APLASTIC ANEMIA

Objectives

* definition of aplastic anemia .
* pathophysiology .
* classification .
* management.

APLASTIC ANEMIA

A reduction or absence of hematopoietic precursors in all 3 cell lineages in the bone marrow resulting in pancytopenia in peripheral blood.

Incidence :

- Rare disease ~ 5 cases/ million annually.
- Wide age range (peak incidence around 20-30 yr).

APLASTIC ANEMIA

- Pathophysiology:
  - The primary defect is a reduction in or depletion of hematopoietic precursor stem cells with decreased production of all cell lines. This is what leads to the peripheral pancytopenia.
    - This may be due to quantitative or qualitative damage to the pluripotential stem cell.
    - In rare instances it is the result of abnormal hormonal stimulation of stem cell proliferation or
    - the result of a defective bone marrow microenvironment or
    - from cellular or humoral immunosuppression of hematopoiesis.

Causes :

primary :-

A - Hereditary : Fanconi's syndrome.

B - Idiopathic, Acquired : Constitute the majority of cases ,diagnosed by excluding other secondary causes of A.A.(detailed H/O exposure to drugs , chemotherapy , radiation , chemicals) .

Secondary :

Irradiation , chemotherapy , chronic benzene exposure, insecticides , post viral infections (Hepatitis)

Drugs : gold, antiepileptic , antithyroid drugs, immunosuppressant .

Classification :

Severity	Criteria
Severe	Bone marrow cellularity <25% (or if <30%, 25-50% residual hematopoietic cells) and at least two of the following: Peripheral blood neutrophil count <500/μL Peripheral blood platelet counts <20,000/μL Peripheral blood corrected reticulocytes <1%
Very severe	As severe, but peripheral blood neutrophil count <200/μL
Non-severe	Hypocellular bone marrow with peripheral blood cytopenias not fulfilling criteria for severe or very severe aplastic anemia

Clinical features :

reflects the pancytopenia :

- Bleeding.
- Infection.
- Symptoms of anemia.

Diagnosis & Investigation :

A - CBC & PBF & Retics :

picture of pancytopenia :

- normo – macrocytic Rbcs. ,Reticulocytopenia.
- Leukopenia : Neutropenia .
- Thrombocytopenia.

- B. marrow aspirate + biopsy :

gross variable reduction in all hematopoietic tissue

which replaced by fat cells leads to hypoplasia or aplasia.

no evidence of blasts or abnormal cells

- Flocytometry " CD55 & CD59 ".

- Cytogenetic study , LFT, viral serology ,

- vitB12 & folate estimation , radiological study.

Complications:

- Progression to more severe disease.
- Evolution to PNH.
- Transformation to acute leukemia.

D/D :- acute leukemia , PNH ,MDS.

APLASTIC ANEMIA: CRITERIA FOR DIAGNOSIS

1. Cytopenia (Hb<6.6 mmol/l; ANC<1,5 G/L; PLT<100 G/L)
2. Bone marrow histology and cytology
   - loss of hematopoietic parenchyma,
   - increased fat cells component,
   - no extensive fibrosis,
   - no malignancy or storage disease
3. No preceding treatment with X-ray or antyproliferative drugs
4. No lymphadenopathy or hepatosplenomegaly
5. No deficiencies or metabolic diseases
6. No evidence of extramedullary hematopoiesis

Causes of pancytopenia :

- B.M. failure : Hypoplasia , aplasia , viral , drugs.

