Aplastic anemia

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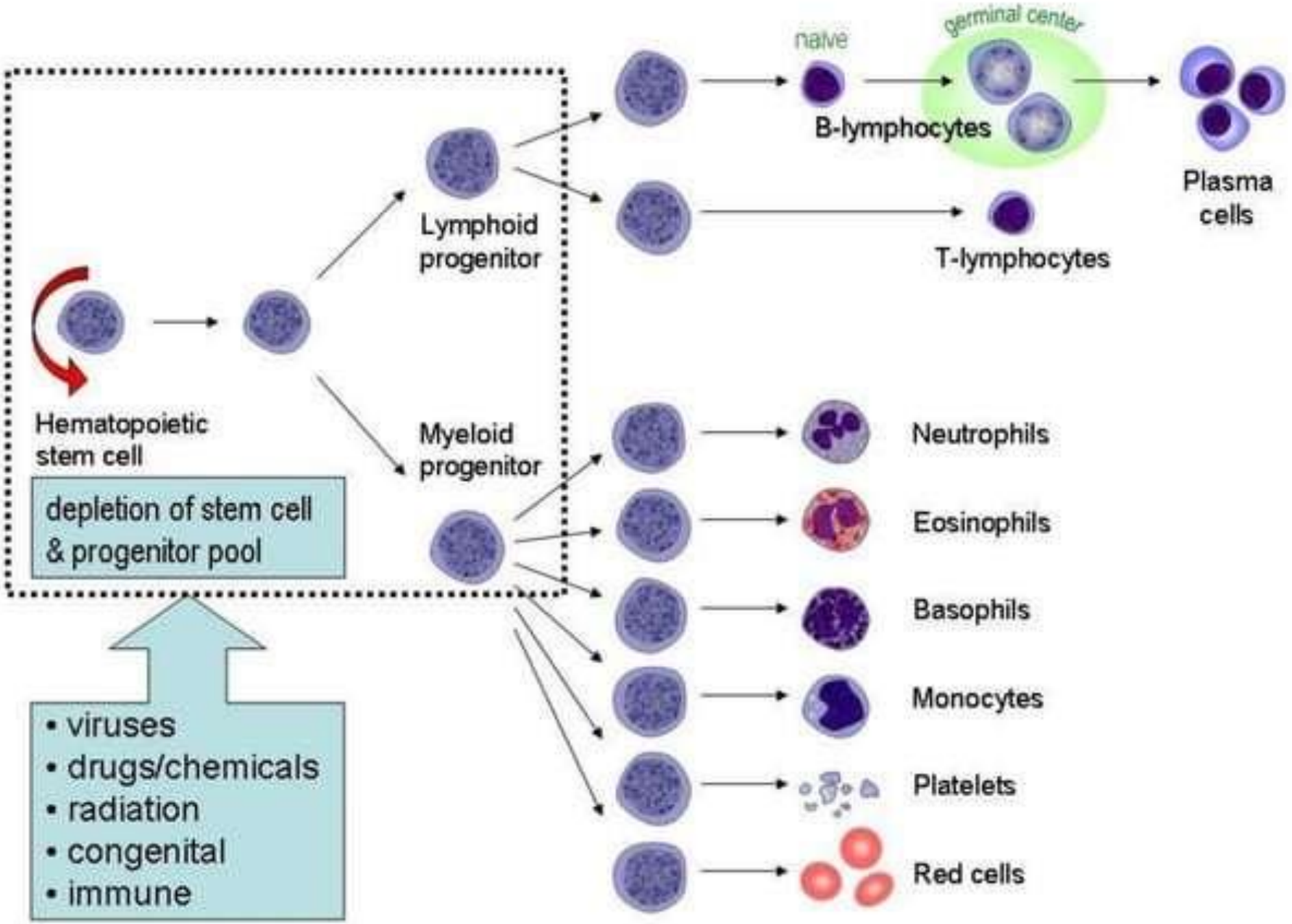
Just like normal and aplastic marrow

The Bone Marrow is the blood Factory

May be exposed to damage or failure


naive
germinal center
B-lymphocytes
Plasma cells
Lymphoid progenitor
T-lymphocytes
Hematopoietic stem cell
Myeloid progenitor
depletion of stem cell & progenitor pool
Neutrophils
Eosinophils
Basophils
Monocytes
Platelets
Red cells
• viruses
• drugs/chemicals
• radiation
• congenital
• immune

Pancytopenia – What??

- Therefore it is the combination of anemia, leukopenia, and thrombocytopenia :-
  - Hb < 13.5 in males & 11.5 in females
  - Leucocyte count < $4x10^9$ /l
  - Platelet count < $100x10^9$ /l

Pancytopenia

- Primary bone marrow disease

1. MDS
2. PNH
3. Myelofibrosis
4. Mylophthisis
5. Hairy cell leukemia
6. Aleukemic leukemia

- Secondary to systemic disease

1. SLE
2. B12 or folate difficiency
3. Hypersplenism
4. Overwhelming infection
5. Brucellosis
6. Sarcoidosis
7. T.B.

Aplastic Anemia

Definition:

- ✓ Pancytopenia with hypocellularity (Aplasia) of Bone Marrow
- ✓ Aplastic anemia is a severe, life threatening syndrome in which production of erythrocytes, WBCs, and platlets has failed.

- Aplastic anemia may occur in all age groups and both genders.
- Failure of the bone marrow percursors to produce mature cells. Characterized by hypocellular marrow and pancytopenia.

Etiology

Acquired: More common
Inherited: Fanconi anemia
Acquired:

Idiopathic: 65%

1. Drugs

Inevitable:

Dose related , reversible.g. cytotoxic drugs, ionizing radiation.

The timing, duration of aplasia and recovery depend on the dose.

Recovery is usual except with whole body irradiation.

e.g., chemotherapeutic drugs)

Idiosyncratic:

Unpredictable to drugs e.g., anti-inflammatory antibiotics, anti-epileptic, these agents usually do not produce marrow failure in the majority of persons exposed to these agents

- Cytotoxic drugs
- Chloramphenicol
- Anti-convulsant
- Antibiotics
- Anti-inflammatory
- Sulphonamides

Aplastic Anemia: (Cont.)

