65
2,7
92

Haematological Diseases :

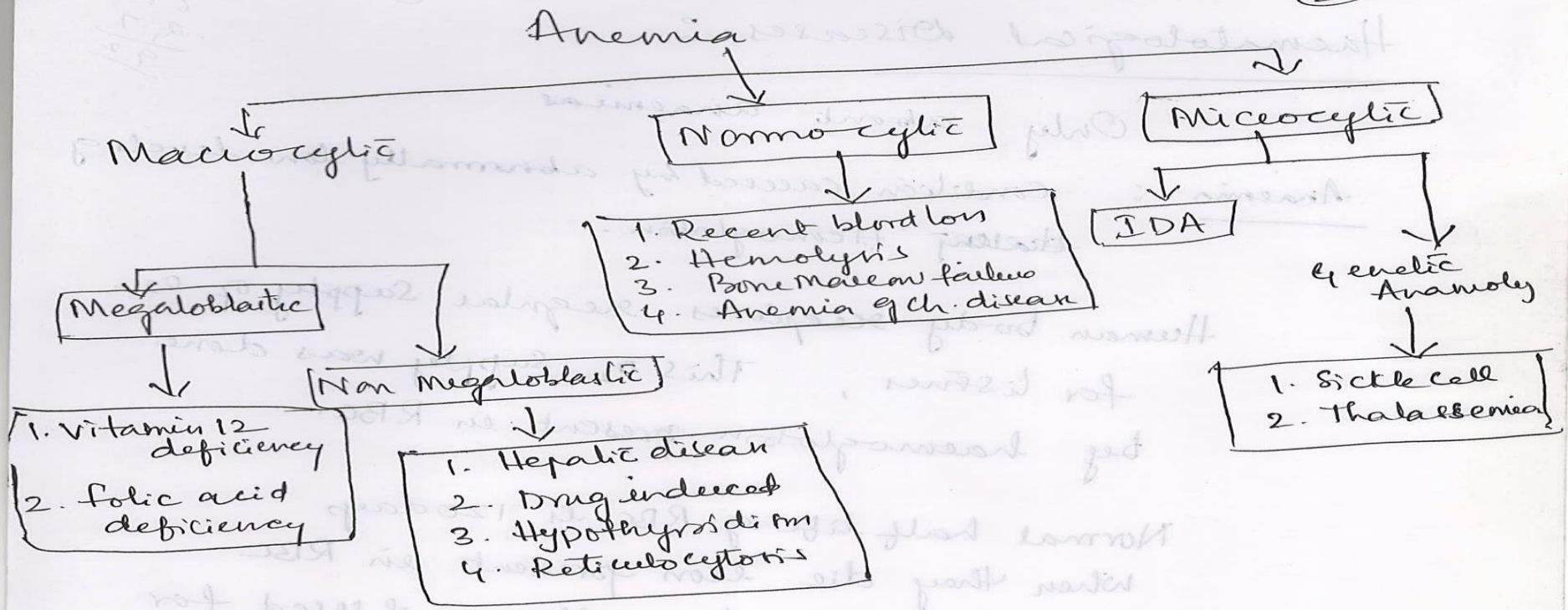
Only about anaemias

Anaemia : Condition caused by abnormally low levels of ~~Healthy~~ Hemoglobin.

Human body requires regular supply of O_2 for tissues, This O_2 supply was done by haemoglobin present in RBC.

Normal half life of RBC is 120 days
When they die iron present in RBC released to the bone Marrow & used for New RBC production.

Anemia develops when heavy bleeding causes significant loss of RBC or when its production slows down or they are destroyed at fast rates.



Iron Deficiency Anaemia

Def: ↓ed O_2 carrying capacity of RBC.

RBC

Results from reduced production of RBC

or

↑ed loss of RBC

RBC are manufactured in bone marrow and

(3)

its life Expectancy is ——— Months i.e 120 days.

To produce RBC
↓
Body needs Iron, B_{12} & folic acid

If their is Lack of any one of the above is lacked
↓
Results Anemia

Etiology : In children it may be due to low Iron diet
Worm infestations

In Adults : Fast blood loss where body can't remake it

Vegetarians lack of Iron in their diet as red meat is main dietary source of Iron

↓ed absorption of Iron from intestines due to
Small intestine diseases
Ulcers in stomach & duodenum

↑ed Iron need occurs during pregnancy
&
during rapid child growth.

Symptoms : Symptoms appear when Hb drops < 10 g%.

First symp : 1. Tiredness
2. Palpitations
3. Shortneng breath
4. Dizzyness

If Anemia is severe 1. Angina (chest pain)
2. Headache
3. Leg pains

Other symptoms dues to long term iron deficiency includes
1. Burning sensation in the tongue
2. Dryness in Mouth, throat, Sores at the corners of Mouth
3. Altered sense of tastes.

In Extreme cases
- Nails become brittle & spoon shaped
- brittle hair
- Difficulty in swallowing
- shortneng breath
- Palpitation
- Angina.

