Dyserythropoietic Anaemia (Qualitative)

Def:

Dyserythropoiesis leads to production of abnormal erythroid series, some of them:

die in BM (ineffective erythropoiesis)

Others: mature & reach the circulation but have a short life span

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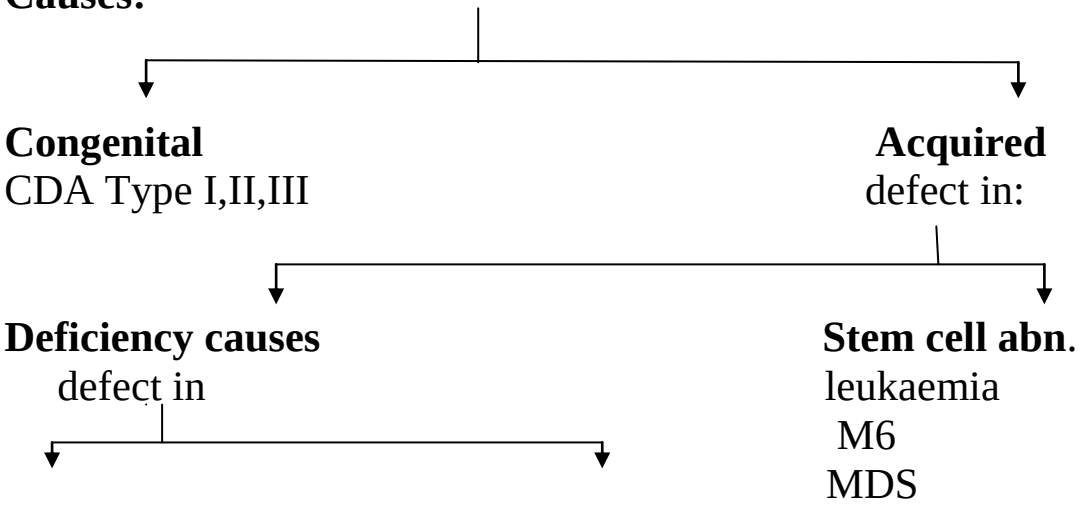
Causes:

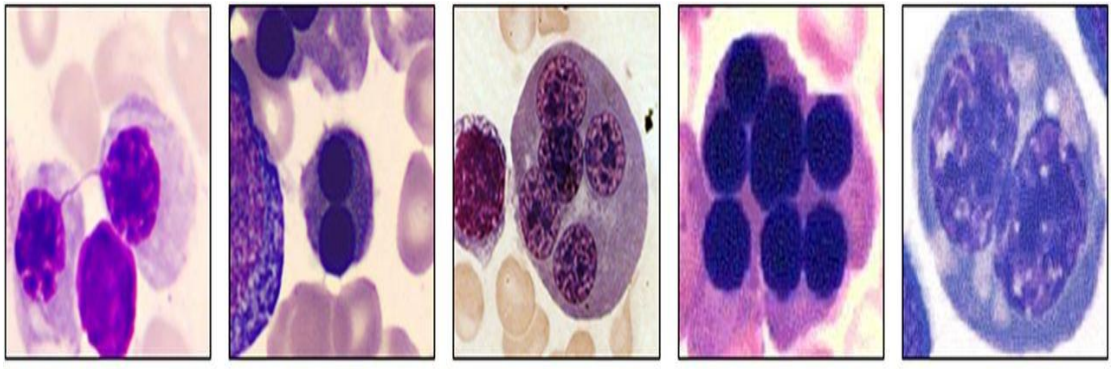


Congenital Dyserythropoietic Anaemia (CDA)

Def, Ch ch :
It is a hereditary refractory anaemia ch ch by:
-ineffective erythropoiesis
-erythroid multinuclearity (abnormal cs)
-2nd tissue siderosis
Types:
Type I, II & III.

