Platelet Disorders

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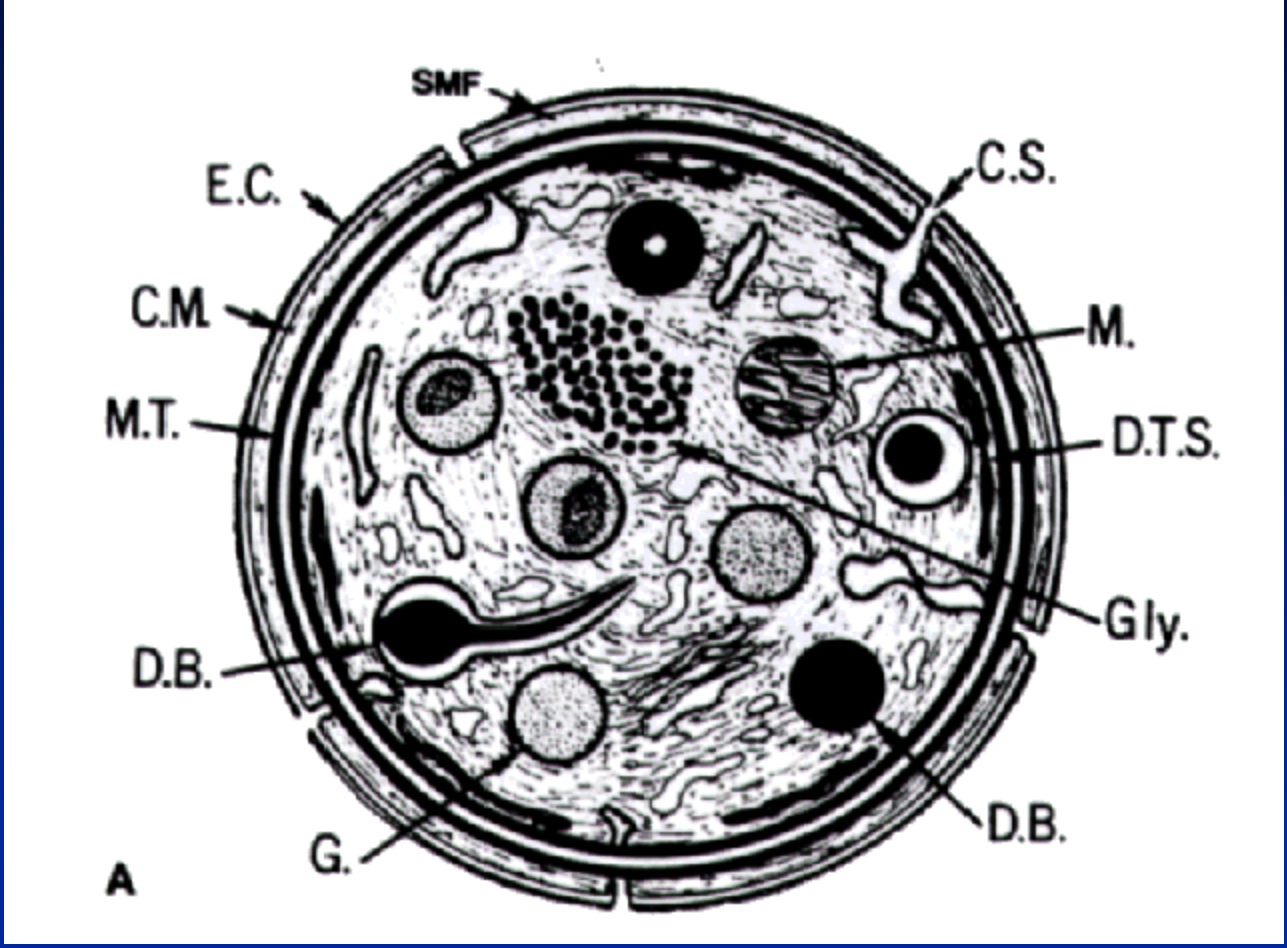
Review of platelet functional anatomy

- Glycocalyx: outer surface, rich in glycoproteins
- Microtubules: sub-membranous band, protein tubulin, provide structural support
- Contractile microfilaments: actin, myosin
- Open canalicular system: direct communication with extracellular environment
- Dense tubular system: derived from smooth endoplasmic reticulum, site for arachidonic acid metabolism

Review of platelet functional anatomy

- Mitochondria
- Glycogen
- Alpha granules: platelet fibrinogen, platelet-derived growth factor, vonWillebrand factor, beta-thromboglobulin, heparin neutralizing factor (PF4)
- Dense granules: adenosine diphosphate, adenosine triphosphate, serotonin, calcium
- Lysosomes

