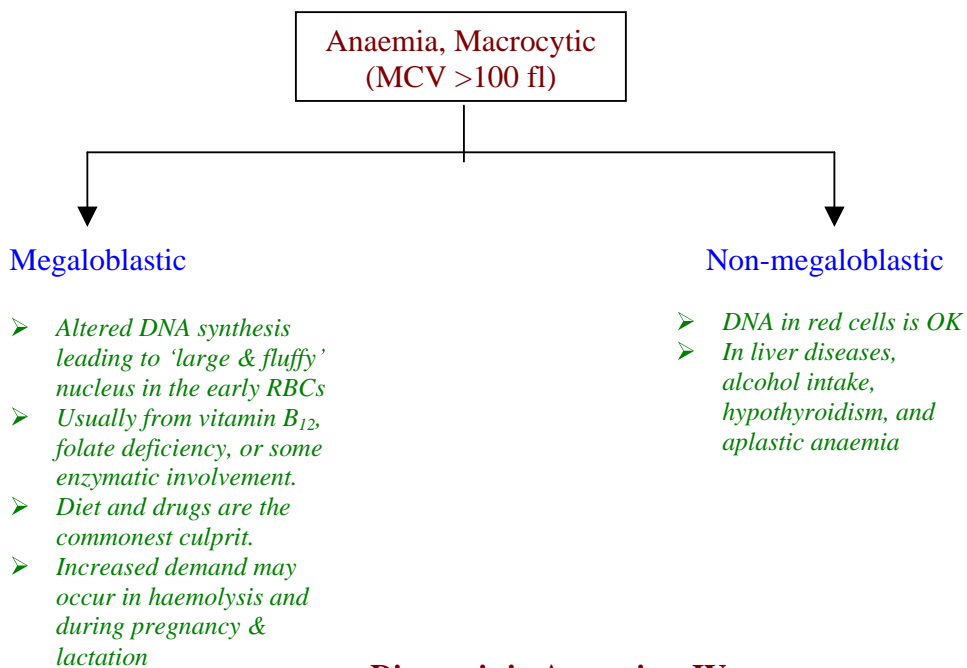
### Diagnosis in Anaemia – I



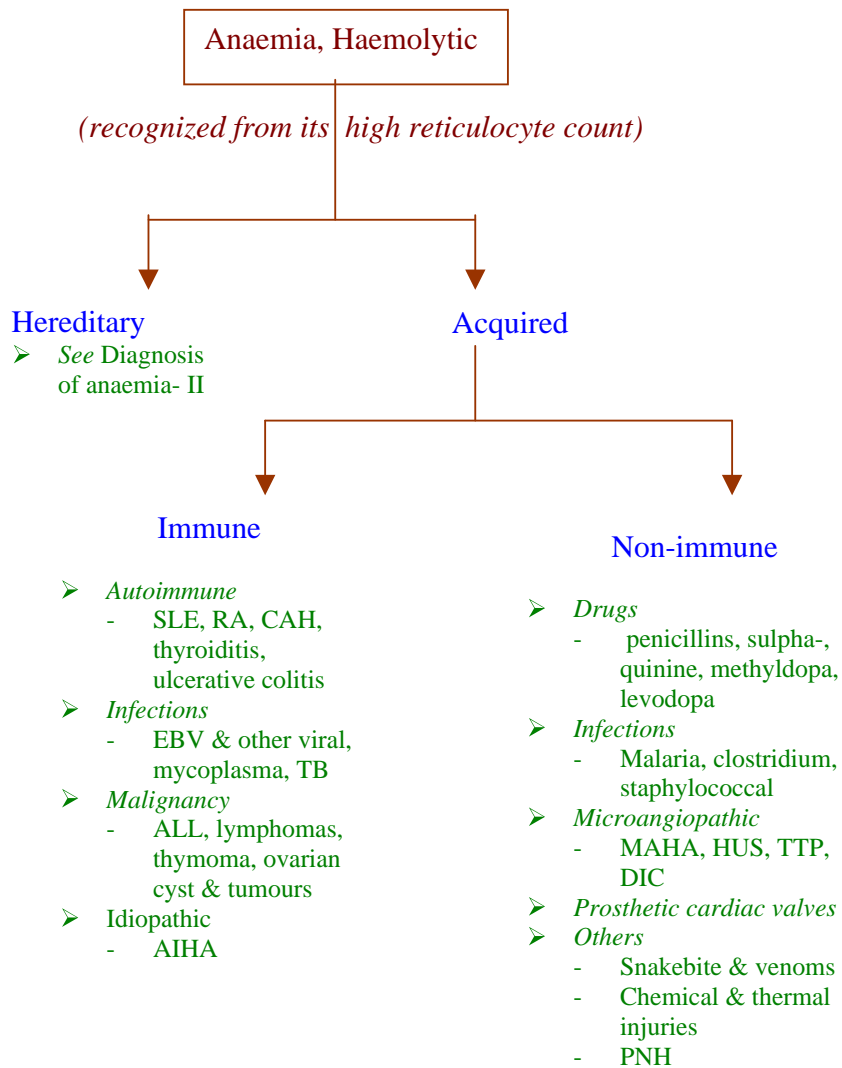
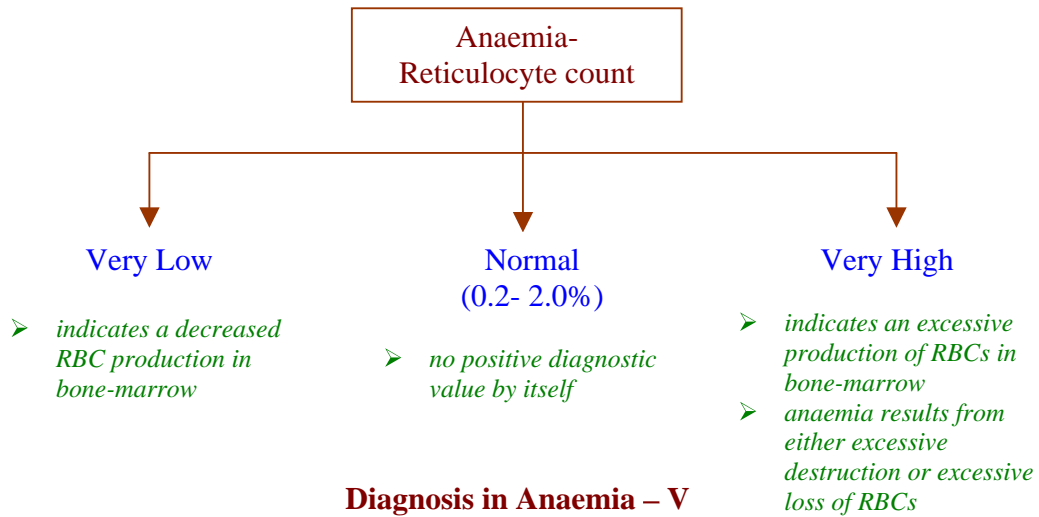
### Diagnosis in Anaemia – II



### Diagnosis in Anaemia – III



### Diagnosis in Anaemia – IV



## **LINE OF MANAGEMENT IN A PATIENT WITH ANAEMIA**

Detailed clinical history, examination, and appropriate laboratory investigations should give a fair idea on the complete diagnosis in a patient with unexplained anaemia. This will facilitate specific therapy in a given case. Other measures include giving supportive medical care. This is true especially in emergency situations when blood (red blood cell) transfusion may be needed.

### **Parameters indicating need for blood (red cell) transfusion in a patient with anaemia**

- a) Anaemia of acute onset
- b) Anaemia of high severity (Hb <6gm/dl or even 8gm/dl in presence of co-morbid conditions)
- c) Anaemia with cardio-respiratory decompensation
- d) Anaemia in presence of active bleeding
- e) Anaemia of a potentially progressive nature e.g. leukaemias, other malignancies
- f) Elective transfusions e.g. thalassaemias, or prior to surgery

### **Steps in emergency care of anaemia requiring transfusion**

- Start an IV line, and take out blood for blood grouping and cross matching  
Request for packed RBC for transfusion.  