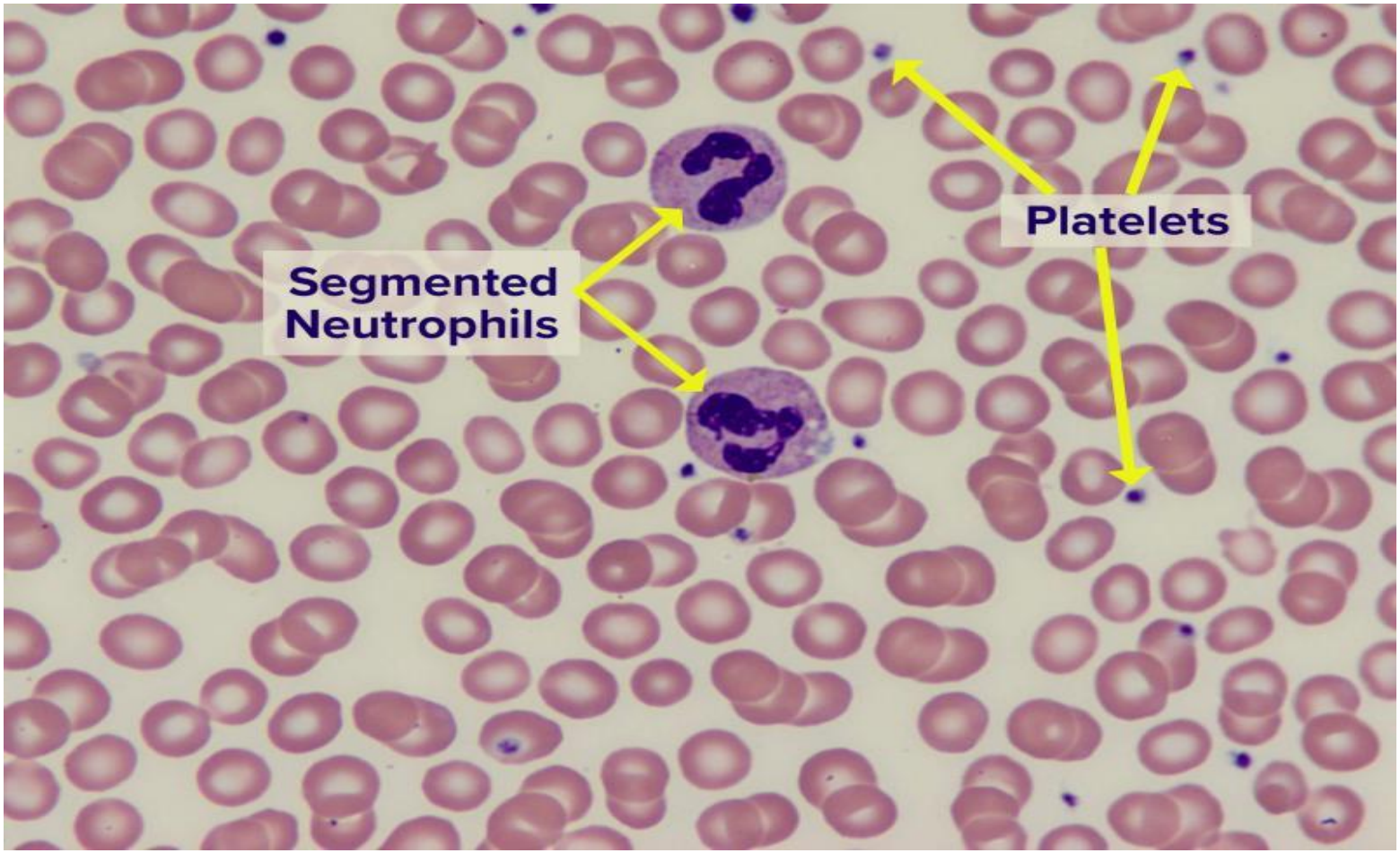
- B.M. infiltration : A.Leukemia , Myeloma ,
Carcinoma , MDS.

- Ineffective hematopoeisis : Megaloblastic Anemia .
AIDS.
- Peripheral pooling/ destruction :
  * Hypersplenism (portal hypertension ,
felty syndrome , malaria).
  * Autoimmune disorders (SLE) .