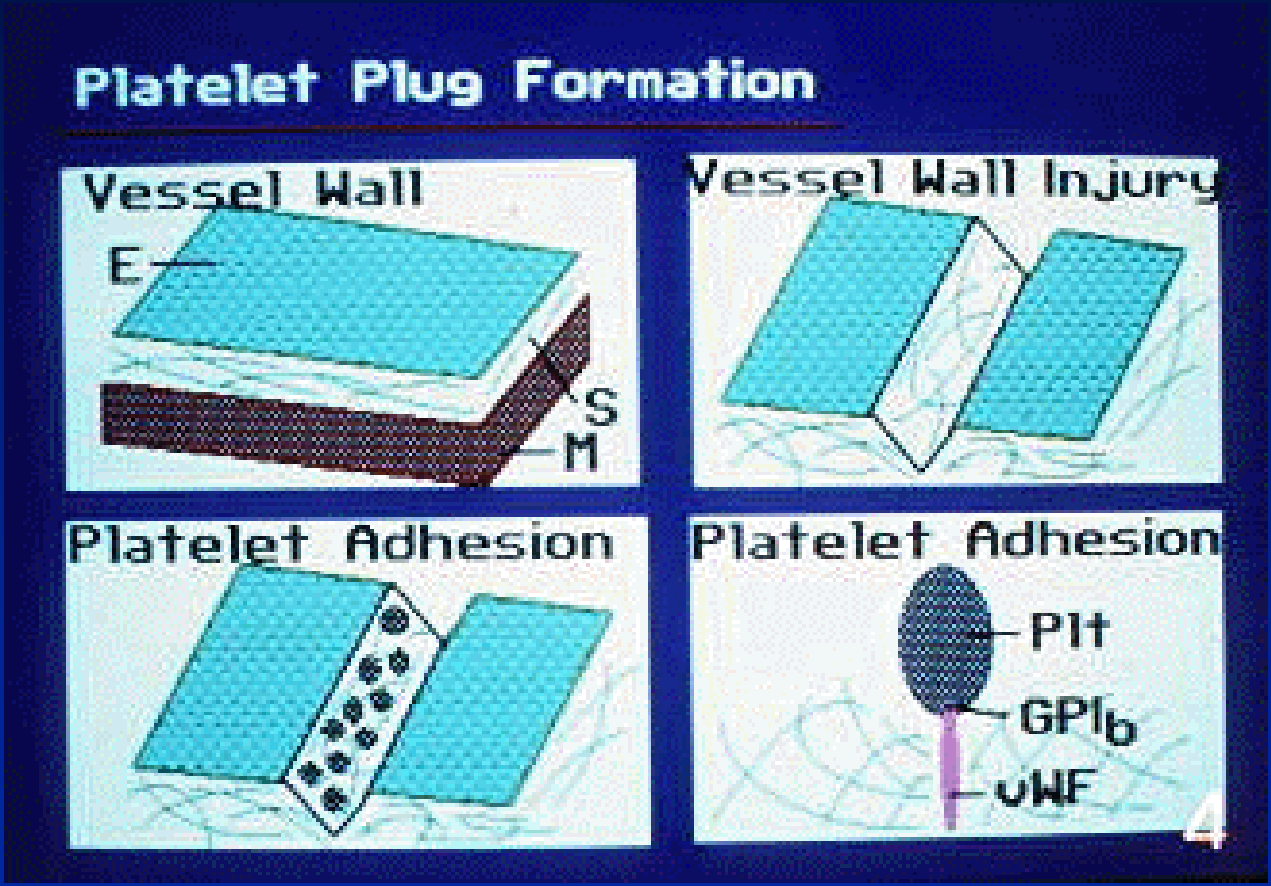
Review of platelet functional anatomy



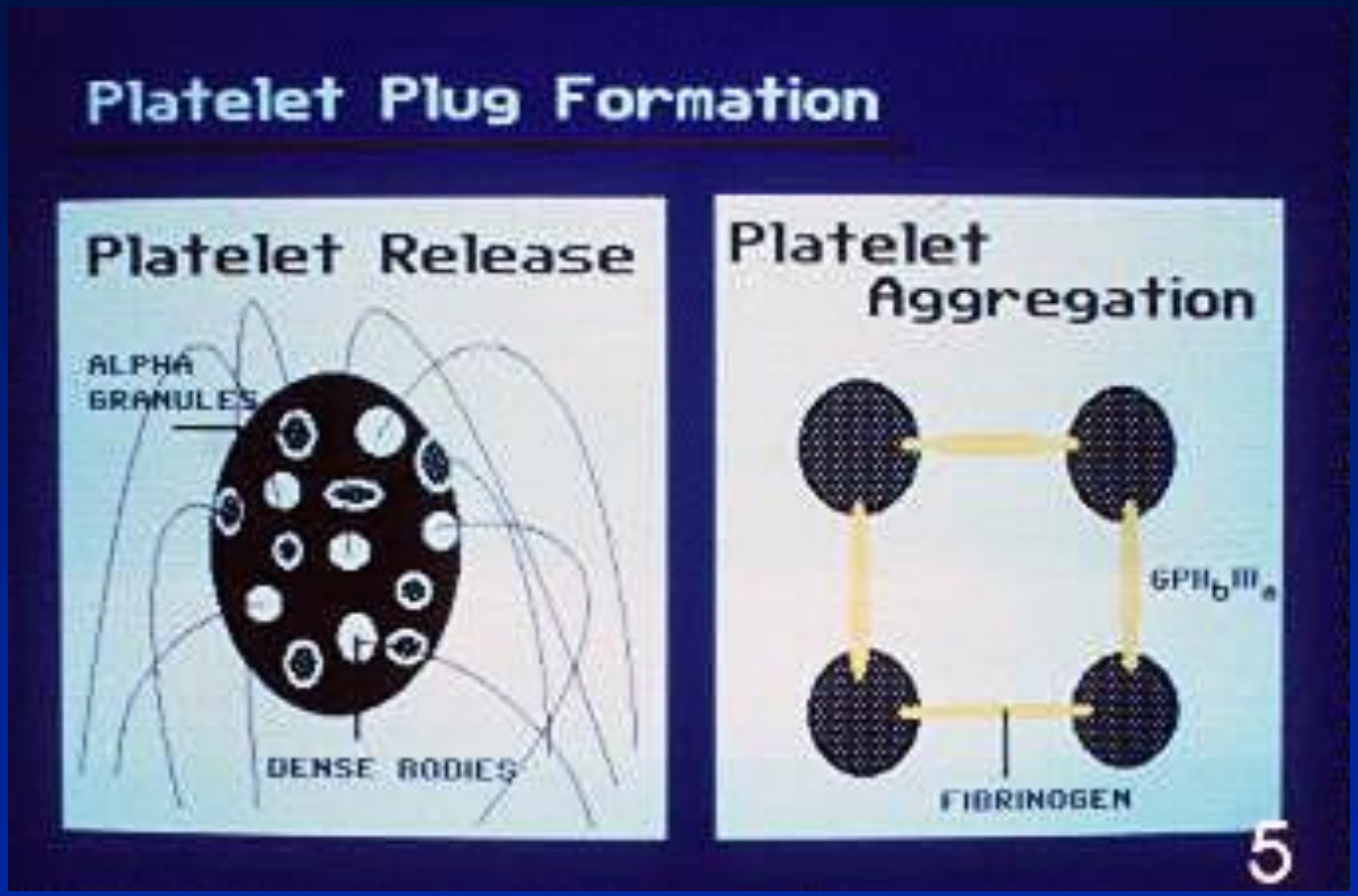
Platelet membrane glycoproteins

- Identified by radio-active labeling of surface glycoproteins, solubilization of the membranes, electrophoresis on polyacrylamide gels
- Clinically important: GP Ib, V, IX, IIb, IIIa

