26th Annual General Pediatric Review & Self-Assessment

Nicklaus Children's Hospital

HEMATOLOGY

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Neonatal Anemia

- Blood loss
- Hemolytic process
  - Anemia, hyperbilirubinemia, high retic count
- Impaired red cell production
  - Low retic count

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Neonatal anemia- Blood loss

- Feto-maternal or feto-fetal transfusion
- Hematoma or rupture of cord or placenta
- Placenta previa or abruptio
- Internal hemorrhage
  - Intracranial
  - cephalhematoma
  - retroperitoneal
  - ruptured liver or spleen

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Newborn hemolytic anemia

- Immune- **Coombs** positive
  - Rh incompatibility- mother Rh negative presents in first 24 hours of life
  - ABO incompatibility- mother /baby
  - Minor group incompatibility (Kell, E, c)
  - Maternal autoimmune hemolytic anemia
  - Drug-induced hemolytic anemia

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Hemolytic anemia- other causes

- Infection
  - Bacterial sepsis
  - Congenital TORCH infections
- DIC
- Cavernous hemangioma
- Galactosemia
- Hereditary red cell membrane defects: HS,HE
- Red cell enzyme deficiency (G6PD, PK, HK)
- Alpha thalassemia syndromes (HbH, Hydrops)

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G6PD Deficiency

- X-linked
- Neonatal jaundice in boys
- Sudden jaundice, pallor, dark urine
- Mediterranean more severe than African
- May get gall stones or aplastic crisis
- Avoid: sulfa drugs, Aspirin, chloroquine, nitrofurantoin, Naphthalene, Fava beans

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Neonatal anemia III

- Impaired Red Cell Production-Low retic
  - Diamond-Blackfan anemia

    Physical anomalies in 30%: short stature, low birth wt, microcephaly, triphalangeal thumb
  - Congenital infection- Rubella, parvovirus
  - Osteopetrosis

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Approach to newborn anemia

- Family history and obstetric history
- Physical exam: anomalies, infection , hemorrhage, hepatosplenomegaly
- Laboratory evaluation
  - Reticulocyte count
  - coomb's test
  - MCV (low in alpha thal. , chronic blood loss)
  - peripheral smear (spherocytosis, ellipto, DIC)
  - RBC enzymes
  - TORCH titers, bacterial cultures

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Physiologic anemia of infancy

- Pathophysiology
  - decreased red cell survival
  - increased plasma volume
  - decreased erythropoietin levels post-natally
- Full term: 8-12 weeks Hb ~ 9.5-10 g/dL
- Premature <1500 gm 4-8 wks Hb~ 6-7 g/dL

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RBC Transfusion

- **10cc/kg of PRBC raise Hgb by 3 gm/dL**

- **Formula:**

$$\text{Volume} = \frac{(\text{Blood volume}) \times (Hct_2 - Hct_1)}{\text{Hct of PRBC } (\sim 65)}$$

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Iron Deficiency Anemia

- Nutritional: Excessive cow milk intake
- Blood loss: GI bleeding, Menorrhagia
- Hypochromic microcytic
- low Fe, high TIBC
- (Fe/TIBCx100=Transferrin saturation <12%)
- low MCV, low Ferritin, High RDW >14
- MCV / RBC >13 (Mentzer index)

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Anemia

- Low Retic
  - Iron Deficiency
  - Hypoplastic
  - Bone marrow infiltration
- High Retic
  - Hemolytic: Coomb's +
  - RBC enzyme (G6PD deficiency- X linked)
  - Hemoglobinopathy (Sickle, thalassemia)
  - RBC membrane defect (spherocytosis)

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Beta Thalassemia *Trait*

- Beta thalassemia trait- Thal Minor
- Low MCV (microcytosis)
- Mild or no anemia
- Occasional mild splenomegaly
- Differential Dx iron deficiency
  - Thal RDW <14. MCV/RBC <13
- Family counseling- No therapy

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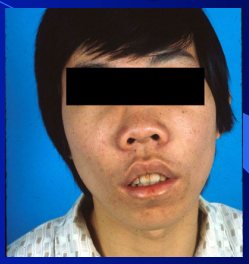
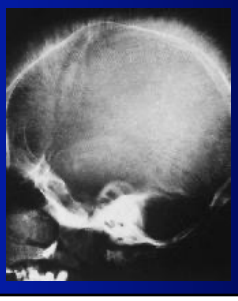
Beta-Thalassemia Major

- Decreased production of *Beta* globin chains
- Severe transfusion-dependent anemia
- Bone marrow expansion- (Thal-facies)
- Chronic transfusions- every 2-3 weeks
- Iron chelation with (Deferasirox) or Deferoxamine (Desferal)
- Ferritin very high





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Alpha Thalassemia aa/aa

- **Single gene deletion**: silent carrier
  normal Hb and MCV, Barts Hb(γ 4) at birth.
- **Two gene deletion:** alpha thal trait:
  Mild or no anemia, Low MCV- Barts at birth
- **Three gene deletion:** Hb H disease
  Moderate hemolytic anemia
- **Four gene deletion**: Severe anemia,
  Hydrops fetalis

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	HB	MCV	Fe	TIBC	Ferritin	FEP
IRON DEF	↓	↓	↓	↑	↓	↑
THAL TRAIT	N↓	↓	N	N	N	N
THAL MAJOR	↓↓	↓	↑	N	↑↑	N
LEAD TOXICITY	N↓	N↓	N↓	N	N	↑↑

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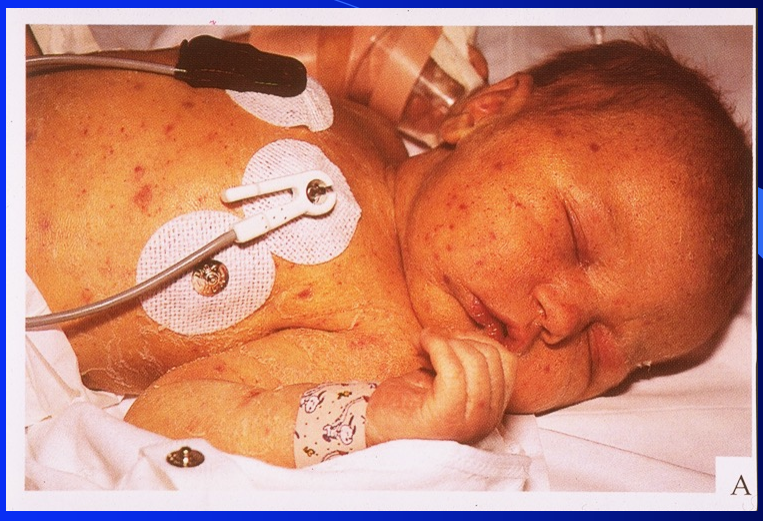

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Neonatal Thrombocytopenia

- Increased Destruction
  - Immune
  - Non-immune
- Decreased Production
- Hypersplenism

