

ANEMIA IN PREGNANCY

EPIDEMIOLOGY

- WHO has classified the world into different zones according to prevalence of anemia:

High Prevalence - >40%

Medium - 15-39%

Low - 5-14.9%

Not a problem - <5%

- Sub Saharan Africa and South East Asia come in high prevalence area
- Globally, incidence is about 30 %
- In developing countries & India, it is around 40 – 90%, compared to 10 – 20 % in developed countries.

DEFINITION

- WHO defines anemia in pregnant women as hemoglobin below 11gm/dl and a hematocrit of less than 33%.
- Centre for Disease Control (CDC) defines : Anemia as Hb conc. < 11gm % in 1st and 3rd trimesters and < 10.5 gm% in 2nd trimester.
- Degree of anemia is graded acc. to ICMR :

Mild	10-10.9
Moderate	7.0-9.9gm/dl
Severe	4- 6.9 gm/dl
Very severe	<4gm/dl

CAUSE OF ANAEMIA

- Low bio-availability of iron in food
- Inadequate intake of iron rich foods
- Inadequate intake of folate.
- Inadequate intake of Vitamin B12.
- Excess consumption of coffee/tea
- Chronic infections like malaria, TB
- Worm infestation
- Menstrual loss of blood

CLASSIFICATION

- Physiological anemia
- Pathological anemia

➤ Compulsory Hb estimation :

- by Cyanmeth-haemoglobin method by using Semi-autoanalyser or photo calorimeter.
- at 14-16 weeks, 20-24 weeks, 26-30 weeks and 30-34 weeks of pregnancy in all pregnant women.
- minimum of 4 Hb estimation ; minimum 4 weeks apart.

➤ Deworming at 14-16th week of gestation (Second Trimester) in all pregnant women – single dose 400 mg of tab. Albendazole.

(WHO recommends deworming with mebendazole(100mg twice daily for three days)or albendazole(400 mg stat) in 2nd or 3rd trimester of pregnancy as the prevalence of iron deficiency anemia due to hookworm infestation is high in high prevalent countries.)

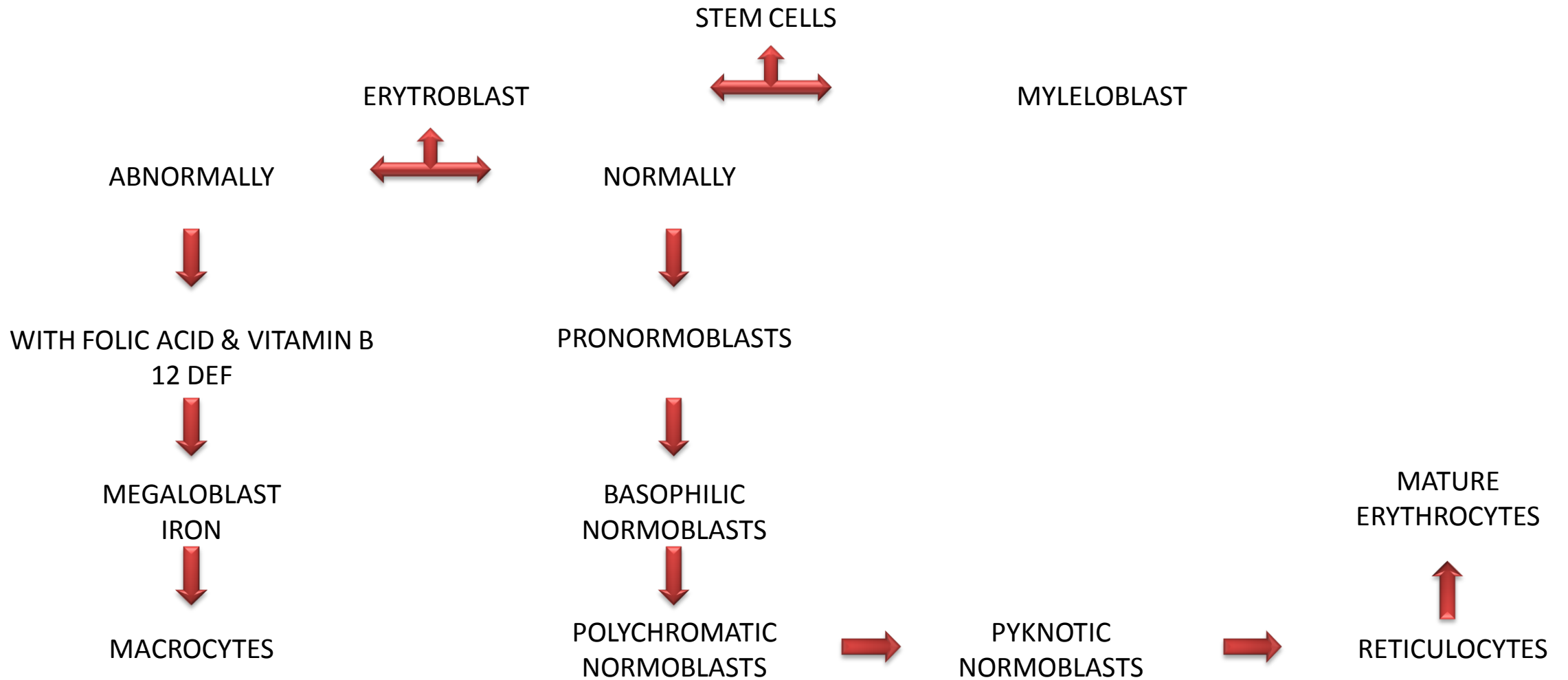
PHYSIOLOGICAL ANEMIA

- Pregnancy causes a state of plethora . The RBC mass increases by 30%,whereas plasma volume increases by 40 to50%, resulting in erythrocyte dilution by 5 to 15% and decrease in hemoglobin concentration by approximately 2g/dl.
- The picture on peripheral smear remain normocytic and normochromic.
- The decrease in blood viscosity facilitate better blood flow through placenta .
- The increased blood volume also offers a protective benefit against blood loss in the third stage of labor.

PATHOLOGICAL ANEMIA

- Deficiency anemia :
 - Iron deficiency (60%)
 - Macrocytic anemia(10%)- Folic A., Vitamin B12 deficiency
 - Dimorphic anemia (30%) – both
 - Protein deficiency – in extreme malnutrition
- Haemorrhagic anemia :
 - Acute – blood loss
 - Chronic - hookworms ,bleeding piles
- Hemoglobinopathies : Thalassemia, Sickle cell anemia
- Aplastic anemia
- Anemia of infection
- Chronic diseases (renal,hepatic,diabetes,thyroid) or neoplasm

LEVEL OF HAEMOPOIESIS AT WHICH VARIOUS DIETARY FACTORS OPERATE



EFFECT OF ANEMIA ON THE MOTHER

➤ Antepartum complications

- Abortions
- Intercurrent infection
- Preeclampsia
- APH
- Preterm labour
- Cardiac failure

➤ Intrapartum

- Uterine inertia
- Dysfunctional labour patterns
- Increased risk of instrumental deliveries
- Fetal distress
- Cardiac failure
- Shock

➤ Postpartum

- Puerperal sepsis
- Subinvolution of uterus
- Failing lactation
- Puerperal venous thrombosis
- Pulmonary embolism
- Cardiac failure
- Delayed wound healing

EFFECTS ON FETUS

- IUGR
- Prematurity
- Increased risk of Iron deficiency Anemia in early infancy
- Congenital malformation
- Still birth
- Intra uterine deaths (severe maternal anoxemia)
- Increased neonatal death / perinatal mortality

SYMPTOMS OF ANEMIA

- Lack of concentration
- Infection
- Palpitation
- Dizziness
- Light headedness
- Irritability
- PICA
- Fatigue
- Weakness
- Dyspnoea on exertion

SIGNS

- Pallor of mucus membrane or nail bed
- Glossitis and Stomatitis
- Platynychia or Koilonychia
- Tachycardia , tachypnea
- Ejection systolic murmur
- Ankle Edema
- Increased juglar venous pressure
- Postural hypotension

WORK UP OF PREGNANCY WITH ANEMIA

➤ Detailed history – age, race, parity, dietary habits, h/o passing worms in stools, h/o bleeding PR, hematuria, hyperemesis, malabsorption, chronic diseases like TB, malaria, bleeding disorders etc. h/o of drug intake, repeated blood transfusions.

➤ Examination

➤ Pallor of mucus membrane and nail bed.

➤ Glossitis , cheilitis

➤ Splenomegaly – hemolytic anemia

➤ Jaundice – hemolytic anemia

➤ Purpura – bleeding disorder

➤ Leg ulcers – sickle cell anemia

➤ Neurological deficit – megaloblastic anemia

➤ Anasarca & signs of cardiac failure in severe cases

APPROACH TO A CASE OF ANEMIA

- Universal screening for iron deficiency anemia with hemoglobin is recommended for all pregnant patients at first antenatal visit.
- With a presumptive diagnosis of iron deficiency anemia , a trial of oral iron for two weeks is recommended in patients with mild to moderate anemia. Further investigations are warranted if patients do not respond to the trial of oral iron(rise in Hb in 2 weeks)
- An empirical trial of oral iron for 2 weeks is advised up to 30-32 weeks of gestation in patients with mild to moderate anemia before considering other tests.

