The Annual General Pediatric Review & Self Assessment

Nicklaus Children's Hospital

HEMATOLOGY

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Disclosure of Relevant Relationship

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Neonatal Anemia

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

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

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

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)

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

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

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

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

RBC Transfusion

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

- **Formula:**

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

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)

Anemia

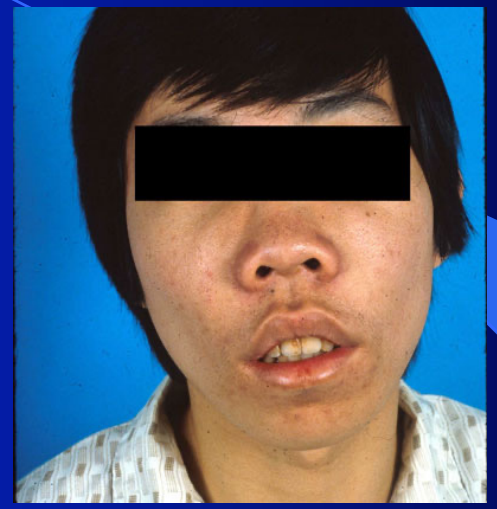
- Low Retic
  - Iron Deficiency
  - Hypoplastic
  - Bone marrow infiltration
- High Retic
  - Hemolytic: Coomb's +
  - RBC enzyme (G6PD deficiency- X linked)
  - Hemoglobinopathy (Sickle, thalassemia)
  - RBC membrane defect (spherocytosis)

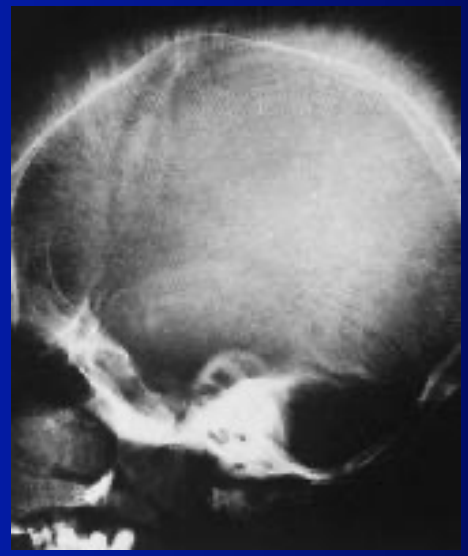
Beta Thalassemia
Trait

- 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

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

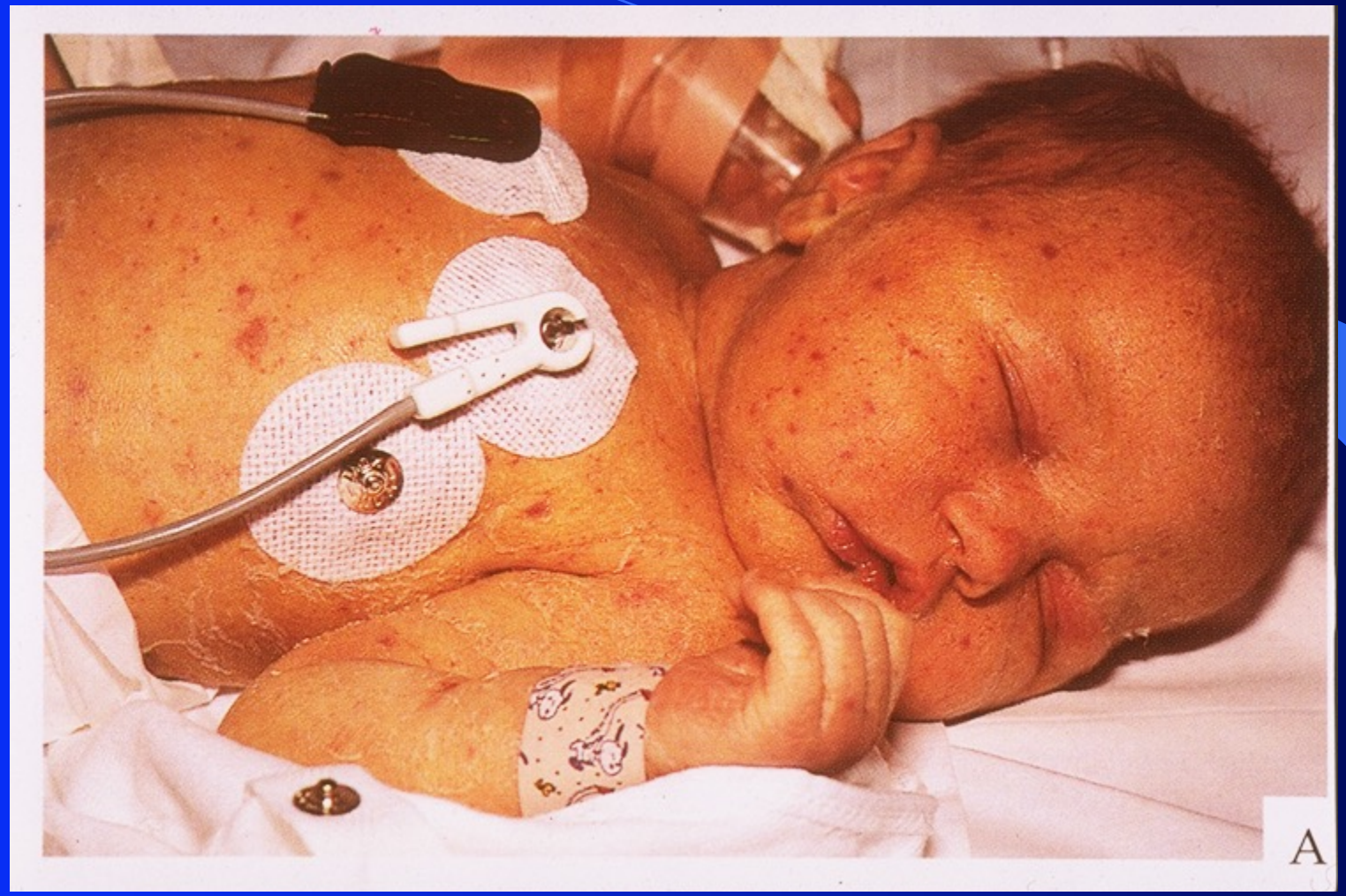




Alpha Thalassemia
aa/aa

- **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

	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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Neonatal Thrombocytopenia