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Immune Thrombocytopenia

- Autoimmune
  - Maternal ITP
  - Maternal SLE
  - Maternal hyperthyroidism, drugs
  - pre-eclempsia

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Neonatal Immune Thrombocytopenia

- Alloimmune or isoimmune
  - Platelet antigen incompatibility - Pl-A1 (HPA-1a) antigen Mother negative , father and baby positive
  - 1: 1000
  - maternal antibodies against paternally derived antigens in infants platelets
  - first born may be affected
  - Severe thrombocytopenia <10,000 + bleeding
  - Rx: IVIG, Platelet transfusion PlA1-ve
  - Prevent bleeding in next pregnancy: give mother IVIG

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Non-immune Destruction of Plts

- Sepsis, DIC, TORCH infections
- Asphyxia
- Perinatal aspiration
- Necrotizing enterocolitis
- Hemangioma
- Neonatal thrombosis
- Respiratory distress syndrome

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Decreased Platelet Production

- Bone marrow replacement
  - congenital leukemia, neuroblastoma, histiocytosis, osteopetrosis
- Bone marrow aplasia
  - TAR: thrombocytopenia with absence of radius
  - Amegakaryocytic thrombocytopenia
  - Fanconi anemia

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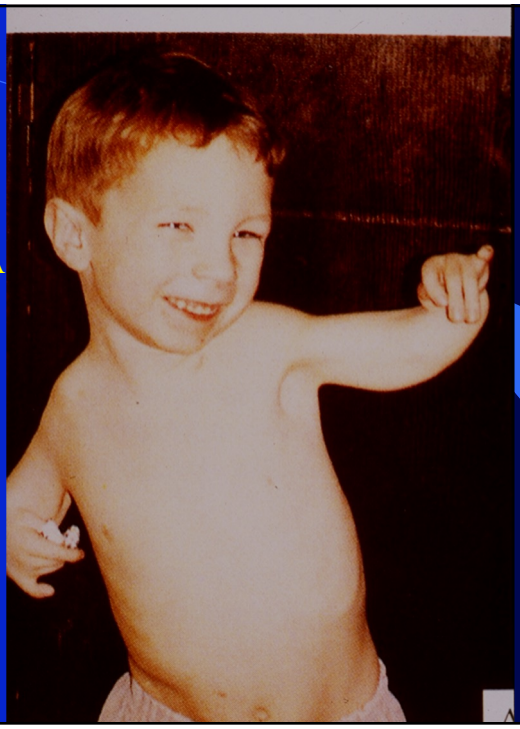
TAR

THROMBOCYTOPENIA
WITH
ABSENT RADIUS



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Thrombocytopenia

- Hypersplenism
  - Sequestration of platelets in enlarged spleen
- Other causes
  - hyperbilirubinemia
  - inborn errors of metabolism: acidemias
  - Wiskott- Aldrich syndrome: small platelets

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Lead Poisoning

- Lead inhibits porphyrin synthesis enzymes d-ALA dehydratase and **ferrochelatase**
- Fe^{++} + protoporphyrin $\xrightarrow{\downarrow}$ Heme
- Lead inhibits iron insertion into protoporphyrin
- Hence an increase in free protoporphyrin **FEP**
- **70 % of Children with Pb 40-49 ug/dL have an FEP >140**

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Lead poisoning

- Acute poisoning
  - encephalopathy: Seizures, coma, death
  - Pb 90-800 ug/dL
- Chronic poisoning
  - abdominal pain, vomiting, malaise, behavioral changes
  - Fanconi renal syndrome
  - Microcytic anemia usually with Fe deficiency
- Low level exposure: neurobehavioral effects

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Lead level screening (ug/dl)

- 0-5 No immediate concern ?
- 5-14 Community/environmental survey
- 15-19 Retest, educational intervention
- 20-24 monitor periodically, house visit
- 25-54 Find Pb source, oral Chemet
- 55-69 Remove Pb source, treat CaNaEDTA
- >70 Emergency hospitalization- treat with BAL+CaNaEDTA-return to clean home

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Sickle Cell Anemia

- Beta chain of hemoglobin- pos 6 Glu to Val
- Newborn screening FS pattern
- Vaso-occlusive crisis
  - Bone pain: back/spine, knee, shoulder, elbow, femur, sternum, ribs etc..
  - Under 5 yrs: Hand- foot syndrome

    puffy swollen warm hands and/or feet

    fever and leukocytosis may be present

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Infections in Sickle cell anemia

- Pneumonia:
  - pneumococcus, H influenza, gram negative rods, mycoplasma, chlamydia
- Meningitis : pneumococcus, H flu
- Osteomyelytis: salmonella, staph aureus
- Sepsis
- UTI

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SCD- penicillin prophylaxis

- To be started at 2-3 months of age in SS disease
- 2 months-3 yrs 125 mg po bid daily
- 3 yrs- 5 yrs 250 mg po bid daily
- Prevnar, Pneumovax (23 valent) at 2 years
- After 5 yrs may stop PCN unless prior sepsis or splenectomized

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SCD- Acute chest syndrome

- pneumonia/ pulmonary infarction
- chest pain, fever, infiltrates, hypoxia, cough
- > 50 % have normal CXR on presentation
- Leading cause of death after age 10 yrs
- RX: supportive care, oxygen, antibiotics, transfusion to Hgb 10 gm/dL, exchange transfusion

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SCD- Abdominal pain

- Vaso-occlusive crisis (mesenteric, abdominal wall)
- Hepatic crisis
- RUQ syndrome (gall stones)
- R/O surgical pain eg: cholecystitis, appendicitis

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Acute sequestration crisis

- Sudden retention of blood in spleen
- leading cause of death in children < 5 yrs
- 50 % may recur
  - Increase spleen size
  - Decrease Hct by 25%
  - Decrease in platelet count <100,000
  - Increase in retic
- Rx: transfusion, splenectomy if recurs

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SCD- Aplastic crisis

- Temporary cessation of erythroid marrow activity
- Parvovirus B-19 infection preceding
- Retic count low (<0.1)
- Due to short sickle RBC survival 15-50 days compared to 120 days normally
- Recovery with or without transfusion

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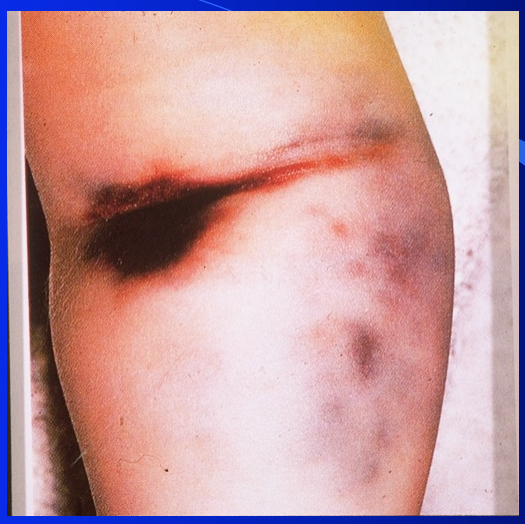