Acquired:

- Radiations
- Chemicals e.g., Benzene and pesticides
- Viruses:
  - Hepatitis A, Non-A and Non-B
  - Herpes simplex
  - E-B virus
  - Parvovirus: Transient
- Immune: SLE, RA (rheumatoid arthritis)

INHERITED(20%)

Fanconi Anaemia

- substantial reduction in the number of haemopoietic pluripotential stem cells, and a fault in the remaining stem cells or an immune reaction against them, which makes them unable to divide and differentiate sufficiently to populate the bone marrow.
- A primary fault in the marrow microenviromnent has also been suggested but the success of stem cell transplantation (SCT) shows this can only be a rare cause because normal donor stem cells are usually able to thrive in the recipient's marrow cavity.

Pathogenesis

Potential mechanisms:

Absent or defective stem cells (stem cell failure).
Abnormal marrow micro-environment.
Inhibition by an abnormal clone of hemopoietic cells.
Immune mediated suppression of hematopoiesis.

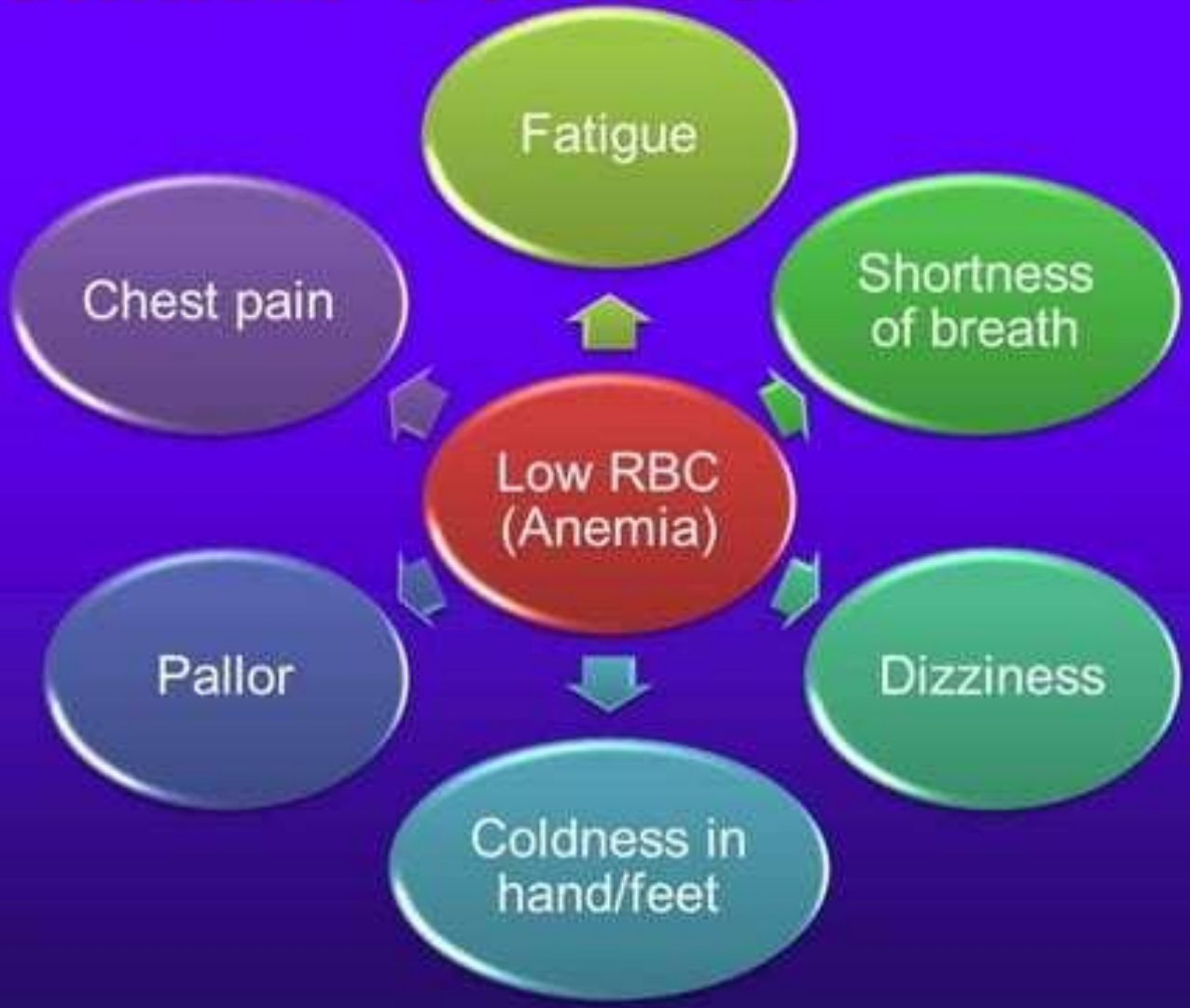
It is believed that genetic factors play a role. There is a higher incidence with HLA (11) histo comp. Antigen. Immune mechanism is involved.

Pathogenesis (Cont..)

The latest theory is:

