III. Anemia:

Q: What are Types and Causes of Anemia ?

- Definition: decrease in RBC mass:
  - Men = hematocrit (Hct) < 41% - OR – hemoglobin (Hb) < 13.5 g/dL
  - Women = Hct < 36% – OR – Hb < 12 g/dL
- **Anemia is classified on the basis of mean corpuscular volume (MCV).**
- Classification of anemia requires the knowledge of reticulocyte-index.
  - **Reticulocyte index (RI)** refers to corrected reticulocyte count.
  - RI is calculated by following formula:
    - RI = reticulocyte count x patient's hematocrit (Hct)/normal hematocrit
    - Normal hematocrit is 45%.
    - RI > 2% means adequate bone marrow response.
    - RI < 2% means hypo-proliferation (inadequate response)

Microcytic Anemia (MCV < 80 μm³)

- Iron deficiency anemia
- Thalassemia
- Anemia of chronic disease
- Sideroblastic anemia

Macrocytic Anemia (MCV > 100 μm³)

- Megaloblastic anemia (Vit. B12 & Folate deficiency) — pernicious Anemia
- Alcoholic liver disease
- Hypothyroidism
- Myelodysplastic syndromes

Normocytic Anemia (MCV 80 - 100 μm³)

Low Reticulocyte Count (<2%)

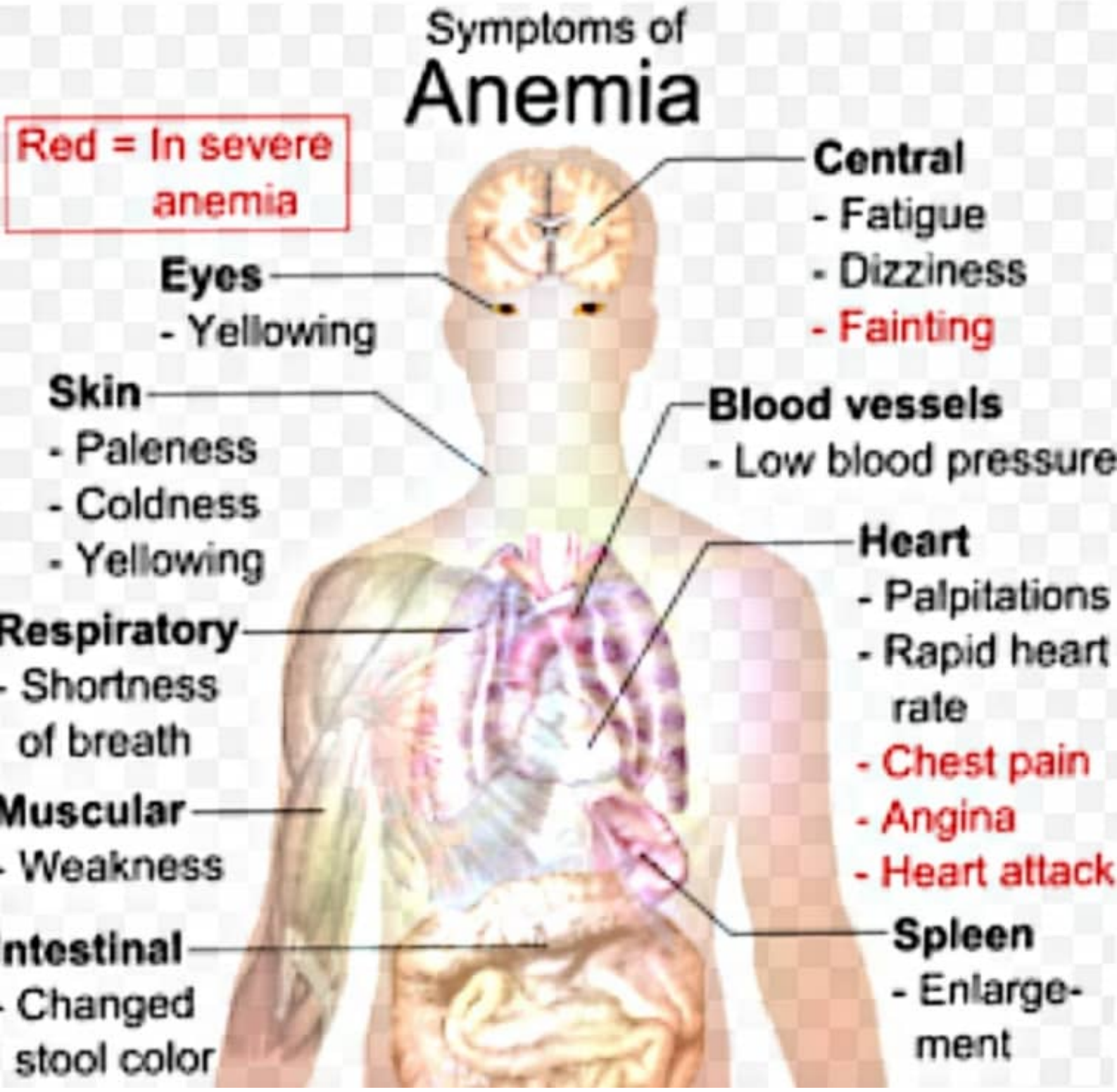
- Blood loss < 1 week.
- Aplastic anemia
- Renal failure
- Early-stage iron deficiency anemia
- Early-stage anemia of chronic disease.

High Reticulocyte Count (> 2%)

- Intrinsic RBC defect:
  - Sickle cell anemia
  - GGPD deficiency
  - Hereditary spherocytosis
  - Paroxysmal nocturnal hemoglobinuria
- Extrinsic RBC defect:
  - Blood loss > 1 week
  - Immune hemolytic anemia
  - Microangiopathic hemolytic anemia
  - Malaria

Scanned with CamScanner

Symptoms of Anemia



Google

clinical presentation of anemia

All Images Videos News Books Finance

The most common symptoms of anemia are **pallor, fatigue and dyspnea**. In biological exams, anemia is classically associated with microcytosis and hypochromia. The origins of microcytic anemia are iron deficiency, inflammatory aetiologies, thalassemia and sideroblastic anaemia. 11-May-2007

I. Iron Deficiency Anemia:

- **Epidemiology:**
  - It is the most common anemia.
  - It is the most common nutritional disorder in the world.
  - Dietary iron is reabsorbed in the duodenum.
  - Oxidized iron (Fe^{+3}) must be reduced (Fe^{+2}) for reabsorption in duodenum.
  - Iron from plants is in a non-heme, oxidized form (Fe^{+3}).
  - Iron from meat is in heme, reduced form (Fe^{+2}).
  - 80% of functional iron is found in hemoglobin; the rest is stored in marrow macrophages, myoglobin, and enzymes.
  - Ascorbic acid (vitamin C) reduces oxidized iron and is therefore important in iron reabsorption.