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Coagulation Disorders

- Pretibial bruising may be normal in active child
- If positive family history or excessive bruising w/o trauma or excessive nose bleeds or post surgical bleeding then:
- Do PT, PTT, Platelets, Bleeding time (PFA)

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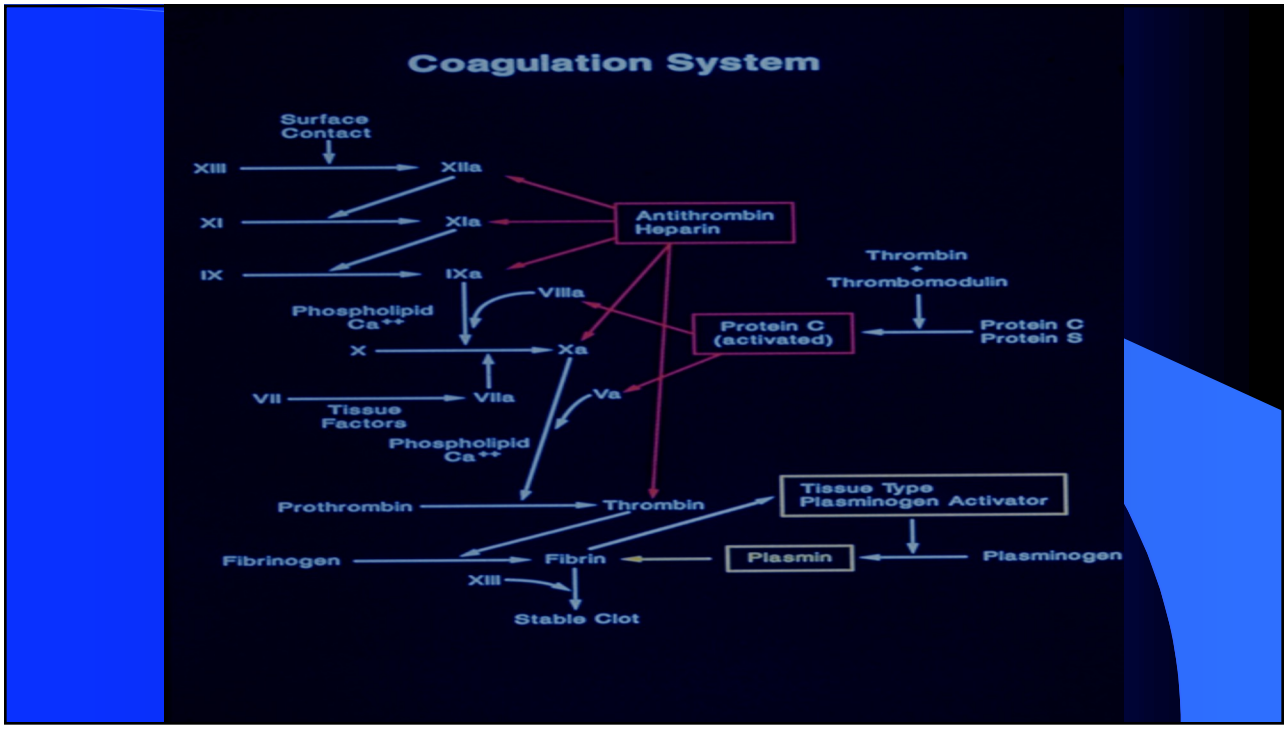

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Prothrombin time PT

Increased : Factor VII deficiency
Liver disease
Vitamin K deficiency
malabsorption, CF

Partial Thromboplastin time PTT

Increased: Factor VIII and IX def
von Willebrand disease
other contact factors

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Hemophilia

- X-linked factor VIII and IX deficiency
- Boys inherit gene from carrier mother
- May **not** bleed with circumcision
- Treat with FFP until factor assay results available