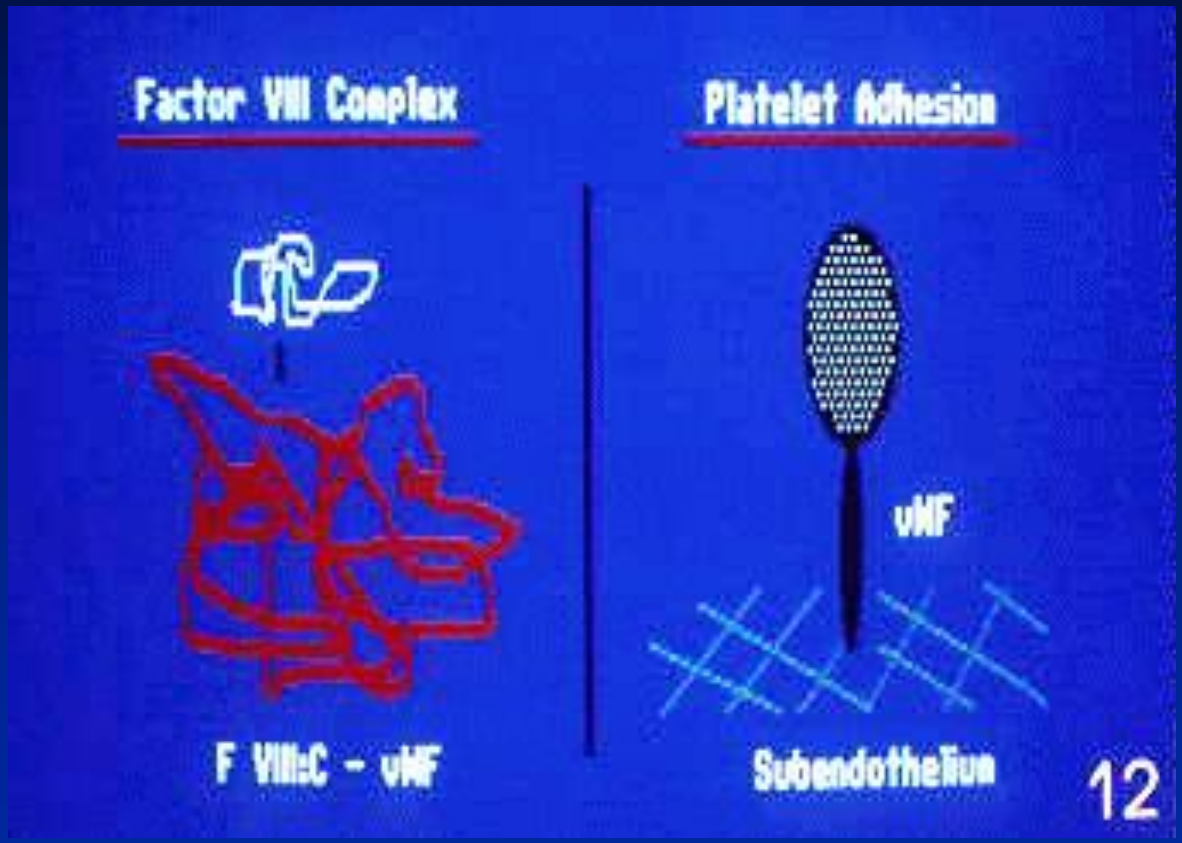
Platelet activities in hemostasis



Platelet activities in hemostasis (cont'd)



Platelet activities in hemostasis (cont'd)



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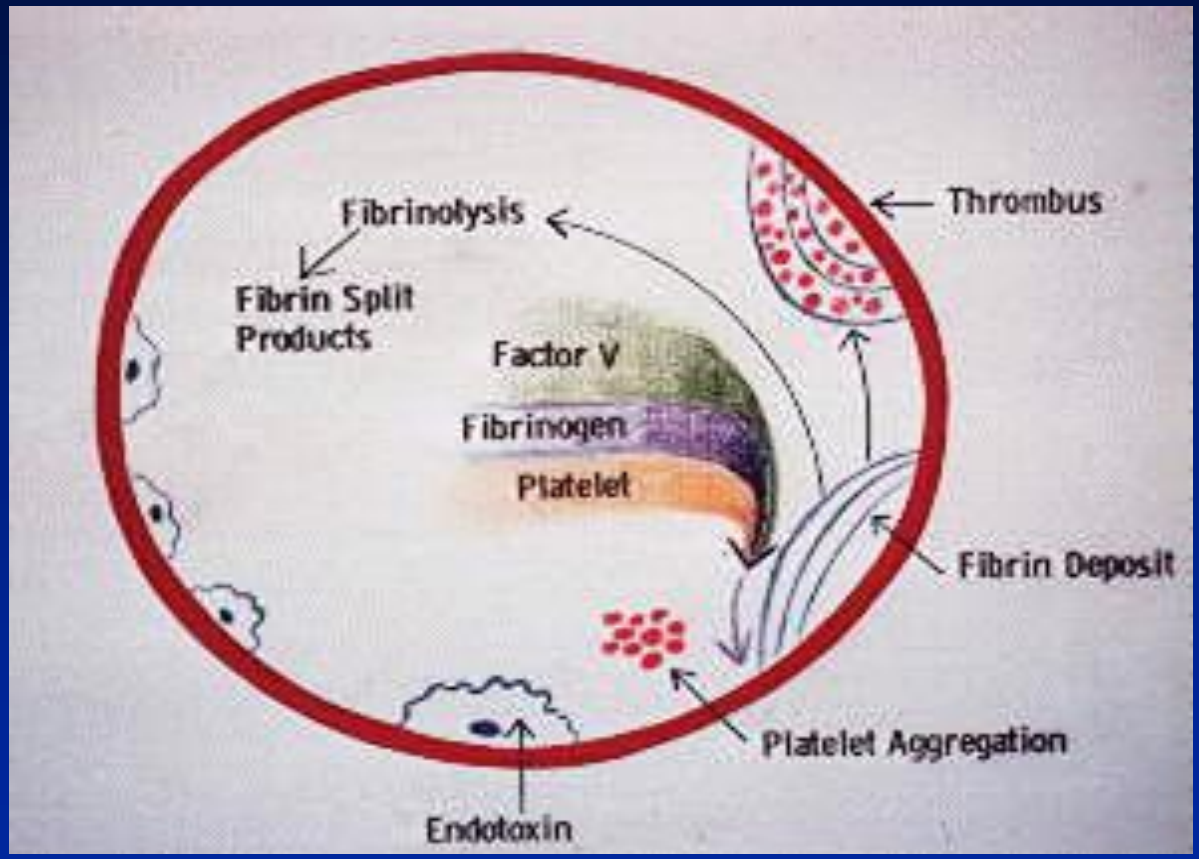
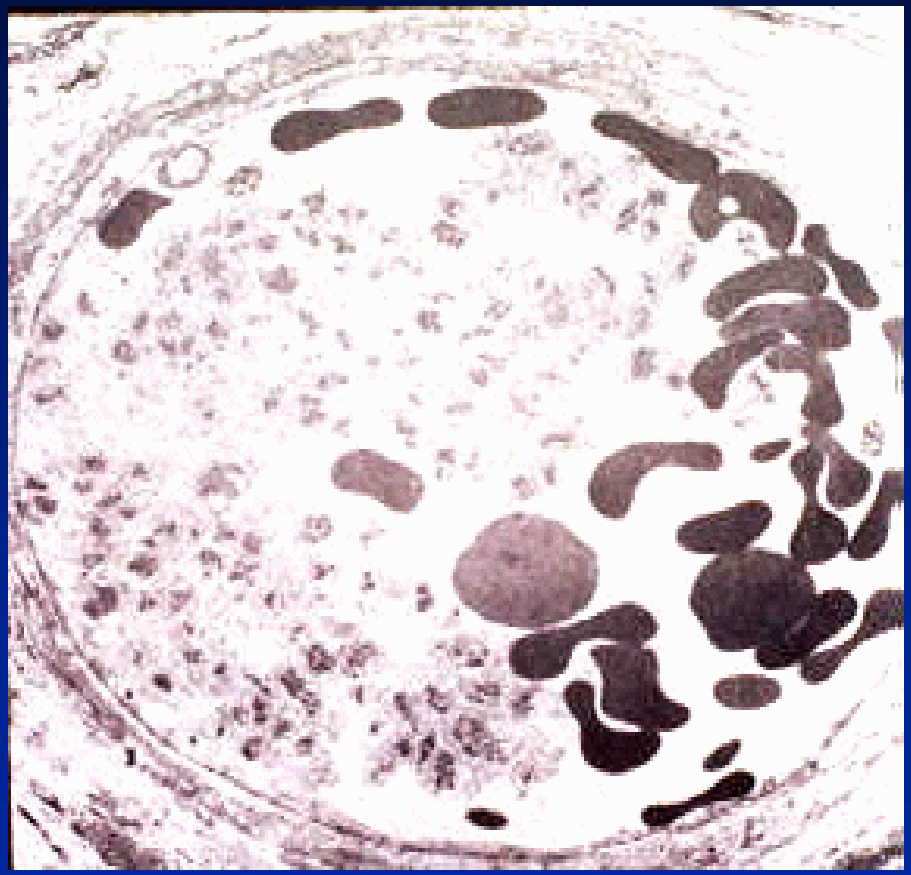


