Qualitative and Quantitative Platelet Disorders

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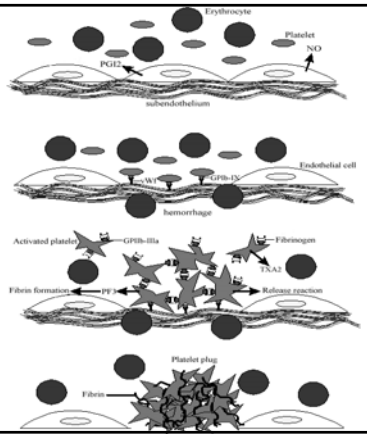
Platelet vs. Coagulation Bleeding

Findings	Coagulation	Platelet
Petechiae	Rare	Common
Hematomas and Hemarthroses	Common	Rare
Delayed Bleeding	Common	Rare
Bleeding cuts	Minimal	Persistent
Gender	Male	Women
Mucosal	Minimal	Typical

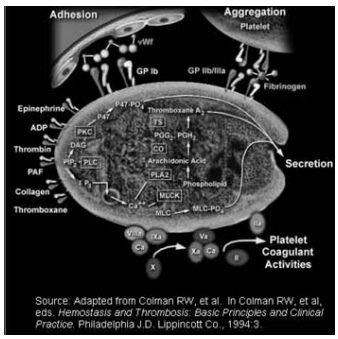
N.B. Some platelet disorders are associated with thrombosis (HIT, TTP)

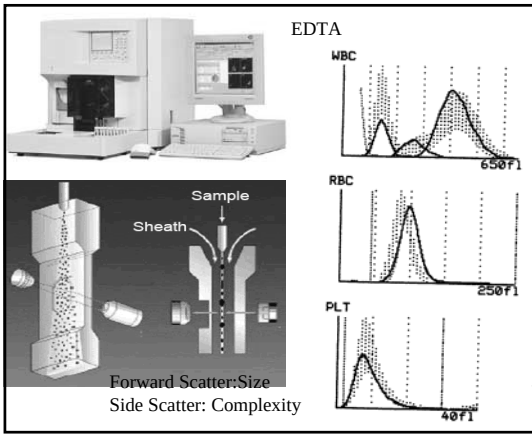


Laboratory Tests

- Automated Cell Counter
  - Platelet Count
  - Mean Platelet Volume
  - Platelet Distribution
- Smear morphology
- Coagulation
  - PT, aPTT, Fib, TT
- Bleeding Time
- Aggregometry
- vWD
  - Ristocetin Cofactor
  - vWf:Ag
  - FVIII:C
  - Multimers

Platelet Signaling

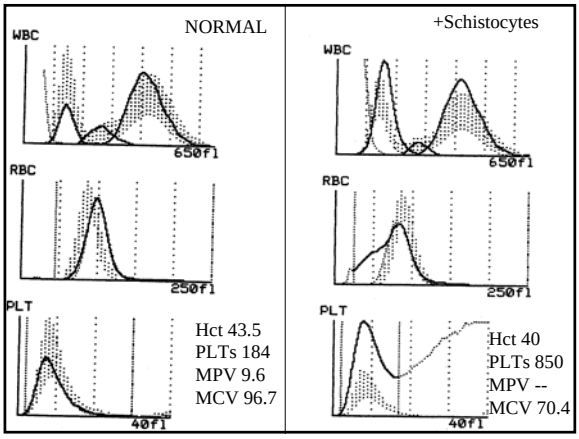


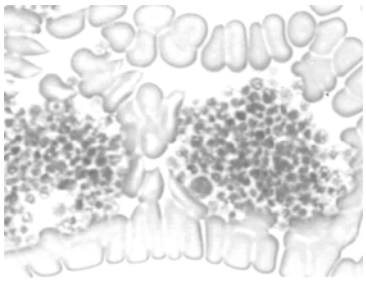


Case

22 year old student athlete undergoes a routine preoperative physical exam and laboratory studies prior to right knee arthroscopy; he has no significant past medical history; no bleeding or family bleeding history; he takes no medications; physical exam is unremarkable