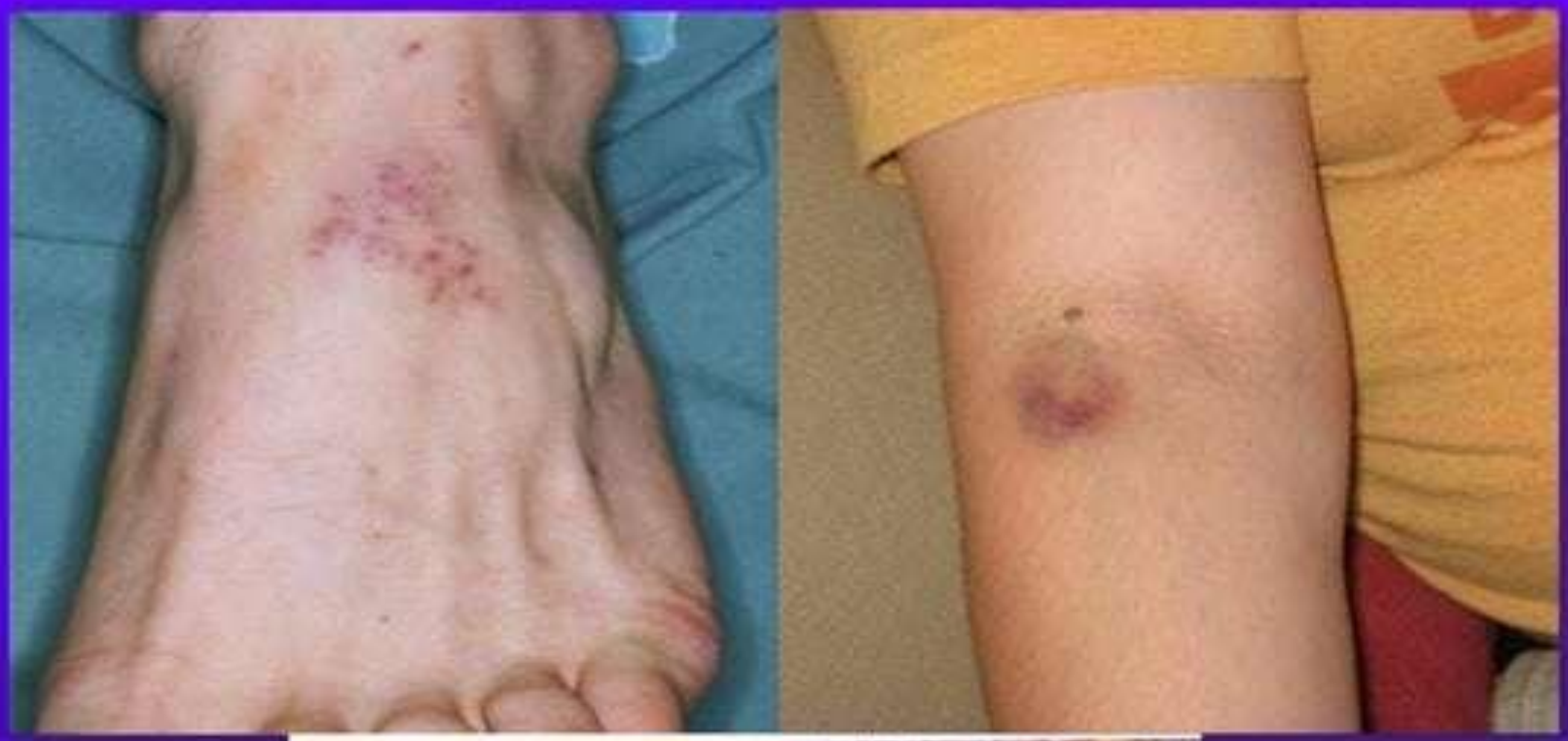
there is an intrinsic derangement
of hemopoietic proliferative capacity, which is consistent
with life. The immune mechanism I,e autoreactive T cell attempt to destroy
the abnormal cells (self cure) and the clinical course and
complications depend on the balance. If the immune
mechanism is strong, there will be severe pancytopenia.
If not, there will be myelodysplasia.

Clinical Features



Clinical Features

- Low WBC (Leukopenia)
  - Fever
  - Infections
  - Flu-like illness
- Low Platelets (Thrombocytopeni
  - Red spots
  - Prolong bleeding
  - Easy bruising



