BONE MARROW FAILURE

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- Primary failure of BM
  - all cell lines
  - one or more cell lines
- Marrow infiltration
  - acute leukaemia
  - fibrosis

APLASTIC ANAEMIA

- **Congenital**

e.g.. - **Fanconi's anaemia**

(- chromosome fragility

- dysmorphism

- family Hx)

- **Dyskeratosis congenita**

- nail / skin changes

- leukoplakia

- X-linked

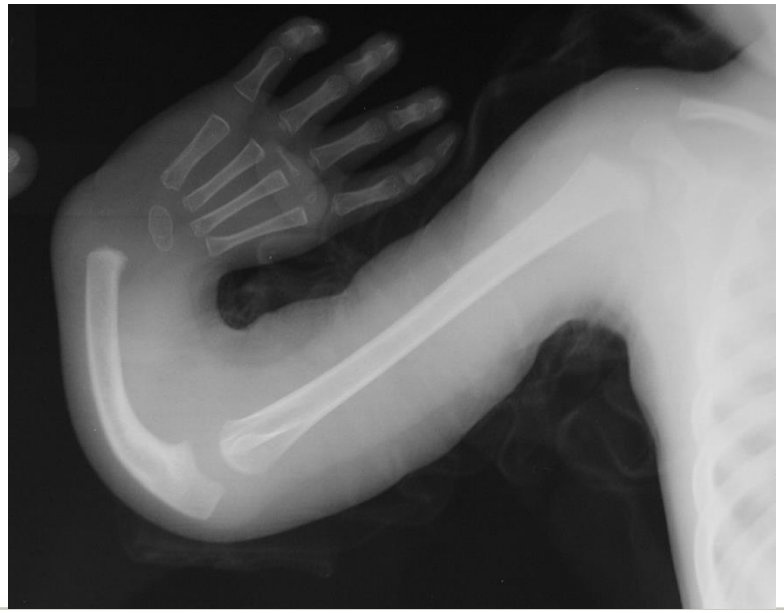
- **Acquired**

Fanconi Anaemia

Radial ray anomalies

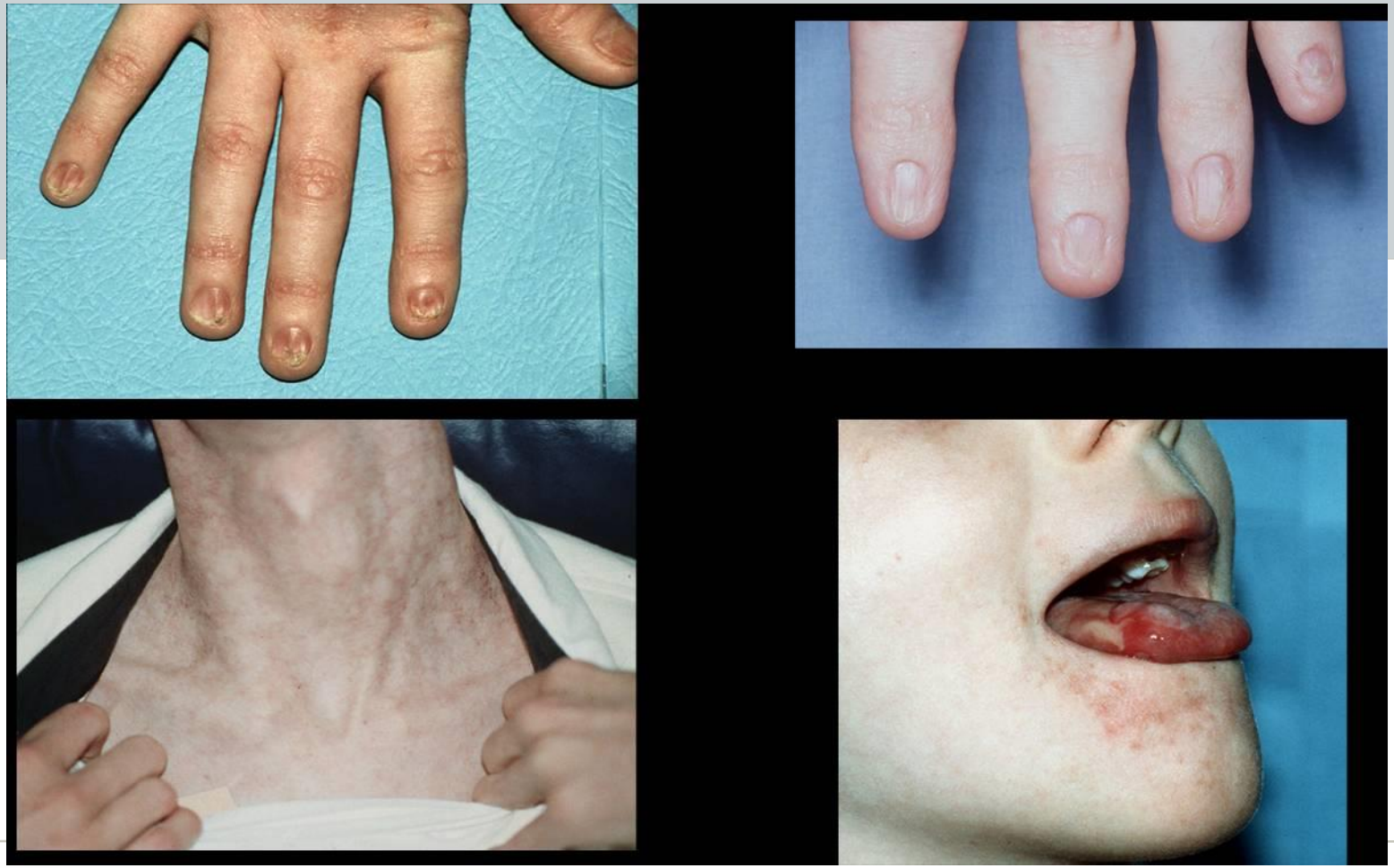
Hands in Fanconi Anemia

- Primarily radial deformities
  - Partial or total absence of preaxial border
  - Bilateral in 50% of cases
  - Ulna thickened, bowed toward absent radius
- Hypoplastic thumb – subgroup of radial deficiency
- Scapula, thenar eminence often reduced in size