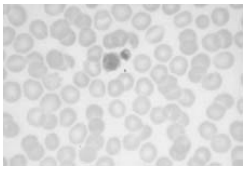
WBC 5.0, Hct 45%, Plt 20K, smear next slide



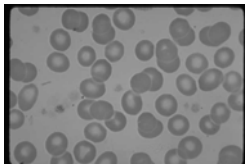


Pseudothrombocytopenia
Anti-coagulant dependent agglutinins associated with EDTA
Re-rerun with citrate or heparin tube

Platelet Morphology

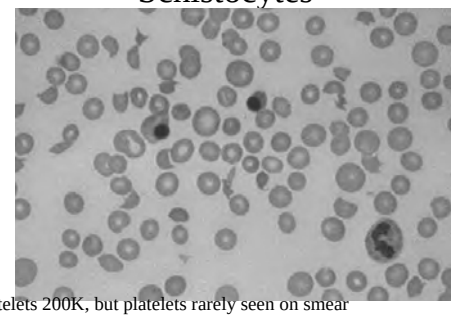


Bernard-Soulier

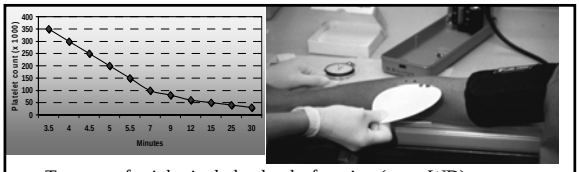


Gray Platelet Syndrome

Real or Spurious Platelet Count: Schistocytes



Platelets 200K, but platelets rarely seen on smear



- To screen for inherited platelet dysfunction (e.g. vWD)
- Done under standardized conditions
  - 40 mmHg
  - Two small punctures on volar surface
  - Absorbed every 30 sec
  - Measured by time in minutes
  - Should not be done if plt<50K, anemia or uremia
- Mainly affected by platelet number and function, hematocrit
- There is no evidence that the bleeding time predicts bleeding
- no correlation between bleeding time and visceral bleeding

Bleeding Time Prolonged

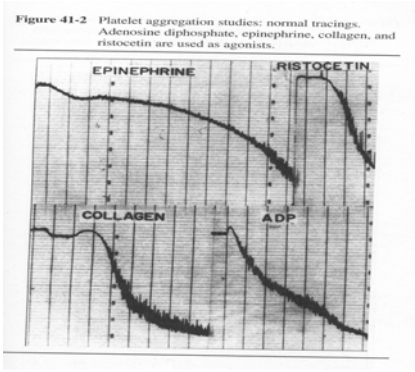
- Congenital
- Drugs (e.g. antiplatelet drugs +/- ASA)
- Alcohol
- Uremia
- Hyperglobulinemias
- Fibrin/fibrinogen split products
- Thrombocythemia
- Cardiac Surgery

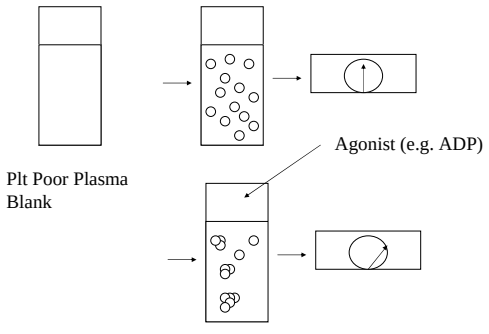
Interpretation

- Evaluate the slope of aggregation; both primary and secondary wave
- Evaluate the extent of aggregation
- Low dose ADP: two waves; high dose a single wave
- Epi biphasic in 80% of normal
- Collagen acts by releasing ADP so only a single wave
- Ristocetin antibiotic that makes vWf bind platelets and induces aggregation; normal tracing does not exclude vWD