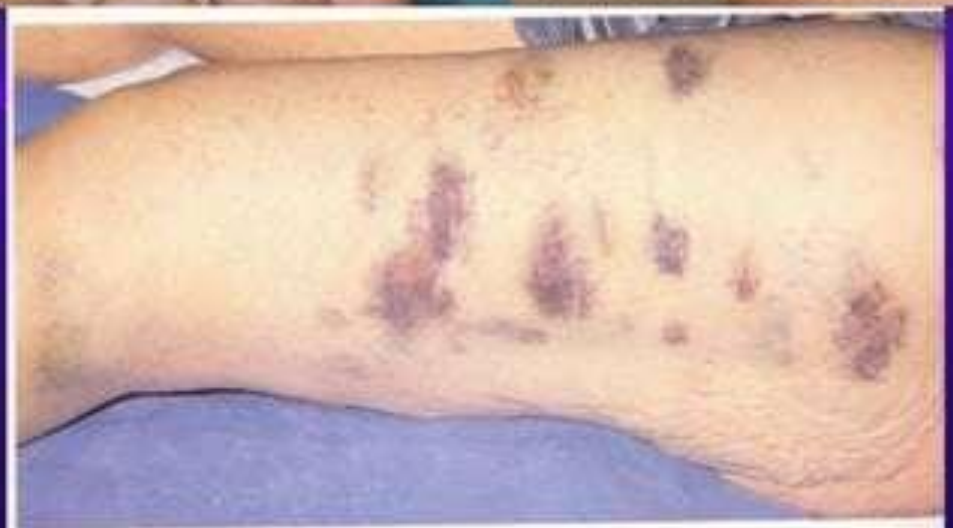


Fig.6.3 Aplastic anaemia: spontaneous bruising over the thigh and leg of a

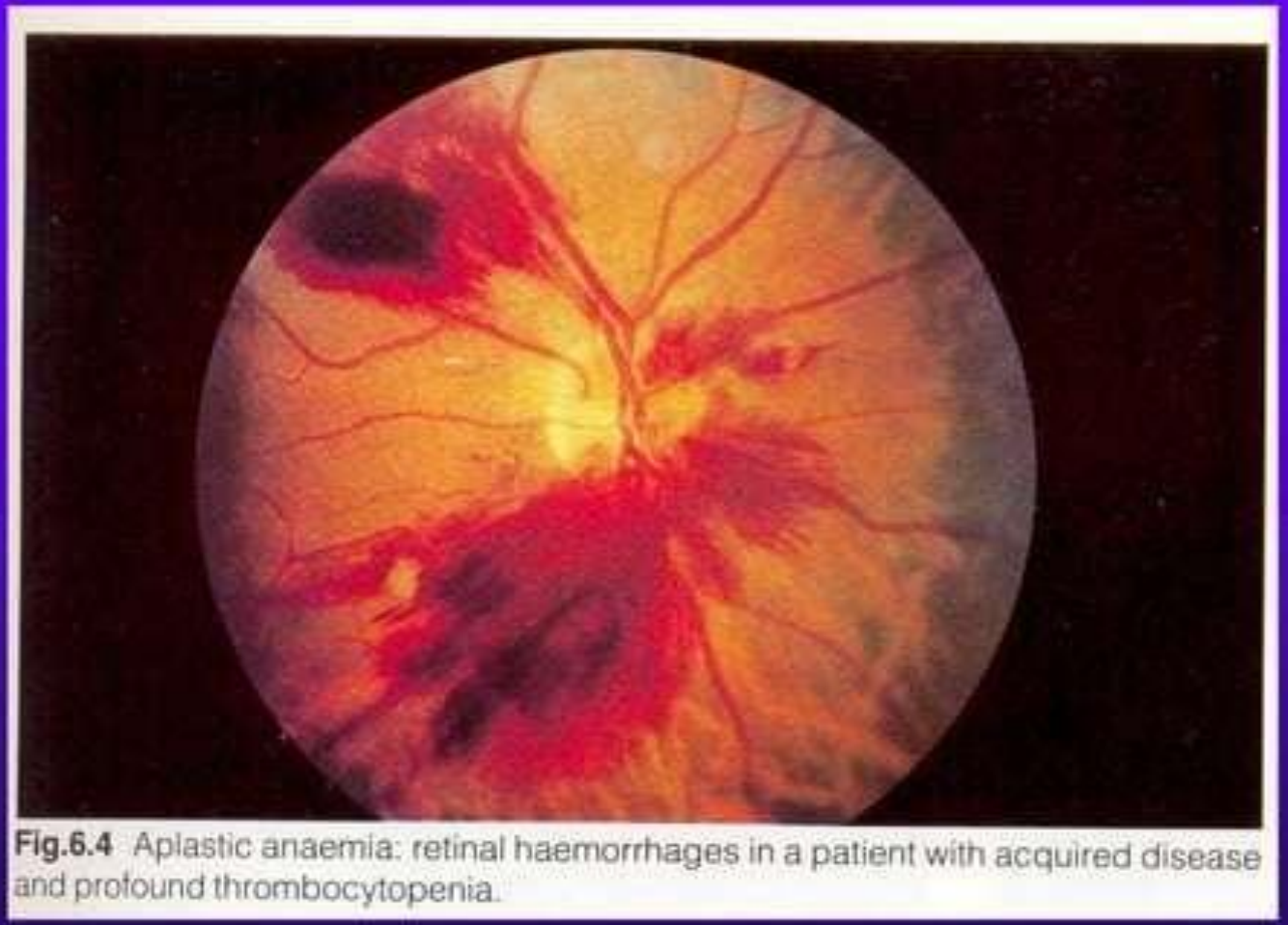


Fig.6.4 Aplastic anaemia: retinal haemorrhages in a patient with acquired disease and profound thrombocytopenia.

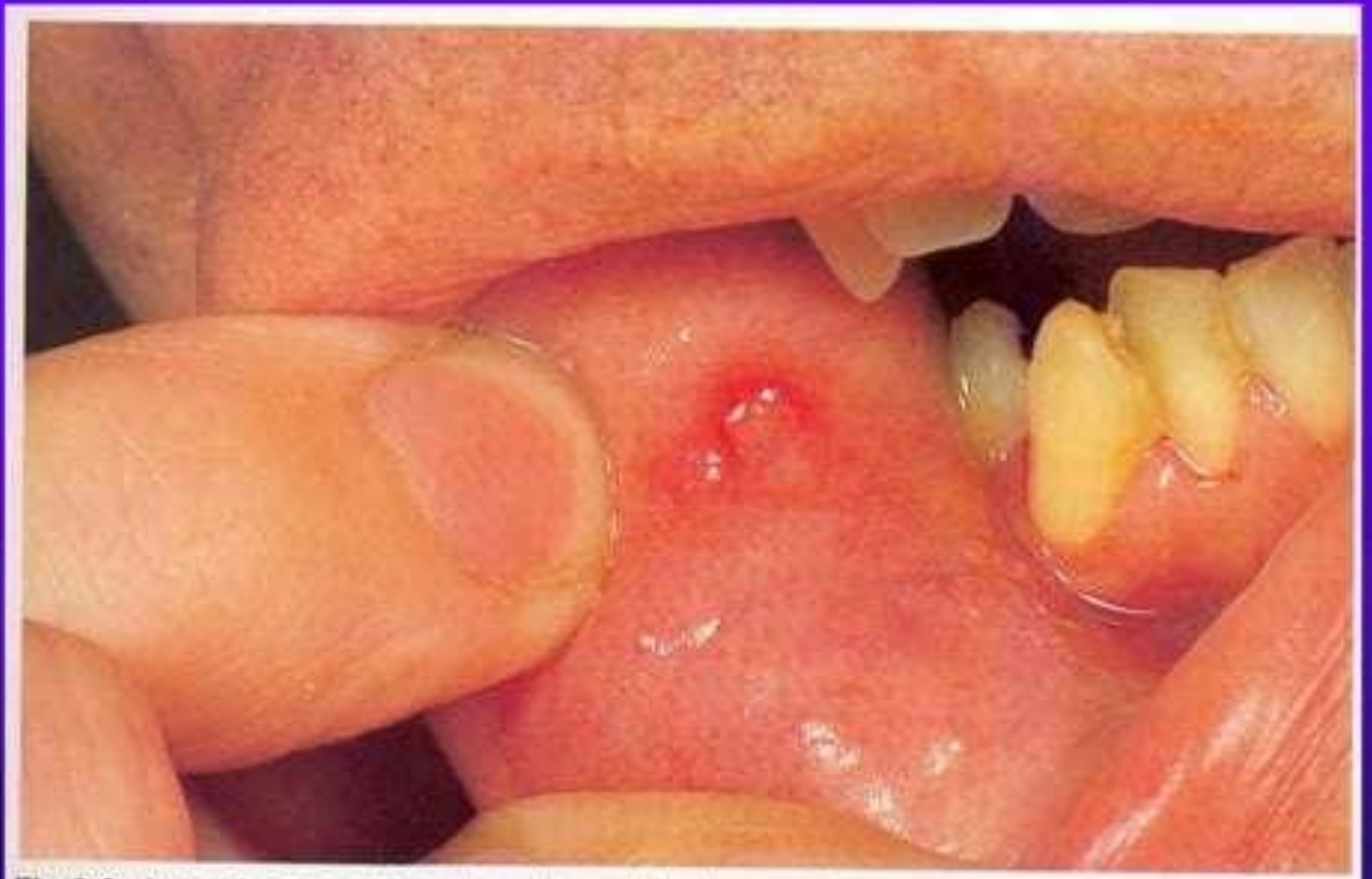
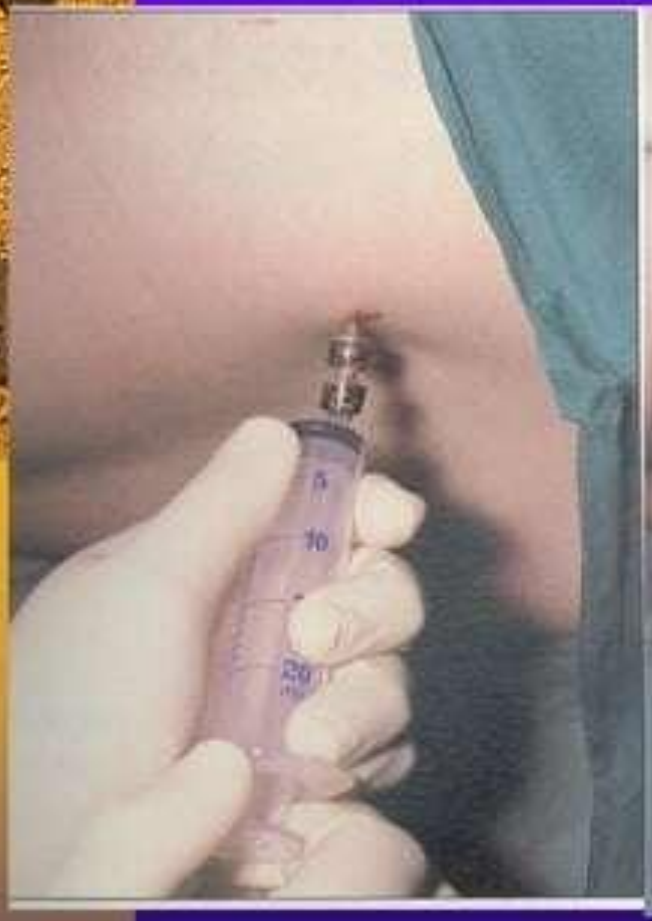