Diagnosis : Blood test diagnoud Microcytic Hypochromic anemia.

Treatment : Iron supplement : Iron tablets
Injectables

To avoid : Iron rich diet includes
Pregnancy → Iron supplements. Green veges. Date palms ← dried fruits
- Red meat
- liver

Megaloblastic Anemia

Agent: Vit B_{12} & folic acid

↓

Food

↓

↓ Vit B_{12} & folic acid oral intake

↓

I.N.G.I.T → Gastric conditions

↓

Destruction of gastric Mucosa which contains Parietal cells secretes Intrinsic factor

Partial or total gastrectomy affecting Distal Duodenum & proximal Small Intestine

↓

↓ Secd or Absence of Intrinsic factor → Faulty gastro intestinal absorption

↓

↓ Vit B_{12} (↓ 200 Pg/ml & ↓ folic acid (↓ 1.8 ng/ml)

↓

Leads to Megaloctosis

↓

↓ Secd production of Matured RBC

Def: Type of anemia where NO of RBC less than normal.

↓

So when there is NO Enough RBC

↓

Tissues & organs don't get enough O_2

- RBC are characterized by Larger cells than normal
  Known as Macrocytic anemia / Megaloblastic anemia / B12 or folate deficiency anemia
- B12 is seen in some foods like Meat, fish, Eggs and milk
- Some people can't absorb B12 from their food leading to Megaloblastic

Symptoms: Fatigue

Vary from person to person

common symp: Shortness of breath
Muscle weakness
Pale skin
Dizziness
Loss of appetite
Nausea
Diarrhea
Tingling in hands & feet.

Pernicious anemia : Type of autoimmune anemia

↓ Intrinsic factor is necessary for absorption of B12

When it is not available B12 can't be absorbed from Gastric Mucosa.

Physiology of B12 absorption :

Gastric Mucosal parietal cells
↓ Secretes
Intrinsic factor
↓
B12 gets attached to this
↓
Forms complex enters Intestines
↓ (Absorption)
Enters blood stream & Released

Infact B12 can only be absorbed when attached to ? ?

Etiology : → When atrophy of Parietal cells - / Surgical removal
Autoimmune disorders affecting the gut, Pancreas & adrenals.
Poisoning & corrosive substances → Destroys the lining of stomach
Intestinal worms like tape worm absorb B12
Ileum disorders (first part) like tropical sprue
Whipple's, Crohn's, tuberculosis &
Zollinger - Ellison syndrome

Symptoms : Affect 3 systems
1. Haemopoietic system
2. Gastrointestinal "
3. Neevous "

Haemopoietic : Abnormal production of RBC
Their reduced O2 carrying capacity
↓ causes
Fatigue, Dizziness, Ringing in ears
Pale skin.
Fast Heart rate, Enlarged Heart
Abnormal Heart sounds (Murmurs)

Gastrointestinal : Sore & brightly red tongue
Loss of appetite
wt loss
Diarrhoea
Abd cramps

Nervous system : Numbness
Tingling
Burning in arms & legs, hands & feet
Muscle weakness
Imbalance while walking
Irritability
Confusion & depression.

Pathophysiology of Pernicious Anemia

Due to failure of gastric parietal cells to produce ?

↓

which affects the dietary absorption of ?

Deficiency of B_{12} also leads to cobalamine deficiency

Cobalamine (B_{12}) binds to IF

Recognition of IF-cbl complex by ileal receptors must occur to transport into circulation

↓

Has to bound by transcobalamine II

Serves as plasma transportee

Cbl-TC complex binds to cell surfaces and is Endocytosed

Transcobalamine is degraded within endosome

↓

Cbl is released into cytoplasm

Here an Enzyme mediated reduction of cobalt occurs

↙ Either or ↘

Cytoplasmic Methylation → To form Methylcobalamine

Mitochondrial adenosylation → To form Adenosylcobalamine

Defect in these steps produces "Cbl dysfunction"

↓

Then Defect will cause Impaired development
Mental Retardation
Macrocytic anemia

Diagnosis: Abnormally large RBC & abnormal shape
Immature forms of RBC "Reticulocytes"
Low in number.

B12 Quantity low in circulating blood.

Schilling test: For Diagnosis

Pat is given Radioactive B12 under 2 different sets of conditions
Once alone and once attached & Intrinsic factor

Normally, large amounts of B12 are absorbed
↓
Circulated through the blood
↓
Enter kidneys
↓
Some amount of B12 passed out in urine.

In Pat ⊂ pernicious anemia
B12 will not be absorbed by Intestine or
↓ Hence
will not pass into urine
↓
Levels of B12 in urine will low.

when given along ⊂ IF
Intestines are able to absorb the vit, urine
levels of B12 will be higher.