- **Causes:**
  - Dietary Lack - children, elderly
  - Increased Utilization - pregnancy, lactation, children
  - Impaired absorption:
    - Celiac disease – absence of villous surface in the duodenum.
    - Gastrectomy – absence of gastric acid, which helps in iron reabsorption.
  - Blood Loss:
    - Gastrointestinal blood loss:
      - **It is most common cause in men and post-menopausal women.**
      - World-wide, hookworm and Schistosomiasis are the most common causes of gut blood loss.
      - It may also occur as result of peptic ulcer disease, gastritis, colorectal malignancy.
    - Menorrhagia (most common cause in women < 50 years)
    - Colorectal cancer (most common cause in patients > 50 years)

- **Clinical Features:**
  - Koilonychia (nail spooning)
  - Angular cheilosis
  - Atrophic glossitis
  - Pica (consumption of non-nutritive substances such as ice, clay)

- **Plummer-Vinson syndrome:**
  - Iron deficiency anemia
  - Esophageal web – dysphagia for solids only (not liquids)
  - Atrophic glossitis
  - Increased risk for squamous cell carcinoma of esophagus.

- **Lab Findings:**
  - Complete Blood Count (CBC)
    - Microcytic anemia (MCV < 80)
    - Thrombocytosis (increased platelet count)
  - Iron Profile:
    - Decreased serum iron
    - Increased total iron binding capacity (TIBC) – TIBC is increased only in this anemia.
    - **Decreased ferritin – best single test to confirm iron deficiency**
    - Decreased transferrin saturation < 15% (Fe/TIBC x 100)
    - Soluble transferrin receptor is increased.

Investigation of causes : GIT : Endoscopy , Barium study
celiac disease :

Rx

Treatment:

- Ferrous sulphate 200 mg 8-hourly:
  - It is given for 3 – 6 months.
  - It provides 195 mg of elemental iron per day.
- Ferrous gluconate 300 mg 12-hourly
  - It is given when the patient is intolerant to ferrous sulphate, e.g. dyspepsia.
  - It provides 70 mg of elemental iron per day.
- Response to therapy:
  - Hemoglobin should rise by 1g/dL every 7 – 10 days.
  - Increased reticulocyte count within 7 days.

Q5a) Causes of:-

- Microcytic anemia:-
  - ✱ Iron deficiency
  - ✱ Thallesemia
- Macrocytic anemia:-
  - ✱ Megaloblastic anemia B12 & folate def
  - ✱ ALD
- Normocytic anemia:-
  - ✱ Sickel cell anemia
  - ✱ G6PD - deficiency
  - ✱ Renal failure

b) Coomb's test:-

- It means that a person has antibodies that act against his RBC's

Increase reticulocyte count:-

- It indicates auto-immune hemolytic anemia.

c) Treat mixed anemia:-

- Ferrous sulphate is the main stay treatment for 2 months.
- Vit B_{12} & F-dic acid supplements

9 A young unmarried female presented to you with severe anemia. Her parents are very much worried about her condition as they are planning for her wedding 03 months later.

a) What are the important investigations you can advise her to confirm anemia, and its possible causes. Discuss in detail, but be specific? (2.5 Marks)

b) What medicines may be prescribed to her?. (2.5 Marks)

① Iron Supplent
② Transfusion RBC
③ IV Iron
④ Food high in Iron
⑤ Ferrous Sulfate Medicine

Q9 a) Investigations:-

- CBC (RBC count, hematocrit, RBC indices, Reticulocyte)
- Blood smear (Poikilocytosis)(Platelet abnormality)
- ~~MCH MCV~~ (if < 8fl = Microcytic hypochromic anemia)(80-100 fl Normocytic Normochromic anemia. >100 fl hyperchromic anemia)
- Schilling test — Urinary excretion, detects Vit
- LFTs, RFTs.
- Serum Iron & transferrin.
- Serum ferritin. - Bone marrow iron staining

Treatment:- Iron supplement

- Trip of vomiting
- Blood transfusion (Packed cell RBC)
- Food rich in iron
- Ferrous sulphate
- Folic acid intake 5mg
- Vit B12 supplement (Methicobal)

Macrocytic Anemia

- It is the group of anemia with MCV > 100.
- It is of two types:
  - **Megaloblastic Anemia:**
    - It is due to impaired DNA synthesis.
    - It is associated with hyper-segmented (> 5 lobes) neutrophils on peripheral smear.
    - It is caused by:
      - Vitamin B12 deficiency
      - Folate deficiency
      - Anti-metabolic drugs (methotrexate, 5-flurouracil)
  - **Non-megaloblastic Anemia:**
    - It is not due to impaired DNA synthesis.
    - It is not associated with hyper-segmented neutrophils.
    - It is caused by:
      - Liver disease
      - Hypothyroidism
      - Alcoholism
      - Lesch-Nyhan syndrome

I. Vitamin B12 Deficiency Anemia:

- **Metabolism:**
  - Vit.B12 is present only in foods of animal origin; total body stores sufficient for 2-3 years.
  - Vit.B12 binds to salivary proteins called "R-binders".
  - R-binders are broken down in the duodenum by the pancreatic enzymes.
  - The released B12 then binds with "intrinsic factor IF", which is produced by gastric parietal cells.
  - Vitamin B12-IF complex is reabsorbed in the terminal ileum.
  - Vitamin B12 binds to transcobalamin-II and is secreted into the plasma.
- **Causes:**
  - Decreased intake:
    - Malnutrition (elderly, alcoholism)
    - Pure vegan diet.
  - Malabsorption:
    - Decreased intrinsic factor – pernicious anemia
    - Decreased gastric acid – cannot activate pepsinogen to pepsin.
    - Pancreatic insufficiency – cannot cleave R-binder

Q.NO.2.(C) A 45 years old lady presented with progressive shortness of breath for last six months, Lab data shows: Hb: 3.8g/dl, TLC: 3000/Cm, platelets: 45.00/Cm, MCV: 112fl, PCV: 0.15, retics: 3%. (Annual 2010)

a. what is the diagnosis? (Sever megaloblastic anemia with pancytopenia)

b. what further investigations are required?

c. what is the treatment?