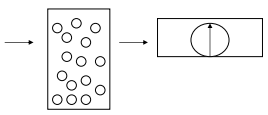
Aggregometry

- Purpose: used to detect abnormalities in platelet function
- Principle: an aggregating agent is added to platelet rich plasma in a cuvette; as the platelets aggregate, the light transmission increases
- **Specimen: platelet rich plasma prepared from citrate whole blood with test completed within 3 hours of the collection**
- Procedure: soft spin to prepare platelet rich plasma prepared; hard spin to prepare platelet poor plasma (blank)



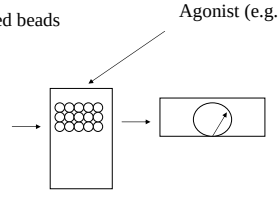


Accumetrics



- Fibrinogen coated beads

Agonist (e.g. ADP)



Evaluate as two groups

- Quantitative
  - Production, Destruction, Sequestration
- OR
- Qualitative
  - Adhesion, Aggregation, Secretion, Other

Case

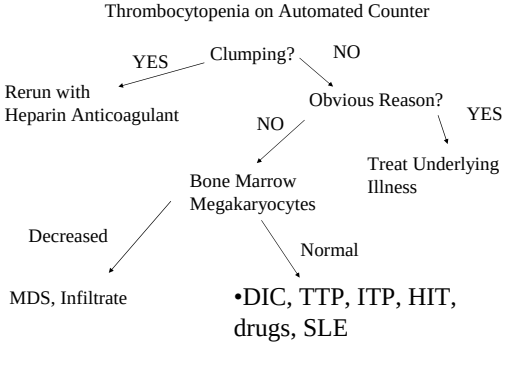
- 75 year-old man with no significant past medical history s/p bowel resection for carcinoma. He spiked a temperature of 103. Blood and urine cultures are positive for GNR. He is noted to have petechiae on his legs. His venipunture sites are oozing. No organomegaly.
- Data: WBC 25K with left shift, Hct 30%, Plts 20K. PT 21s, PTT 120s, Fib 80, D-Dimer>20 , schistocytes
- DDx: ITP, TTP/HUS,DIC, HIT

Quantitative

- Production
  - Reduced Megakaryocytes
    - Infiltration (e.g. tumor)
    - Aplasia (e.g. chemicals)
    - Congenital (e.g. WAS)
  - Ineffective
    - Megaloblastic anemia, myelodysplasia, ETOH
- Destruction
  - Immune
    - Autoantibody e.g. ITP
    - Alloantibody
      - NAIT, HIT
  - Consumption
    - DIC
    - TTP
    - Mechanical
- Sequestration
- Hemodilution
- Real or Spurious?

Case

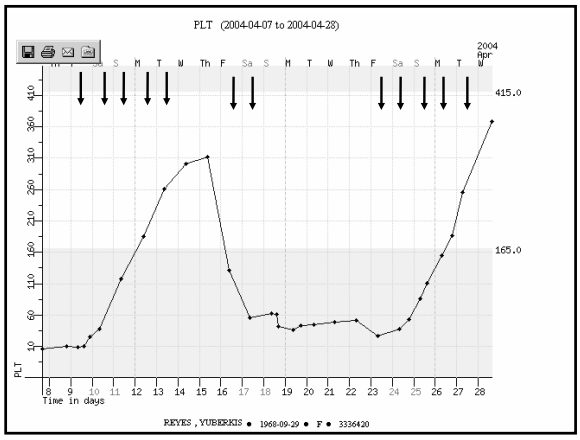
- 35 year-old F previously in good health, developed URI sx's 1 wk PTA. A few days later, felt "hot" with headache, and developed bruising on ant shins. Went to urgicare, sent home. Then was called back for admission in the evening, due to PLT 5
- PE: T 99, VS stable, marked ecchymosis on B/L extremities, especially LE, a few on body.
- Lab:
  - PLT 5, WBC 7.7, H/H=11.3/ 34.3
  - PT/PTT 12.4/30.7, fib 327
  - TB/DB 2.6/0.4, AST/ ALT 65/ 13
  - BUN 11, Cr 0.5
  - Urine: hemoglobin 2+, RBC 15, WBC 0-2, Prot. neg
  - PB smear: schistocytes > 5/HPF
  - ANA, Speckled nuclearplasmic patterns
- DDx: ITP, HELLP, HUS,DIC, HITetc.