Fig.6.6 Aplastic anaemia: ulceration of the buccal mucosa associated with severe neutropenia. Herpes simplex virus was grown from the ulcers. *Total leucocyte count:0.8x10^9/l; neutrophils:20%.*

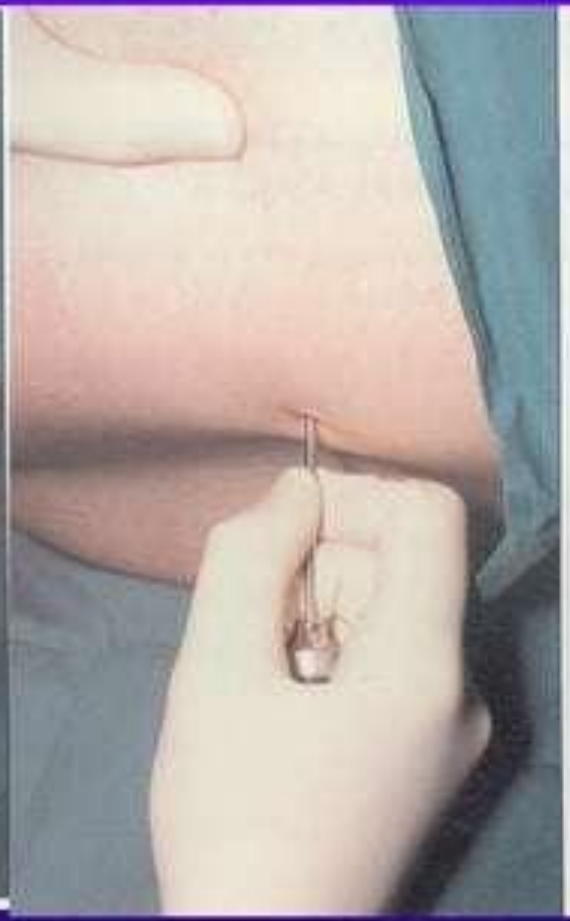
Hematological findings:

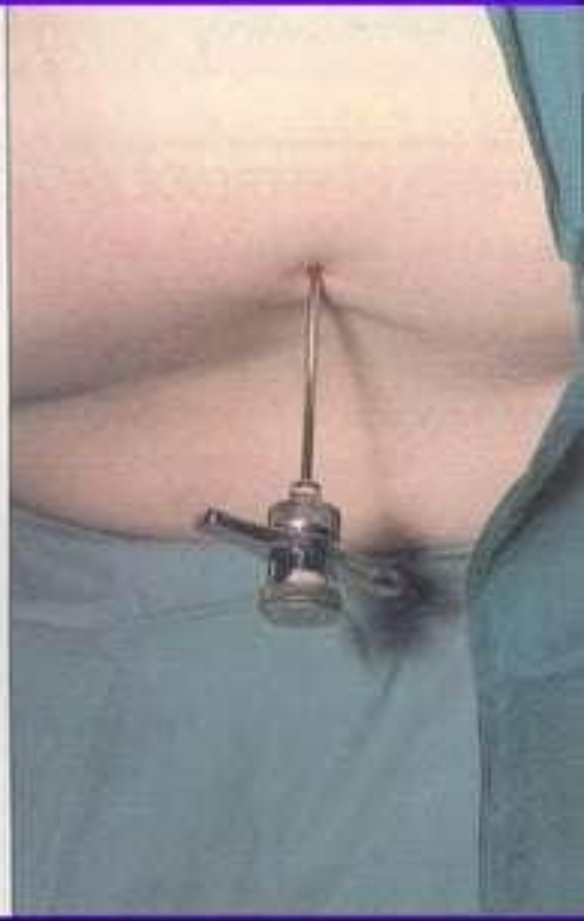
CBC:

- Pancytopenia: initially only 1 or 2 parameters
- WBC < 2.0,
- Hb < 10.
- Plt. < 100.
- No gross morphological abnormalities.
- Anemia is usually NCNC.
- Reticulocytopenia.