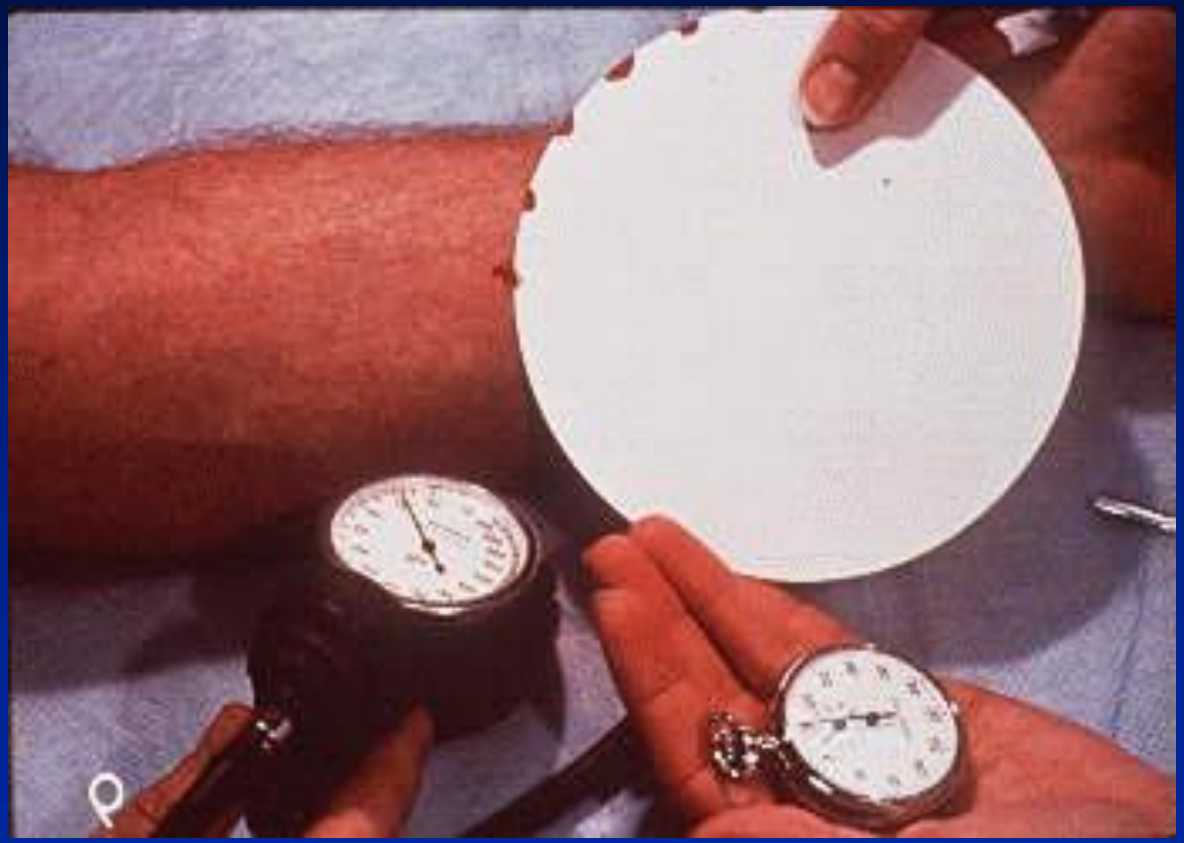
Platelet activities in hemostasis (cont'd)



Laboratory evaluation of platelets

- Platelet count: reference range 150,000-400,000 $x10^9$ /L
- Bleeding time: reference range < 9 min