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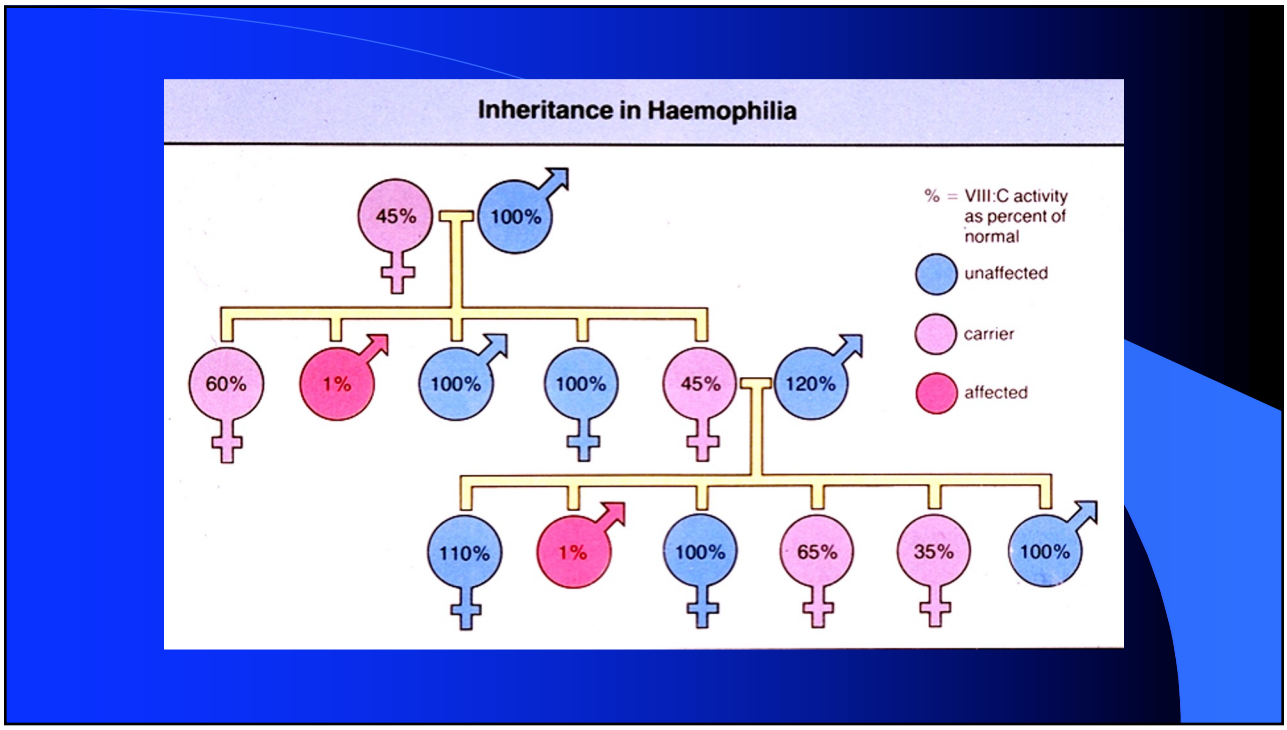
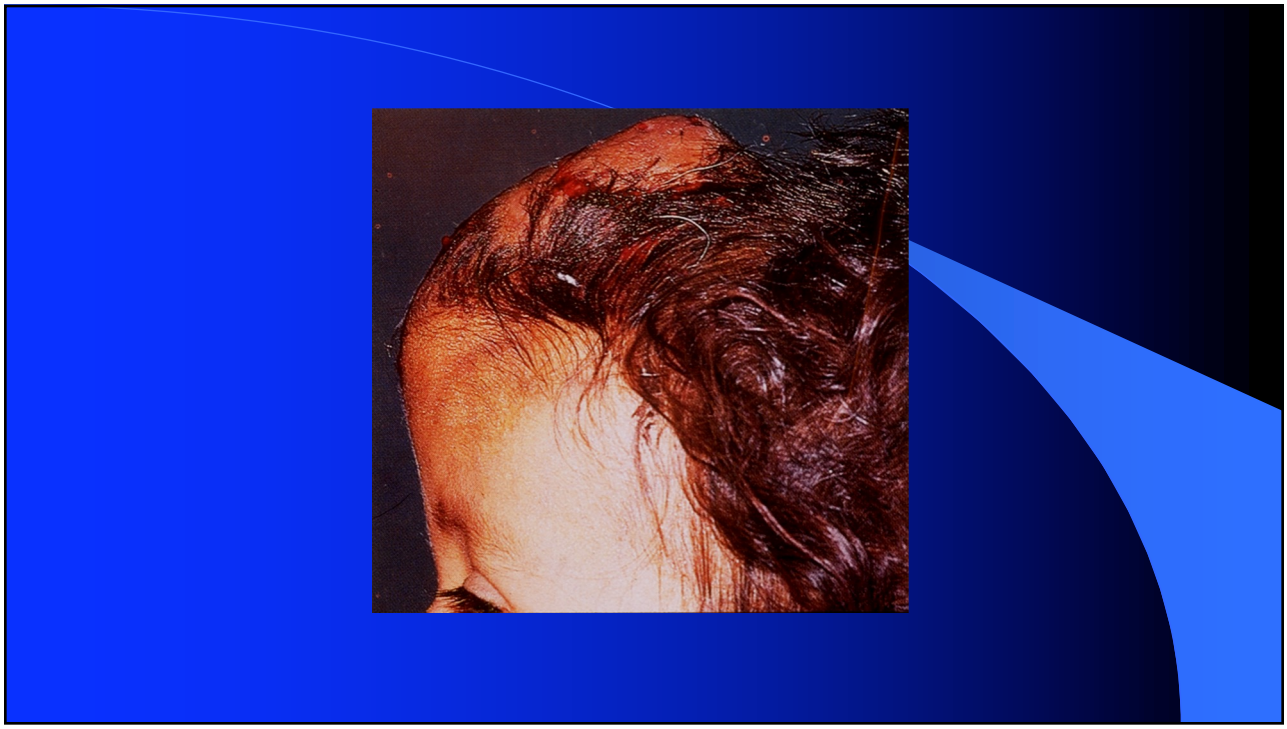

Inheritance in Haemophilia
45%
100%
% = VIII:C activity as percent of normal
unaffected
carrier
affected
60%
1%
100%
100%
45%
120%
110%
1%
100%
65%
35%
100%

42



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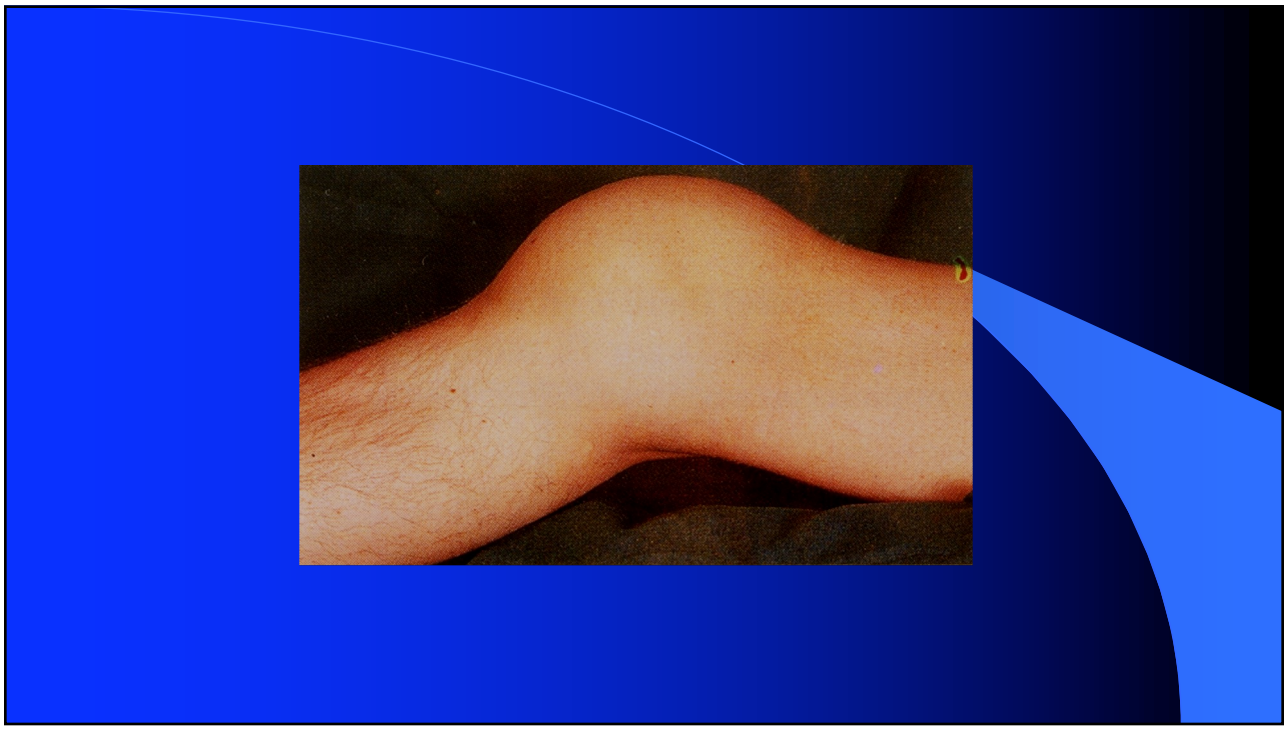