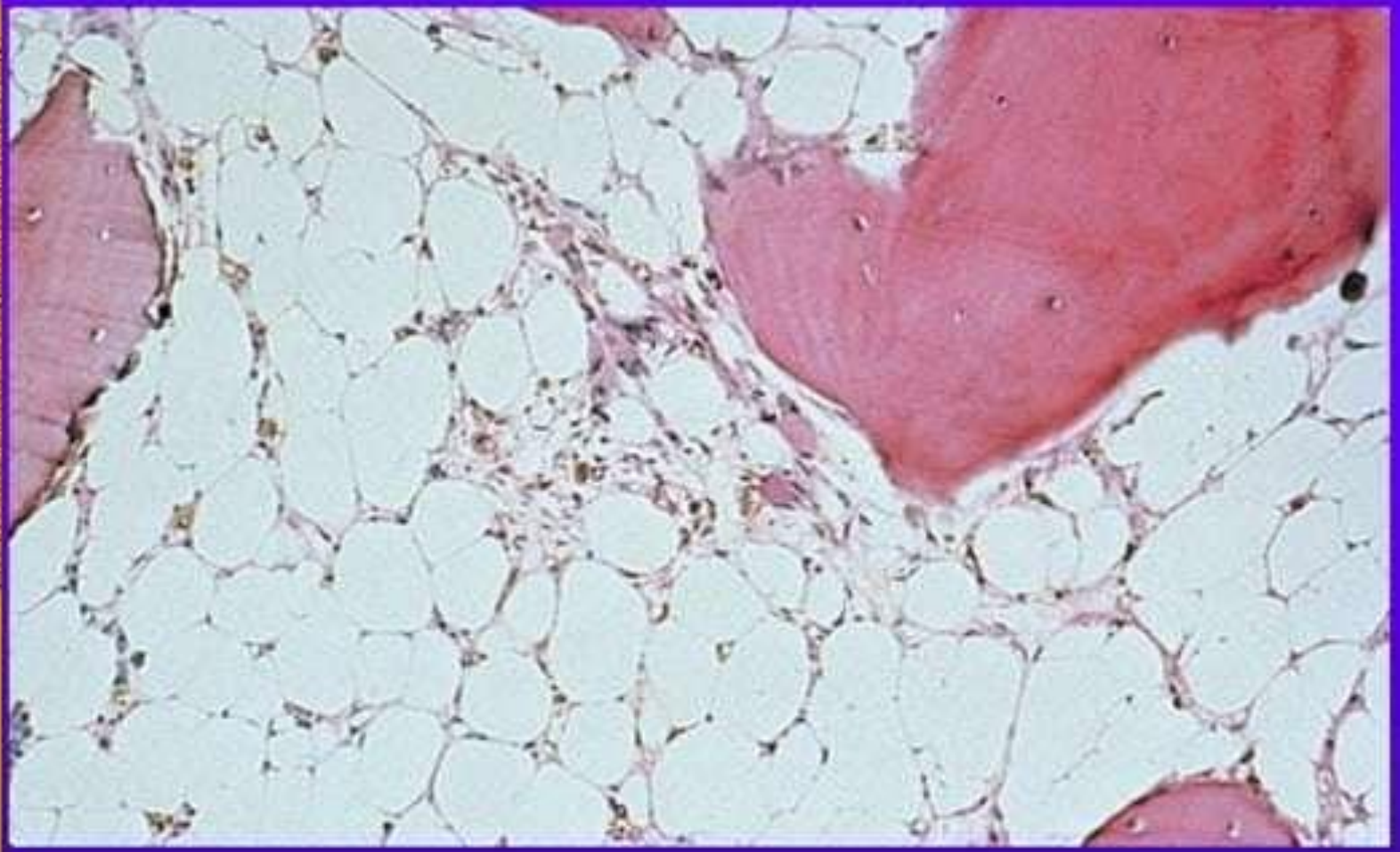


BM Aspiration



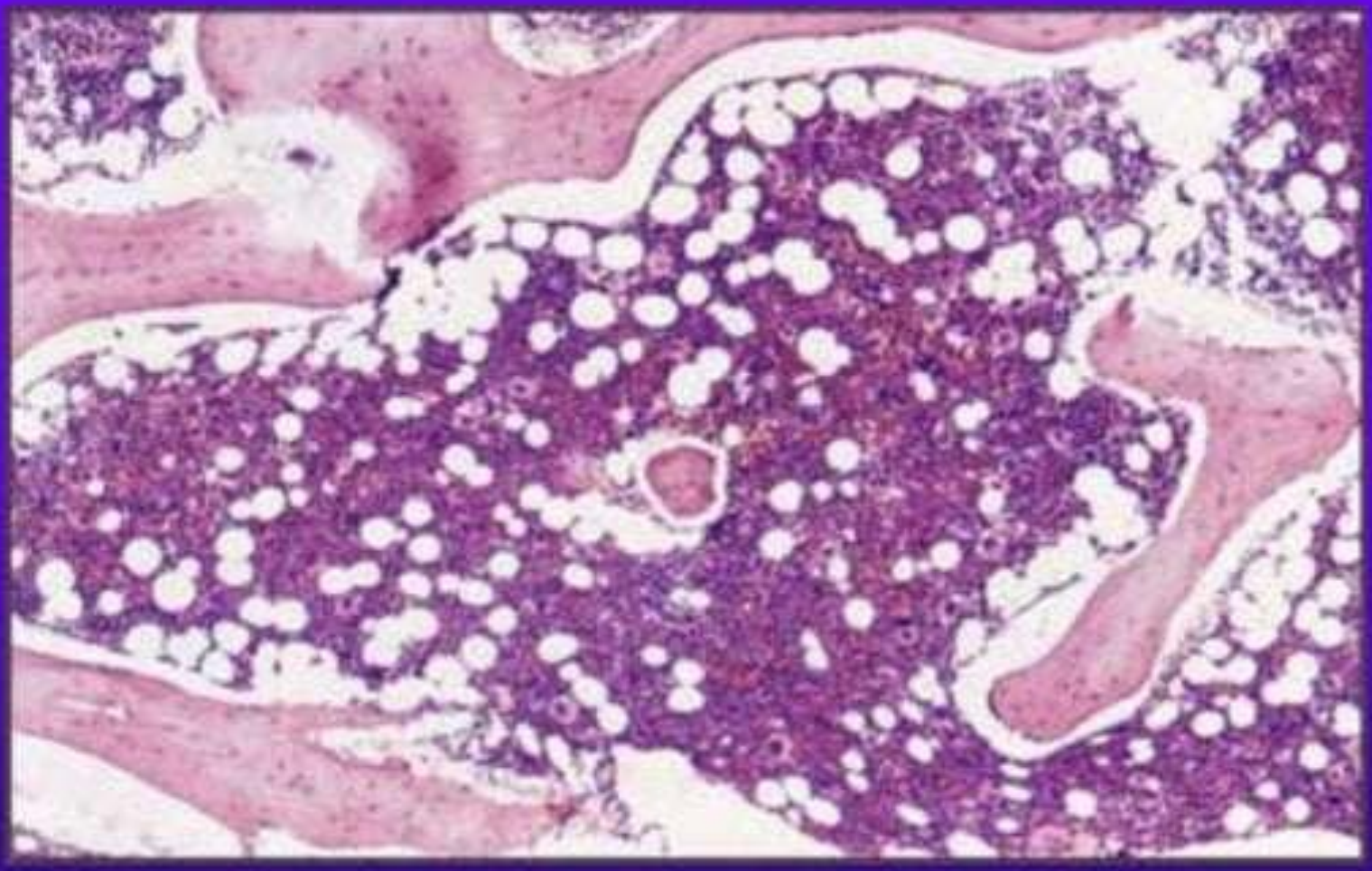


BM Biopsy



BM biopsy

hypocellular ,increased fat spaces



Hematological findings: (Cont…)

Bone Marrow:

- Hypocellular:

  <50% of normal cellularity Trephine biopsy is the most important for diagnosis.
- Most of the cells present are lymphocytes, plasma cells.
- Iron stores: increased

Treatment

- Withdrawal of etiological agents.
- Supportive.
- Restoration of marrow activity:
  - Bone marrow transplant
  - Immunosuppressive treatment
    - Prednisolone
    - Cyclosporin
    - Splenectomy
    - Antilymphocyte glob.
    - Anti T cells abs.
  - Androgens