Bleeding time



Causes of a prolonged bleeding time

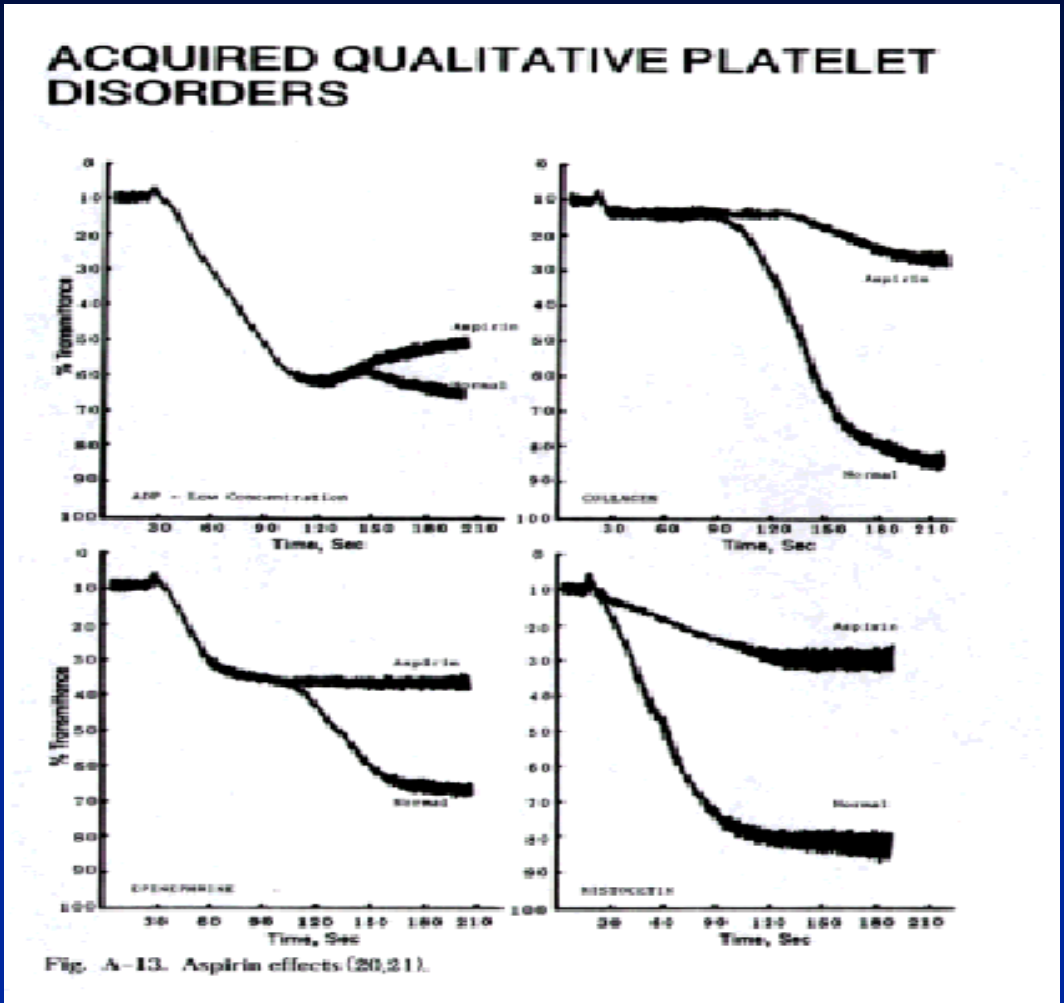
- Asprin, other NSAID
- vonWillebrand disease
- Dysfunctional platelets: storage pool disease, Glanzmann thrombasthenia, Bernard Soulier syndrome, uremia

Platelet aggregation study

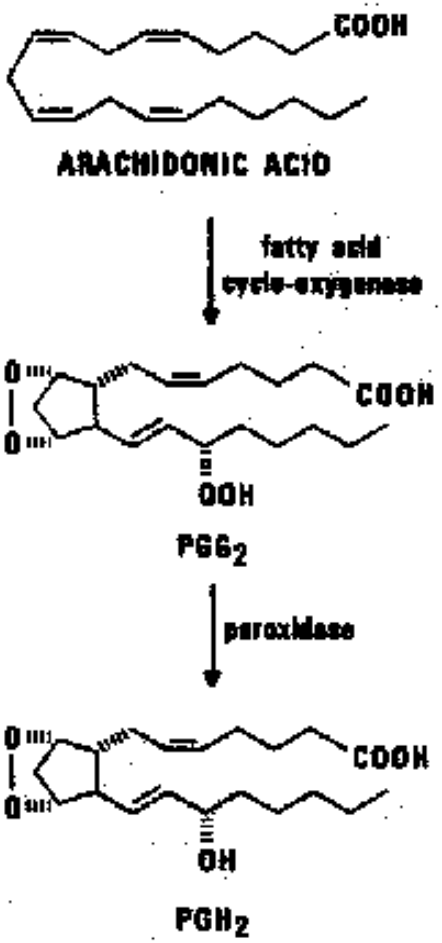
- Principle: aggregation in response to an added chemical stimulus can be monitored by change in transmittance
- Stimulating agent: arachidonic acid, ADP, collagen, epinephrine, and ristocetin
- Platelet functional disorders have typical aggregation patterns