Send for urgent CBC, reticulocyte count, blood smear, and blood biochemistry.
- Start O<sub>2</sub> by mask at 6-8L/minute
- Restrict physical activities of the patient
- Engage measures to stop out going active bleeding, if any
- If anaemia is from acute or active bleeding (Trauma or severe bleeding as haemoptysis, epistaxis, oromucosal bleed, haematuria, bleeding *per rectum*, bleeding *per vaginum*, or hereditary bleeding disorder etc.), start i.v. line with rapid normal saline infusion.
- Rate of infusion is governed by HR, IBP, IVP, urine output, and cardiac condition
- Switch over to colloid volume expanders as soon as possible (until blood is available).
- Whole blood is not transfused these days.
- Transfuse packed RBC only for anaemia
- Each unit of RBC is transfused promptly within 2-3 hours
- Monitor and watch out for transfusion-reactions during period of transfusion
- Number of units to be transfused is determined from clinical assessment and the response to transfusion
- Expect a rise of 1gm/dl in Hb concentration from a single unit of transfusion of packed RBC

**Unnecessary transfusion must be avoided.** Also, apart from transfusion reactions, blood is a source of infection, volume overload, and iron overloaded

This management for stabilization of patient takes precedence over a detailed assessment (*vide supra*) of the anaemia and of any other co-morbid medical conditions.