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

Immune Thrombocytopenia

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

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

Non-immune Destruction of Plts

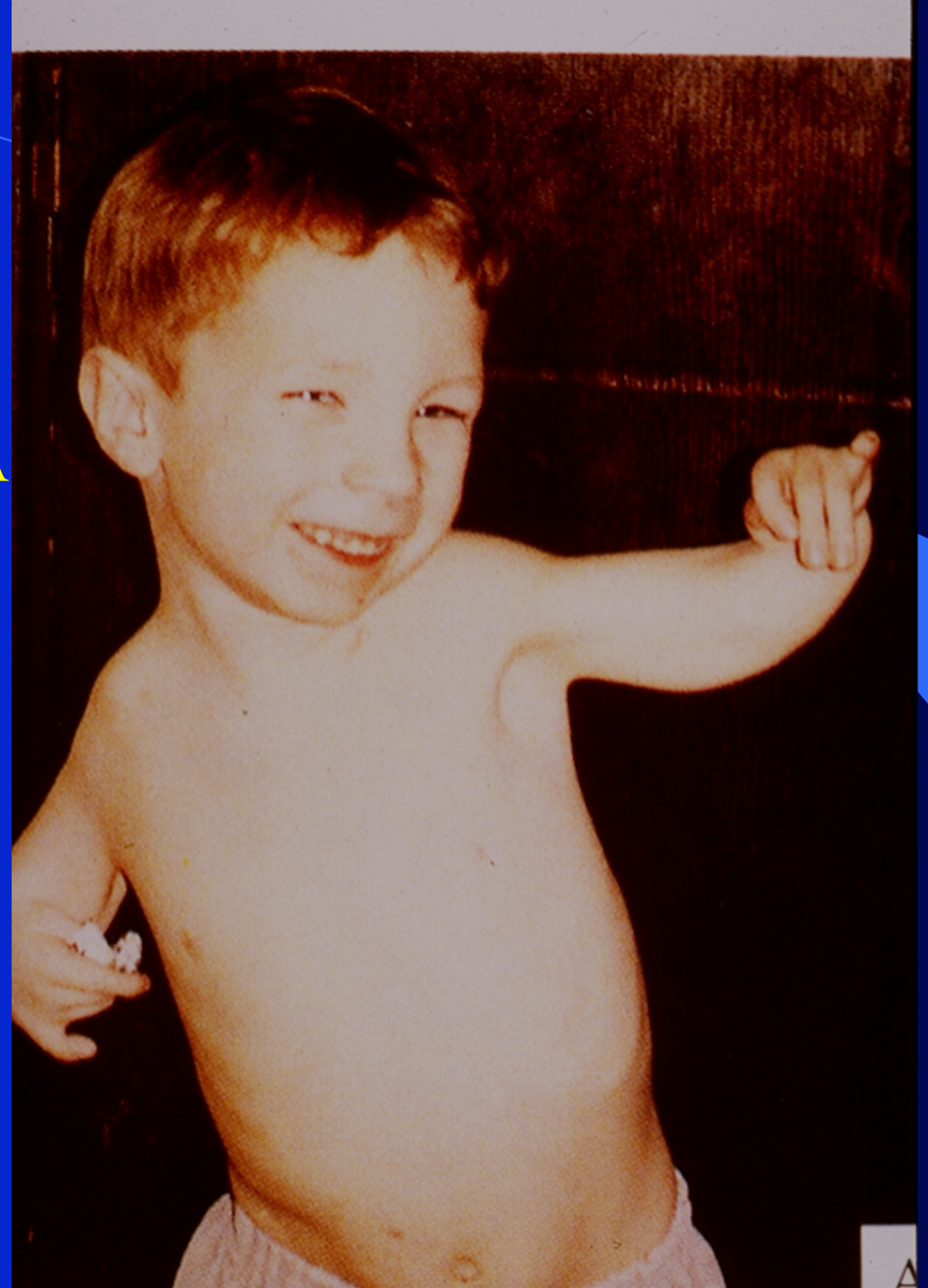
- Sepsis, DIC, TORCH infections
- Asphyxia
- Perinatal aspiration
- Necrotizing enterocolitis
- Hemangioma
- Neonatal thrombosis
- Respiratory distress syndrome

Decreased Platelet Production

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

TAR

THROMBOCYTOPENIA
WITH
ABSENT RADIUS



Thrombocytopenia

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

Lead Poisoning

- Lead inhibits porphyrin synthesis enzymes d-ALA dehydratase and **ferrochelatase**
- Fe^{++} + protoporphyrin $\xrightarrow{\text{ferrochelatase}}$ 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**

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

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

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

Infections in Sickle cell anemia

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

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

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

SCD- Abdominal pain

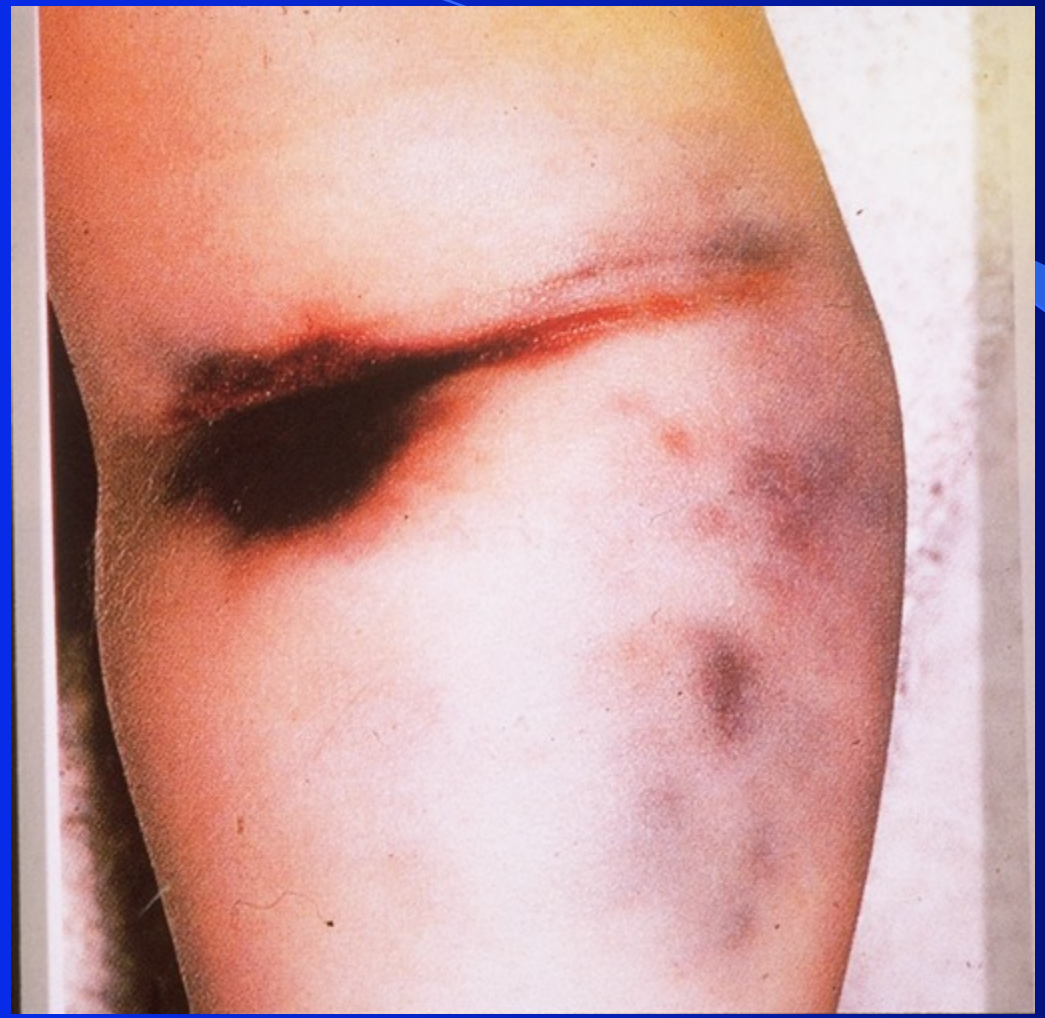
- Vaso-occlusive crisis (mesenteric, abdominal wall)
- Hepatic crisis
- RUQ syndrome (gall stones)
- R/O surgical pain eg: cholecystitis, appendicitis