Aggregometer

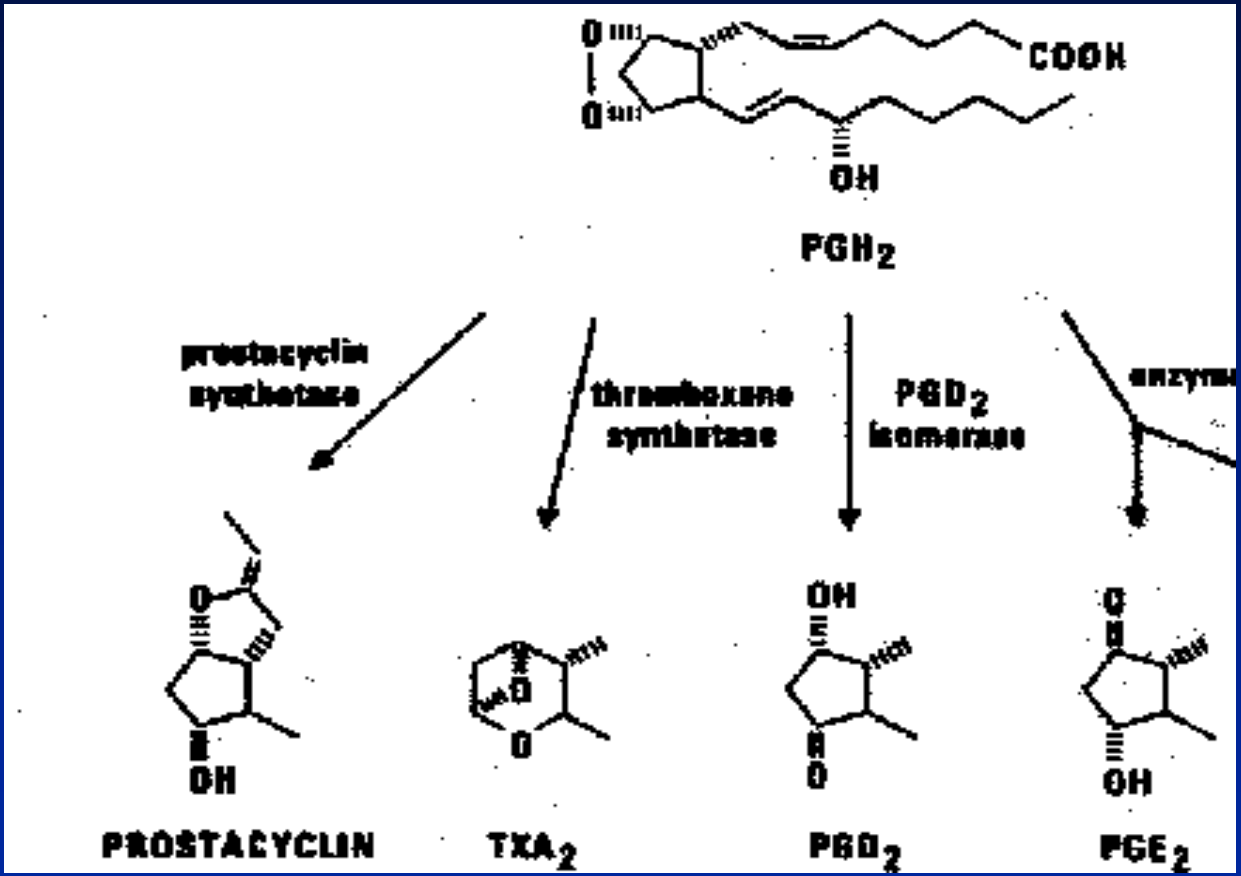
Platelet aggregation patterns



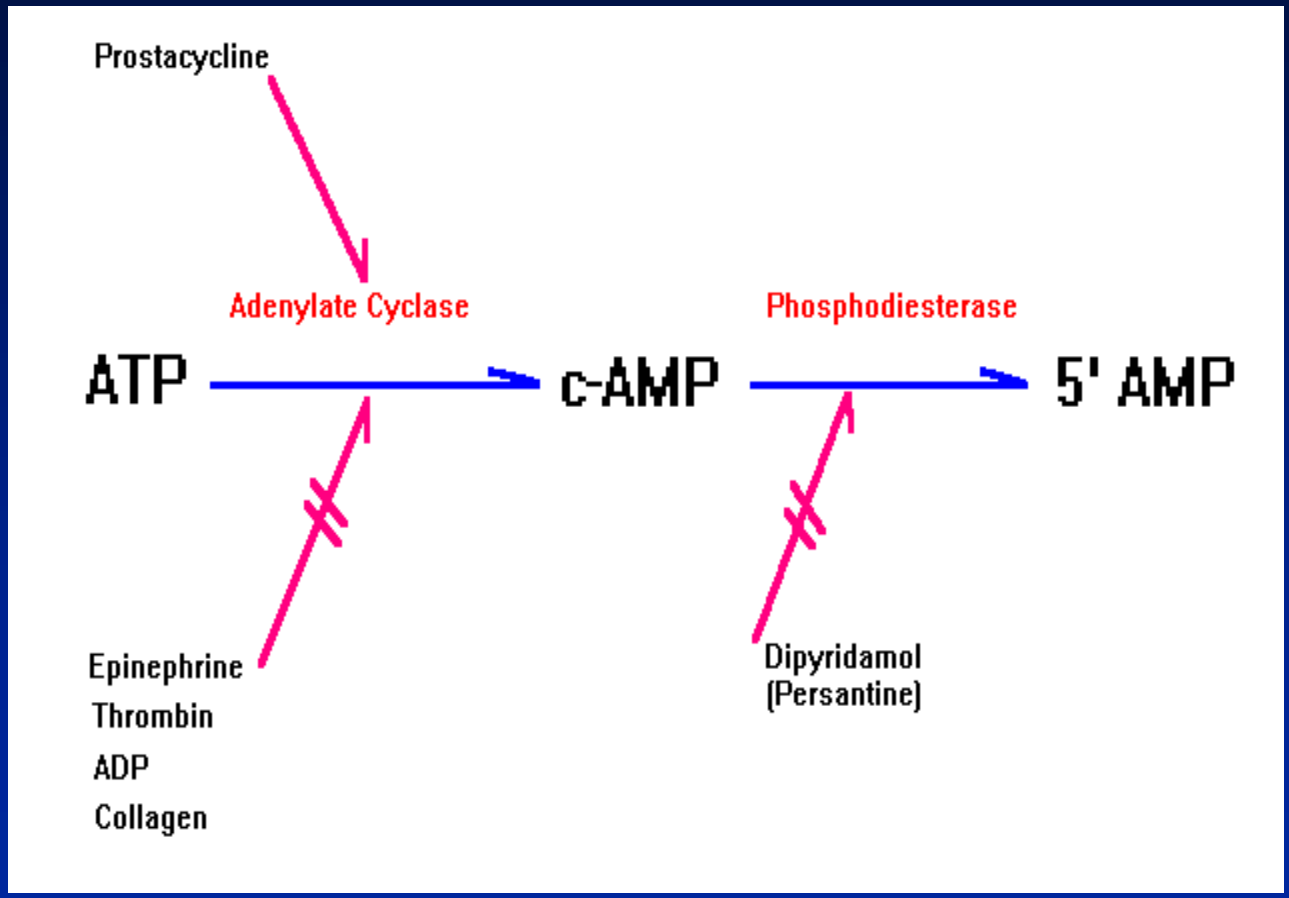
Pathway of platelet activation



Pathway of platelet activation (cont'd)



Pathway of platelet activation (cont'd)



Quantitative platelet disorders, mechanism

- Decreased platelet production:
  1. Hereditary: Fanconi's anemia, thrombocytopenia with short radii syndrome (TAR), May-Hegglin
  2. Acquired: radiation, drugs, marrow replacement, splenomegaly, B12 / folate deficiency
- Destruction: DIC, TTP, HUS, ITP, HIT

Acute ITP

- Peak age incidence: 2-6 y/o
- Sex predilection: none
- Antecedent infection: 1-3 weeks prior
- Onset of bleeding: abrupt
- Platelet count: < 20,000
- Duration: 2-6 weeks
- Spontaneous remission: in 80% of cases

Chronic ITP

- Peak age incidence: 20-40 y/o
- Sex predilection: F:M=3:1
- Antecedent infection: unusual
- Onset of bleeding: insidious
- Platelet count: 30,000-80,000
- Duration: months or years
- Spontaneous remission: uncommon

Heparin induced thrombocytopenia (HIT)

- Other name: heparin associated thrombocytopenia (HAT)
- Occurs in 1-5% of patients on Heparin, typically 5-10 days after initiation of heparin
- Testing:
  1. Heparin-induced platelet aggregation: patient's serum and normal platelets with heparin, look for positive response (aggregation > 25%)
  2. ELISA