These anaemia (3 types) have common features:

- Mild to severe anaemia presented early in life.
- Splenomegaly.
- Evidence of ineffective erythropoiesis.
- Ferrokinetics:
  rapid plasma clearance.
  accumulation of radioactivity in BM.
  ↑ iron in BM.
  ↓ red cell iron utilization.
- RBCs life span N or slightly ↓
- Retics : N or slightly ↑
- CBC: anaemia, anisocytosis, poikilocytosis & macrocytes



CDA type I | CDA type II | CDA type III familial | CDA type III sporadic | CDA variants

Table 1:BM:

	Type I	Type II (HEMPAS)	Type III
It affects:	Pro erythroblasts & early normoblasts	Late erythroblasts	All erythroid series
By light microscope:	Megaloblastic changes: Nucleo-cytoplasmic dissociation , stippled chromatin , internuclear bridges -Macrocytosis	Bi nuclearity or multi nuclearity (2-7 n) -Karyorrhexis (degenerative changes)	Multi nuclearity up to 12 nucleii -Giant erythroblast -Basophilic stippling or siderotic granules -Must be D.D from M6 (x blasts)
By electron microscope:	Nuclear membrane integrity is lost e' oozing of nuclear material. -Ribosomes r attached to nuclear membrane -Widened nuclear pores -Presence of cytoplasmic microtubules	Excess endoplasmic reticulum appearing as double cell membrane.	Clefts & blebs up to nuclear bridges (due to abn. in nuclear division (incomplete separation) -Auto lytic areas in cytoplasm -Iron filled mitochondria
Inheritance:	AR	AR	AD
Pathogenesis:	Main defect is in nuclear membrane e' failure of protein synthesis.	Abnormal RBC membrane protein (band 3,4.5) → ↑Susceptibility to lysis)	

Table 2:

•**Serology: Comparisons of in vitro lysis test:**

	Acidified Serum Lysis test (Ham's test)		Anti I		Anti i		Sucrose Lysis test
	Donor Serum	Patient Serum	Lysis	Agglutination	Lysis	Agglutination	
Normal adult	-	-	-	±	-	-	-
PNH	+++	++	+++	+	±	±	+++
CDA Type I	_	_	±	±	-	-	-
Type II (HEMPS)	+	_	++	++	++	++	-
Type III	_	_	++	+++	++	+++	-

Acidified serum lysis test (Ham's test):
Acidification of serum to a ph of 6.5-7⟶ activates Alternative pathway of complement.
PNH:
Lysis in both patient & donor serum (no protective mechanism against complement mediated lysis) due to Red Cell defect (sensitivity to lysis by complement).
Normal cells: No lysis.
HEMPAS:
Lysis in donor's serum not patient's by cold Abs (anti I),
Serum of donor + RBCs of patient ⟶ agglutination/ lysis.
↘
Contain Ab against hidden Ag.

Sucrose Lysis test:
Patient RBCs + sucrose solution ⟶ activation of Classic Pathway of complement.
PNH: +ve lysis.
HEMPAS: no lysis.

Table 3: D.D : of HEMPAS:

	HEMPAS	PNH
Sucrose Lysis test:	-ve	+ve
Acidified serum lysis test (Ham's test):	Cells r lysed by donor serum **Only** & not by patient's serum	Cells r lysed by acidified patient's or donor's serum (**by both**)
Cause:	Presence of IgM , complement fixing naturally occuring Abs≠ specific Ag on RBCs of HEMPAS	↑ sensitivity to Complement

Table 4: D.D of CDA type III:

	Type III CDA	Erythroleukaemia (M6)
Degree of anaemia:	mild	Severe
Thrombocytopenia:	-	+
CBC:	No myeloblasts No normoblasts	Myeloblasts normoblasts
Retics:	N or slightly	
BM:	Giant erythroblasts contain 12 nucleii Basophilic stippling	Pro erythroblasts Myeloblasts

Management of CDA:

Mild anaemia ⟶ no intervention.
Severe anaemia ⟶ minimal transfusion to avoid iron overload.
If regular transfusion is needed ⟶ iron chelation.