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

SCD- Aplastic crisis

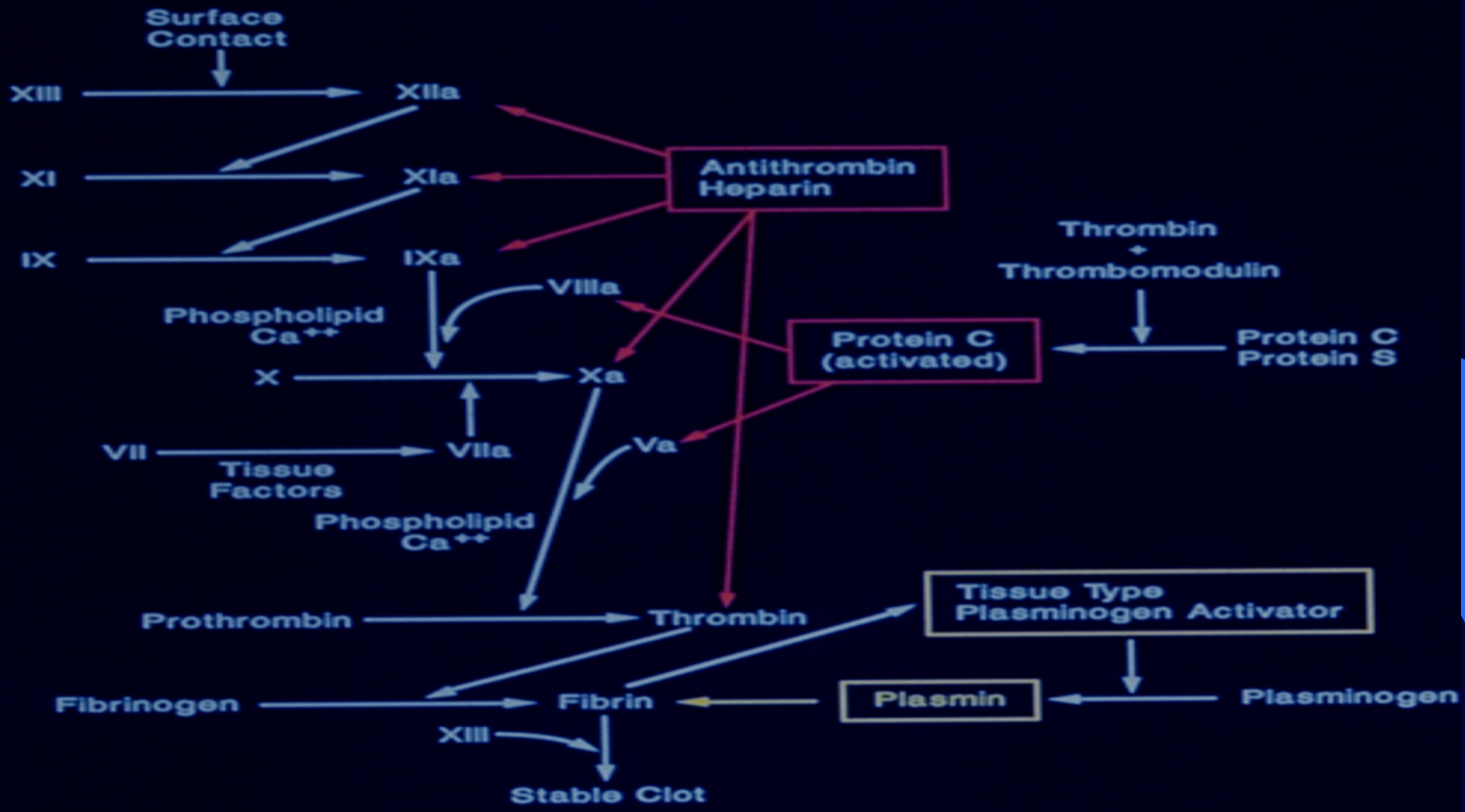
- Temporary cessation of erythroid marrow activity
- Parvovirus B-19 infection preceding
- Retic count low (<0.1)
- Due to short sickle RBC survival 15-50 days compared to 120 days normally
- Recovery with or without transfusion



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)