Treatment : Life long B12 Inj Administration
↓
Enter directly into blood stream
No need for IF to get absorb through Intestine
First Needed few wks and later weekly once monthly

Pathophysiology of Anemia

Predisposing factors
Age = 13–30 yrs.
Condition: Pregnancy
Excessive Menstruation
Alcoholic
Disease like Cancer
Kidney disease
DM.
Gender = female

Precipitating factors
↓ dietary intake Iron vit B_{12} folic acid
↓ set Erythropoietin
Malabsorption: Lack of Intrinsic factor
Gastrectomy
Inflammatory bowel syndrome

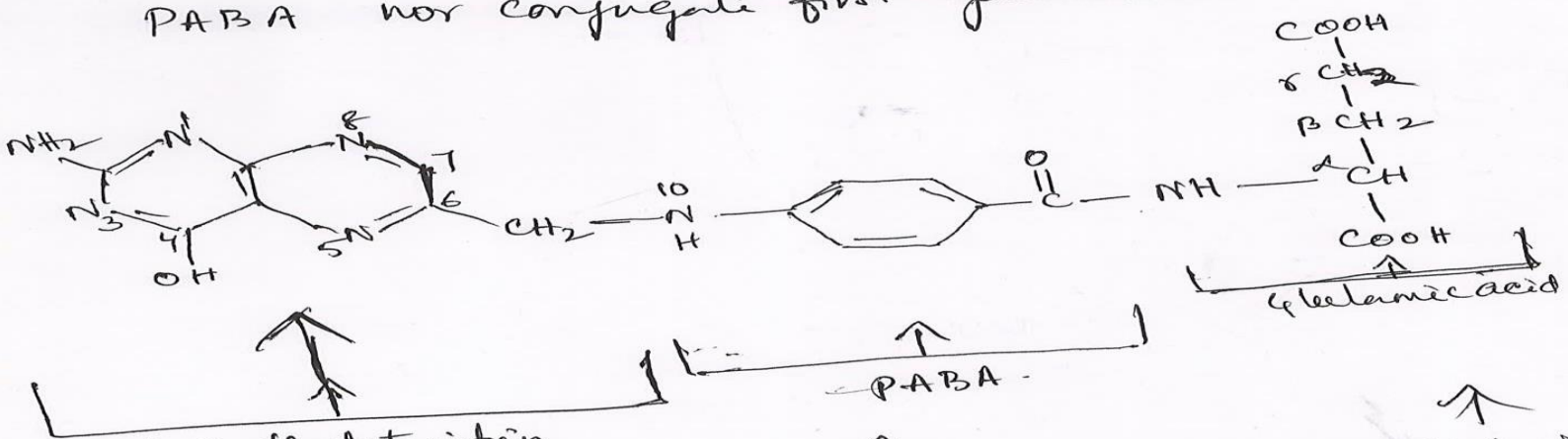
B_{12} Def
Folic acid Def
Iron Def
Lack of Hb in RBC
Proliferation of large immature dysfunctional RBC
Alteration of Normal RBC Production
↓ set O_2 carrying capacity
Hypoxia
Organ Dysfunction
Organ failure
Death

Manifestation
1. Paresthesia of hands & feet
2. Impaired coordination and position sense
3. Diarrhea

- age
- alcoholism
- Birth control pills.
- anticonvulsant therapy
- Sulfa antibiotics
- Smoking
- Stress

Pathophysiology : Folic acid structure composed of pteridine ring connected to PABA and conjugated to one or more glutamate residues.

Humans do not synthesize folate bcoz they cannot synthesize PABA nor conjugate first glutamate



Folates present in the form of poly glutamates in cells.

In plasma & urine they are as monoglutamates as they are transported across membranes in this form

Enzymes in Intestines — (proximal Jejunum where absorbed)

↓

Convert poly to mono

In plasma folate is present as 5 methyltetrahydrofolate form and loosely attached to albumin in circulation.

5 Methyl THFA Enters the cell via ATP dependent H+ co transported

Once it is in, 5 Methyl THFA may be demethylated to THFA which is active form & Participates in folate dependent Enzymatic reactions

Q-6

Cobalamin (B_{12}) is required for this conversion

if it is absent folate remains as 5 Methyl THFA in the cell.

and folate doesn't undergo in eli Metabolic pathways resulting Megaloblastic Anemia

THFA Plays a Key role in transfer of 1-carbon units such as Methyl, Methylene & formyl groups of the Essential Substrates

↓

involved in synthesis of RNA & DNA & proteins.

It is involved in Enzymatic reaction Necessary for synthesis of Purine, thymidine & aminoacid

Healthy Individual has 500 – 20,000 mcg of folate in the body stores.

50 to 100 mcg of folate / day necessary inorder to replace daily degradation & loss through urine & bile.

Otherwise signs & symptoms of deficiency can manifest after 4 Months.

Diagnosis : Blood tests to investigate Hb%.
Results compared after folic acid supplementation

Treatment :
~~Administer~~ folic acid
Self care like avoiding alcohol
Non herbal tea
Antacids
Phosphates