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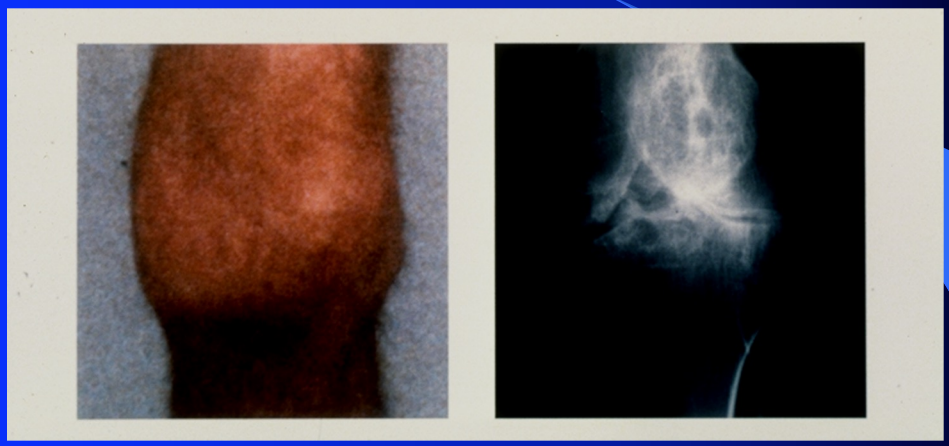
Hemophilia
Joint Damage with No Prophylactic Therapy



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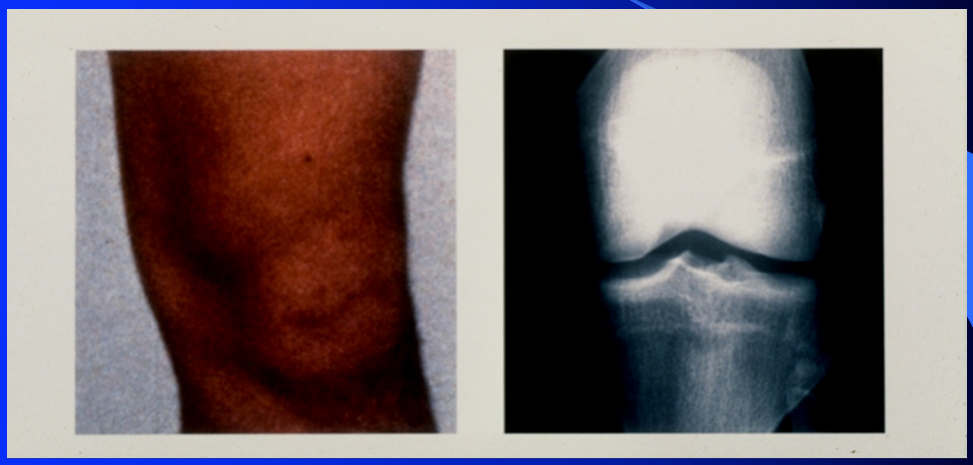
Prevention of Joint Damage with Chronic Prophylactic Therapy



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Platelet Function Disorders

- Von Willebrand disease (lack of plasma factor necessary for platelet adhesiveness)
- Glanzmann thrombasthenia (Gp IIb/IIIa)
- Bernard-Soulier syndrome (Gp Ib deficiency)
- Storage pool defect
  - Alpha granule-gray platelet syndrome
  - Dense granule deficiency (Hermansky-Pudlak etc.)

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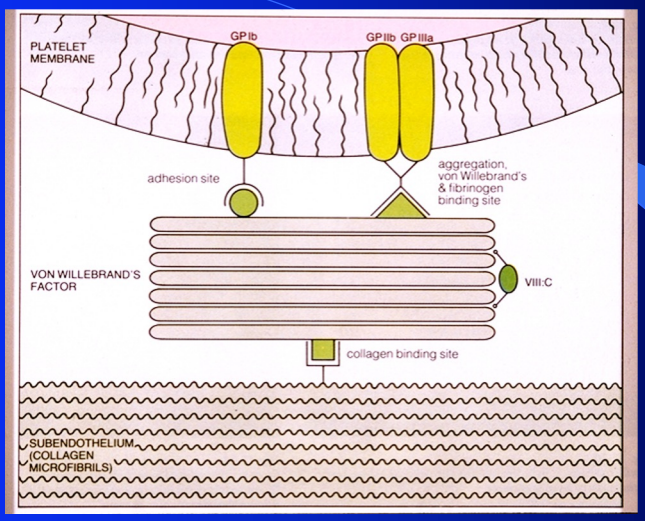

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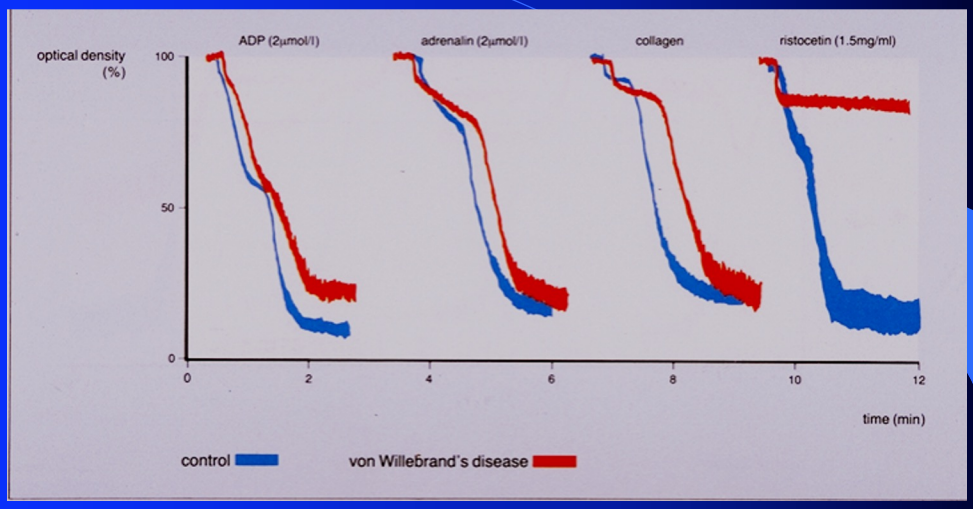
Measurement of Platelet Aggregation