**Specific management would start as soon as the primary disease gets diagnosed.**

Thus in a patient having anaemia from **IRON DEFICIENCY**, give

- a. Oral iron (ferrous sulphate) as tablets, equivalent to 200mg elemental iron per day (Tab *Fersolate* 1 tab TDS)
- b. Avoid sustained release or 'fancy' or expensive preparation of iron
- c. Ascorbic acid enhances iron absorption
- d. Avoid giving antacids concomitantly
- e. Oral iron is administered for at least 3 months beyond normalization of Hb so as to replenish body stores
- f. Parenteral iron may be given if oral iron is not tolerated or oral iron therapy is ineffective
  - Total Dose Iron / (T.D.I) in mg  
= (15- Hb of patient) x body weight in kg x 3
  - This can be given as a slow intravenous infusion over 8-10 hours
  - Iron dextran or iron gluconate or hydroxide sucrose comp. preparations are available (*Imferon, Venofer*)
  - Iron sorbitol (*Jectofer*) is for intramuscular route only
  - Intramuscular route is painful and causes local discolorations. It is not a preferred route.
  - If must, intramuscular injections must be administered deep
- g. Anthelmintics may be used for concomitantly for de-worming (hook worm is a common cause of iron deficiency anaemia)
- h. Primary disease is to be managed appropriately to prevent recurrence of bleeding, iron deficiency, or anaemia.

**Specific treatment in MEGALOBLASTIC ANEMIA**

Megaloblastic anaemia is common amongst vegetarians because vegetarian diet lacks in vitamin B<sub>12</sub>. Foliates are water-soluble vitamins with limited body stores, and sensitive to destruction during cooking or processing of food. An absorptive defect of either is seen in medical or surgical diseases. Blood levels identify the deficient vitamin.

If vitamin B<sub>12</sub> deficiency is the cause of megaloblastic anaemia, give

- Oral Vitamin B<sub>12</sub> if absorption is not a problem.
- Else vitamin B<sub>12</sub> is administered by intramuscular route.
- Initial dose
  - 1,000 µg daily x 7 doses
  - 1,000 µg twice weekly x 7 doses
  - 1,000 µg weekly x 7 doses
  - 1,000 µg every month thereafter
- Oral dose is administered daily in a dose of 100 – 1000 µg. (Normal requirement is 1 µg daily)
- A lifelong supplementation is mandatory in presence of defects of absorption or assimilation, and is advisable for vegans.

If folic acid deficiency alone is responsible for megaloblastic anaemia, give

- Oral folic acid as tablet, 1 mg daily.
- Folic acid is a water-soluble vitamin
- Folic acid needs to be administered as long as the causative pathology persists.

### **Specific treatment in anaemia of CHRONIC RENAL FAILURE**

- Appropriate management of chronic renal failure, CRF, including renal replacement therapy,
- and complications of CRF
- Treatment of any associated infections
- Treatment of any associated deficiency states
- Treatment of any associated bleeding diathesis
- In absence of adequate response, recombined erythropoietin, **rhEPO** is very beneficial in anaemia of CRF. It is administered subcutaneously, 2000i.u. x 2-3 times in a week. Expect a rise in Hb, while watching for any rise in BP or fall in body iron. The latter mandates iron supplementation.

### **Specific treatment in THALASSAEMIAS/ Haemoglobinopathies**

For thalassaemias and other 'Transfusion Dependent' hereditary haemoglobinopathies,

- Regular packed RBC transfusion (generally 2 units to an adult) is needed every 2-3 weeks.
- Such regular transfusion is a source of iron overload. Hence, concomitant iron-chelation therapy (e.g. with *Desferal*) is required.
- Folate supplementation is helpful in preventing anaemia.
- Therapeutic splenectomy is beneficial in selected cases.
- Curative gene transplant therapy is now possible for these genetic disorders.
- Genetic counselling

### **Specific treatment in anaemia of CHRONIC SYSTEMIC DISEASE**

- Management of primary disease and its complications
- Supportive care (RBC transfusion etc.) may be undertaken wherever warranted.