INVESTIGATIONS

- Severity of anemia – Hb & Hematocrit
- Type of anemia – PBF, red cell indices
- Bone marrow activity – reticulocyte count (N – 0.2-2%)

RED CELL INDICES

- RBC count – N (4-4.5 million/cumm)
- PCV / Hematocrit - (N 32-37%)
- MCV (PCV / RBC count) – average volume of a red blood cell(82-96 fl)
- MCH (Hb / RBC count) - average mass of Hb in picogm(27-33 pg)
- MCHC – (Hb / PCV) - avrage concentration of Hb in a given volume of packed RBCs(33-37%)

Classification of anemia according to

MCV

MICROCYTIC(<80)

Sideroblastic anemia

Iron deficiency anemia

Anemia of Chronic Ds

Thalassemia

MACROCYTIC(>100)

Megaloblastic anemia

Liver disease

Hypothyroidism

Cytotoxic drugs

NORMOCYTIC (80-100)

HIGH RETICULOCYTE COUNT

Sickle cell anemia

Hereditary spherocytosis

Autoimmune hemolytic anemia

PNH

Acute blood loss

LOW RETICULOCYTE COUNT

Aplastic anemia

Renal failure

Myelofibrosis

PBF

- Normal smear – normocytic (normal size RBC), normochromic (normal colour RBC)
- Iron deficiency – microcytic (small RBC), hypochromic (pale RBC), anisocytosis (variation in size), poikilocytosis (variation in shape), with or without target cells
- Malarial parasites can be seen
- Aplastic anemia shows low/no counts
- Sickle cells can be demonstrated.
- Triad of oval macrocytes, howel jolly bodies and hypersegmented neutrophils seen in megaloblastic anemia
- Abnormal blast cells
- Target cells in thalassemia

IRON INDICES

- **Serum ferritin** – abnormal if $< 20\text{ng/ml}$ (N 40-160 ng/dl), assess iron stores
- **Serum iron** – N 65-165mcg/dl
- **Serum iron binding capacity** – It reflects the availability of iron binding sites. Normal - 300-360 mcg/dl, increases with severity of anaemia
- **Percentage saturation of transferrin** – ratio of S.Fe/TIBC.35-50%, decreases to less than 20% in Fe def anaemia
- **RBC protoporphyrin** – 30mcg/dl, it doubles or triples in Fe def anaemia (substrate to bind with Fe, can not be converted into Hb in Fe def)
- **Soluble transferrin receptor** - it is the only measurement to accurately reflect the iron deficit between the point of storage iron depletion and development of anemia. It precedes reduction in MCV or rise in EFP.

OTHER INVESTIGATIONS

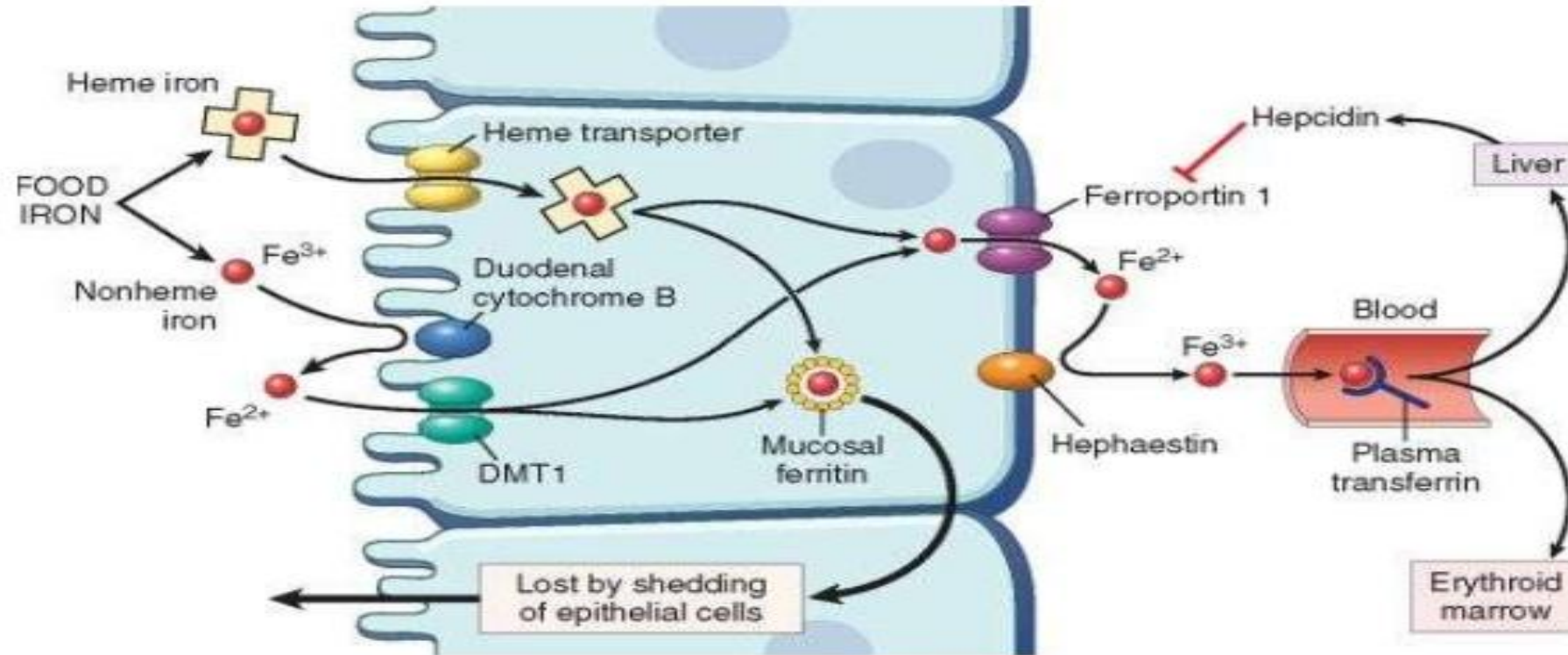
- BUN/ Serum creatinine – renal disease
- LFT- Hepatic disease.
- Urine examination – RBC, casts
- Stool examination – occult blood, ova
- Bone marrow examination – refractory anemia
- X-ray chest – pulmonary TB
- USG Whole abdomen

IRON DEFICIENCY ANEMIA

IRON REQUIREMENT IN PREGNANCY

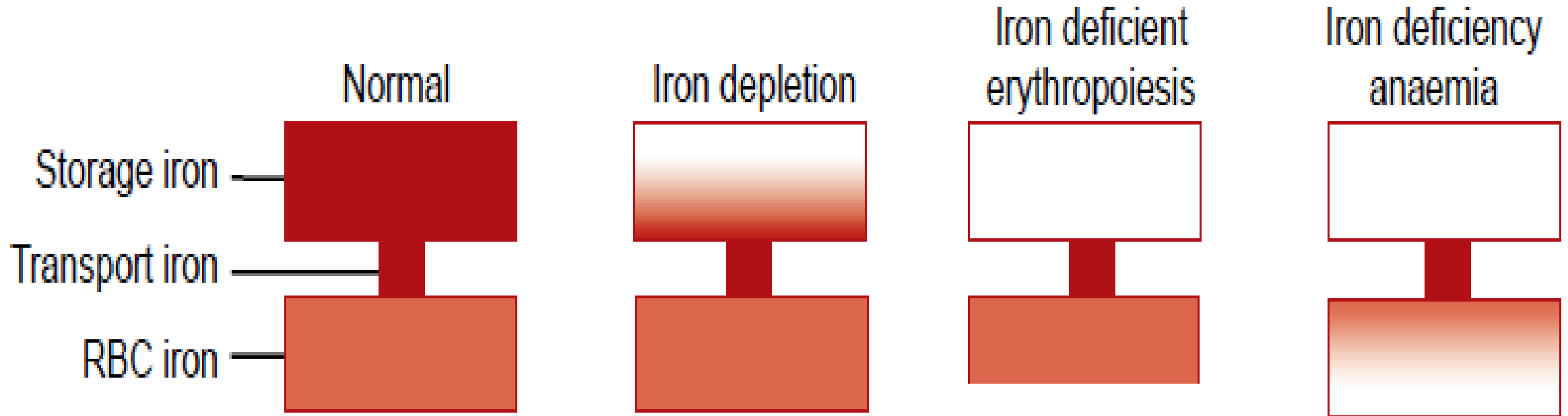
- Total iron demand in pregnancy – 900mg (700-1400 mg)
 - uterus (fetus + placenta) – + 500 - 600 mg
 - blood loss during delivery – + 150 – 200 mg
 - lactation - + 150 – 200 mg
 - Basal loss – 200 mg
 - increase in Hb mass - + 500 mg
 - 225 mg of iron is saved as a result of amenorrhoea of 9 months
- Average requirement is 4-6mg/day.
 - 2.5 mg/day in early pregnancy
 - 5.5 mg/day from 20-32 weeks
 - 6-8 mg/day from 32 weeks onwards

PHYSIOLOGY OF IRON ABSORPTION



DUODENAL EPITHELIAL CELL UPTAKE OF HEME AND NONHEME IRON.