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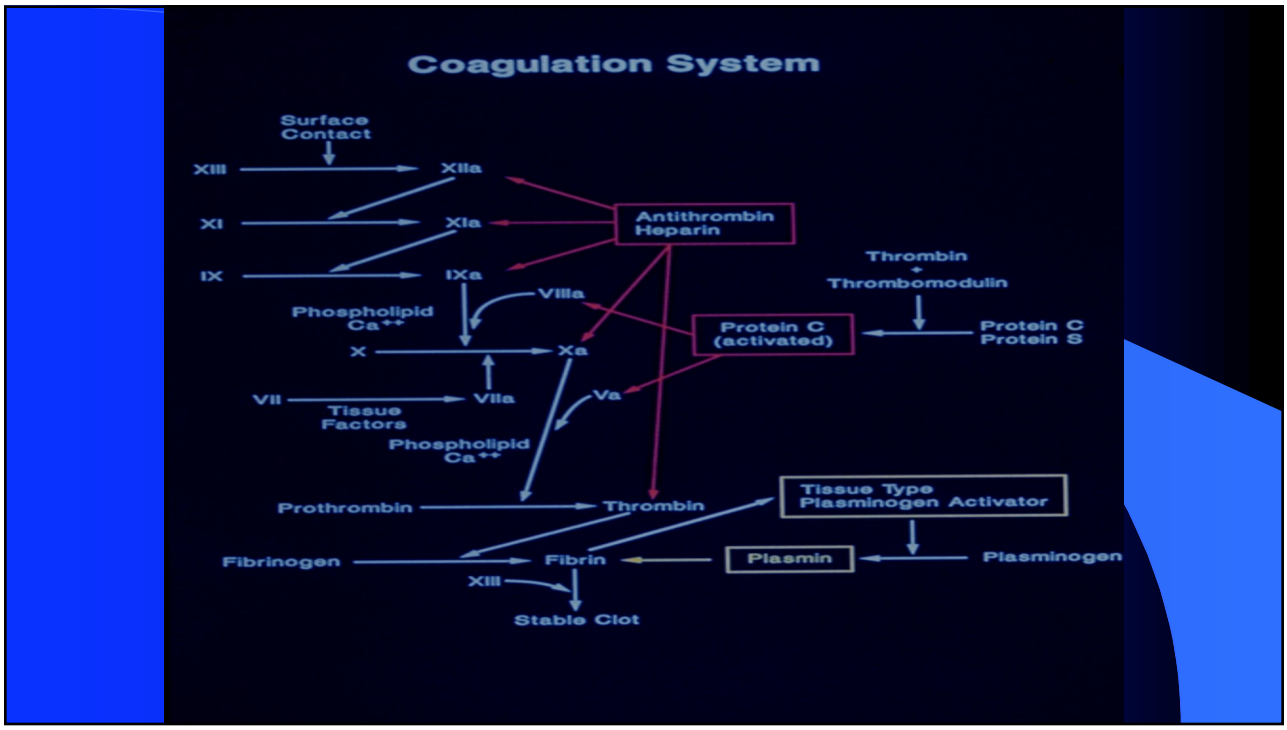

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Hypercoagulability

- Protein C or S deficiency
- Activated protein C resistance
- Factor V Leiden Mutation
- Antiphospholipid/anticardiolipin antibodies
- Antithrombin III deficiency
- Prothrombin 20210 mutation
- Hyper-homocysteinemia

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Assessing Neutrophils
The Absolute Neutrophil Count (ANC)

ANC = Total WBC x % of neutrophils (bands and segs)

Example:

- **WBC = 2,000/mm^3**
- **Segmented neutrophils = 55%**
- **Band neutrophils = 1%**

ANC = 2,000 x 0.56 = 1,120/mm^3

Reference: 1

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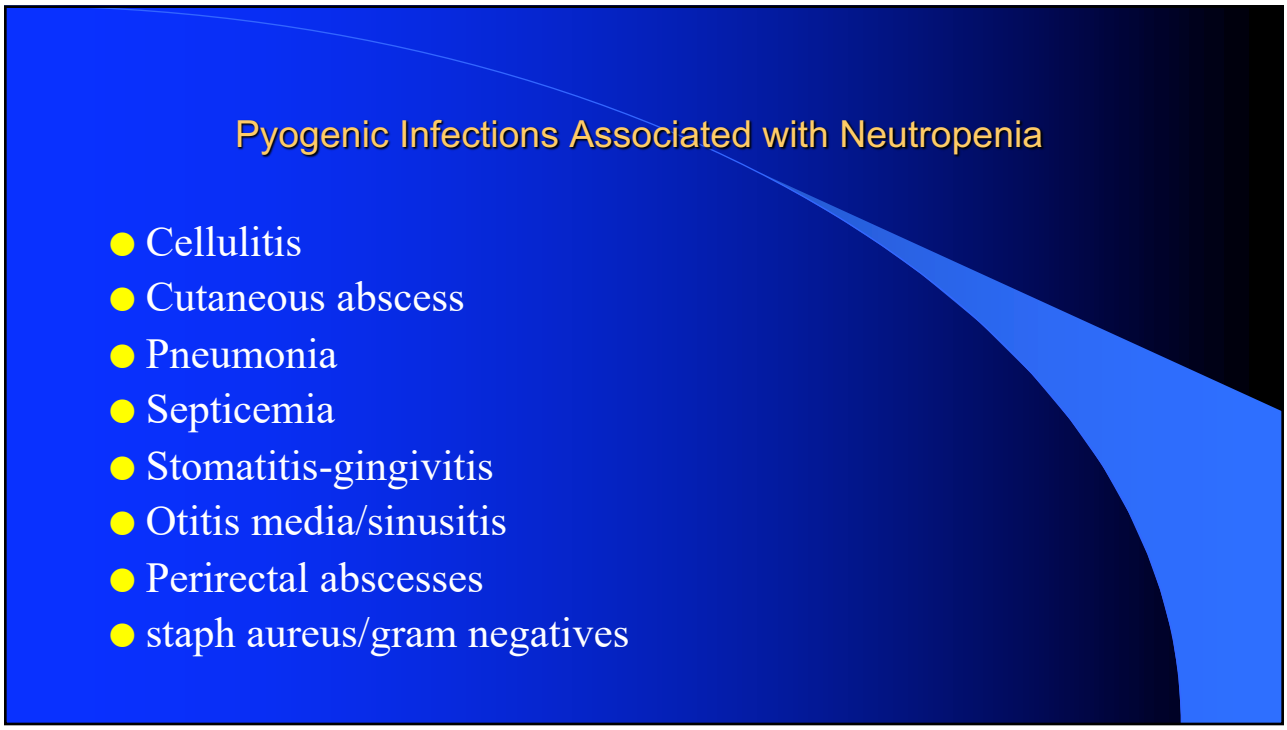
Pyogenic Infections Associated with Neutropenia
Cellulitis
Cutaneous abscess
Pneumonia
Septicemia
Stomatitis-gingivitis
Otitis media/sinusitis
Perirectal abscesses
staph aureus/gram negatives