Anaemia of chronic renal failure

Mechanisms:

1- Dilutional anaemia:

due to ↑ plasma volume.

2- Aplastic anaemia:

due to : failure of Epo production, or failure to respond to Epo.

3-Haemolytic anaemia:

urea, creatinine ⟶ direct injury to RBCs ↓ life span.
instability of membrane ATPase & glutathione.
burning of RBCs: by heat labile non dialyzable material.

4- Deficiency anaemia:

A- Microcytic hypochromic anaemia:

- Fe def. anaemia due to hge from GIT or menorrhagia.
- In nephrotic syndrome: loss of many proteins including Transferrin.
- Defective iron reutilization ⟶ an. of chronic dis.

B- Megaloblastic anaemia:

due to loss of folate in dialysis.

5- Bleeding tendency:

due to platelet dysfunction as bleeding from GIT & mennorrhagia.

C/P:

manifestations of renal failure.

C/P of anaemia.

Lab:

CBC:

- NNA e' ↓ retics.
- Sometimes MHA or even megaloblastic an.
- RBCs r burr shaped or triangular.
- WBCs & platelets r N.

BM:

- Normocellular e' no abnormal cells.
- Sometimes hypocellular.
- There may be compensatory ↑ in erythroid activity.

ttt:

- Mild anaemia → no ttt.
- Ideal ttt → dialysis + Epo.
- Transfusion if necessary.

Anaemia of Endocrinal diseases

It is due to ↓ Epo & other hormones.

Types:

A- Anaemia of pituitary deficiency: (Hypo pituitirism):

Leads to aplastic an. 2ry to thyroid H., GH, adrenal & gonadal H.

B- Anaemia of thyroid gland:

1-Hypothyrodism:

aplastic an. NNA

MHA: due to menorrhagia, ↓HCL, ↓ Fe absorption.

macrocytic: due to IF Abs.

2- Hyper thyrodism:

Haemolytic an. due to shortened life span of RBCs.

C- Anaemia of adrenal gland: (Addission's disease):

Aplastic an. NNA.

D- Anaemia of Gonadal disease: (Hypo gonadism):

↓ Androgens → Aplastic an.

Myelophthesic Anaemia
= BM Replacement
= Alteration of HIM

Def:

Anaemia or pancytopenia due to BM infilteration (BM is replaced by non marrow elements) e.g: leukaemia, associated e' leucoerythroblastic reaction.

Causes:

- Metastasis → Ca breast.
- Leukaemia, lymphoma, MM.
- Miliary T.B.
- Metabolic disorders : Gaucher, Neimen Pick.

Pathogenesis:

- Replacement of marrow by ectopic cells → compete e' haemopoietic cells for essential nutrients.
- Ectopic cells secrete inhibitory factors → inhibit haemopoietic cs.
- BM become crowded by infiltration → ineffective erythropoiesis.
- Lodge in spleen → extra medullary haematopoiesis.
- This infilteration disturbs HIM → release of immature cs in P.B.

Ectopic cs multiply in BM → irritation of BM → release of immature cells in P.B.

Diagnosis:

CBC:

RBCs:

NNA e' anisocytosis, poikilocytosis & tear drops (in M.F).

↓ Retics.

WBCs & platelets: N or ↓ or ↑ according to the cause.

Leucoerythroblastic picture:

immature RBCs (normo) & immature WBCs (staff, Juv).

BM:
Infilteration e' metastatic cs (or according to cause).
BM biopsy:
From tender bone is essential for diagnosis .

Table 5: causes of pancytopenia:

Decreased bone marrow function
Aplasia **Acute leukaemia, myelodysplasia, myeloma** **Infiltration with lymphoma, solid tumors, tuberculosis** **Megaloblastic anaemia** **Paroxysmal nocturnal haemoglobinuria** **Myelofibrosis** **Haemophagocytic syndrome**
Increased peripheral destruction
Splenomegaly