Stages of Iron Deficiency



Causes of iron def. anemia in pregnancy

- Increased demand~1000 mg
(growing fetus + placenta + blood loss during labor)
- Decreased intake:
 - Faulty eating habits
 - Loss of appetite
 - Vomiting
- Disturbed metabolism-low erythropoiesis
- Pre pregnancy iron status/ Anemia
- Repeated pregnancies
- Hookworm infestations.
- Bleeding piles

Diagnosis



- TIBC raised
- RBC Protoporphyrin increased
- S.Transferrin receptors- increased



- Serum Iron
- % saturation < 16%
- S.Ferritin low

Differential diagnosis of Microcytic Hypochromic anemia

Test	Iron Deficiency	Chronic disease	Thalassaemia	Sideroblastic
Hb	Dec	N / Dec	Dec	
Ferritin	Dec	N / Inc	N / Inc	N / Inc
Se Iron	Dec	N / Dec	N / Inc	N / Inc
TIBC	Inc	Dec slight	N	N
TS	Dec	N / Dec	N / Inc	N / Inc
MCV	Dec	N / Dec	Dec	N
Reticulocytes	Dec	N / Dec	Inc	

Differential diagnosis of Microcytic Hypochromic anemia

Test	Iron Deficiency	Chronic disease	Thalassaemia	Sideroblastic
Hb Electrophoresis	Normal	Normal	High HbA2, Hb F	Normal
RDW	High	N	N	N
STfR	High	N / low	N	N / High
FEP	High	N / High	N / high	High

Mentzer index is an index used to differentiate IDA from thalessemias.

Formula is MCV/RBC count

Value for IDA >13

Value for thalessemia <13

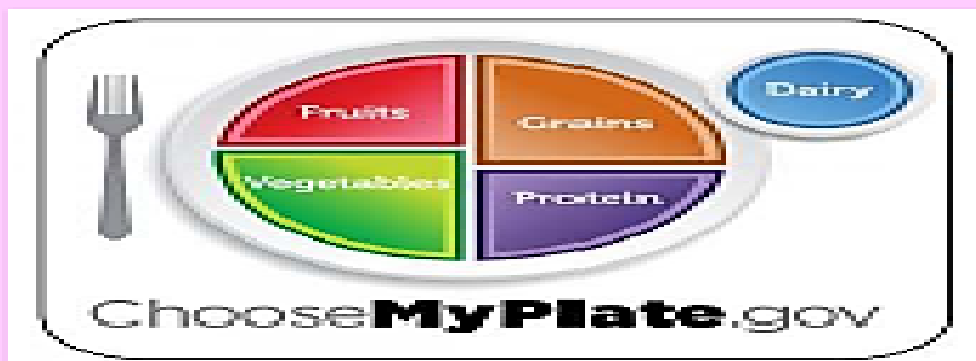
PROPHYLAXIS AND TREATMENT

IRON IN INDIAN DIET ?

- No matter in which form iron is being taken –only 10% of it is absorbed.
- Typical vegetarian Indian diets contain **large quantities of inhibitors**
- Indians obtain **non-heme iron** from cereals, pulses, vegetables & fruits
- Indian diet is plagued by **low iron content & poor absorption**
- Impossible for Indian population to meet iron requirement by normal diet (does not provide >10-15 mg iron per day)
- **National Nutrition Monitoring Bureau (NNMB)** survey shows that **intake of dietary iron is grossly inadequate** in most of the states in India, meeting **less than 50% of RDA**
- Therefore, **iron supplementation during pregnancy is recommended** universally even in non-anemic women

Principles

Create Healthful Prenatal Meals with the Daily Food Guide.



Eat at Least Three Meals Each Day.



Avoid foods that may be harmful during pregnancy

Suggestions

Food Group	Minimum # Servings
bread, cereals, rice, pasta	7+
serving = 1 slice bread, ½ cup rice or noodles	

vegetables	3-5
serving = 1 cup raw, ½ cup cooked	

fruits	2-4
serving = 1 med	

milk, yogurt, cheese	3
serving = 8 oz milk/ yogurt, 1 ½ oz cheese	

meat, poultry, fish, eggs, beans, nuts or nut butters	3
serving = 2 oz meat, 1 cup beans, 2 eggs, or 2 Tbsp peanut butter	

Try not to skip meals. Too many hours without food can affect your unborn baby.

Be sure to have breakfast.

Rely on foods rather than vitamin supplements for good nutrition. Vitamin pills cannot replace the nutrition in good food.

Fish to avoid: (mercury)
shark swordfish albacore tuna
mackerel tilefish

IRON RICH FOODS

➤ **Meat & Eggs**

- Ham, chicken, beef, pork, Liver, eggs

➤ **Sea Food**

- Oysters, Tuna, sardines, shrimps

➤ **Bread & Cereals**

- Whole wheat bread, wheat products, corn meal, oats, rye bread, brown rice, Lobia, soybeans

➤ **Fruits**

- Strawberries, figs, watermelon, dried apricots, dried peaches, raisins, dates













➤ **Beans & other foods**

- Beans, tomato products, Molasses, Dark chocolate

➤ **Vegetables**

- Potatoes, spinach, sweet potatoes, peas, broccoli

Common Iron Rich Foods

<p>Chickpea <i>Chana Sag</i></p>		<p>Spinach <i>Palak</i></p>	
<p>Amaranth <i>Kantewali Chaulai</i></p>		<p>Onion Stalks <i>Pyaz ki kali</i></p>	
<p>Mustard Leaves <i>Sarson ka sag</i></p>		<p>Fenugreek Leaves <i>Methi</i></p>	
<p>Mint <i>Pudina</i></p>		<p>Colocasia leaves <i>Arvi Ka Sag</i></p>	
<p>Lentil <i>Dal</i></p>		<p>Bengal Gram, Whole <i>Kala chana</i></p>	
<p>Soyabean</p>		<p>Gingelly Seeds <i>Til</i></p>	

Red Gram Dhal
Arhar



Plantain Green
Kuchcha Kela



Black Gram, Dhal
Urad Dal or Kaskalay



Water Melon
Tarbooz



Pumpkin
Seethaphal



Mutton
Gosht



Common Vitamin C Rich Foods

Cabbage
Patta Gobhi



Drumstick Leaves
Saijan Patta



Coriander Leaves
Dhaniya



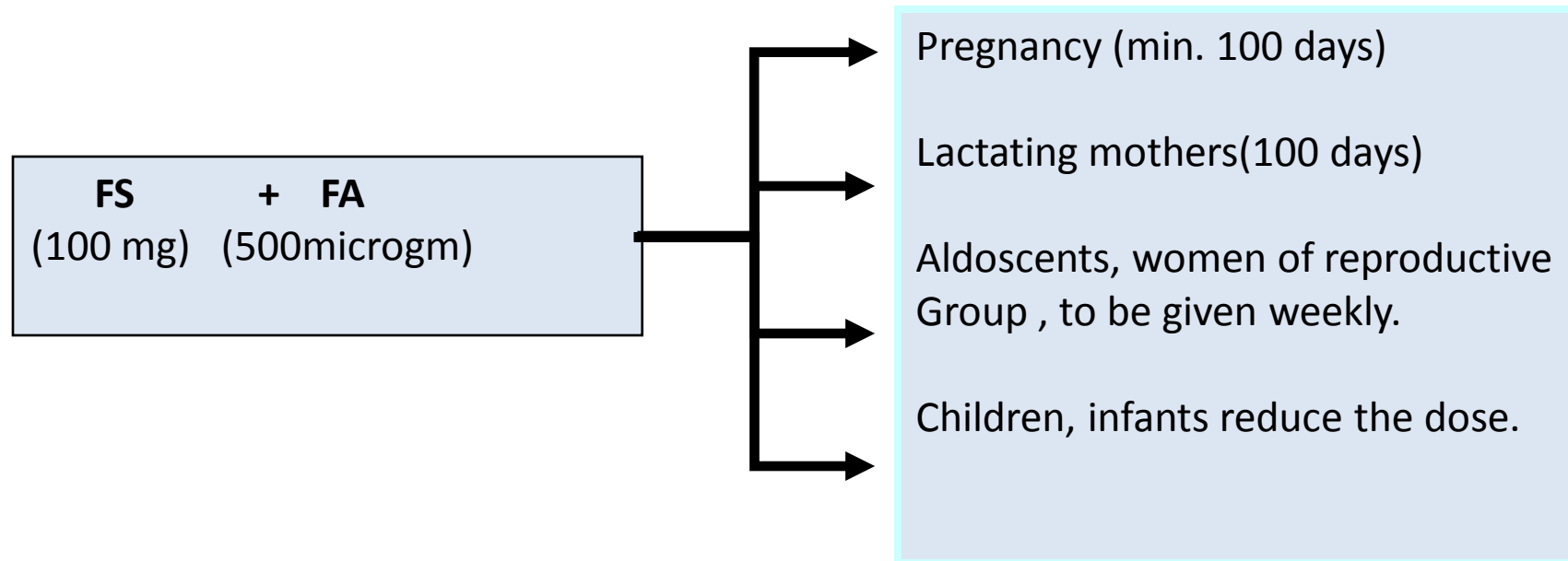
Gooseberry
Amla



IMPAIRED IRON ABSORPTION

- Tea and coffee
- Calcium, found in dairy products such as milk
- Antacids (medication to help relieve indigestion)
- Proton pump inhibitors (PPIs), which affect the production of acid in your stomach
- Some wholegrain cereals contained phytic acid