### **Specific treatment in anaemia secondary of CHRONIC BLEEDING DISORDERS**

(hereditary or acquired)

- Can of primary disease to stop and prevent any further bleed.
- Treatment of secondary deficiency of iron, folic acid and at times vitaminB<sub>12</sub> using appropriate supplements.
- For management of anaemia secondary to acute bleed, see above.

### **Specific treatment in anaemia secondary to LEUKAEMIA & HAEMATOLOGICAL MALIGNANCES**

- Full supportive care including blood transfusions
- Supplements for the expected deficiency states
- Immunosuppressive agents if anaemia is immuno-haemolytic

- Treatment of the primary disease
- All efforts to be made to keep the patient free of nagging symptoms.

### **Specific treatment in IMMUNE HAEMOLYTIC ANAEMIA**

- Blood transfusions are tricky in these situations. The antibodies against RBCs may destroy the transfused RBCs.
- Mainstay of treatment is use of immunosuppressive agents.
- Vitamin supplements are essential owing to increased requirements.

### **PROGNOSIS**

Prognosis in a patient with anaemia is a function of the underlying primary disease. Thus in anaemias secondary to malaria, acute infections, iron or folate/ vitamin B<sub>12</sub> deficiency may show 100% response to treatment and may never occurs again (unless the primary disease reoccurs). On the other hand, haemoglobinopathies and other hereditary haemolytic anaemia require life-long blood transfusion and other supportive care. Potential cure may be possible with bone-marrow or stem-cell transplantation. Leukaemia and other haematological malignancies have greatly improved treatment, with potential long-term cures. Anaemia of chronic disease lingers on *pari pasu* with primary causative disease. Anaemia of CRF responds beautifully to recombinant erythropoietin therapy. Anaemias secondary to bleeding disorders can be generally controlled, but prognosis varies depending on the aetiology.

### **WHEN TO REFER A PATIENT WITH ANAEMIA to a specialist?**

#### **The following clinical situations warrant a specialist referral:**

- i) Anaemia requiring transfusion
- ii) Acute or active bleeding resulting in anaemia
- iii) Moderate to severe anaemia in a child or elderly or a pregnant lady.
- iv) Anaemia showing no response or inadequate response to transfusions.
- v) Anaemia showing no response or poor response to medical treatment.
- vi) A chronic or recurrent anaemia.
- vii) Anaemia of chronic renal failure
- viii) Recurrent or long standing bleeding disorders
- ix) Anaemia of systemic disease, if disproportionate to disease or of moderate-severe degree
- x) Anaemia secondary to bleeding disorders, leukaemia or haematological malignancies.
- xi) Where the underlying causative disease is likely to result in progressive or persistent anaemia
- xii) Anaemia where the underlying causative disease is undiagnosed or not clear.
- xiii) Where surgery or other intervention procedure is contemplated.
- xiv) When there are co-existent abnormalities of platelet or leukocyte.
- xv) When you are uncertain of your diagnosis or treatment.

## SUMMARY

- Anaemia is not a disease *sou moto*. It is only a clinical manifestation of an underlying disease.
- Hb level alone does not determine the clinical manifestations of anaemia.
- Clinical and laboratory assessment of anaemia leads to correct diagnosis of primary disease.
- Clinical assessment should revolve around the SIX KEY ISSUES (*vide supra*)
- Assessment should include
  - an accurate & complete diagnosis
  - understanding the elements of this diagnosis
  - understanding response of patient's body to this diagnosis.
- Know
  - whether to treat?
  - when to treat?
  - how to treat?
  - when to refer?
- Treatment of primary disease is single most important determinant of the ultimate prognosis in a patient with anaemia.
- In anaemias, a right treatment may bring patient back to life whereas an inappropriate or delayed treatment may take life away.

\*\*\*\*\*

This article is a copyright. Correspondence to:  
Naresh Gupta, M.D.  
Professor of Medicine and Head, Clinical haematology  
Maulana Azad Medical College, and associated Hospitals, New Delhi-110002, India  
[Email: doctornaresh@bol.net.in](mailto:doctornaresh@bol.net.in)

This document was created with Win2PDF available at <http://www.win2pdf.com>.  
The unregistered version of Win2PDF is for evaluation or non-commercial use only.