Q.NO.2.(D) A 58 years old lady is complaining of easy fatigue, breathlessness as well as numbness and pins and needles in her feet and legs. She also says that immediately after taking meals she develops nausea, bloating, sweating and palpitations. In her past medical history it is noted that she is underwent partial gastrectomy seven years ago. Her Hb is 8.8mg/dl and MCV 104 fl. She is negative for H.pylori. (Supplementary 2011)

a. what may the cause of her anemia?

b. how would you explain her post-prandial symptoms?

c. what is the explanation of her numbness and pins and needles?

Q.2.(D)A 40 year old woman presents with shortness of breath on exertion which has been gradually increasing for last 7 months. She also complains of fatigue. She has recently developed paresthesias of extremities and a sore tongue. On examination she is pale and has loss of ankle jerks. Dietary history is insignificant. She is taking treatment for Graves's disease which has been well controlled. Her Hb is 4.5, TLC 4000, Platelet count of 100,000, MCV 119. Her blood film shows hypersegmented polymorphs. TSH is 2 IU/L, HbA1c is 5.6%%. (Annual 2020)

a) What is the most likely diagnosis?
b) How will you manage this patient?

a) Megaloblastic anemia due to pernicious anemia
b) 1000ug vitamin B12 I/M in 5doses (2-3days apart)
Followed by maintenance therapy of 1000ug every 3months for life.

Megalobalstic anemia:

Clinical features:

Symptoms:

- Malaise (90%)
- Paraesthesiae (80%)
- Weight loss
- Gray hair
- Poor memory & depression
- Hallucination
- breathlessness (50%)
- sore mouth (20%)
- altered skin pigmentation
- impotence
- personality change
- visual disturbance

Signs:

- smooth tongue
- vitiligo
- heart failure
- angular cheilosis
- skin pigmentation
- pyrexia

Post prandial syndrome:

Nausea, vomiting, palpitation, sweating, bloating, these symptoms develop after partial gatrectomy known as dumpling.

Causes of numbness and pins and needles:

Vitamin B12 deficiency can result in peripheral neuropathy and subacute degeneration of the spinal cord. Subacute degeneration resulting in diminished vibration sense and proprioception leading to sensory ataxia.

Investigations:

- Hb ↓
- CBCs: (↓RBCs & WBCs +platelets low or normal
- (↑MCV, RDW, MCHC)>120fl
- Reticulocyte count: low
- Peripheral blood picture:
  1. macrocytosis (oval mycrocyte)
  2. anisocytosis
  3. poiklocytosis
  4. hypersegmentation of neutrophil
- Bone marrow examination:
  1. hypercellular fragments
  2. megaloblast
  3. myloid series shift to lift
- Serum indirect bilirubin level: increased
- Plasma LDH: elevated
- Serum ferritin: elevated
- Decreased haptoglobin
- Decreased serum vit B12 level
- Two Part Schilling test: to rule out the cause of vit B12 deficiency (pernicious)
- FIGLO test: differentiate either the anemia is due to vitB12 or folic acid
- Anti-parietal antibodies: positive in case of pernicious anemia
- serum folate level: low

Management:

- Before result of test: (folic acid + vit B12)
- Vitamin B12 deficiency:
  - Inj. Hydroxycoblamin: 1000ug I/M five doses 2 or 3 days apart followed by

maintenance therapy 1000ug every 3 months for life.

- Follow up: Retics count will peak at 5^{th}-10^{th} day & Hb: 10g/l every week.
  The response of marrow: fall in K level & rapid depletion of iron.
  If the blood picture is dimorphic: add iron therapy
- counseling: Sensory neuropathy may take 6-12 months to correct

■ Folate deficiency:

- Tab. Folic acid 5mg OD for 3 weeks (acute deficiency)& 5mg weekly (maintenance)
- Prophylactic Folic acid: pregnancy, autoimmune hemolytic A, haemoglobinopathies.
- Supraphysiological supplementation: 400ug/day ↓ risk of coronary & cerebral vascular diseases by reducing homocysteine.
- Transfusion: in case of sever angina or heart failure: if there is decompensation, Exchange transfusion or slow administration of 1 unit each day with diuretic.

II. Sickle Cell Disease:

- It is an autosomal recessive disorder, with intrinsic defect and extravascular hemolysis.
- It is a type of normocytic anemia with high reticulocyte count.
- **Genetics:**
  - It is caused by a point mutation at position 6 of the β-globin chain resulting in substitution of valine for glutamic acid.
  - Heterozygous Condition:
    - It is known as Sickle cell trait i.e. *HbAS*.
    - It contains 60% normal Hb, and 40% is sickle Hb (HbS).
    - It produces no anemia.
    - Protective against falciparum malaria.
  - Homozygous Condition:
    - It is known as Sickle cell anemia i.e. *HbSS*.
    - It contains 100% HbS, with no normal Hb.
    - It produces anemia.
    - Not protective against falciparum malaria.
- **Pathogenesis:**
  - HbS when deoxygenated undergoes aggregation and polymerization.
  - HbS polymerization causes RBCs to assume a sickle shape and decrease RBC deformability, resulting in hemolysis and microvascular occlusion.
  - Sickling is precipitated by hypoxia, acidosis, dehydration, and infection.
  - Early stages = splenomegaly

- **Lab Diagnosis:**
  - CBC = normocytic anemia with raised reticulocyte count.
  - Peripheral film:
    - Sickle cells
    - **Howell – Jolly bodies** (which are nuclear remnants of RBCs)
  - Sickling Test:
    - Metabisulfite, an O_2-consuming reagent is used.
    - It reduces O_2 tension, and induces sickling.
    - It can't differentiate sickle cell anemia from sickle cell trait.
  - Hb Electrophoresis:
    - It is the most accurate test.
    - HbAS profile = HbA 60%, HbS 40%
    - HbSS profile = HbS 95%, HbF 5%, HbA 0%.
    - Both parents of affected individual will have sickle cell trait.