NATIONAL NUTRITION ANEMIA PROPHYLAXIS PROGRAMME (NNAPP 1971 - 72)



For T/t of anemia, double dose is given f/b 3-6 m post partum

WHO RECOMMENDATION FOR PROPHYLAXIS OF ANEMIA

- Based on the prevalence of anemia.
- 60mg of elemental iron + 400 microgm of folic acid/day
- Recommended for 6 months where the prevalence is <40%.
- This dose is to be supplemented for another 3 months if prevalence is >40%.

**RECOMMENDATIONS-
MANAGEMENT OF IDA IN
PREGNANCY AND POSTPARTUM**

- Awareness and health education strategies should continue with a greater momentum to encourage antenatal mothers to consume iron – rich foods and diets that enhance iron absorption.
- Daily iron supplementation(60-100mg) of iron and folic acid(500mcg)for all non-anemic pregnant women at first antenatal visit is recommended for primary prevention of anemia with repeat hemoglobin at least once in each trimester.
- In pregnant women with established mild to moderate anemia , with a period of gestation less than 30-32weeks, and those who respond to a trial of oral iron, the treatment should continue with 100mg elemental iron twice daily and 500mcg of folic acid with an assessment for the rise in hemoglobin. Repeat hemoglobin is recommended after 4 weeks of oral iron.

- After achieving the normalization of hemoglobin a prophylactic daily iron supplementation(60-100mg and 500mcg of folic acid) is recommended for atleast 6 month during pregnancy and should be continued in postpartum for another 6 months.
- Pregnant women on oral iron supplements should be counseled about steps to reduce gastrointestinal side effects. These include consuming the tablet at least about one hour before a meal , along with absorption enhancers(like vit c)

- Parenteral iron is recommended for pregnant women with anemia who do not respond or are intolerant to oral iron. Among the newer intravenous formulation, iron sucrose is approved for use during pregnancy though it is better avoided during the first trimester.
- Parenteral iron is also recommended for pregnant women with severe anemia who require rapid restoration of iron stores in the second and early 3rd trimester of pregnancy.
- Packed red cell transfusion should be reserved for those with severe anemia at any period of gestation.
- Deworming using albendazole is routinely recommended after the first trimester to avoid the soil-transmitted helminthic infestation.

1st Estimation of Hb
At 14 -16 weeks

Hb estimation and deworming

Hb < 7 gm/dl
Blood tranfusion and further
management.

Hb 7 – 10.9 gm/dl
Therapeutic dose
Fe SO₄ 100 mg + FA 0.5mg BD
With Vit B12 15mcg + Vit C 100
mg OD (100 tab)

Hb >= 11gm/dl
Prophylactic dose
Fe SO₄ 100 mg + FA 0.5mg OD
With Vit B12 15mcg + Vit C 100
mg OD (100 tab)

2nd Estimation of Hb

At 20-24 weeks

After consumption of prophylactic / therapeutic dose

Hb < 7 gm/dl

Blood tranfusion
and further
management.

Hb 7 – 8.9 gm/dl

Inj iron
sucroseinfusion
intravenous – 4doses
of100Mg over a
period of 2 weeks
with2-4 days interval

Hb 9 – 11 gm/dl

Therapeutic dose
Fe SO₄ 100 mg + FA 0.5mg
BD
With Vit B12 15mcg + Vit C
100 mg OD (100 tab)

Hb >= 11 gm/dl

Prophylactic dose
Fe SO₄ 100 mg + FA
0.5mg OD
With Vit B12 15mcg
+ Vit C 100 mg OD (100 tab)

3rd Estimation of Hb

1 month after the 4 doses (gestational age < 30 weeks)

Hb < 7 gm/dl

Blood tranfusion
and further
management

Hb 7 – 8.9 gm/dl

Not received Inj
Iron sucrose prev
in current
pregnancy

Inj iron sucrose infusion
intravenous – 4doses
of 100Mg over a period of 2
weeks with 2-4 days interval

Received Inj Iron
sucrose previ in
current pregnancy

Two top up doses of
Injection iron sucrose
infusion intra venous –
100 mg(each).

Hb 9 – 11 gm/dl

Prophylactic dose

Fe SO₄ 100 mg + FA 0.5mg OD
With Vit B12 15mcg + Vit C 100
mg OD (till del)

Hb >= 11 gm/dl

Prophylactic dose

Fe SO₄ 100 mg + FA 0.5mg OD
With Vit B12 15mcg + Vit C 100
mg OD (till del)

Estimation of Blood Hemoglobin at
30-34 weeks of gestation

Hb < 9 gm/dl

Blood tranfusion and further
management

Hb > 9 gm/dl

Prophylactic dose
Fe SO₄ 100 mg + FA 0.5mg OD
With Vit B12 15mcg + Vit C 100 mg OD (till del)

IRON THERAPY

Specific therapy

- Oral therapy
- Parenteral therapy

ORAL IRON

- Hb 8-11gm%, early pregnancy
- Contraindications to oral iron therapy
 - Intolerance to oral iron
 - Advanced pregnancy
 - Non compliant
- Failure to respond
 - Inaccurate diagnosis (folate / vit B12 def or thalassemia)
 - Faulty absorption
 - Continuous blood loss
 - Co-existent infection
- Indicators of response to therapy
 - Feeling of well being
 - Improved look of patient
 - Better appetite
 - Reticulocytosis in 7-10 days.
 - Rise in Hb 0.8 gm/dl per week (starts after 3 weeks)

ORAL IRON

- Commonly available **Ferrous Preparations**-
 - Ferrous Sulphate - cheapest
 - Ferrous Gluconate
 - Ferrous Fumarate
 - Ferrous Succinate
 - Carbonyl iron.
 - **Administration**- 2 Hours before or 1 hour after meals preferably with Orange juice.
- **GIT Intolerance** is most commonly observed side effect.

ORAL IRON PREPARATIONS

S.NO.	NAME OF PREPARATION	ELEMENTAL IRON (mg/gm)
1)	FERROUS GLUCONATE	120
2)	FERROUS GLYCINE SULPHATE	200
3)	FERROUS ASCORBATE	200
4)	FERROUS SULPHATE	200
5)	FERROUS SULPHATE DRIED	300
6)	FERROUS FUMERATE	330
7)	FERROUS SUCCINATE	350
8)	FERROUS CARBONATE ANHYDROUS	480
9)	CARBONYL IRON	1000
10)	FERRIC PYROPHOSPHATE	120
11)	HEME IRON	1000

NEW THERAPEUTIC ALTERNATIVE



- Carbonyl iron
- Iron ascorbate
- **Advantages :**

- Outstanding GI tolerance.
- Very safe with no poisoning even in high doses
- No interaction with food stuff
- Non metallic taste and don't stain the patient ' teeth
- Compliance is very high

➤ Side effect

- Constipation- having prune juice may help relieve the problem, also it is a good source of iron
- Heartburn- avoid taking the tablet at bedtime as lying down may increase the discomfort
- Abdominal discomfort
- Nausea, vomiting, Diarrohea (rare)

BIOAVAILABILITY OF VARIOUS IRON

- Ferrous sulphate-26.7%
- Ferrous ascorbate-40%
- Ferrous fumerate-28%
- Ferrous bisglycinate-99.9%

DIETARY FACTORS AFFECTING BIOAVAILABILITY OF IRON

Enhancers

Heme iron present in Meat, Fish, Poultry and Seafood.

Ascorbic acid (Vitamin C) present in citrus fruits, fruit juices, green leafy vegetables, cabbage, cauliflower, tubers

Some germinated or fermented foods (germinated or fermentation reduces phytate content) e.g. soya sauce

Inhibitors

Phytates present in cereal bran, cereal grains, high extraction flour, legumes, nuts and seeds.