ACQUIRED APLASTIC ANEMIA - CAUSES

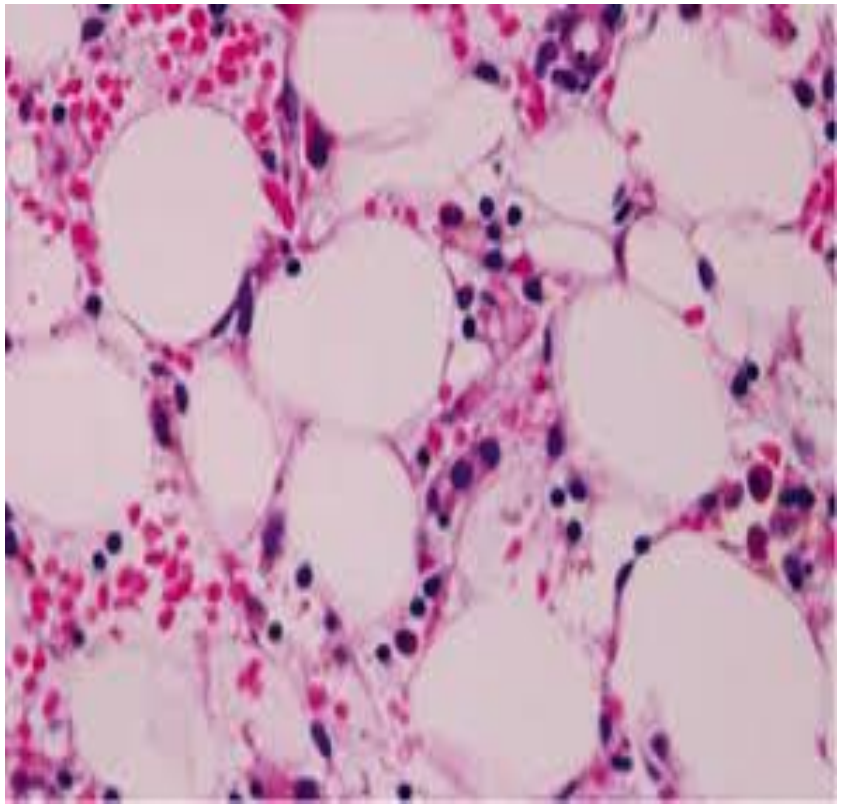
- **Radiation**
- **Drugs and chemicals**
  - chemotherapy
  - benzene
  - chloramphenicol
  - antiepileptics
- **Viruses:**
  - CMV
  - EBV
  - Hep B, C,D
  - HIV
- **Immune diseases:**
  - eosinophilic fascitis
  - thymoma
- **Pregnancy**
- **PNH**
- **Marrow replacement:**
  - leukemia
  - myelofibrosis
  - myelodysplasia