Coagulation System



Prothrombin time PT

Increased : Factor VII deficiency

Liver disease

Vitamin K deficiency

malabsorption, CF

Partial Thromboplastin time PTT

Increased: Factor VIII and IX def

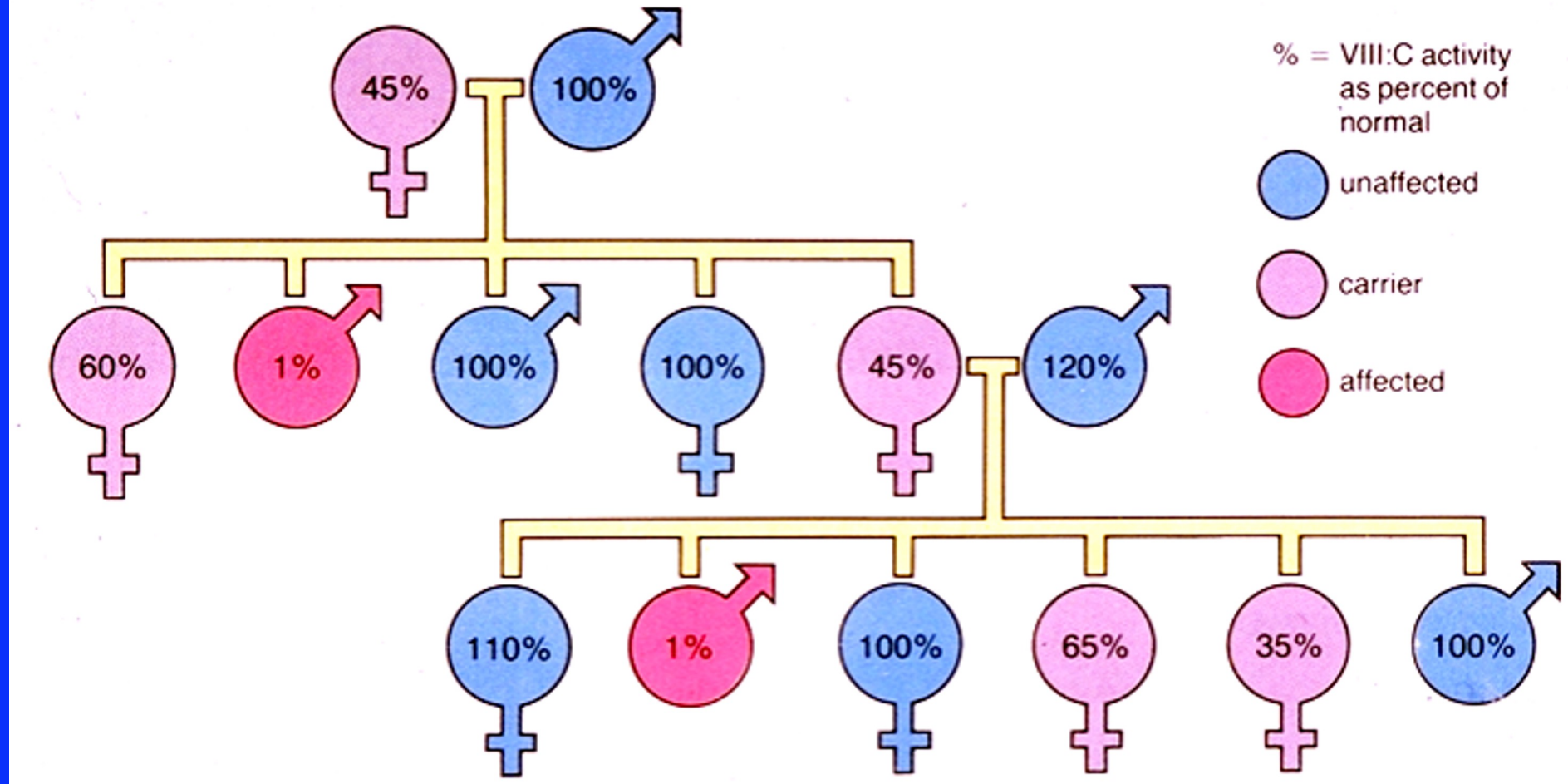
von Willebrand disease

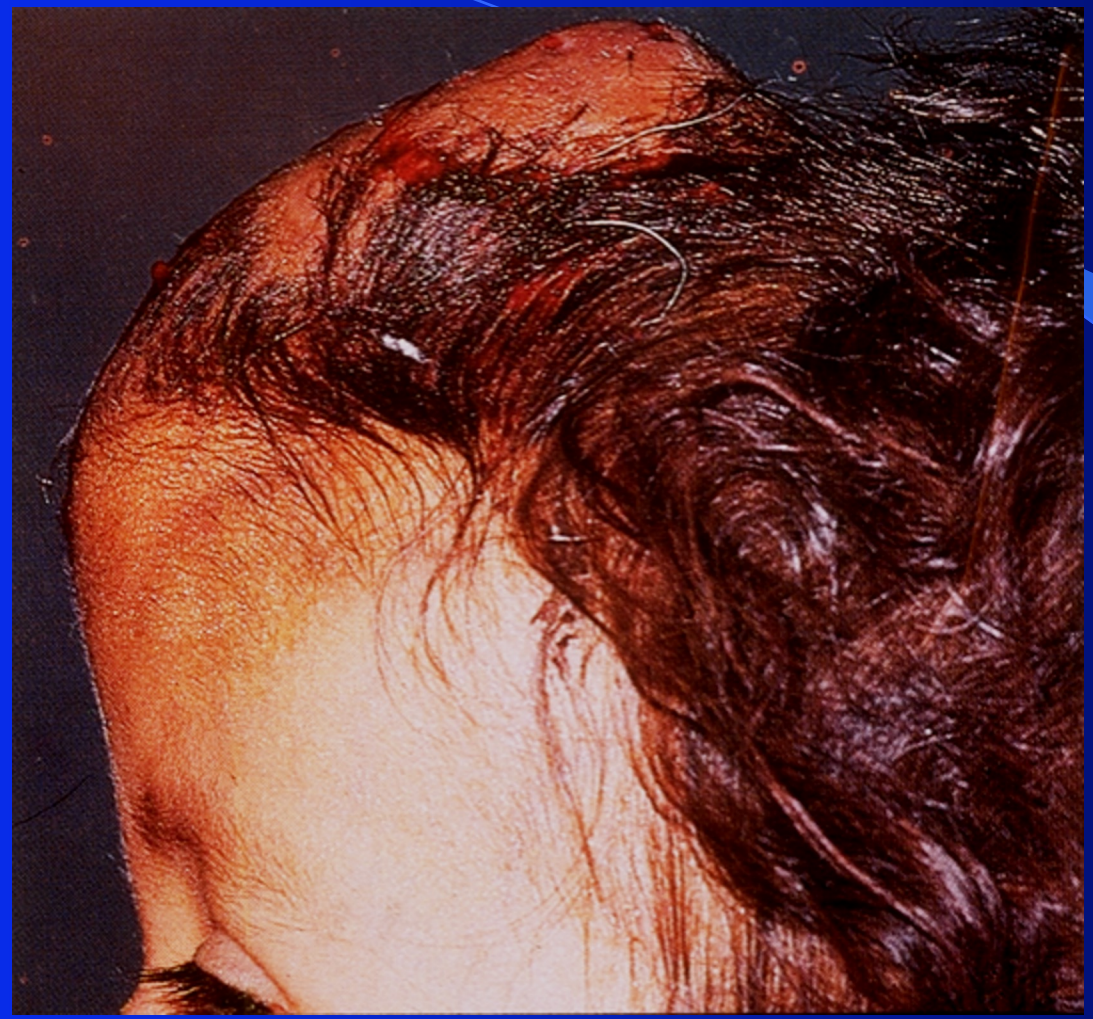
other contact factors

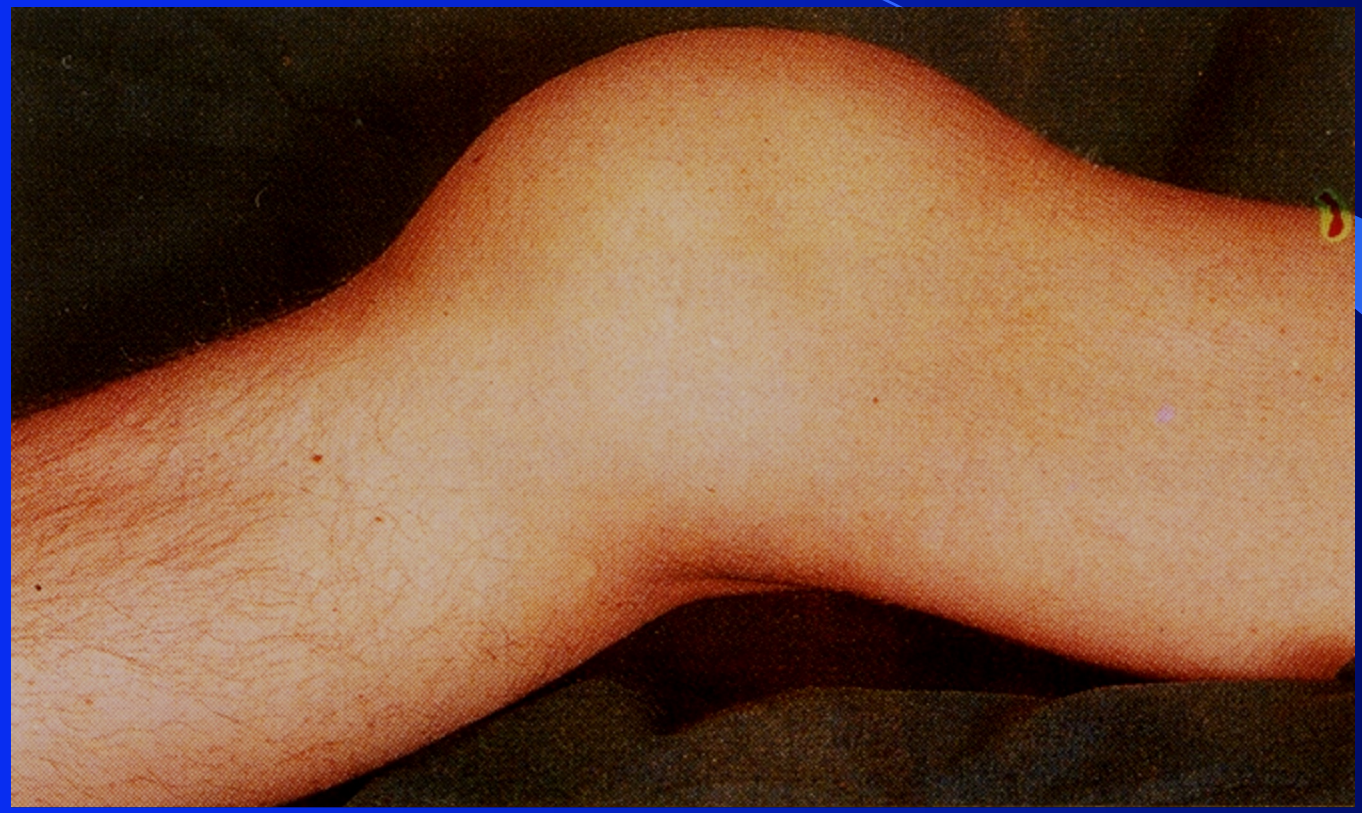
Hemophilia

- 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

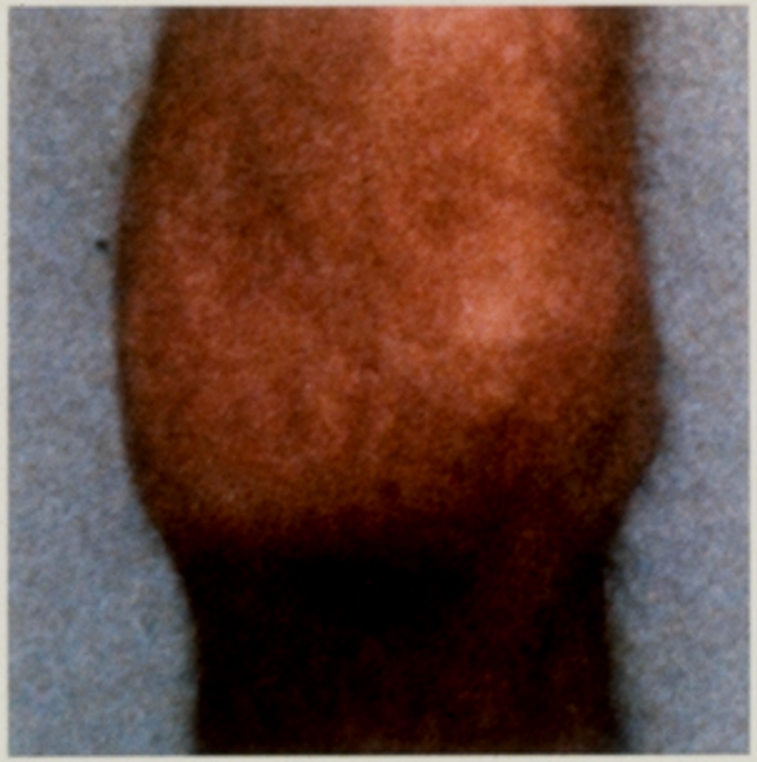