Treatment:

- **Vaso-occlusive crisis:**
  - Aggressive rehydration
  - Oxygen therapy
  - Analgesia
  - Antibiotics
  - Hydroxyurea
    - It is used in treatment of this disease.
    - It increases HbF and prevents sickling.
    - It can form NO, a vasodilator.
    - It prevents red cells stasis due to its anti-inflammatory effect.
- **Prophylaxis:**
  - Folic acid supplementation
  - Penicillin V (protects against pneumococcal infection)
  - Vaccination against encapsulated organisms:
    - Encapsulated organisms – pneumococcal, meningococcal, H. influenzae
    - Hepatitis B vaccination

VI. Aplastic Anemia:

- It is normocytic anemia with low reticulocyte count.
- It results most commonly from suppression of stem cell function by activated T cells
- **Causes:**
  - Idiopathic = most common
  - Inherited = Fanconi anemia
  - Drugs :
    - Most common known cause.
    - Alkylating agents
    - Chloramphenicol
    - Streptomycin
  - Infections:
    - Cytomegalovirus
    - Epstein-Barr virus
    - Hepatitis
    - Varicella Zoster
- **Clinical Findings:**
  - Anemia = weakness
  - Neutropenia = infection

  - Thrombocytopenia = bleeding
  - Splenomegaly is characteristically absent.
  - Diagnosis:
    1. CBC = pancytopenia
    2. Bone marrow biopsy:
       - It is the most accurate method.
       - It shows hypocellularity, and contain fat cells
    3. Low Reticulocyte count
    4. peripheral Blood Picture
       normocytic normochromic Anemia

Rx

Treatment:

- Supportive:
  - Anemia = blood transfusion
  - Infection = antibiotics
  - Bleeding = platelets
- Young patients (< 30 years) = allogeneic bone marrow transplantationis curative
- Old patients = immunosuppressive therapy with cyclosporin and anti-thymocyte globulin

MEgaloBlastic Anemia

Presence of erythroblast in bone marrow with Delayed maturation
↓
Because Defect of DNA synthesis

Pernicious Anemia:

- CBC
- Peripheral smear
- Schilling TEST (Diagnostic)
  ① ↑ urine methylonic acid
  ② ↑ Homocysteine
  ③ ↓ Vit. B12

① Blood TransFusion
② Rx OF infection
③ Packed platelets
④ Vit. B12
⑤ Folic acid
⑥ iron:

SickIE cell Anemia

It caused by:
Point mutation at position 6 - B Globulin chain
↓
Resulting in substitution of valine → Glutamic acid

InvEstigations:

- CBC
- peripheral smear
- sickling TEST
- Hb - Electrophoresis (Diagnostic)

Treatment:

vaso-occlusive crises

Rehydration
Oxygen
Antibiotic
Analgesic
Hydroxyurea

Prophylaxis:
Folic acid
Penicillin V
Vaccination

Aplastic Anemia

Defined as:
Peripheral Blood Pancytopenia
① (↓ RBC, WBC, Platelets) ② & Aplasia ↓ inability to Produce Blood cell

Suppression of Pluropotential stem cell
↓
By activated T-cell

vaso-ocul
- CBC
- peripheral smear
- ↓ Reticulocyte count
- Bone marrow (Diagnostic)

Supportive:
Anemia → Blood Transfusion
infection → Antibiotic
Bleeding → Platelets

Young pts <30year:
Bone marrow Transplant

Old pts
immunosuppressants
Anti-Thymocyte globulin

Platelet Disorders:

I. Idiopathic Thrombocytopenic Purpura (ITP):

- It is a disease caused by IgG antibodies against Glycoprotein IIb/IIIa receptors.
- It is an isolated thrombocytopenia; hematocrit and WBC count are normal.
- Spleen is normal-sized.
  - Primary ITP = ITP occurring in the absence of any known risk factors
  - Secondary ITP = ITP associated with other diseases or drug exposure.
- **Lab Findings:**
  - Smear = micro-spherocytes
  - Coomb's test is positive

C/F:

1. insidious onset
2. bruising
3. epistaxis
4. menorrhagia
5. Acute ITP in children 2-3 week after viral infection
6. chronic ITP in adult women 20-50 years

Diagnosis:

1. CBC: Anemia, ↓ platelets, WBC normal
2. Peripheral blood picture: normal
3. infection: rule out HIV
4. connective tissue disorders: (ANA, Double strand DNA)
5. BT: ↑
6. PT & APTT: normal
7. Bone marrow aspiration: megakaryocytes ↑
8. platelets associated IgG, IgM
9. detection of platelets autoantibodies

Comb's Test = he

D/D

1. Leukemia: (blast cells)
2. aplastic anemia:(pancytopenia)
3. DIC: (PT & APTT) ↑
4. Lymphoma: (lymphadenopathy)
5. SLE

Management:

Supportive:

1. avoid trauma
2. avoid anti-platelets drugs

Specific:

- platelets count>30,000, no treatment (no symptoms)

- if platelets count>20,000, symptoms
  - 1st line: predinisolone 1 mg/kg (1-4 weeks)
  - IVIG where rapid rise in platelets is required: 1g/kg/day (1-3 days)
  - in case of relapse→reintroduce: corticosteroid
- 2nd line: if two relapses: splenectomy + vaccination
- If splenectomy failed:
  - low dose corticosteroid
  - IVIG (block Fc receptors on macrophages on spleen)
  - I.V anti D 50-75 ug/kg/day for 2 days
  - danazol: patient not responding to predinsolone & splenectomy 600mg/d
  - immunosuppressive agents: azathioprine, cyclophasphamide
  - Rituximab, vica alkaloid
  - repeated infusion of IVIG
  - platelets Transfusion: when platelets count is less than 10,000/ul ①
  - Thrombopoiesis protein,

Short term: Prednisolone i.v & i.v immunoglobulin
Long term: Splenectomy + oral steroids

② Troublesom Bleeding such as : epistaxis
③ Life Threatening condi GI hemorrhage

ACUTE LEUKEMIAS

Acute Myelogenous (or myeloid) Leukemia (AML) is about 8-times more common than lymphoblastic leukemia (ALL) in adults. In young children lymphoblastic variety is more common.

PATHOLOGY

They have the following characteristic pathological features:

- Failure of maturation
- Proliferation of cells which do not mature leads to an increasing accumulation of useless cells which take up more and more marrow space, suppressing the normal cells from bone marrow resulting in anemia, thrombocytopenia and infection.

  These proliferating cells spill into blood causing widespread infiltration in liver, spleen, lymph nodes and other sites throughout the body.

CLINICAL FEATURES

Symptoms

- *Symptoms of anemia:* Headache, fatigue, faintness, palpitation and breathlessness.
- *Infections:* Perianal and skin infection.
- *Hemorrhagic manifestations:* Skin petechiae, bruises, bleeding from gums, nose or persistent bleeding after tooth extraction or tonsillectomy.
- *Bone pain*: Especially sternal tenderness
- *Organ infiltration:* Marked gum hypertrophy.