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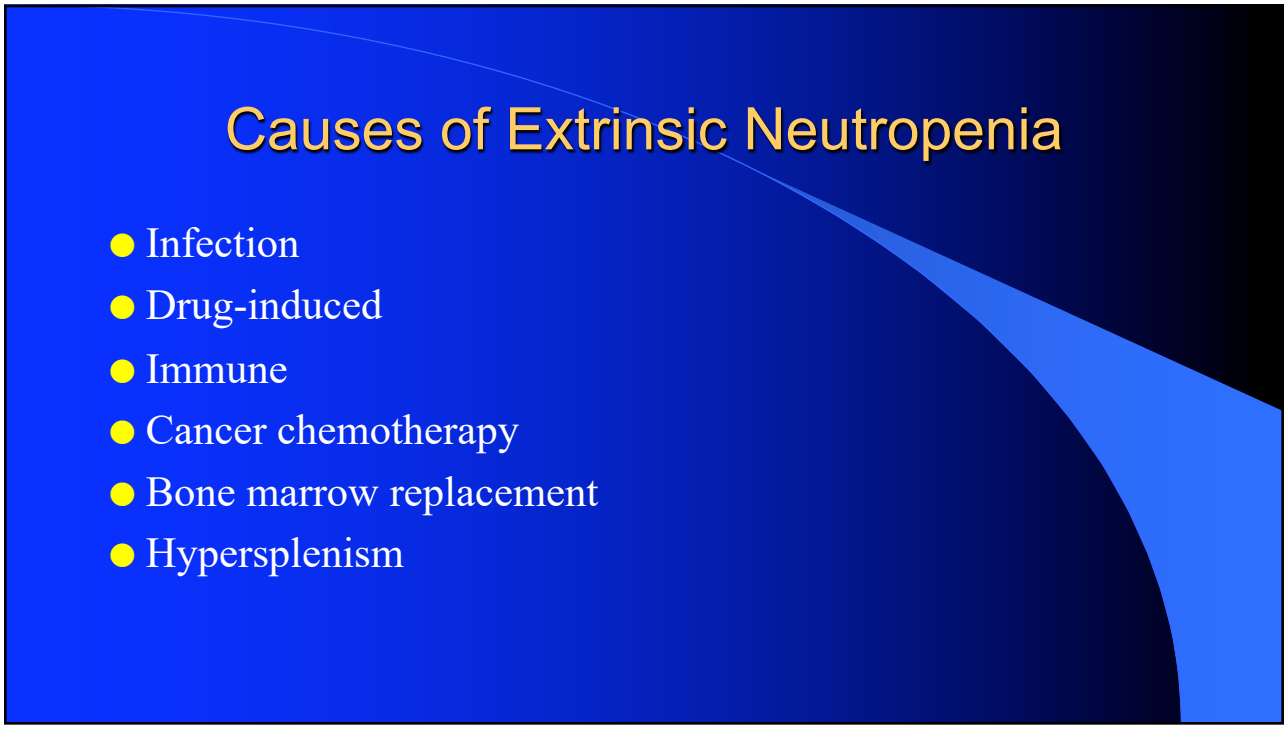
Causes of Extrinsic Neutropenia
Infection
Drug-induced
Immune
Cancer chemotherapy
Bone marrow replacement
Hypersplenism

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Intrinsic Neutropenia

- Cyclic neutropenia
- Severe congenital neutropenia-Kostmann
- Chronic benign neutropenia
- Neutropenias associated with phenotypic abnormalities

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Congenital Disorders of Stem Cells and Myeloid Precursors

- Severe Congenital Neutropenia (Kostmann's Syndrome)
- Cyclic Neutropenia
- Shwachman-Diamond Syndromes
- Myelokathexis/WHIM Syndrome
- Chédiak-Higashi Syndrome
- Glycogenosis Ib
- Neutropenia with associated metabolic diseases
- Neutropenia with immune disorders

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Febrile Neutropenia

- Evaluation : history + physical
- CBC, blood cultures, line CX
- CXR if symptomatic
- CT scans chest, abdomen, sinuses if needed
- Gm-stain, Culture bacterial fungal all lesions or drainage
- GI panel
- Karius

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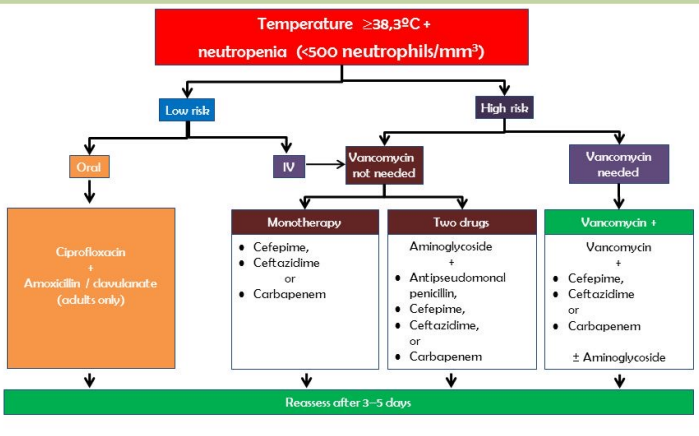
ALGORITHM FOR INITIAL MANAGEMENT OF FEBRILE NEUTROPENIA



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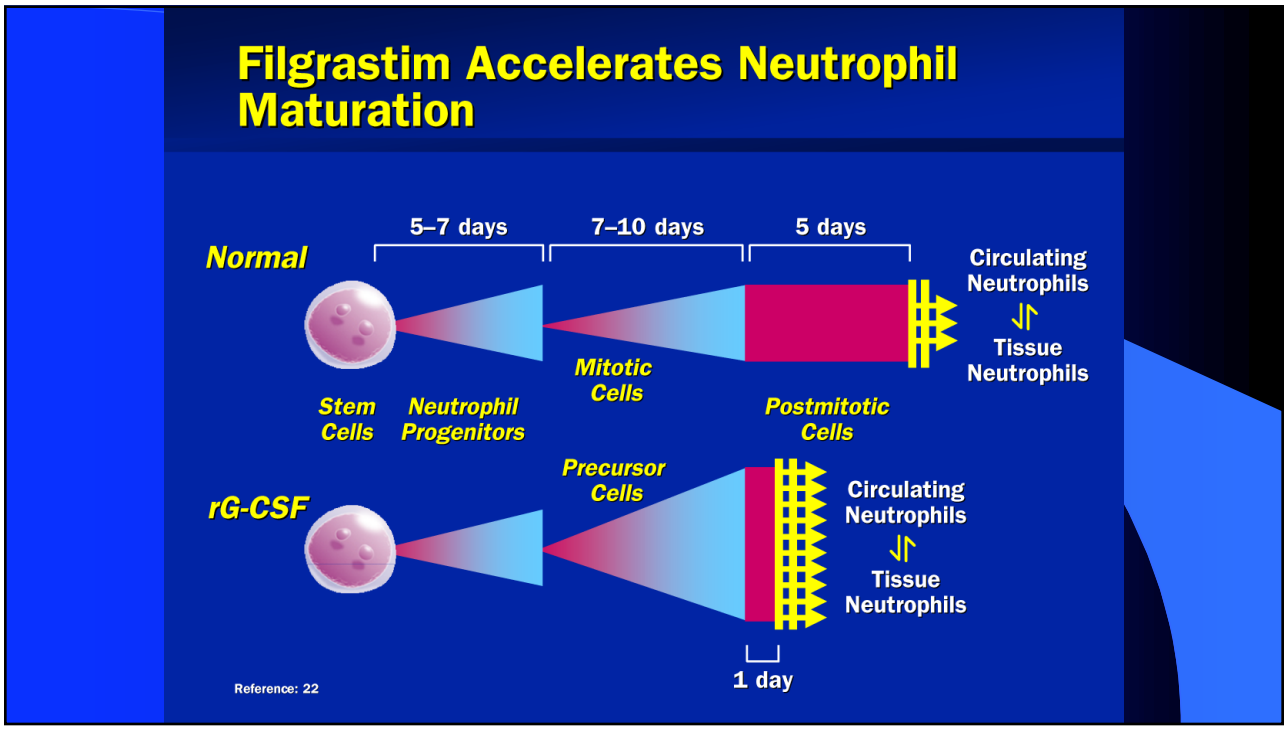