Inheritance in Haemophilia

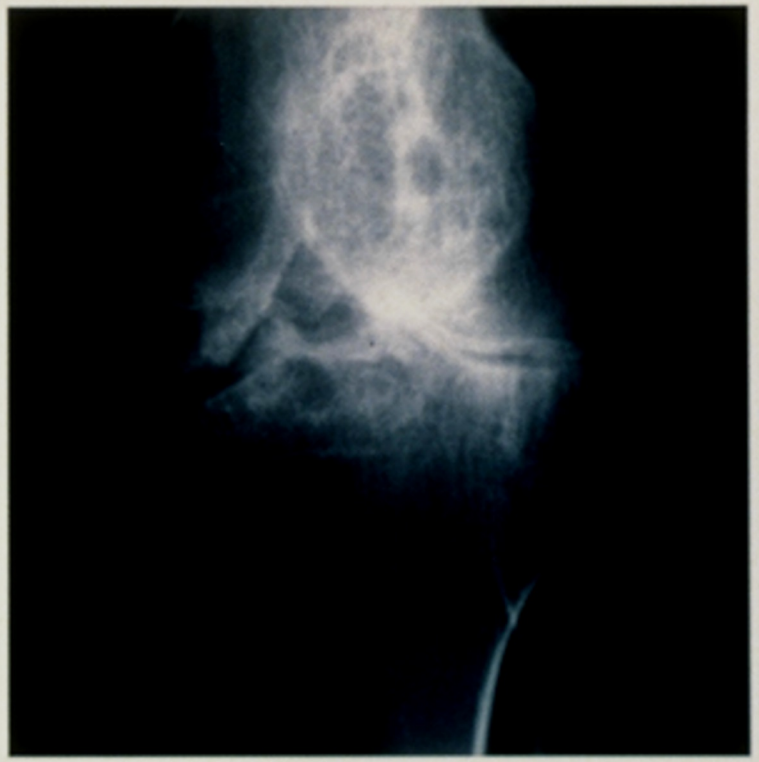




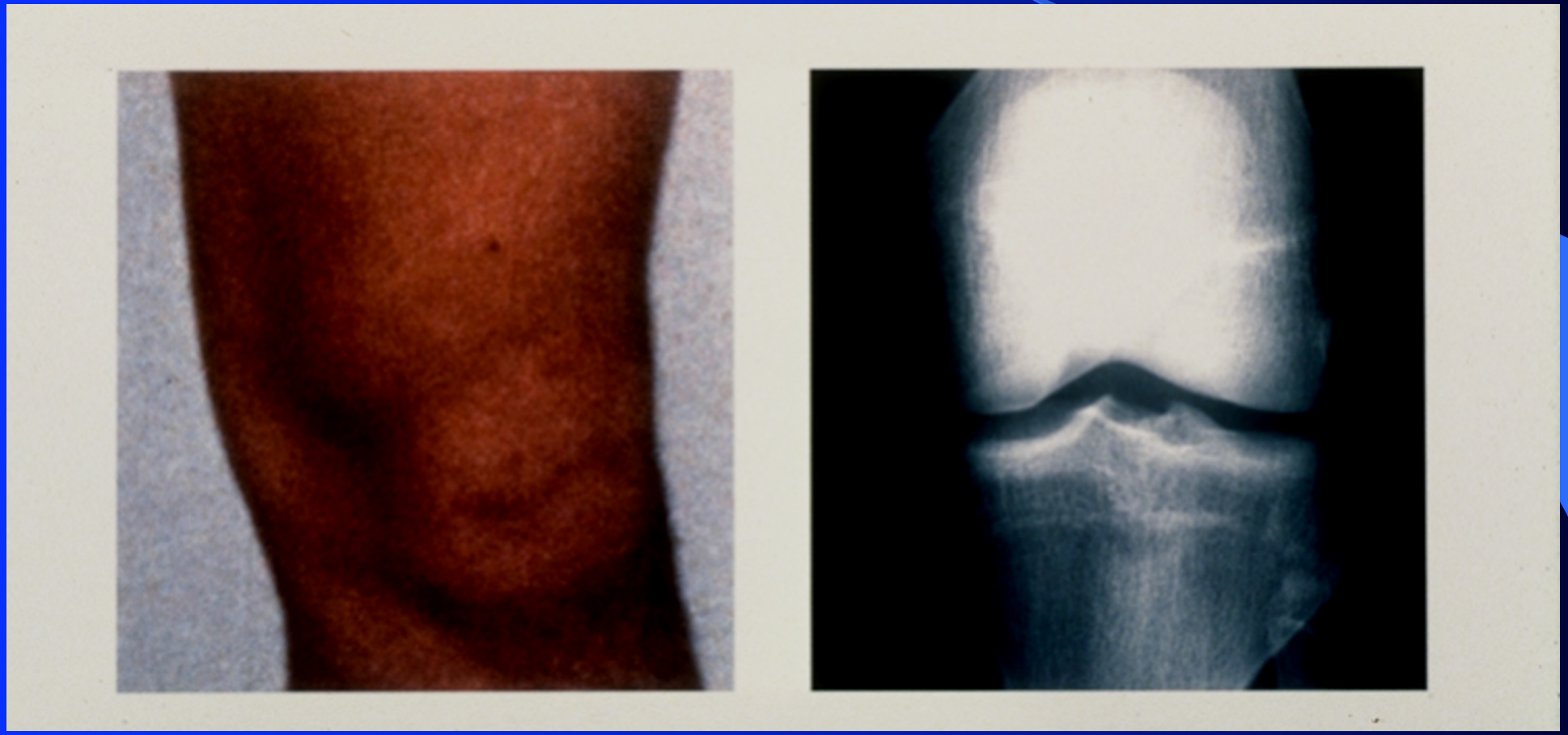


Hemophilia
Joint Damage with No Prophylactic Therapy



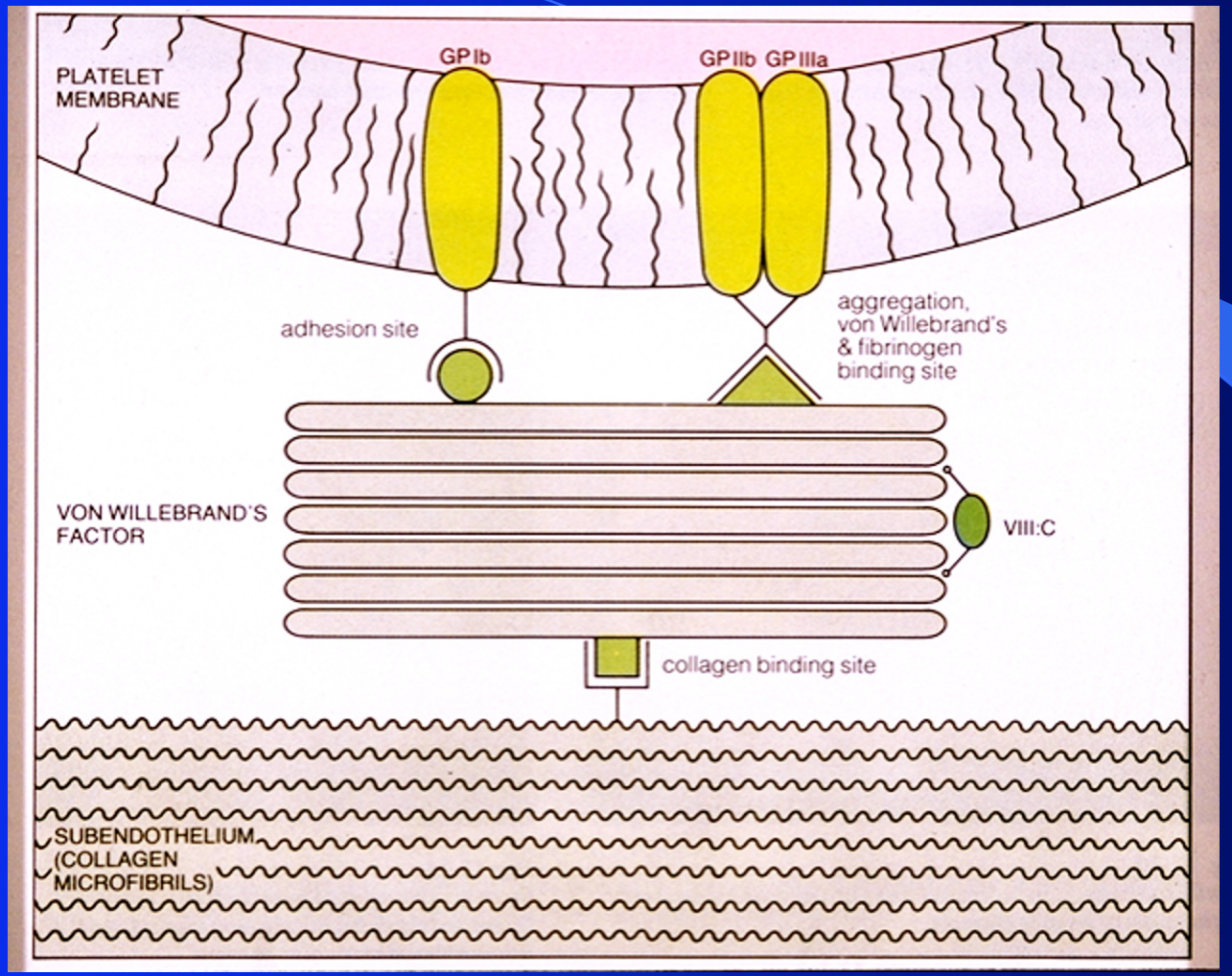


Prevention of Joint Damage with Chronic Prophylactic Therapy

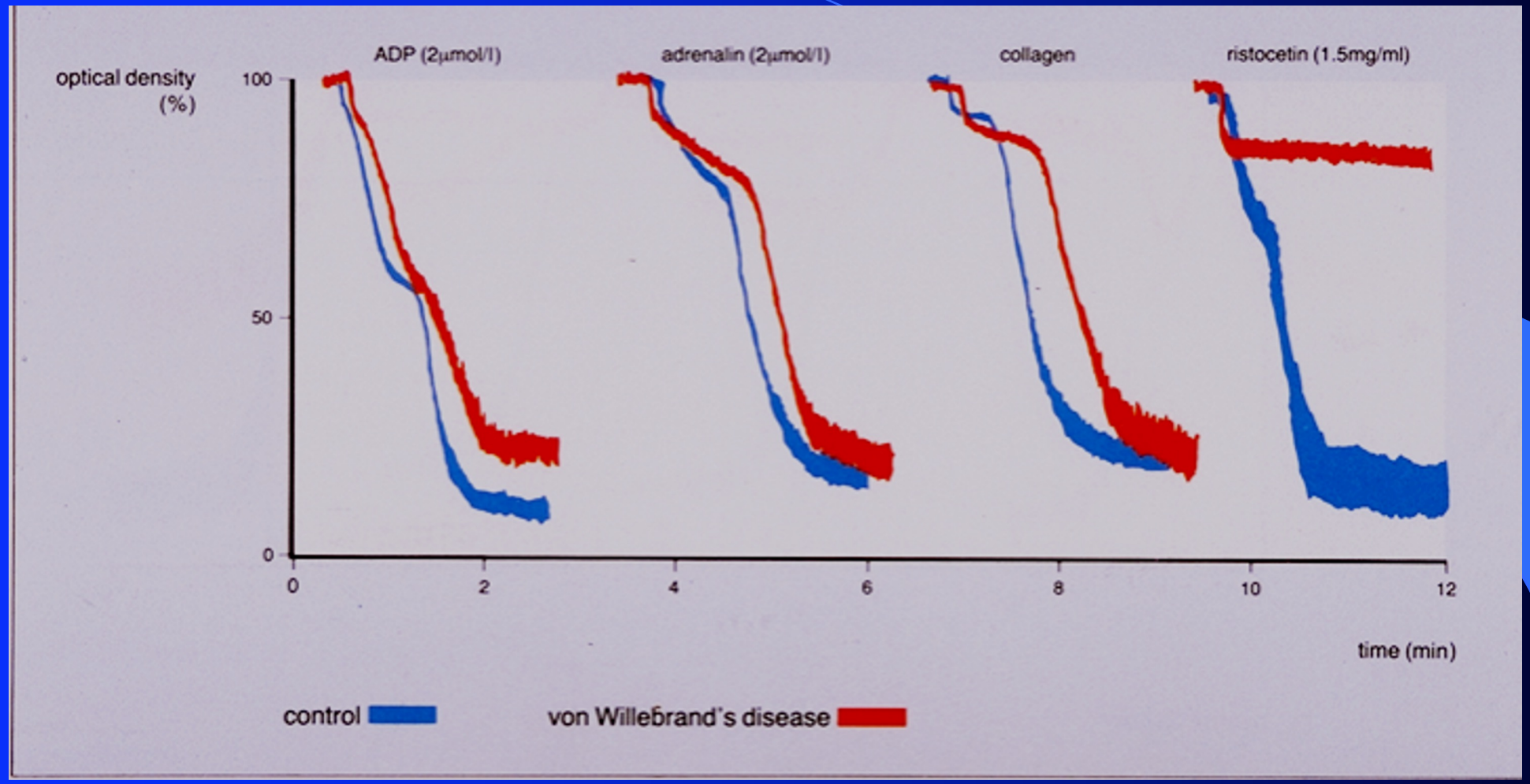


Platelet Function Disorders

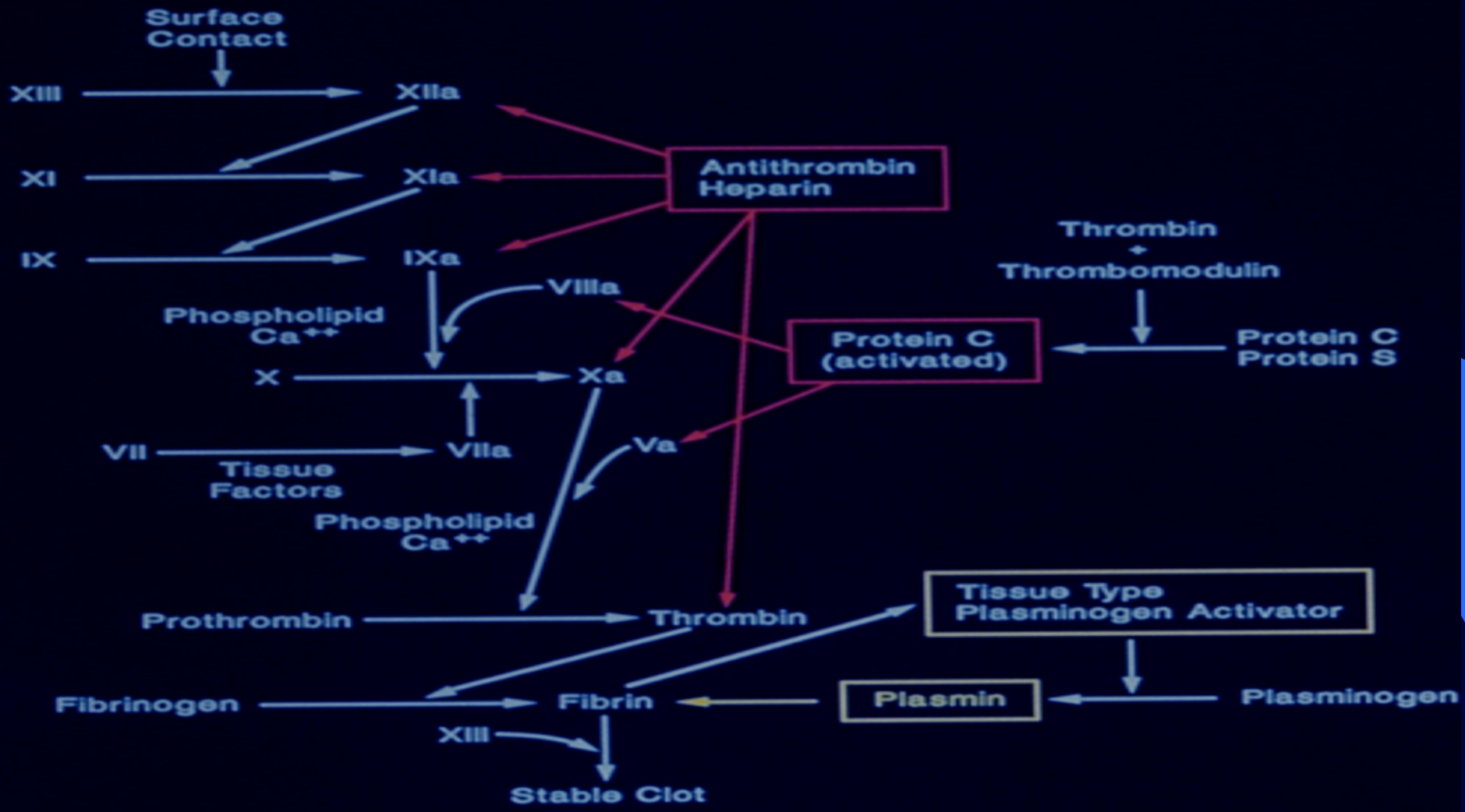
- Von Willebrand disease (lack of plasma factor necessary for platelet adhesiveness)
- Glanzmann thrombasthenia (Gp IIb/IIIa)
- Bernard-Soulier syndrome (Gp Ib deficiency)
- Storage pool defect
  - Alpha granule-gray platelet syndrome
  - Dense granule deficiency (Hermansky-Pudlak etc.)


PLATELET MEMBRANE
GP Ib
GP IIb GP IIIa
adhesion site
aggregation, von Willebrand's & fibrinogen binding site
VON WILLEBRAND'S FACTOR
VIII:C
collagen binding site
SUBENDOTHELIUM (COLLAGEN MICROFIBRILS)

Measurement of Platelet Aggregation



Coagulation System



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

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

Pyogenic Infections Associated with Neutropenia

- Cellulitis
- Cutaneous abscess
- Pneumonia
- Septicemia
- Stomatitis-gingivitis
- Otitis media/sinusitis
- Perirectal abscesses
- staph aureus/gram negatives

Causes of Extrinsic Neutropenia

- Infection
- Drug-induced
- Immune
- Cancer chemotherapy
- Bone marrow replacement
- Hypersplenism