Signs

- Pallor
- Bruising petechiae, bleeding gums and gum hypertrophy
- Lymphadenopathy
- Splenomegaly–Sight to moderate
- Hepatomegaly
- Hemorrhage in the optic fundus

INVESTIGATIONS

1. Blood CBC

The hallmark of acute leukemia is combination of pancytopenia with circulating blasts. However blasts may be absent in peripheral blood in about 10% of patients called aleukemic leukemia. Platelet count is decreased.

2. Bone marrow biopsy:

The marrow is hypercellular with replacement of normal elements by leukemic blast cells in varying degree. More than 20% blasts are required for diagnosis of acute leukemia.

3. Other investigations

- Serum uric acid: Hyperuricemia
- Serum calcium
- Blood culture
- X-ray chest: Patients with lymphoblastic leukemia may have mediastinal mass visible on chest X-ray.
- CSF: Meningeal leukemia will have blast cells in CSF in about 5% of cases at diagnosis.

These investigations are done to see tumor lysis syndrome in which rapid destruction of leukaemic cells, liberation of phosphate and other intracellular components result in hyperphosphatemia, hypercalcemia, hyperkalemia and hyperuricemia.

Differentiation between myeloid and lymphoblastic leukemia

Acute myelogenous leukemia

The Auer rod, an eosoinphilic needle-like inclusion in cytoplasm of blast cells, is pathognomonic of acute myelogenous leukemia.

To confirm the myeloid nature of the cells, histochemical stains demonstrating myeloid enzymes such as myeloperoxidase may be useful.

Acute lymphoblastic leukemia

Diagnosis is confirmed by demonstrating surface markers characteristic of lyphoid cells as following:

Terminal Deoxynucleotidal Transferase (TdT) is present in 95% cases of acute lymphoblastic leukemia.

MANAGEMENT

- Supportive treatment
- Specific treatment

Bone marrow Transplantation

SUPPORTIVE TREATMENT

- **Anemia:** Blood transfusion (packed cell volume)
- **Thrombocytopenia:** Platelets transfusion
- **Infections:** Antibiotics

Bacterial:

Antibiotics are given according to the organism isolated from culture; mean while gentamicin + azlocilin is given for 9 days. The organisms most commonly associated with severe neutropenia are gram-negative bacteria such as E, coli, pseudomonas and klebsiella, and gram-positive bacteria such as staphylococcus areus. Patients with lymphoblastic leukemia are suspected to infection with pneumocystis carinii which causes severe pneumonia. Treatment is with high dose cotrimoxazole.

Fungal:

- Prophylactic for oral infection nystatin suspension 1ml held in mouth
- Established infection: Nystatin suspension 1ml QID.
- Systemic infection I/V amphotericin
- Topical gentian violet paint for severe infection.

Viral

Herpes simplex around the mouth and nose is treated with Acyclovir cream applied to the lesion QID OR Tab. Acyclovir 200 mg 5 times/day for 5-10 days.

07

PREPARATIONS FOR SPECIFIC THERAPY

- Existing infection should be identified and treated (e.g. urinary tract infection, oral candidiasis, dental, gingival and skin infections).
- Anemia corrected with red cell concentrate infusion.
- Thrombocytopenic bleeding controlled with platelet transfusion.
- If possible, insertion of silastic catheter in to the neck veins for venous access.
- Careful explanation of the therapeutic regimen to the patient.

SPECIFIC TREATMENT

The aim of treatment is to destroy the leukemic clone of cells without destroying the residual normal stem cells. There are three phases of treatment as following:

- Remission induction phase
- Remission consolidation phase
- Remission maintenance phase

1. Remission induction phase

In this phase bulk of the tumor is destroyed by combination chemotherapy. The patients go to periods of marrow hypoplasia requiring intensive supportive therapy.

2. Remission consolidation phase

If remission has been achieved by induction therapy, residual disease is attacked by therapy during this (remission consolidation) phase. This consists of a number of courses of chemotherapy. In acute lymphoblastic leukemia it is necessary to give therapy to the central nervous system (intrathecal methotrexate) along with cranial radiation.

3. Remission maintenance phase

When bulk of tumor is reduced to a minimum, maintenance therapy is given in acute lymphoblastic leukemia for a period of about 2-3 years. This phase is not required in acute myelogenous leukemia.

DRUGS COMMONLY USED IN THE TREATMENT OF ACUTE LEUKEMIA

Phase	Lymphoblastic	Myelogenous
Induction phase	Vincristine IV Prednisolone oral L-asparaginase IV Daunorubicin IV Methotrexate (intrathecal)	Daunorubicin IV Cytarabine IV Etoposide IV oral Tioguanine oral
Consolidation phase	Daunorubicin IV Cytarabine IV Etoposide IV oral Methotrexate IV	Cytarabine IV Amsacrine IV Mitoxantrone IV
Maintenance phase	Prednisolone oral Vincristine IV Mercaptopurine oral Methotrexate oral	

TREATMENT OF RECURRENCE (RELAPSE)

ALL

A proportion of patients are cured with initial therapy. In the rest of them, disease recurs and ultimately proves fatal unless second remission is achieved with chemotherapy and bone marrow transplantation.

Common sites for relapse: Bone marrow, CNS, testis

- Bone marrow relapse–marrow transplantation
- CNS relapse–intrathecal drugs and craniospinal irradiation.
- Testicular relapse–irradiation and re-induction of therapy.

AML

- With modern combination chemotherapy, approximately 70-80% of patients of acute leukemia under age 60 years achieve complete remission.
- However within 1-3 years disease recurs in at least 60% of patients. In young patients if second remission is achieved cure may be possible with allogenic or autologous bone marrow transplantation.
- Older patients with AML achieve complete remission in up to 50% of cases. In recurrence intensive chemotherapy, antibiotics, blood transfusion and hydroxyurea.