TTP In Brief

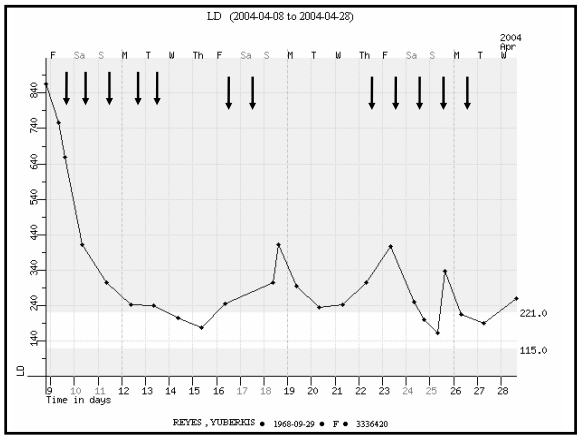
Pentad
- Microangiopathic hemolytic anemia (vessel narrowing) with schistocytes (mechanical injury to RBCs)
- Severe Thrombocytopenia
  - (systemic PLT aggregation)
- Neurologic abnormalities
  - (CNS ischemia)
- Acute renal insufficiency
  - (renal ischemia)
- Fever
- Associated with thrombosis

- Plasmapheresis w FFP infusion
  - Prednisone



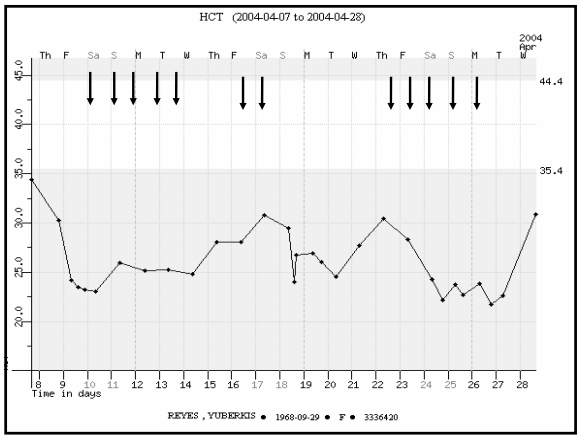
Qualitative

- Inherited
  - Bernard-Soulier
  - Glanzmann's
  - Storage pool disease (ChediakHigashi, Wiscott-Aldrich, Hermansky-Pudlak, Gray Platelet Syndrome)
- Acquired
  - Drugs (e.g. ASA, ADP, Iib/IIIa)
  - Uremia, Post-bypass
  - Primary marrow disorders; MDS, Dysproteinemias



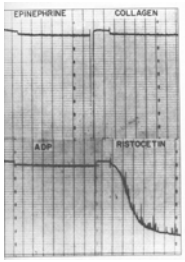
Inherited

- Adhesion
  - Bernard-Soulier
- Aggregation
  - Glanzzmann's
- Secretion
  - E.g. Gray Platelet Syndrome



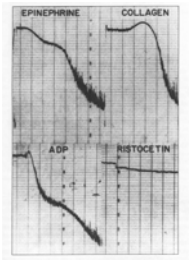
Glanzmann's Thrombasthenia

- Rare Condition
- Inherited absence of GPIIb/IIIa (AR)
- Severe Bleeding manifestations
- GPIIb/IIIa a key platelet glycoprotein required for aggregation
- Absence of aggregation with ADP, Epi, Collagen
- Normal ristocetin



Bernard-Soulier

- Rare inherited bleeding disorder
- Lack of GPIb which is necessary for the formation of the hemostatic plug by binding to subendothelial von Willebrand factor
- Aggregation with ADP, Epi and collagen; absent ristocetin