Calcium particularly in milk and milk products

Tannins present in tea coffee, cocoa

Phosphates in egg yolk

Oxalates in vegetables

Excess of dietary fibers

MALABSORPTION OF IRON

- Adult Coeliac Disease (Gluten Enteropathy)
- Patient allergic to gluten in wheat
- Diagnosis
 - t-TG Antibody IgA ↑
 - UGI Endoscopy & D2 Biopsy
- Villous Atrophy
- Treatment
 - Gluten free diet (lifelong)
 - I/V Iron for Anemia

PARENTERAL THERAPY

INDICATION

- Contraindications of oral therapy
- Patient not co-operative to take oral iron
- Cases seen for the first time during the last 8-10 weeks with severe anaemia
- Malabsorption
- Small bowel resection
- When haemorrhage is likely to continue

CONTRAINDICATION

- H/O anaphylatic reaction to parenteral therapy.
- First trimester, chronic liver disease, Hbpathies (BT, SCA), active infection (acute or chronic)
- Oral iron is stopped atleast 24 hours before to avoid toxic reaction.

SIDE EFFECTS

- Fever, arthralgia, skin rashes
- Lymphadenopathy local pain & Black staining, Anaphylactic reaction.
 - The rise in Hb levels after parenteral therapy is 0.7-1gm per week which is same as seen with oral therapy. The main advantage of parenteral therapy is certainty of its administration

CALCULATION OF IRON REQUIREMENT

➤ $250\text{mg} * \text{Hb \% deficit} + \text{another } 50\% \text{ for replenishment of stores.}$

OR

➤ $2.4 * \text{pre pregnancy wt(kg)} * \text{Hb deficit} + 1000\text{mg (for storage).}$

(1000mg is taken for complete restoration of the stores in patients with continuing blood loss otherwise 500 mg is adequate.)

#Hb deficit =desired Hb-actual Hb

PARENTERAL IRON PREPARATIONS

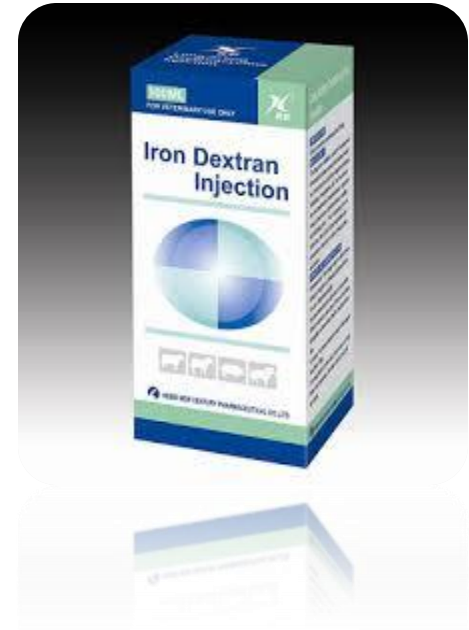
S.NO.	NAME OF PREPARATION	ELEMENTAL IRON
	IM PREPARATIONS	
1)	IRON DEXTRAN (IMFERON)	50mg/ml
2)	IRON SORBITOL CITRIC ACID COMPLEX (JECTOFER)	50mg/ml
	IV PREPARATIONS	
1)	IRON DEXTRAN	50mg/ml
2)	IRON SUCROSE COMPLEX (VENOFER)	20mg/ml
3)	FERRIC CARBOXY MALTOSE (FERRINJECT)	50mg/ml
4)	FERRIC ISOMALTOSIDE (MONOFER)	100mg/ml
5)	FERUMOXYTOL (FERAHEME)	30mg/ml

INTRAMUSCULAR THERAPY

- Iron dextran (1ml contains 50mg elemental iron & 1amp =2ml)complex of ferric hydroxide + dextran
- Dose : 100mg im OD or on alternate days till the total dose over
- Drawbacks – painful injection ,skin discoloration ,local abscess, allergic reaction, Fe over load, category C drug, gluteal sarcoma.
- Acute anaphylactic reactions may occur.epinephrine should be given immediately in a dose of 0.5 ml of a 1:1000 solution by s.c. or i.m. injection.
- A test dose of 0.5 ml should be given at the injection site. The full dose should be given at least after 1 hr ,if there is no adverse reaction to the test dose.
- The drug should be injected deeply with a 2 or 3 inch 20-22 gauze needle with z track technique.

INTRAVENOUS PREPARATION

- Iron dextran (Imferon)(50 mg/ml)
- Iron sucrose (20mg/ml)
- Sodium ferric gluconate (ferrlecit) (12.5mg/ml)



INTRAVENOUS PREPARATION

➤ Iron Dextran

- The advantage of iron dextran is the possibility of giving larger doses of iron ,up to 1000 mg in one sitting.
- A test dose should be given before every infusion.
- 25mg of iron dextran is added to a 50ml bag of NS and run over 10-15 minutes. Patient should be monitored for another 15-20 minutes. If there are no signs of adverse reactions the rest of the dose diluted in a 500ml bag of S should be administered over 2-6 hours; the rate of infusion should not exceed 500mg per hour.

ADVERSE REACTIONS

- Increased anaphylaxis incidence with TDI.
- Onset is 24-48 hrs after administration.
- Effects subside within 3-4 days.
- Dose related:
 - Arthralgia, backache, chills, dizziness, moderate to high fever, headache, malaise, myalgia, N/V.
- Non-dose related:
 - Hypersensitivity reactions characterized by anaphylactic shock, CV collapse, cardiac arrest, bronchospasm, oral or pharyngeal edema, or dyspnea.
- Treatment
 - Stop infusion
 - Give antihistaminic,
 - corticosteroids, adrenaline.

IRON SUCROSE(VENOFER)

- Commonly used ,best in chronic kidney diseases
- Iron hydroxide sucrose complex in water
- Mw 34,000-60,000 D
- Each ml contain 20 mg of Fe, total of 5 ml
- After IV administration it dissociates into iron & sucrose
- T_{1/2} is 6 hrs

IRON SUCROSE

- No test dose is required.
- May be administered Iv push undiluted @1ml/min max dose being 100mg,i.e over 5 minutes as 5ml contains 100mg iron.
- Another way is to dilute 200 mg to be diluted with 200ml NS, infuse at least 20 min.
- Marked increase in reticulocyte count expected in 7-14 days.
- **Three times weekly.**
- 200 mg max dose per sitting
- Rate of administration should not more than 20mg/min.

ADVERSE REACTIONS

- Experienced in > 5% of patients:
 - Hypotension
 - Cramps/leg cramps
 - Nausea
 - Headache
 - Vomiting
 - Diarrhea

PRECAUTIONS

- Iron overload or infusing too rapidly can cause:
- Hypotension, headache, Nausea, vomiting, dizziness, joint aches, paresthesia, abdominal & muscle pain, edema, & CV collapse
- Tx - IV fluids, hydrocortisone, or antihistamines
- Or slow down rate of infusion

SODIUM FERRIC GLUCONATE

- No test dose is required.
- available as 12.5mg/ml(10ml=125mg)
- Administered in:
 - Small installments of 125 mg Fe or less diluted in 100 mL of NS and infused over 60 min.
 - Or undiluted as a slow IV injection at a rate not exceeding 12.5 mg/min (1 mL/min).5ml contains 62.5mg

ADVERSE REACTIONS

- Hypotension/flushing
- Associated with rapid administration
- Not associated with hypersensitivity reactions
- Resolves within 1-2 hours

ADVANTAGES OF IRON SUCROSE OVER OTHER

- No test dose recommended
- It has minimal side effects.
- It is usually not associated with anaphylactic reaction
- Preferred in haemodialysis patient as it has low molecular weight.
- All iron preparations were capable of causing tissue peroxidation except iron sucrose
- Less oxidative injury
- Less risk of tissue parenchymal injury by free iron
- Higher availability for erythropoiesis than iron dextran
- Safe in dextran sensitive patient

NEWEST FAST ACTING IV MOLECULES

➤ Ferric Carboxymaltose (FERRINJECT):

- It is a novel iron complex that consists of ferric hydroxide core stabilized by a carbohydrate shell, allow for controlled delivery of iron to target tissues.
- Rapidly taken up by the RE cells, liver, spleen on i.v.
- T1/2: 16 hrs
- Dose : Single dose of 1000mg over 15 minutes (maximum 15mg/kg by injection or 20 mg/kg by infusion)
- Rapid increase in Hb and stores.
- Less antigenic.
- Pain at injection site,rashes,headache,nausea,hypotension.
- Not recommended <14 years and in first trimester.
- US FDA approved.
- Act on neutral and physiological pH.therefore it forms a more stable complex and can be given in high doses.



FERUMOXYTOL(FEREHEME)

- USA FDA approved this drug in 2009 for iron replacement in patients with Iron deficiency Anaemia &CKD
- No test dose required
- Can be given large dose (510mg/vial) infused over 15 min once followed by a second dose 3-8 days later
- No significant side effects



FERRIC ISOMALTOSIDE (MONOFER)

- Strongly bound iron in spheroid iron carbohydrate particle providing slow release of bioavailable iron to iron binding proteins
- Rapidly up taken by RES and little risk of free iron for tissue damage
- Dose : 1000mg in a single infusion
- Erythropoietic response seen within days
- Serum ferritin returns to normal by 3 wks

INDICATION OF ERYTHROPOETIN

- Rapid correction of anemia in less than 2 weeks, chronic kidney diseases.
- Anemia not responding to parenteral therapy alone
- Treatment of moderate to severe iron deficiency as an alternate to blood transfusion.