POOR PROGNOSTIC FEATURES IN ACUTE LEUKEMIA

- Increasing age
- Male sex
- High leukocyte levels at diagnosis
- Cytogenic abnormalities
- CNS involvement at diagnosis

Lymphomas

- Lymphomas are neoplasms that arise from lymphoid tissues.
- Lymphoid neoplasms are classified into;
  - Hodgkin lymphoma (HL)
  - Non-Hodgkin lymphoma (NHL)

	Hodgkin Lymphoma	Non-Hodgkin Lymphoma
1	It is mostly localized to a single axial group of nodes.	It mostly involves multiple peripheral nodes.
2	Contagious spread	Non-contagious spread
3	Mesenteric nodes and Waldeyer's ring rarely involved.	Mesenteric nodes and Waldeyer's ring commonly involved
4	Extranodal involvement uncommon.	Extranodal involvement common.
5	Reed-Sternberg cells present	Reed-Sternberg cells absent.

I. Hodgkin Lymphoma:

- **Clinical Features:**
  - Lymph node enlargement; most often of the cervical nodes.
    - Lymph nodes are painless with a rubbery consistency
    - Lymph nodes are involved in a **"contagious pattern"** i.e. orderly anatomic spread to adjacent nodes
  - Hepatosplenomegaly
  - Systemic "B" symptoms:
    - Fever
    - Drenching night sweats
    - Weight loss of > 10% bodyweight.
- **WHO Classification:**
  - Classic HL:
    - Nodular sclerosis
    - Mixed cellularity
    - Lymphocyte-rich
    - Lymphocyte depletion
  - Non-classic HL:
    - Lymphocyte predominance

D/Ds:

1. Hodgkin Lymphoma
2. Lymphocytic Lymphoma
3. Thymoma
4. Sarcoidosis

Diagnosis:

① ○ CBC = normal, or may show normochromic normocytic anemia, lymphopenia

② ○ ESR = raised

○ Serum LDH = raised level is associated with poor prognosis.

Radio-imaging

○ CXR = mediastinal widening ± lung involvement

○ CT scan chest, abdomen and pelvis

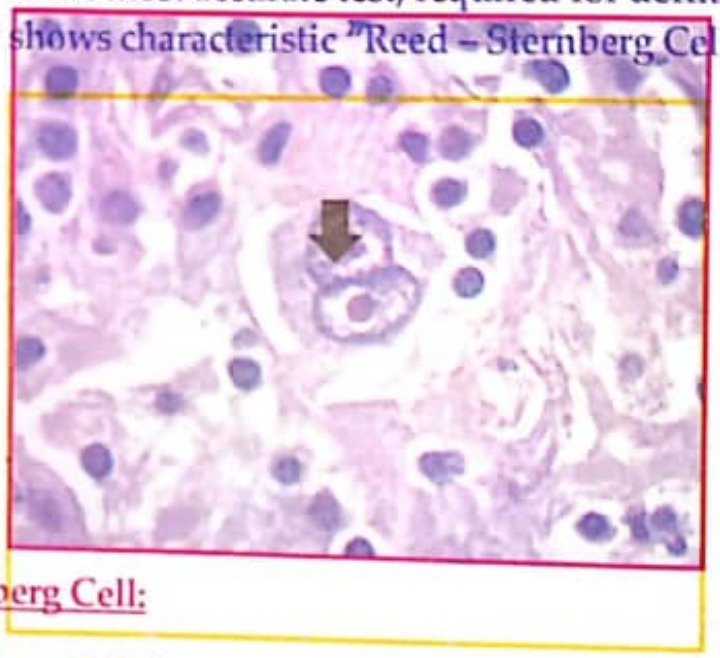
○ Positron emission tomography (PET) scan – for staging and assessing response to therapy

③ ○ Excisional Lymph Node Biopsy:

- It is the most accurate test, required for definitive diagnosis.
- It shows characteristic "Reed – Sternberg Cells".

OTHERS

LFTs, RFTs



④ Reed-Sternberg Cell:

Reed-Sternberg Cell: Large B-cell with Bi-lobular Nuclei with halves As mirror-images ("owl's eyes") and eosinophilic nucleoli

Treatment of HL:

- Local Disease (Stage IA & IIA):
  - Chemotherapy (ABVD regimen) + Radiotherapy
- Advanced Disease (Stage III, IV, or any B-symptom):
  - Chemotherapy (ABVD regimen) only (6 – 8 cycles):
    - A = Adriamycin (or doxorubicin)
    - B = Bleomycin
    - V = Vincristine (or vinblastine)
    - D = Dacarbazine
- Relapse after radiotherapy = chemotherapy
- Relapse after chemotherapy = high-dose chemotherapy + bone marrow transplantation

6. A 28 years old male was referred to you for work up of cervical lymph nodes enlargement which he noticed about 4 months back. He had occasionally low grade fever which responded well to antipyretics, He denies any contact history of tuberculosis On examination, both cervical and axillary lymph nodes are enlarged bilaterally , rest of the examination is unremarkable Complete blood count is normal?

a) What is your differential diagnosis? (01Mark)
b) What is most likely diagnosis? And why? (02Marks)
c) How would you investigate this patient? (02Marks)

6ba) Differential Diagnosis -
- Sarcoidosis
- Lymphocytic lymphoma
- Thymoma
- Hodgkin's lymphoma

b) Hodgkin lymphoma because of enlargment of cervical & axillary lymphnodes along with fever.

c) Investigation:
- CBC: Anemia, TLC↑
- ESR↑ CRP↑
- Biopsy (Reed-sternberg cell)
- Bone marrow examination.
- CT-scan, Pet scan, MRI
- Other test:- LFT's, RFT's

Causes of low platelet count:

1. Leukemia
2. viral infection : Hep.C & HIV
3. Heavy Alcohol consumption
4. ITP (common cause)

If a patient comes to you with severe chronic anemia and her immediate surgery is require for strangulated hernia. There is a dire need of multiple transfusion.

a) Describe briefly the ABO system regarding blood transfusions.
b) Which infections can be transmitted through blood transfusions?
c) Which blood groups are universal donors and universal recipients?

Hepatitis B, C
HIV,
Syphilis, Cytomegalovirus,
Malaria

O−

AB+

Blood Type	Antigens on rbcs	*Antibodies* in blood	Safe transfusions	
			To	From
A	A	B′	A , AB	A , O
B	B	A′	B , AB	B , O
AB	A , B	-	AB	A , B , AB , O
O	-	A′ , B′	A , B , AB , O	O

SALMAN MANZOOR

BLOOD TRANSFUSION

Annual 2021 :

A 50 year old undergoes Partial Hepatectomy For 2rdary metastasis. The operation proceeded smoothly For 1st couple of hour After which surgical Team noticed unusal Bleeding in the Form of oozing from wound site. The Pts has 2 IV cannula sites through one of which he is on his First unit of Blood.