  - Growth factors

Inherited Anemia

Fanconi's Anemia:

- The most common type of inherited aplastic anemias.
- Associated with anomalies e.g., skeletal, skin.
- Autosomal recessive.

Genetics:

- Increased sensitivity of the cells to chromosomal damage by DNA cross linking agents.
- 13 genes are responsible

- IV54 mutation, is associated with multiple dysmorphism, severe pancytopenia, higher incidence of AML.

Inherited Anemia

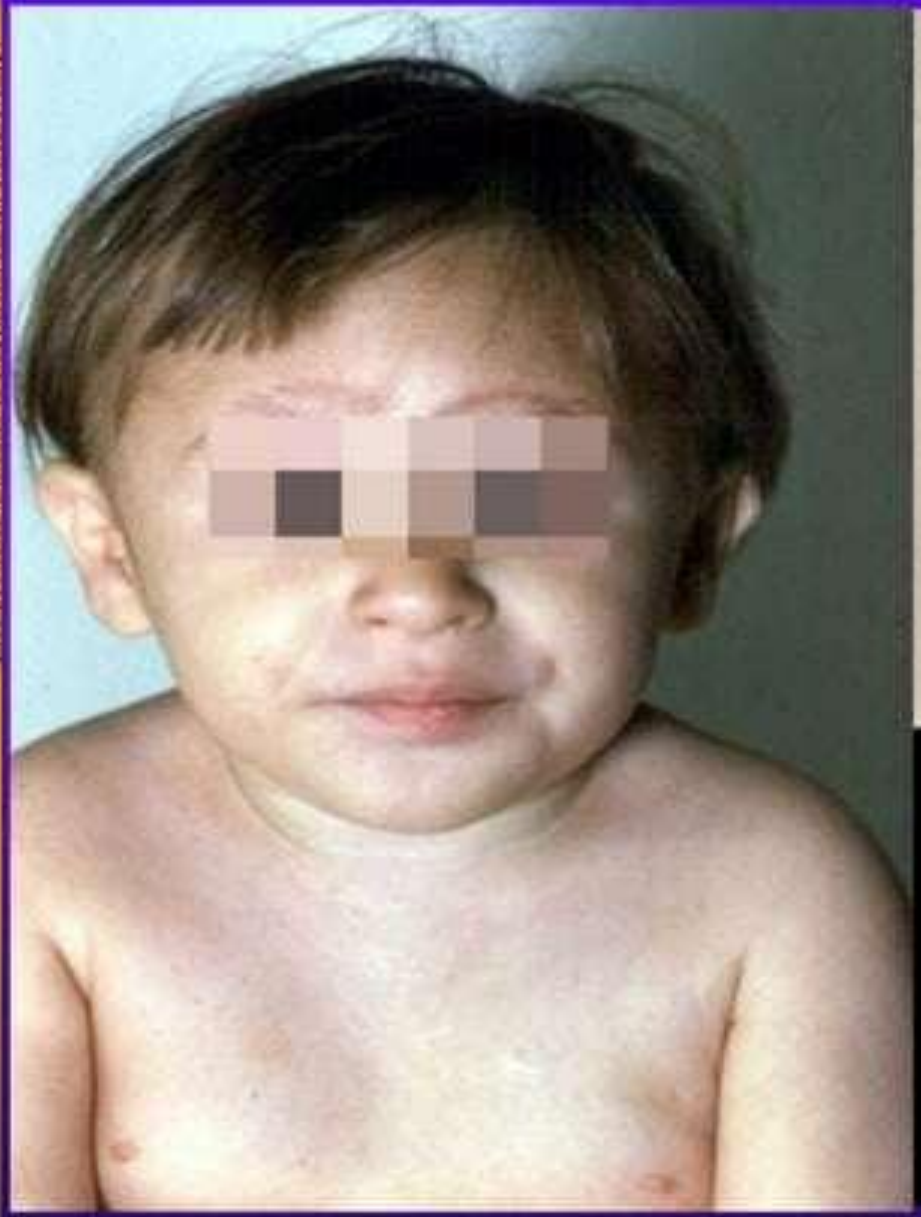
Clinical Features:

- Skeletal and skin anomalies seen at birth e.g., microcephally.
- Manifestations of marrow failure, usually later at age 5-10 yrs. Present as anemia, mucusal bleeding e.g. nasal.