Thrombocytosis

- Autonomous: essential thrombocythemia, other myeloproliferative disorders (p. vera, myelofibrosis, CML)
- Reactive: iron deficiency, inflammation, splenectomy

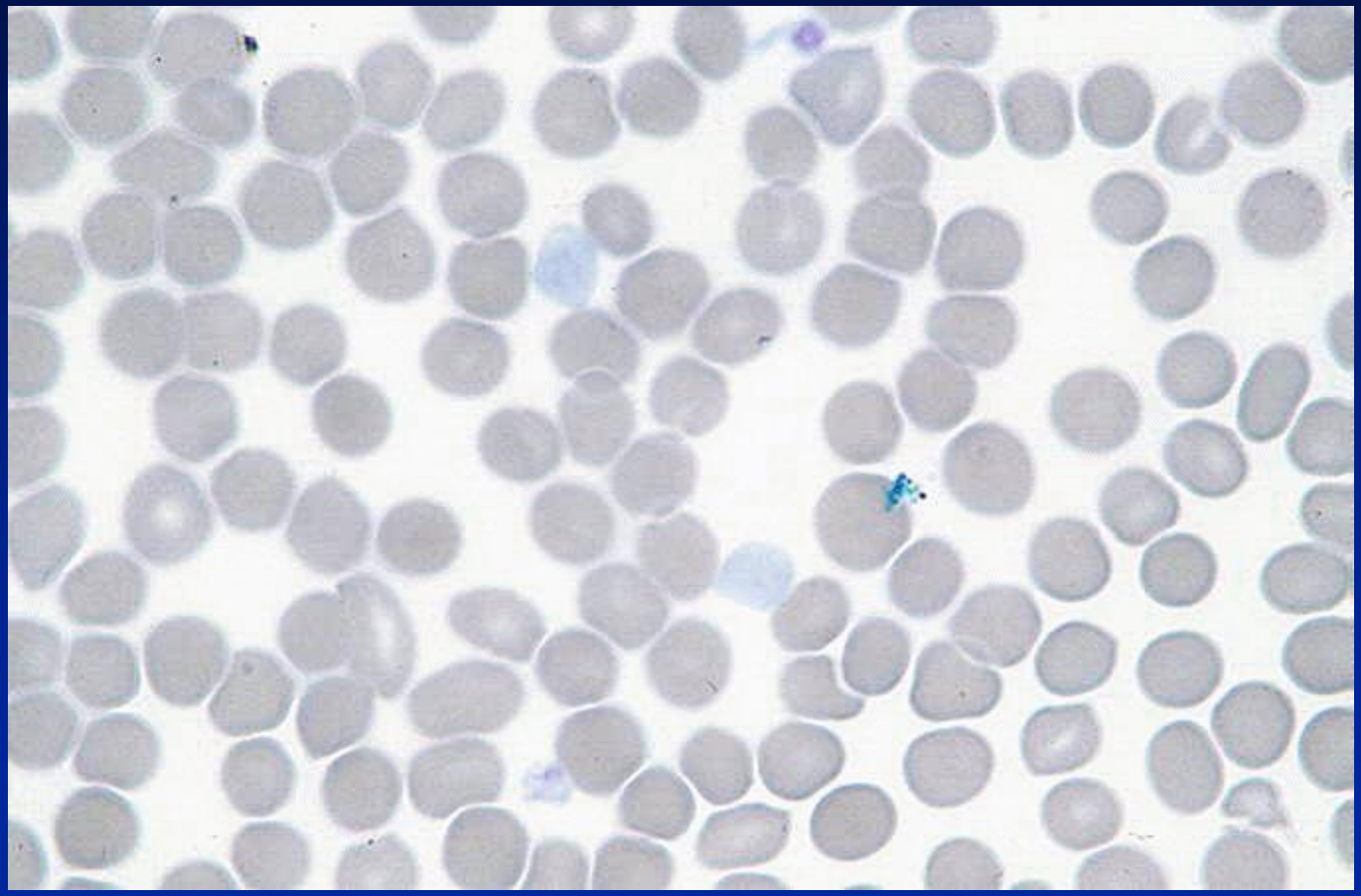
Inherited disorders of platelet function: surface membrane defects

- Glanzmann thrombasthenia: autosomal recessive, defective GP IIb/IIIa
- Bernard Soulier syndrome: autosomal recessive, thrombocytopenia, large platelets, defective GP Ib,V,IX
- Collagen receptor defect: defective thrombospondin
- Platelet-type vWD: autosomal dominant, high affinity for vWF, borderline thrombocytopenia, addition of cryo-> aggregation

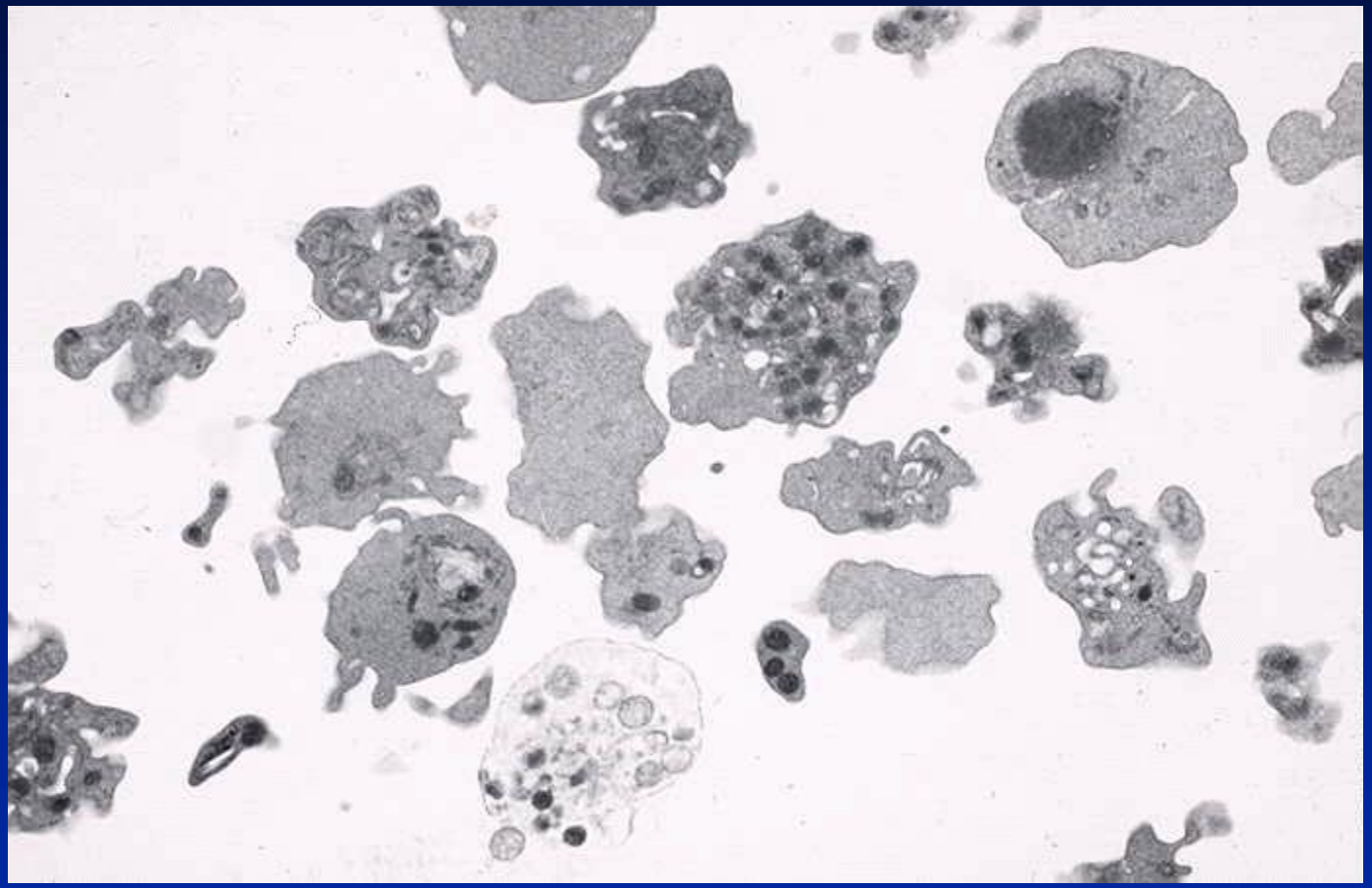
Inherited disorders of platelet function: granule defects