DOSAGE REGIMEN CONTAINING ERYTHROPOETIN

- Inj erythropoetin – can be given along with parenteral iron in a dose of 50-150 U/kg given s.c. twice/thrice weekly.
- First dose after subcutaneous sensitivity test.
- Adrenaline, hydrocortisone injection oxygen to be kept ready.
- Produces 3gm % rise in Hb over a 2wk period

‘Transfusion should be prescribed ONLY for conditions for which there is NO OTHER
TREATMENT’

BLOOD TRANSFUSION

INDICATIONS OF BLOOD TRANSFUSION

Table 11 Indications of blood transfusion in pregnancy(197, 198, 199)

Antepartum Period
1. Pregnancy <34 weeks
a. Hb <5 g/dL with or without signs of cardiac failure or hypoxia
b. Hb 5-7 g/dL – in presence of impending heart failure
2. Pregnancy >34 weeks
a. Hb <7 g/dL even without signs of cardiac failure or hypoxia
b. Severe anemia with decompensation
3. Anemia not due to hematinic deficiency
a. Hemoglobinopathy or bone marrow failure syndromes
b. Hematologist should always be consulted
4. Acute hemorrhage
a. Always indicated if Hb <6 g/dL
b. If the patient becomes hemodynamically unstable due to ongoing hemorrhage
Intrapartum Period
a. Hb <7 g/dL (in labor)
b. Decision of blood transfusion depends on medical history or symptoms
Postpartum Period
a. Anemia with signs of shock/acute hemorrhage with signs of hemodynamic instability.
b. Hb <7g% (postpartum): Decision of blood transfusion depends on medical history or symptoms

Whole blood Description:

- 450 mL whole blood in 63 mL anticoagulant-preservative solution of which Hb will be approximately 1.2 g/dL and haematocrit (Hct) 35-45% with no functional platelets or labile coagulation factors (V and VIII) when stored at +2°C to +6°C.
- Storage: Between +2°C and +6°C in an approved blood bank refrigerator, fitted with a temperature monitor and alarm.
- Indications: Red cell replacement in acute blood loss with hypovolaemia. Exchange transfusion.
- Contraindications: Risk of volume overload in patients with: Chronic anaemia. Incipient cardiac failure.
- Complete transfusion within 4 hours of commencement.

Red cell concentrates [packed red blood cells (PRBC)]

- Description: 150-200 mL red blood cells from which most of the plasma has been removed. Hb concentration will be approximately 20 g/100 mL (not less than 45 g per unit) and Hct 55-75%.
- Indications: Replacement of red cells in anaemic patients.

ADVANTAGES & SIDE EFFECT

One unit of whole blood/PRBC can increase Hb by 1g/dL in an adult or Hct by 3%

Advantages

- Increase oxygen carrying capacity of the blood
- Stimulates erythropoiesis
- Hb from the haemolysed red cells may be utilised for the formation of new red cell
- Supplies the natural constituents of blood
- Improvement is expected after 3 days

Side Effect

- Risk of transmission of HIV, Hepatitis B, C, malaria, rubella, etc.
- Transfusion reactions.
- Risk of incorrect cross - matching and transfusion negative impact on immune system.
- Onset of preterm labour
- Pulmonary edema

TRANSFUSION REACTIONS

- Fatal Hemolytic reactions → 1 in 1,00,000
- Non hemolytic febrile reactions → 3-4%
- Anaphylactic reactions → 1 in 1,50,000
- GVHD → 0.1 to 1%
- TRALI → 0.1-0.2%
- HBV → 1 in 50,000
- HCV → 1 in 3000
- HIV → 1 in 1,50,000



TREATMENT OF RELATED CONDITIONS

- **Malaria** causes anaemia in pregnancy due to **rupture of RBCs**. It leads to low birth weight babies, parasitaemia in neonates and becomes a persistent source of infection. Therefore malaria in pregnancy should be treated without any hesitation. The preferred drug is **chloroquine**. Malaria prophylaxis should also be given to pregnant women in areas where malaria is endemic.
- **Hookworm infection** causes anaemia due to chronic blood loss. **Albendazole or mebendazole** is recommended to all pregnant women after the first trimester of pregnancy. To prevent recurrence, patients should be advised to use **footwear, improve sanitation, and personal hygiene**.

Keep the nails trimmed

Wear chappals/ footwear

Keep the environment clean

Safe Mother



Healthy Child

Wash the vegetables before eating or cooking

Use sanitary toilets

Wash hands with soap after defecation

Wash hands with soap before eating food

MANAGEMENT DURING LABOUR

First stage:

The patient should be in bed or propped up
Oxygen inhalation ,intermittent chest auscultation
Strict asepsis
Labour monitoring by partograph, ctg monitoring
Sedation and analgesic, fluid restriction

Second stage:

Asepsis
oxytocin concentrated form, restrict fluid
Prophylactic low forceps or vacuum delivery to cut short second stage of labour.

Third stage:

Active management of 3rd stage
Blood loss with fresh packed cell transfusion
Diuretics prior to transfusion
Close monitoring of vitals
look for any genital trauma.

MANAGEMENT – PUERPERIUM:

- (1) Prophylactic antibiotics
- (2) iron therapy for at least 3 months .
- (3) contraception advice

MEGALOBLASTIC ANEMIA

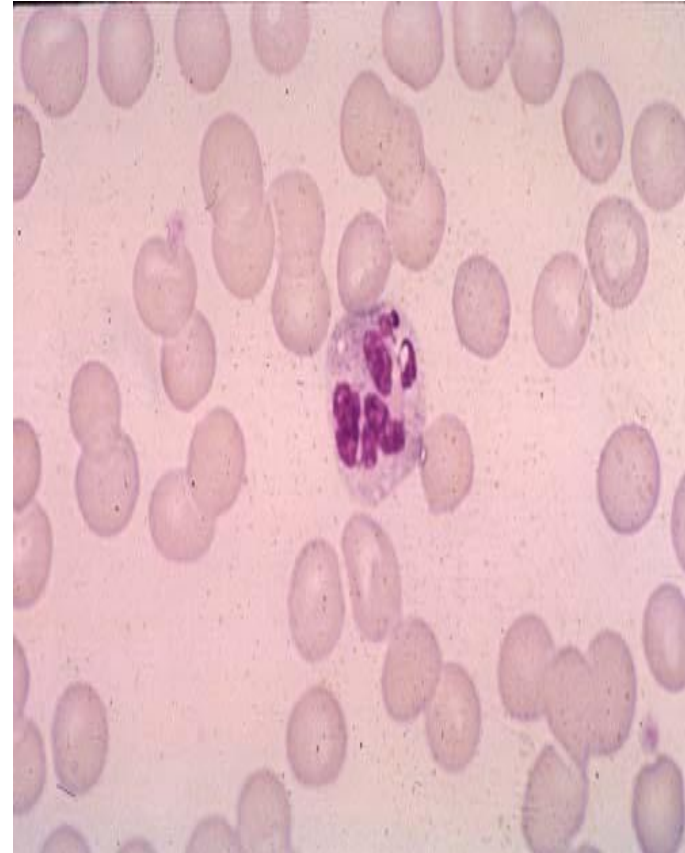
- Megaloblastic anemia
- Derrangement in red cell maturation due to impaired DNA synthesis
- Etiology-
 - Folate deficiency
 - Vitamin B12 deficiency
- Folic acid is necessary for the synthesis of purines and pyrimidines, which ultimately take part with vit B 12 in the synthesis of nuclic acid and nucleoproteins.
- Incidence – 0.2 - 5%
- In pregnancy cause is almost always folate deficiency.
- Folate stores last for 2-4months,vit B12 for 2-3 years, vit B12 deficiency occurs only in pure vegetarians.
pernicious anemia associated with infertility.

SIGN AND SYMPTOMS

- Insidious onset, mostly in last trimester
- Anorexia and occasional diarrhoea
- Pallor of varying degree
- Ulceration in mouth and tongue
- Hemorrhagic patches under the skin and conjunctiva
- Enlarged liver and spleen

LAB INV.

- Hb<10gm%
- Hypersegmentation of neutrophil'
- s.Oval macrocytes and pancytopenia
- Macrocytosis.
- MCV>100micrometer³
- MCH>33pg, but MCHC is Normal
- S.folate levels<3ng/ml
- S.vit B12 LEVELS<100 pg/ml
- Serum Fe is Normal or high, TIBC is low
- Bone marrow shows megaloblasts



TREATMENT

- Prophylactic

- all woman of reproductive age should be given 400mcg of folic acid daily(ACOG 2003)

- Curative

- daily administration of Folic acid 5mg orally cotinued for atleast 3 months postpartum.