(a) What Complications is suspected

(a) Transfusion Reaction (single)

- Acute immune hemolytic Reaction
- Delayed immune hemolytic Reaction
- Allergies
- Febrile convulsion
- Transfusion Related acute lung injuries
- Graft versus host Disease

(b) infections

- Bacterial infection
- HBV
- HCV
- HIV
- Malaria
- Syphills
- CMV
- Pseudomonas

(c) Storage complication

- Hyperkalemia
- Hyperammonia
- metabolic acidosis
- Hypothermia
- Hypocalacemia

Massive Transfusion

- Hyperkalemia
- Hypokalemia
- Hypocalcemia
- Hypothermia
- Coagulopathy
- metabolic acidosis
- ARDS

(b) **How will you manage this patient**

① Rapid recognition is essential & immediate stopage of Blood

② Shock Therapy - Steroids, vesopressors, respiratory ventilation
maintenance of Renal System

③ Antihistamine

④ I/v Antibiotic

⑤ mannitol & Large Fluids (Avoid colloid & crystalloids)

⑥ If DIC is suspected
Fresh Frozen Plasma
Platelets
Fibrinogens

⑦ Vitals monitoring

⑧ sent Clotted Blood Sample to the Laboratory

April-2019

How Transfusion Complication can prevented.

Preventions :

1. Proper cross matching
2. monitoring while Given Blood
3. Stop Transfusion immediately
4. Fever – paracetamol
5. Prophylactic antibiotic

Safety Criteria / measures

ABO Blood Grouping & RH incompetability Prior to collection

Cross matching

Detection of Antibodies

Screening for - HIV, HCV, HBV, malaria, syphilis

Blood donor should be Fit

Paraproteinemias

- Gammopathy refers to over-production of one or more classes of immunoglobulin.
- Polyclonal gammopathy means that a single clone of plasma cells produces different immunoglobulins (Ig).
- Monoclonal gammopathy means that a single clone of plasma cells produces identical immunoglobulins (Ig).
- Monoclonal immunoglobulins are called "M-proteins", or "Paraproteins".

I. Multiple Myeloma (MM):

- **Introduction:**
  - It is a plasma cell neoplasm (plasma cells are formed by B-cells).
  - It is the most common **symptomatic** monoclonal gammopathy.
  - Peak age is 70 years; rare under 40 years of age.
- **Pathogenesis:**
  - In multiple myeloma, plasma cells are monoclonal i.e. a single clone of plasma cells produces identical immunoglobulins.
  - Monoclonal immunoglobulins show "M-spike" on protein electrophoresis.
  - Most common types of monoclonal Ig or Paraproteins are:
    - IgG =55%
    - IgA =25%
    - Light-chain only =22%
- **Clinical Features:**
  - Skeletal System:
    - Multifocal destructive (lytic) bone tumors
    - Bone pain and hypercalcemia – due to increased osteoclast activity.
    - Pathologic fractures.
    - Common site: axial skeleton:
      - Vertebral column – most common
      - Ribs; Skull; Pelvis & femur
  - Hematologic:
    - Normocytic anemia
    - Rouleaux formation due to increased serum M-proteins
    - Increased erythrocyte sedimentation rate (ESR) > 100
    - Coagulopathy and increased bleeding time.

- Renal Disease:
  - **Bence Jones Nephropathy:**
    - Bence Jones proteins refer to light-chain proteins in the urine.
    - BJ proteins cause "cast- nephropathy", which is renal failure due to toxic effect of filtered light-chains.
    - BJ proteins damage tubular epithelium with intra-tubular multinucleated giant cell reaction.
  - Nephrocalcinosis:
    - It presents as renal failure in multiple myeloma.
    - It is metastatic calcification of tubular basement membranes in the collecting ducts.
- Amyloidosis:
  - It is AL (amyloid light-chain) type.
  - It is due to secretion of amyloidogenic Ig light chains.
  - It presents as nephrotic syndrome.
- Infections:
  - It is the **most common cause of death** in MM.
  - Recurrent infections due to decreased normal immunoglobulins.
  - Streptococcus pneumoniae, S. aureus, and E. coli are the common pathogens.
  - Cellular immunity is relatively unaffected.

- Protein Electrophoresis
- ↓ Anion Gap
- Beta-2 microglobulin
- Bone marrow Biopsy

- **Diagnosis:**
  - Protein Electrophoresis (PEP):
    - Serum PEP = increased Ig in serum > 3 gm/dL.
    - Urine PEP = increased BJ (light-chains) in urine (more than 6 gm/dL)
  - Increased ESR (> 100) and CRP
  - Decreased anion gap.
  - **Beta-2 Microglobulin – corresponds to disease severity (useful in prognosis)**
  - **Raised serum LDH – corresponds to disease severity (useful in prognosis)**
  - Elevated blood urea nitrogen (BUN) and creatinine
  - Elevated total protein with normal albumin.
  - Bone marrow biopsy:
    - Increased plasma cells > 10% on bone marrow biopsy.
    - Russel bodies (PAS positive intra-cytoplasmic Ig-containing inclusions)

CBC
↑LDH
ESR, CRP

- Dutcher bodies (PAS positive intra-nuclear Ig-containing inclusions)

- Skeletal survey = characteristic lytic lesion, mostly seen in the skull.

Clinical Pearl:

Multiple Myeloma Diagnostic Criteria:

- 2 out of 3 diagnostic features should be present:
  1. Serum and/or urinary paraprotein.
  2. Increased malignant plasma cells in the bone marrow
  3. Skeletal lytic lesions

Treatment:

- Transplant Candidates (age < 70):
  - High dose chemotherapy
  - Hematopoietic stem cell transplantation (HSCT)
- Non-transplant Candidates (age > 70):
  - Melphalan + Prednisolone, PLUS:
  - Thalidomide – OR – Lenalidomide
- Adjuvant:
  - Bone = bisphosphonates
  - Anemia = transfusion and erythropoietin
  - Infections = broad-spectrum antibiotics
  - Renal:
    - Avoid NSAIDs & IV contrast,
    - ① Rehydrate, and ensure adequate fluid intake
    - ② Dialysis may be indicated in acute renal failure

Q.8.A 32 yew old females comes with recent onset complaints of low grade fever and yellow discoloration of eyes and urine. One examination she has palpable spleen. While the investigation shows Hb 8 gm/dl with Retics 5%. Bilirum 5mg/ dl with 4mg Indirect bilirubin and urinary urobrilinogen +ve while HBsAg and Anti HCV are negative by ELISA. (Supple 2018 held in 2019)

a) What is the probable diagnosis? If the disease is caused by autoantibodies without any infection then what can be the four possible causative factors?
b) What abnormalities can be seen on peripheral blood picture of this patient? How will you treat this patient?