Intrinsic Neutropenia

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

Congenital Disorders of Stem Cells and Myeloid Precursors

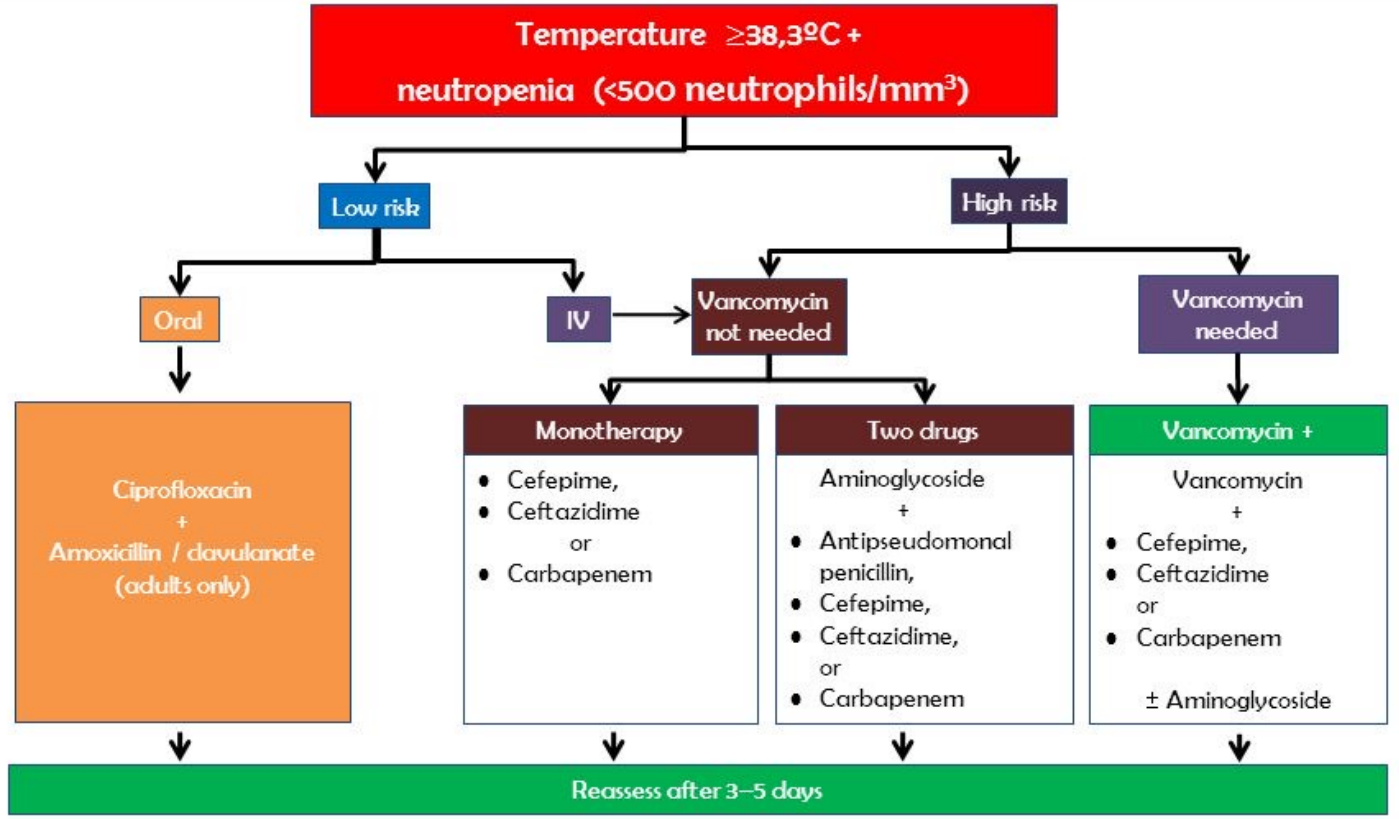
- Severe Congenital Neutropenia (Kostmann's Syndrome)
- Cyclic Neutropenia
- Shwachman-Diamond Syndromes
- Myelokathexis/WHIM Syndrome
- Chédiak-Higashi Syndrome
- Glycogenosis Ib
- Neutropenia with associated metabolic diseases
- Neutropenia with immune disorders

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

UKK INFEKSI PEDIATRI TROPIS

ALGORITHM FOR INITIAL MANAGEMENT OF FEBRILE NEUTROPENIA



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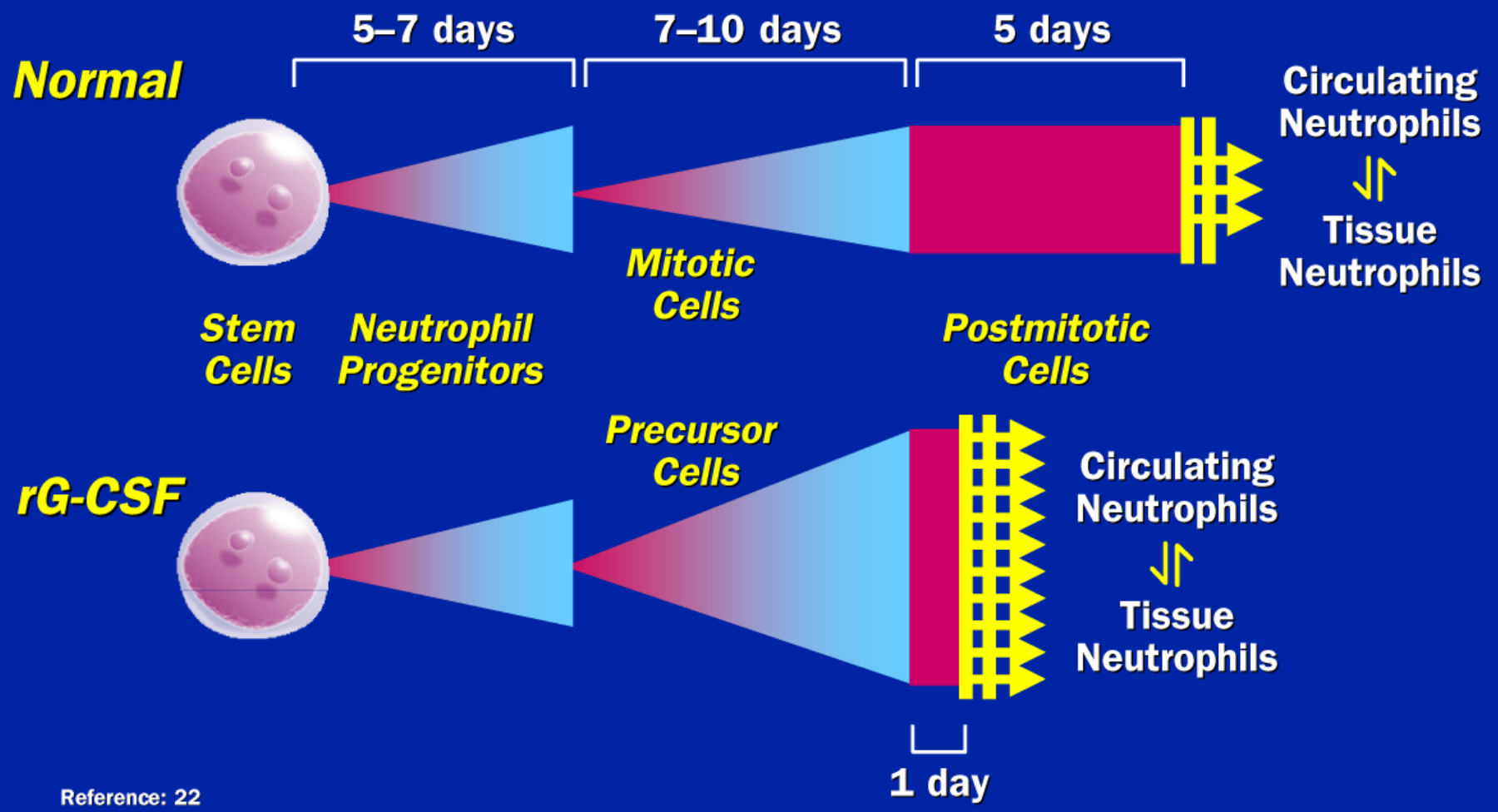
Filgrastim Accelerates Neutrophil Maturation



Reference: 22

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

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

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

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

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

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

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

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

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

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 90,000 k/sL

A. Evaluate blood smear

B. Obtain bone marrow aspirate

C. Refer to hematology

D. Start broad spectrum antibiotics

E. All of the above