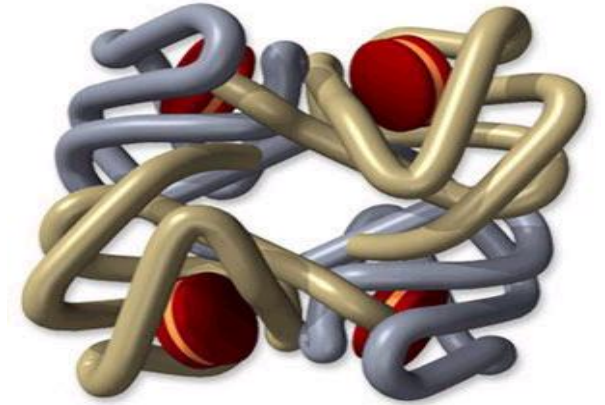
- Vit B12-1mg im on alternate days for 2 weeks followed by 1 mg im once amonth for 6 months.

VITCOFOL

- FOLIC ACID 15 mg/ml
- Nicotinamide 200mg/ml
- Cynocobalamine 0.5mg/ml
- Route of administration –parenteral – 1ml/i.m alternate day
- 10 ml injection

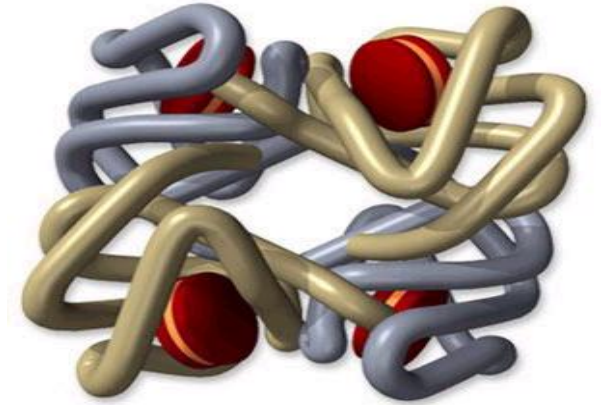
HEMOGLOBINOPATHIES

- Normal adult hb is a conjugated protein with a molecular weight of about 68000, which contains a globin fraction bound to 4 haem molecules.
- Abnormalities of heme synthesis are responsible for porphyrias.
- The hemoglobinopathies are concerned with the disorders within polypeptide chains that comprise globin fractions.
- There are 4 possible chains, namely alpha, beta, gamma & delta.



THERE ARE 4 POSSIBLE CHAINS, NAMELY ALPHA, BETA, GAMMA & DELTA.

- HbA---97%, = 2 alpha + 2 beta globin chains
- HbA2---(1.5-3.5%), = 2alpha+2 delta globin chains
- HbF --<1%. = 2 alpha+ 2 gamma globin chains
- Two classes of abnormality of Hb A synthesis can result in decreased portion of HbA
 - Quantitative defect(thalessemias)
 - Qualitative defect(sickle cell disease)



THALESSEMIA

➤ The synthesis of globin chain is partially or completely suppressed resulting in reduced Hb. content in red cells, which have shortened life span

➤ Result is ineffective erythropoiesis, haemolysis & varying degree of anaemia

Incidence: 1 in 300 – 500 pregnancies

➤ TYPES

➤ Alpha thalassaemia (impaired production of Alpha chain).

➤ Beta thalassaemia: (impaired production of beta chains)

➤ Major

➤ Intermedia

➤ Minor

THALESSEMIA INTERMEDIA AND MINOR

- Low MCV,MCHC.near normal or normal MCHC.
- Diagnosis is confirmed by a raised concentration of Hb A2.
- If Patient is found to have thalessemia partner should be tested if both have thalassemia trait the couple is offered prenatal diagnostic testing.
- pregnancy termination can be offered if fetus found to be Thalassemia major.
- In thalassemia minor oral iron and folate prescribed but never parenteral preparations.

B-THALESSEMIA MAJOR

- Rarely encountered.
- Homozygous inheritance from both parents.
- Both beta chains are missing.
- Severe anaemia.
- Diagnosed in paediatric age.
- Hypogonadotropic hypogonadism, diabetes & thyroid diseases, so reduced fertility.
- T/m: is blood transfusion
- Desferrioxamine discontinued during pregnancy due to possible harmful effect on fetus and risk of iron deficiency in neonate.
- Vit C should also be stopped.
- prenatal diagnosis

ALPHA THALESSEMIA

- 4 types-alpha major,intermediateform or Hb H disease and two minor traits.
- Alpha major is usually incompatible with life and pregnancy ends in a hydropic fetus.
- Management of carrier state is as in case of beta thalessemia minor.
- They should receive routine iron and folate supplements.

SICKLE CELL DISEASE

- Structural Hb variant
- substitution of Valine for glutamic acid at 6 position of β chain.
- Exists in homo(Hb-SS) & heterozygous forms(Hb-SA)
- Under hypoxic conditions, HbS polymerizes, gels or crystallizes.
- hemolysis of cells, & thrombosis of vessels in various organs
- In long standing cases, multiple organ damage.
- Constant sickling & desickling leads to membrane damage & cells may be irreversibly sickled
- Slow rbc transit through microcirculation contributes to vaso-occlusion



IN PREGNANCY

- Abortion and still birth
- Intra uterine growth restriction
- Premature birth
- Intrapartum fetal distress
- Increased perinatal mortality
 - Aplastic , megaloblastic sequestration & haemolytic crisis
- Diagnosis: Hb. Electrophoresis

MANAGEMENT: PRE PREGNANCY COUNSELLING

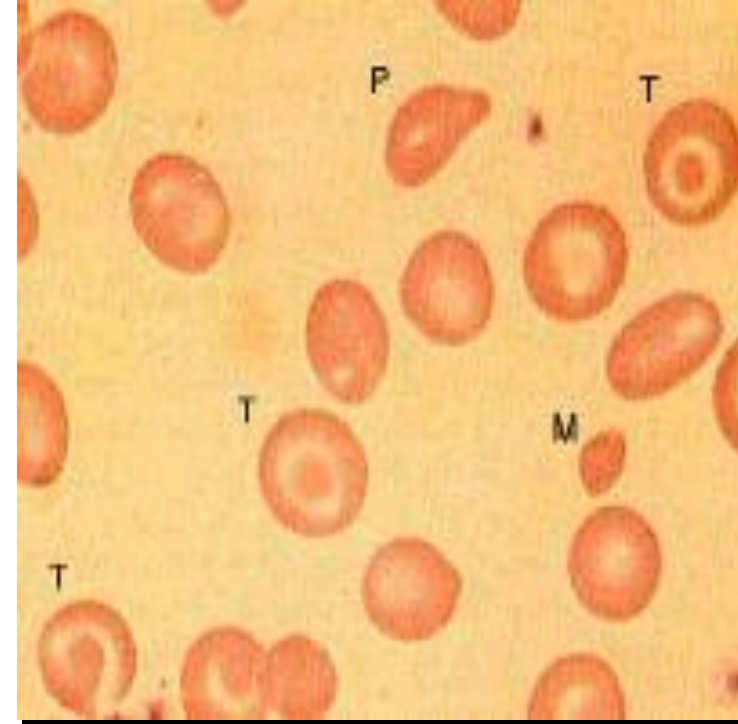
- Risk during pregnancy(stress ,hypoxia,overexertion can precipitate anemia)
- Partner's hb electrophoresis should be done and couple should be counselled about risk of baby being born with SCD.
- A complete evaluation for the status of disease and chronic disease complication should be done.

ANTENATAL MANAGEMENT

- Well hydration, effective analgesia, prophylactic antibiotics, O2 inhalation, folic acid(5 mg/day, oral iron supplement (I/V iron is C/I), blood transfusion
 - BT reduces pain, prevents crises , not shown to improve perinatal outcome
 - Some advocate exchange transfusions .
- Low dose aspirin is recommended as SCD is considered a mild risk factor for thrombotic episodes.
- Heparin should be prescribed for thromboprophylaxis.