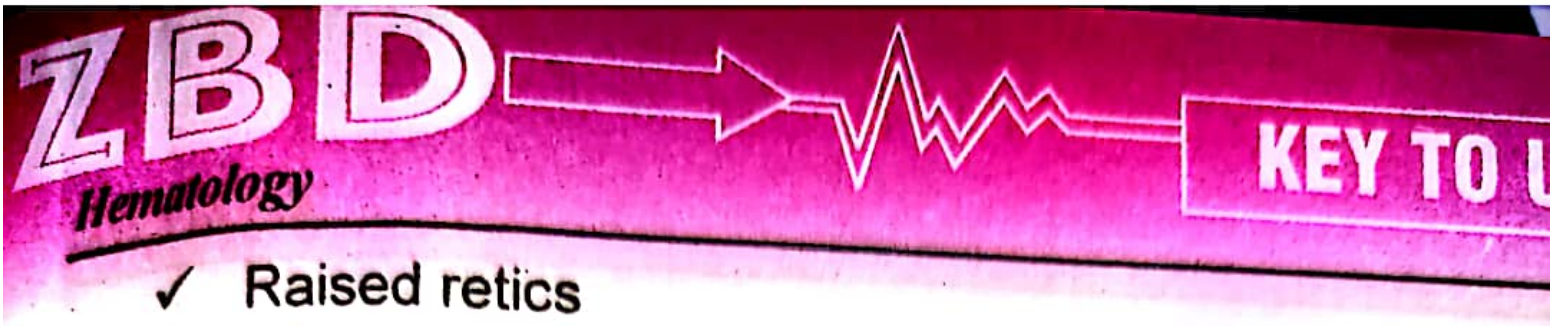
a) Diagnosis: Autoimmune hemolytic anemia

Causes of autoantibodies hemolysis without infections:

1. Idiopathic
2. Lymphoproliferative disorders (Lymphoma)
3. Autoimmune (SLE, RA)
4. Drugs: L-dopa, methyldopa, mefenamic acid
5. CLL, myeloma
6. UC

b) *Peripheral pictures of hemolysis:*

- ✓ Polychromasia
- ✓ Spherocytes



- ✓ Raised retics

Treatment:

- Treat the cause
- Stopp offending drug
- Prenisolone 1 mg/kg
- Transfusion support for life threatening anemia
- Immunosupression
- Splencetomy
- Anti-CD20 monoclonal antibody (Rituximab)

Q.NO.6 A 23 years old primigravida has been found to have mild anemia during outline antenatal examination. Her husband, who is his first cousin, also has mild anemia. Blood tests of the patient show Hb: 10.6gm/dl with hypochromic microcytic picture. (S/2008)

a. Name TWO major causes of this type of anemia.

b. What further investigations should be performed to determine the cause of anemia?

c. What are the possible risks to the baby?

d. How could you prevent any serious complication in this baby?

a. Thalassemia minor
Iron deficiency anemia

b. see below

c. **Risks:**
i) Thalassemia major
ii) Abortion, hydrops fetalis
iii) IUGR, IUD

d. **see below**

Beta-Thalassemia

Definition : inherited disorder of microcytic hemolytic anemias characterized by the Absence or decreased synthesis of the beta globin chain of hemoglobin.

Types:
1. Heterozygous states: Thalassemia minor
2. Homozygous states: Thalassemia intermedia & major

Clinical Manifestations:
1. patients are symptomatic by 12 months of age (often as early as 3 months)
2. sever anemia & icteric tinge
3. mandibular prominence, depressed nasal bridge, frontal bossing
4. abdomen become protuberance due to massive hepatosplenomegaly
5. iron overload results in:
   - hepatic fibrosis & cirrhosis
   - darkening of skin
   - sideroblastic cardiomyopathy (arrhythmias, CCF)
   - Endocrinopathies (DM, hypothyrioidism)

Diagnosis:
1. CBC: Hb: 5-6 or less
2. Retics: increased 5-10% leukocytosis
3. RBC morphology: Microcytic hypochromic anemia, Anisocytosis, poikilocytosis, Target cell, nucleated RBCs & Heinz bodies HbF↑, HbA2↑
4. Hemoglobin Electrophoresis: it is diagnostic ↑ Serum Ferritin
5. Serum: • serum iron is elevated • TIBC • normal or elevated bilirubin
6. Imaging studies: Hair on end pattern & thinning of long bone cortices on X-ray

Complications:
1. Iron overload:
   - Cardiomyopathy
   - Heart failure
   - Arrhythmias
   - Hepatic fibrosis, cirrhosis
   - Endocrinopathy
     - Hypothyroidism
     - Hypoparathyroidism
     - Diabetes mellitus
     - Hypogonadism
     - Delayed puberty
3. Bone disease
   - osteopenia
   - osteoporosis
4. Infections: prone to infections caused by HBV, HCV & Yersinia enterocolitis
5. Hypercogulopathy: • pulmonary embolism • cerebral ischemia • DVT

6. Alloimmune & RBCs autoimmunization:

Management:

1. General:
   - Discussion should be done with parents about the nature, prognosis & Rx
   - Goals of therapy: maintain normal Hb level, prevent iron accumulation & promote iron excretion.
2. Transfusion therapy:
   - packed RBCs transfusion (15-20ml/kg) should be given every 4-8 weeks to Maintain hemoglobin above 10 g/dl (hyper-transfusion) or above 12 g/dl.
   - Required amount of packed cells: Desired Hb - present Hb × Wt in kg × 3
   - Each unit of blood contains 200mg of iron.
3. Chelation therapy:
   - Deferoxamine (Desferal) 20-60 mg/kg Sc over 8 hours by an infusion pump for a minimum of 5 nights/week
   - Deferoxamine is initiated b/w 4-5 yrs of age when serum ferritin is greater than 1000 ng/ml & transferrin is ▯ 50% saturated
4. Ascorbic acid, folic acid
5. Splenctomy
6. Bone marrow transplantation (Permanent solution)
7. Gene therapy
8. Hydroxyurea

Prevention:

- Genetic counseling