Normal PBF

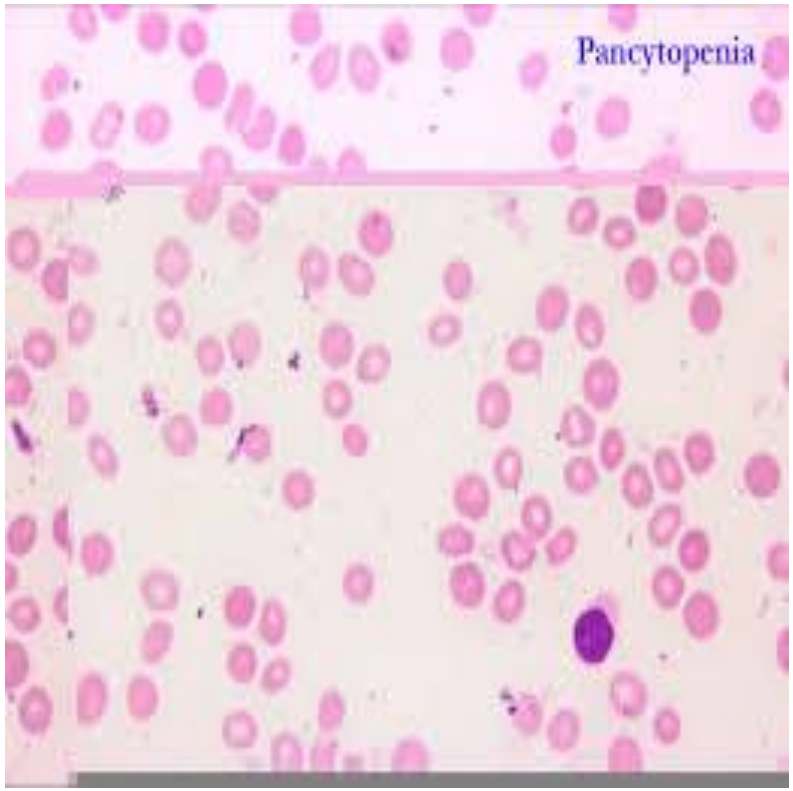


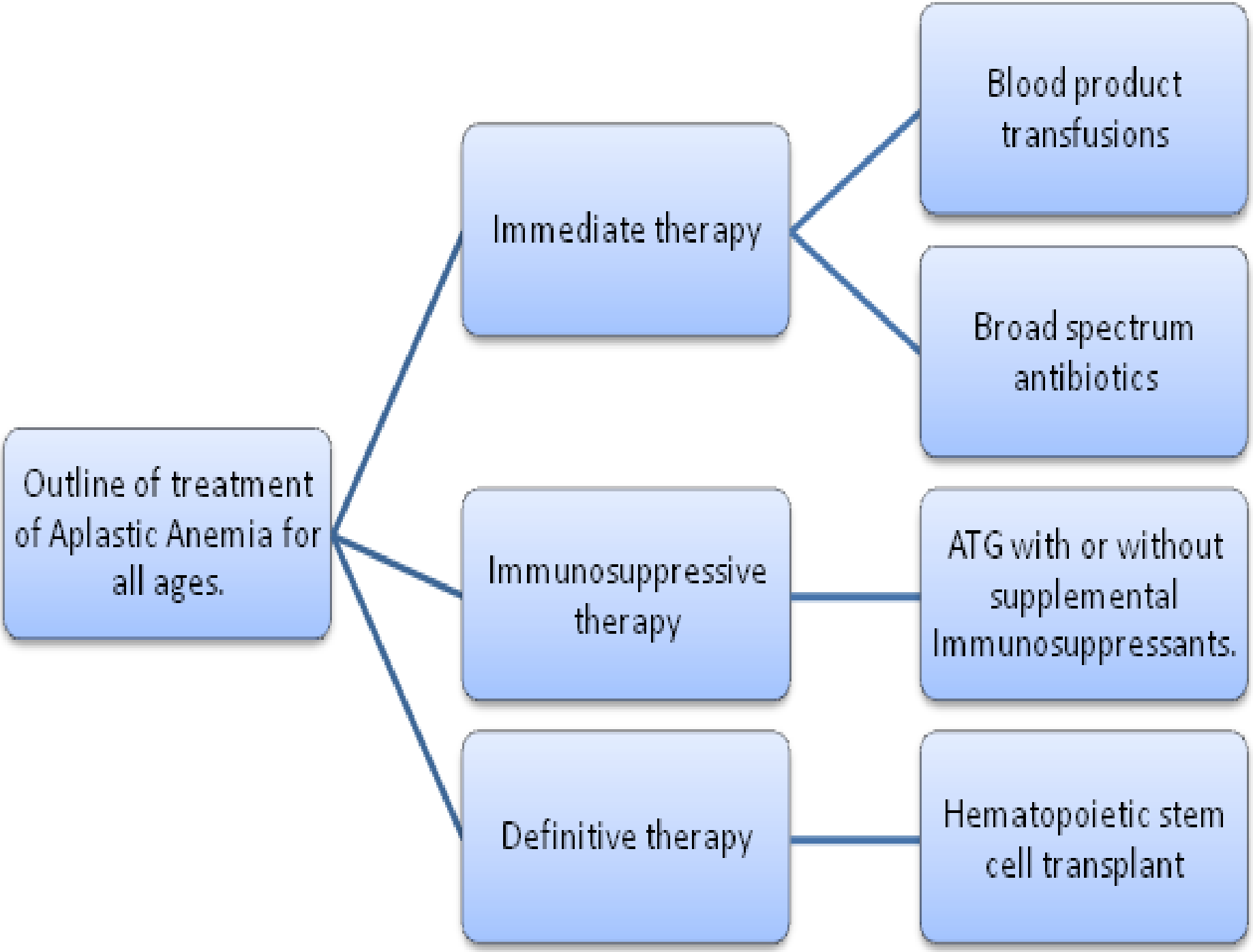

Normal BM Aspirate

B.M in A.A.



PBF in A.A.




Outline of treatment of Aplastic Anemia for all ages.
Immediate therapy
Blood product transfusions
Broad spectrum antibiotics
Immunosuppressive therapy
ATG with or without supplemental Immunosuppressants.
Definitive therapy
Hematopoietic stem cell transplant

Treatment :

- ***Mild cases:*** close observation and supportive treatment according to presentation.

- ***Sever cases :***

1- supportive (plts . Blood . Antibiotics)

2- Immunosuppressive therapy by :

- Antilymphcyte globulin ± cyclosporine.
- Cyclosporine alone.
- Androgens or danazole.

3 - Sibling allogeneic transplant.

Prognosis :-

- >50% of severe aplastic anemia cases who were treated with supportive therapy only will die in the first year .
- A better survival (60%) has been reported in cases who were treated with B.M.Trans-plantation or immunosuppressive agents.

… THANK YOU