DIAGNOSIS

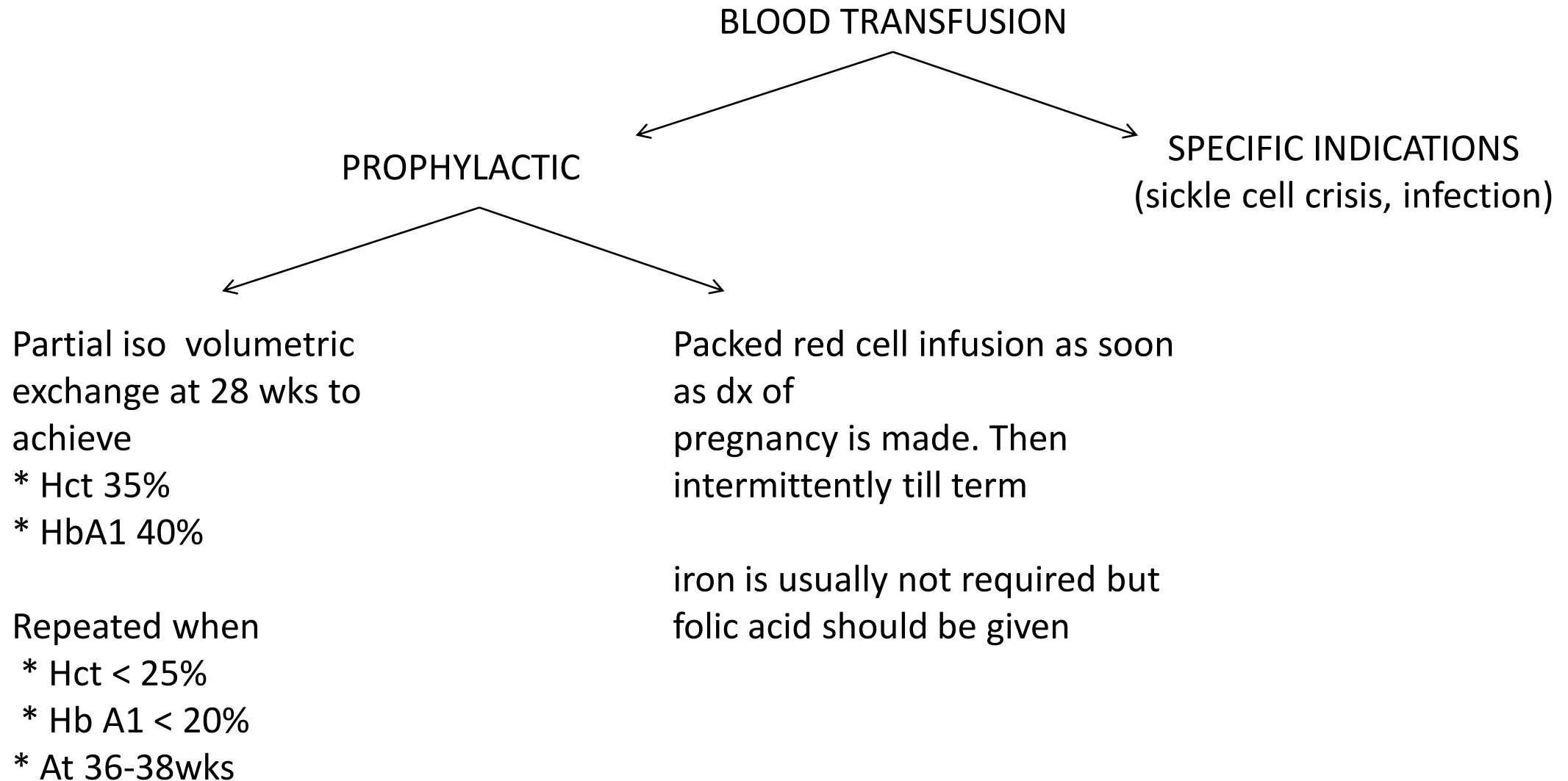
- Hb estimations
- Peripheral smear
- Decreased MCV, MCHC
- HbA2 levels
- Diagnostic test:
- Hb electrophoresis



MANAGEMENT OF SICKLE CELL CRISIS

- HOSPITALISATION
- HYDRATION AND OXYGENATION
- PAIN RELIEF
- TRANSFUSION
- IV ANTIBIOTIC

TREATMENT OF SICKLE CELL ANEMIA



HEMOLYTIC ANEMIA

CLASSIFICATION OF HEMOLYTIC ANEMIAS

	INTRACORPUSCULAR DEFECTS	EXTRACORPUSCULAR FACTORS
HEREDITARY	<ul style="list-style-type: none">•HEMOGLOBINOPATHIES•ENZYMOPATHIES•MEMBRANE-CYTOSKELETAL DEFECTS	<ul style="list-style-type: none">•FAMILIAL HEMOLYTIC UREMIC SYNDROME
ACQUIRED	<ul style="list-style-type: none">•PAROXYSMAL NOCTURNAL HEMOGLOBINURIA	<ul style="list-style-type: none">•MECHANICAL DESTRUCTION [MICROANGIOPATHIC]•TOXIC AGENTS•DRUGS•INFECTIOUS•AUTOIMMUNE

INTRAVASCULAR HEMOLYSIS

- HEMOGLOBINEMIA
- HEMOGLOBINUREA
- LOW HAPTOGLOBIN
- METHAMOGLOBINEMIA
- METHAMOGLOBINURIA
- INCREASED UNCONJUGATED BILIRUBIN
- JAUNDICE

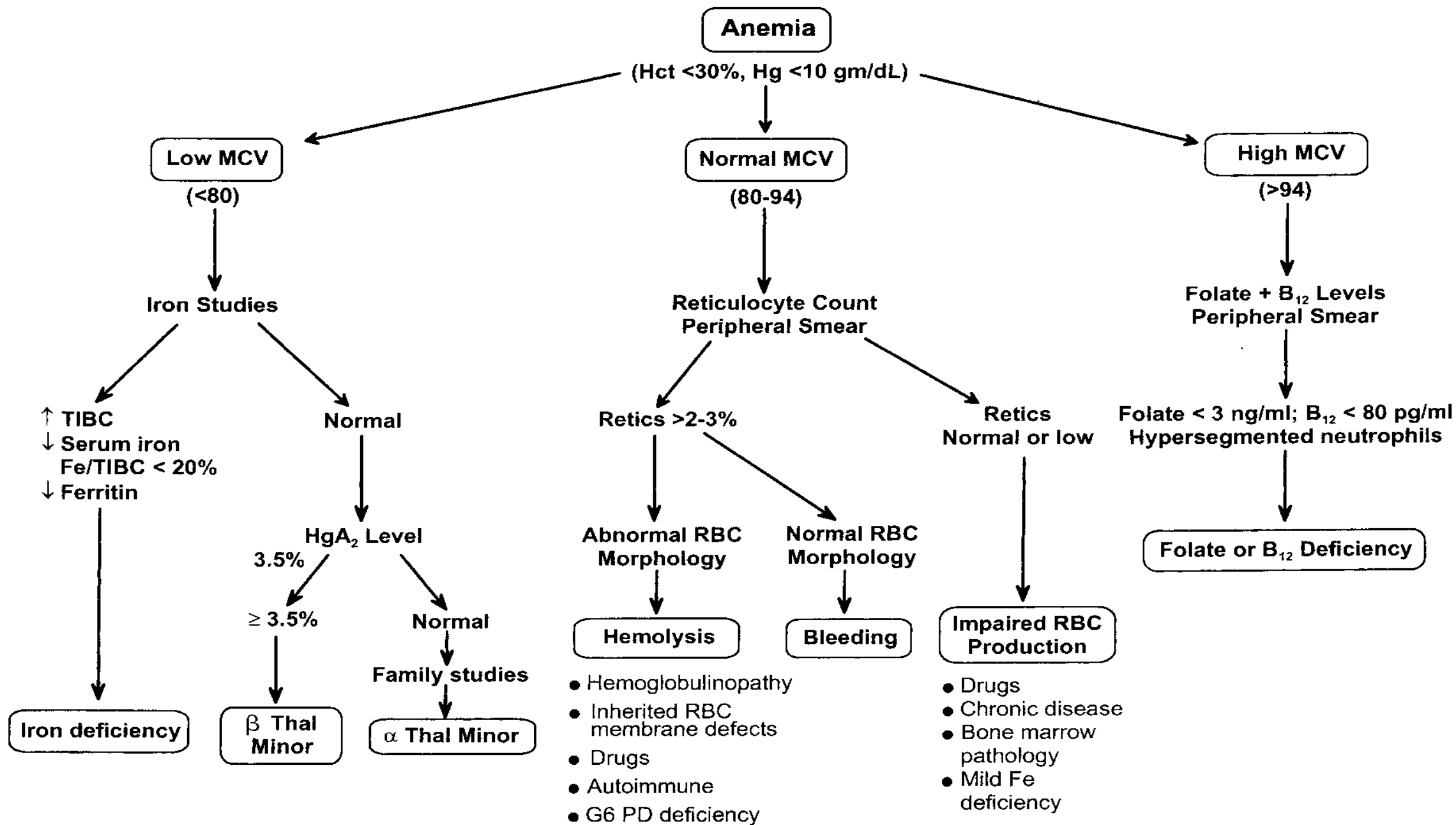
EXTRAVASCULAR HEMOLYSIS

- RBC DESTRUCTION IN SPLEEN AND LIVER
- HEPATOMEGALY
- SPLENOMEGALY
- JAUNDICE
- NO HEMOGLOBINEMIA, HEMOGLOBINURIA OR METHAMOGLOBINEMIA

APLASTIC ANEMIA

- Disorder characterised by marrow failure associated with Pancytopenia.
- Causes-
 - inherited -Fanconi anemia
 - acquired - stem cell defect
 - irradiation
 - viral infections
 - chemical agents

- PBF is normocytic normochromic
- Bone marrow shows dry tap
- Clinical features are caused by anemia(pallor),thrombocytopenia (petechiae), neutropenia (recurrent infections).
- Characteristically splenomegaly is absent and reticulocytopenia is the rule.
- Treatment is with either bone marrow transplantation (in young patients) or antithymocyte globulin(in old patients).





THANK YOU