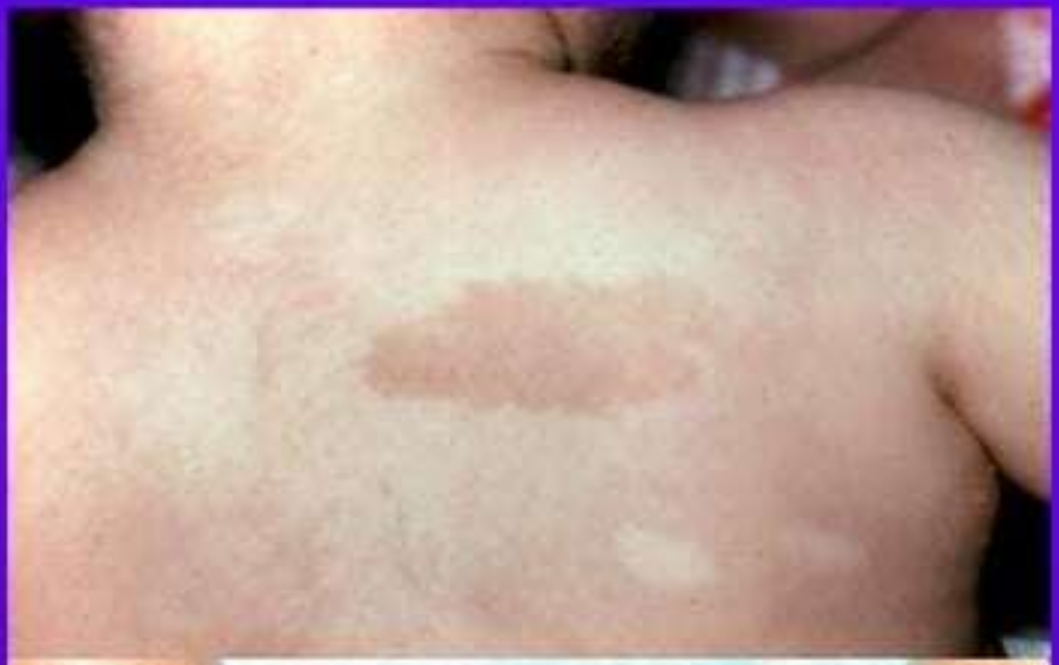
Clinical Features of Fanconi's Anemia

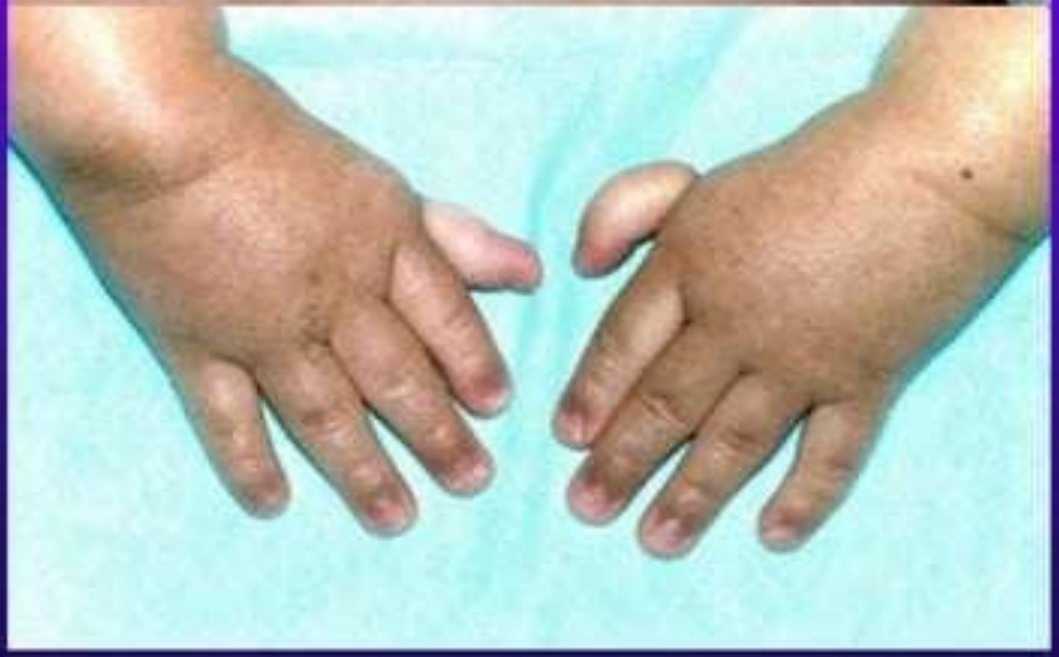
Common Findings:

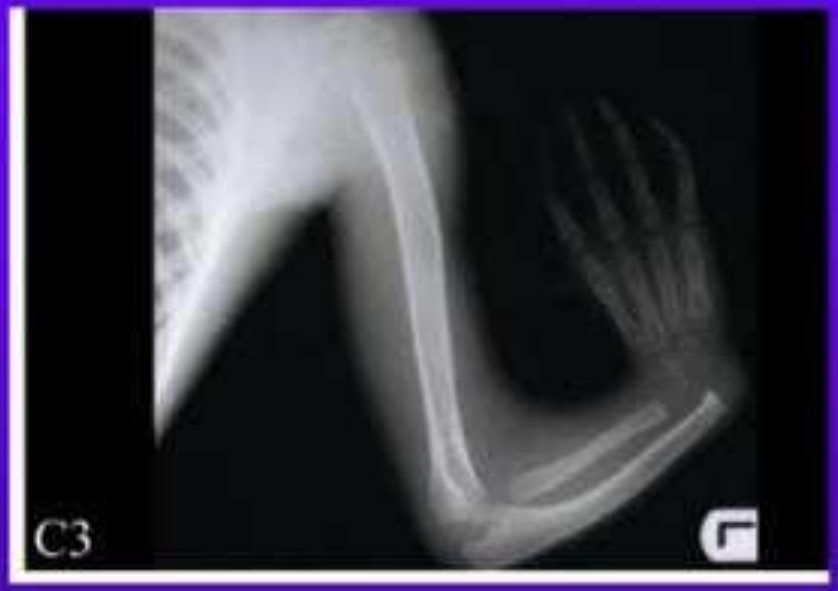
- Low birth weight
- Short stature
- Microcephaly
- Microphthalmia
- Microstomia
- Skeletal abnormalities, particularly of thumbs and radii
- Generalized increased pigmentation of skin




80
60
40
20






C3


Postgraduate Haematology
A1
A2


Thank You