Images courtesy of Scott Kozin MD – Shriners Hospital Philadelphia

Dyskeratosis Congenita (DC)



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Dyskeratosis Congenita

- Ectodermal dysplasia – DNA repair defect
- Triad – reticulated skin hyperpigmentation, dystrophic nails, mucous membrane leukoplakia – develops with age
- Aplastic anemia develops in up to 50% in 2nd to 3rd decade
- Solid organ cancers (head, neck, gastrointestinal) and leukemia at an early age in 3rd to 4th decades
- AML
- Carcinomas of bronchus, tongue, larynx, esophagus, pancreas, skin

Diamond Blackfan Anaemia

- At least 47% of all patients
  - 50% cranio-orofacial (tow colored hair, blue sclerae, glaucoma)
  - 38% upper extremity (thumbs, may be subtle)
  - 39% genitourinary
  - 30% cardiac
- Over 20% with more than one anomaly
- Short stature and bony abnormalities common, and often overlooked!
- Neutropenia, and rarely thrombocytopenia also

DBA

Thrombocytopenia Absent Radii Syndrome: Clinical Features

Absence of radii with presence of thumbs

Courtesy of Dr. Jeff Lipton

Acquired Aplastic anaemia

Features -

- Peripheral blood pancytopaenia
- Hypocellular marrow

  Replaced by fat

  no ↑ of reticulin or fibrosis

  no dysplastic cells
- No morphologically abnormal cells in circulation or marrow
- No evidence of a malignant disease

Epidemiology

- Uncommon
- 2 per million / year
- 2 peaks

  - young
  - after 60 yrs

Aetiology

- 70 –80% not known
- Rest

Drugs - difficult to prove

e.g.. Chloramphenicol

- usually a delay of 2-3 months before it develop

Viruses - Hepatitis A*

(B)

- Parvo virus B 19

Disease mechanism / Pathophysiology

- Stem cell problem
- Some abnormalities of immune mechanism

Diagnosis

- Manifestations of pancytopaenia
  - anaemia
  - neutropaenia
  - thrombocytopaenia

- No lymphadenopathy

- Liver, spleen not enlarged
  * if +ve → ? leukaemia

Investigations

- FBC, blood film
- ↓ Hb, macrocytic (slight)
- No abnormal cells
- Retic count
- ↓ WBC →

  no left shift
- Platelets small in size

Severity of Aplastic anaemia

	Blood	**BM**
V. Severe	(N) $<0.2*10^9$/L (P) $<0.2*10^9$/L (R) $<0.2*10^9$/L	<25% normal cellularity
Severe	N (0.2-1.5 $*10^9$/L) Otherwise as for v.severe	= v. severe
Non-severe	(N) (0.5-1.5)$*10^9$/L (P) (20-100)$*10^9$/L (R) (20-60)$*10^9$/L	hypocellular

- Bone marrow

  Aspiration - Easy

  If hard → think elsewhere

  Hypocellular

  ↑ fat cells

  No dysplasia

- Cytogenetics

  less than in MDS

Management

1. Supportive Rx

2. Restoration of stem cell function

   (Immunosuppressive Rx or BMT)

Supportive Treatment

- RBC transfusion

  (watch out Iron overload)

- Platelet transfusions

  (keep platelet >$10*10^9$/L)

  below this spontaneous bleeding.

Supportive treatment

- Granulocyte transfusion

  -febrile pts with severe neutropenia

  value?

  -When neutrophil count <200 ($0.2*10^9$) : isolate
  + prophylactic antibiotics

  -count >$0.5*10^9$/L - safe

Immunosuppressive Tx

- Produces a remission

- (= freedom from Tx and

neutrophil count $0.5*10^9/L$)

- remission - complete (normal counts)

- partial

Agents

- ATG (antithymocyte globuline)

  (horse, rabbit immunized with human T cells & their Ig purities)

  - ATG must be given in protective isolation.

  - 65% achieve remission.

  - Effective for all ages.

- Cyclosporin + ATG - remission rate

- Cyclosporin alone (less effective than ATG)

- Immunosupp. Most effective for non-sever AA.
- If 1st course not effective, a repeat course in 6/12 time.
- Usually takes 6/52 to show response.

Bone marrow Transplantation

- Cures the disease
- Young children with severe aplasia
- Young adult patients <40 yrs

Myelodysplastic syndrome (MDS)

- Abnormal, clonal, marrow cell proliferation with varying degree of cytopaenias, maturation defects in one or more cell lines.

- Causes cytopaenias.

  Usually marrow is hypercellular.

  But dysplastic cells

- Leukaemic potential (pre-leukaemic)
- Patients >50yrs
- May have been Rx by RT or chemotherapy for other cancers.

Symptoms

- Those of cytopaenias

Treatment

- For some merely supportive
- Others……..

  combination of chemo +/- BMT

- Specialist affair