- Dense granule deficiency (δ SPD): isolated deficiency or in association with Hermansky-Pudlak, Chediak-Higashi, Wiskott-Aldrich
- Alpha granule deficiency (α SPD): gray platelet syndrome
- Combined granule deficiency (α δ SPD)

Combined granule deficiency: blood smear



Combined granule deficiency: EM



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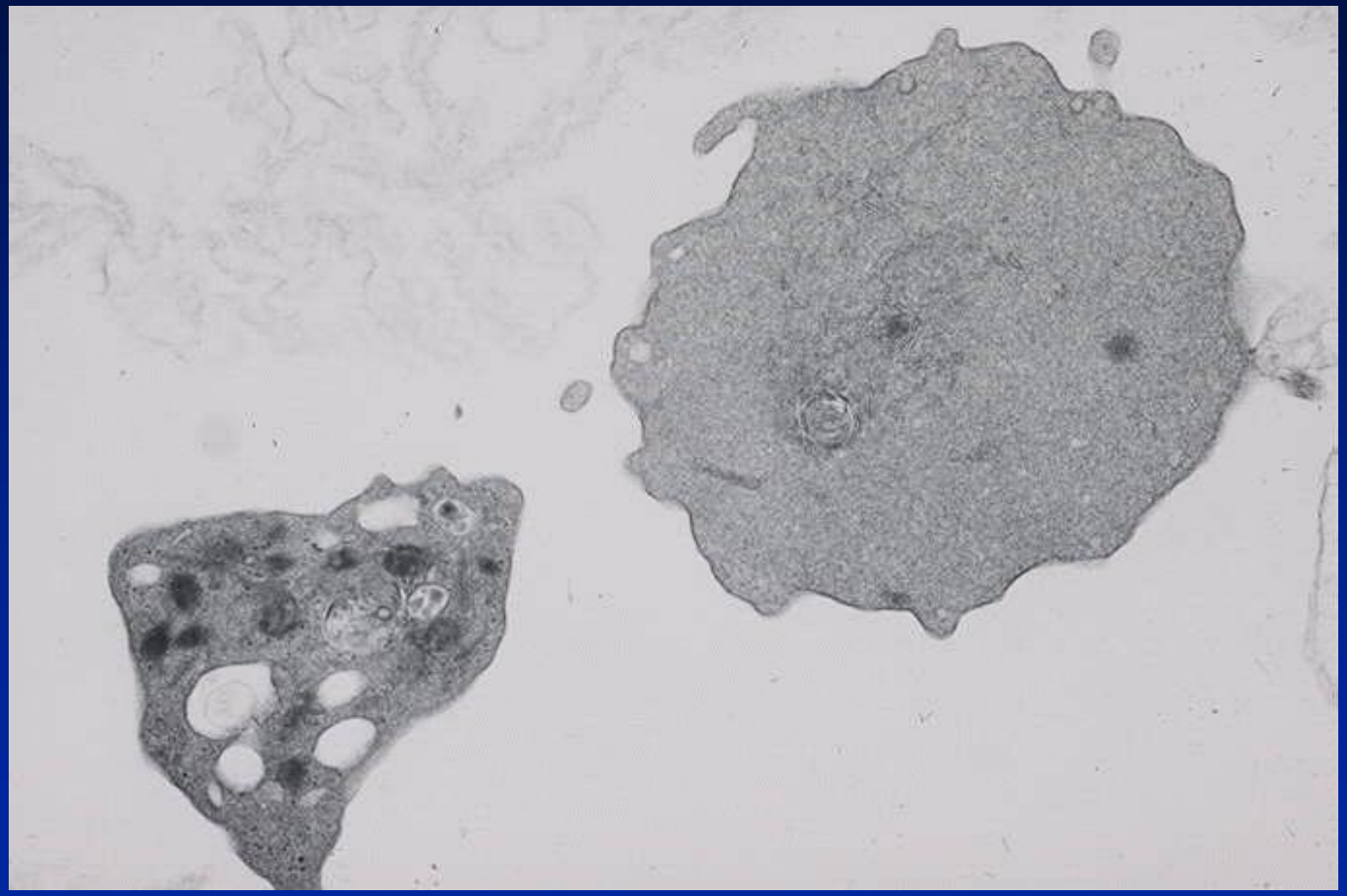

Defects in platelet arachidonic acid metabolism: aspirin-like defects

- Cyclooxygenase deficiency
- Thromboxane synthetase deficiency

Acquired disorders of platelet function

- Medication: aspirin, other NSAID, dipyridamole, penicillins, cephalosporins, tricyclic antidepressants, phenothiazines, heparin, antihistamines, etc
- Uremia
- Myeloproliferative disorders
- Paraproteins
- Cardiopulmonary bypass