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Disorders of Granulocyte Function

- Disorders of Adhesion-LAD
- Disorders of Chemotaxis- complement
- Disorders of Recognition and Ingestion
- Disorders of Degranulation- Chediak-Higashi
- Disorders of Oxidative Metabolism- CGD

61

23-month-old hispanic boy is found to be anemic on a routine visit. He drinks 3 bottles of whole milk a day and 3 at night.

Hgb 7.1 gm/dL MCV 54 fl RDW 22 Retic 1.5%

What is the most likely cause of his anemia?

A. Thalassemia
B. Lead poisoning
C. Iron deficiency
D. Anemia of chronic disease

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Two year old African American girl found on a well baby visit to have this CBC. Adequate diet , No family Hx of anemia

TEST	RESULT				FLAG
WBC	8.8	K/uL			
LYM	5.5	R1	62.3	%L	H
*MID	0.8		9.2	%M	
GRAN	2.5	R3	28.5	%G	
RBC	4.70	M/uL			
HGB	10.1	g/dL			L
HCT	32.3	%			L
MCV	68.8	fL			L
MCH	21.5	pg			L
MCHC	31.3	g/dL			
RDW	15.3	%			H
PLT	320.	K/uL			
MPV	9.3	fL			

What is the Diagnosis?

A. Iron deficiency
B. Beta thalassemia trait
C. Alpha thalassemia trait
D. Sickle cell anemia

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15 yo boy with recurrent epigastric pain. Which of the following is the most appropriate plan?

TEST	RESULT		FLAG
WBC	12.5	K/uL	
LYM	1.8	14.5 %L	
*MID	1.8	14.1 %M	
GRAN	8.9	71.4 %G	H
RBC	4.68	M/uL	L
HGB	11.3	g/dL	L
HCT	35.4	%	L
MCV	75.7	fL	L
MCH	24.1	pg	L
MCHC	31.9	g/dL	
RDW	15.9	%	H
PLT	297.	K/uL	
MPV	11.4	fL	

A. Reassure all is normal
B. Give iron therapy for 3 months and F/U in 6 months
C. Refer to gastroenterology for endoscopy

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6 yo girl with anemia not responding to oral iron. Father has anemia also.

TEST	RESULT			FLAG
WBC	4.3	K/uL		L
LYM	2.5	57.7 %L		
*MID	0.3	7.1 %M		
GRAN	1.5	35.2 %G		L
RBC	5.35	M/uL		H
HGB	9.8	g/dL		L
HCT	30.7	%		L
MCV	57.3	fL		L
MCH	18.3	pg		L
MCHC	31.9	g/dL		
RDW	17.4	%		H
PLT	394.	K/uL	URI	H
MPV		fL		

Retic 0.7%

What is the most likely diagnosis?

A. Iron deficiency
B. Inflammation
C. Lead poisoning
D. Thalassemia

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15 month old white female, was noted 6 months ago to have mild anemia. She has not responded to iron therapy. She had neonatal jaundice requiring phototherapy. The spleen is palpable 2 cm bcm. Which of the following is correct?

TEST	RESULT			FLAG
WBC	12.7	K/uL		
LYM	7.3	R1 57.6	%L	H
*MID	1.5	11.7	%M	
GRAN	3.9	R3 30.7	%G	
RBC	3.02	M/uL		L
HGB	7.7	g/dL		L
HCT	22.1	%		L
MCV	73.3	fL		L
MCH	25.5	pg		
MCHC	34.8	g/dL		
RDW	31.3	%		H
PLT	281.	K/uL	URI	
MPV		fL		

Ret C 5.7%

A. Most likely diagnosis is G6PD
B. Refer for immediate splenectomy
C. Give intravenous iron sucrose
D. Obtain osmotic fragility test

70

A 16 month old boy with progressive pallor is otherwise well.

- Hemoglobin is 6.0 gm/dl,
- hematocrit 17%
- MCV 84 fl
- reticulocytes <0.1%.
- WBC 4300 /mm3
- platelets 225,000 /mm3.
- Peripheral blood smear is normal.

- Most likely diagnosis?

A. Transient erythroblastopenia of childhood
B. Iron deficiency
C. Diamond-Blackfan anemia
D. Autoimmune hemolytic anemia

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4-year-old African-American male with fever otitis was given trimethoprim/sulfa and suddenly develops pallor and tea-colored urine

- Hgb 5.4 gm/dl
- MCV 96 fl
- WBC count 17,000 / mm^3
- platelets 180,000 / mm^3
- reticulocytes 12%,

Most likely Diagnosis?

A. Autoimmune hemolytic anemia

B. Hereditary spherocytosis

C. G6PD deficiency

D. Sickle cell anemia

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11 yo Puerto Rican boy with recurrent back pain

TEST	RESULT			FLAG
WBC	3.6	K/uL		L
LYM	1.6	43.5	%L	
*MID	0.4	12.0	%M	
GRAN	1.6	44.5	%G	L
RBC	5.72	M/uL		H
HGB	13.2	g/dL		
HCT	39.1	%		
MCV	68.4	fL		L
MCH	23.1	pg		L
MCHC	33.8	g/dL		
RDW	18.6	%		H
PLT	230.	K/uL	URI	
MPV		fL		

A. Bone marrow aspiration indicated

B. Check rheumatoid factor

C. Obtain hemoglobin electrophoresis

D. Test for urine porphyrins

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15 year old girl with fatigue and fever?

TEST	RESULT			FLAG
WBC	1.3	K/uL		LL
LYM	0.4	33.7	%L	L
*MID	0.3	26.9	%M	
GRAN	0.5	RM 39.4	%G	L
RBC	2.57	M/uL		L
HGB	8.1	g/dL		L
HCT	25.1	%		L
MCV	97.7	fL		
MCH	31.5	pg		H
MCHC	32.3	g/dL		
RDW	17.6	%		H
PLT	44.	K/uL		LL
MPV		fL		

Estimated plt 95,000 k/uL

A. Evaluate blood smear

B. Obtain bone marrow aspirate

C. Refer to hematology

D. Start broad spectrum antibiotics

E. All of the above

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