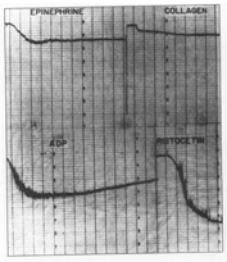


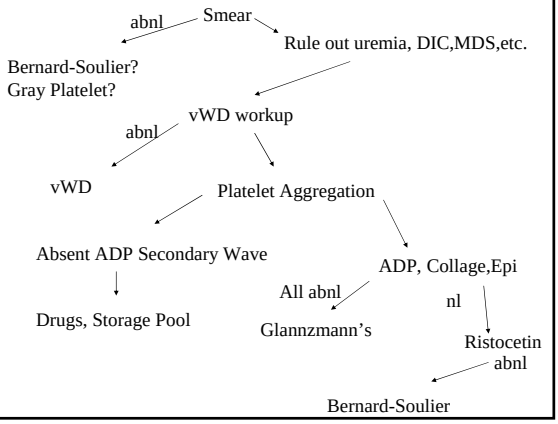
von Willebrand's Disease

- Inherited bleeding disorders
- Absent or decreased levels of vWf or lack of large and medium sized multimers
- Work up includes vWf:Ag level, FVIII:C activity, Ristocetin Cofactor Activity, Platelet Aggregation studies

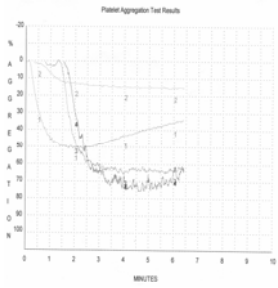
Thrombocytopathies

- Common
- Abnormality in the release reaction
- Storage Pool Disease (no ADP in granules)
- Release defect (defects in mechanism of release)
- Resembles same pattern as aspirin





Hermansky-Pudlak



- 21 month old male with bruisability and bleeding
- albino features
- Oculomotor nystagmus
- Delayed development
- tyrosinase-positive oculocutaneous albinism (Ty-pos OCA), bleeding diathesis, and systemic complications associated to ceroid-lipofuscin–like lysosomal storage disease.

Case

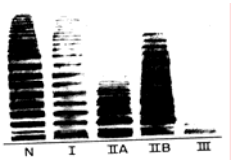
- 33 year old woman with menorrhagia
- History of epistaxis since childhood
- Cousin with similar problems
- Aspirin for headaches; no other meds
- PT, PTT, TT, Platelets normal count
- Blood smear platelet morphology normal

Differential Diagnosis

- Inherited
  - Bernard-Soulier
  - Glanzmann's
  - Storage Pool Defect
  - vWD
- Acquired
  - DIC, MDS, uremia, drugs, dysproteinemia

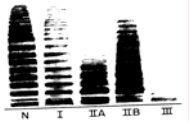
Type I vWD

- Most frequently encountered
- All polymeric forms are present, but to a decreased level
- Bleeding time usually prolonged; can be normal if mild deficiency



vWD Lab Workup

- Bleeding Time
- Ristocetin Cofactor (functional)
- Ristocetin Aggregation
- vWf Ag (quantitative)
- Factor VIII:C
- Multimeric Analysis

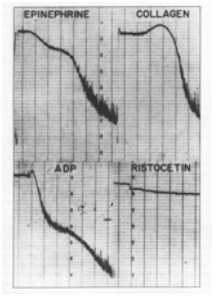


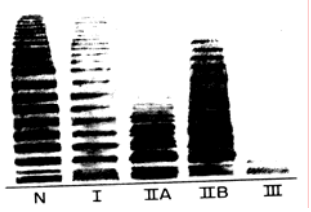
Type II vWD

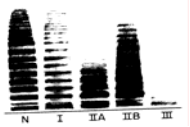
- Type IIA
- Amount synthesized may be normal
- Failure to form intermediate or large multimers
- BT usually prolonged
- FVIII decreased or normal

- Type IIB
- Less common
- May not respond to DDAVP
- Largest multimers are absent
- Concentration too low to induce aggregation

vWD







Type III

- Severe bleeding disorder
- Very low levels of all multimers; low vWf:Ag, FVIII:C, Ristocetin Cofactor activity

Test	IA	IIA	IIB	III
BT	V	V	V	V
FVIII	D	D or N	D or N	D
vWAg	D	N or D	N or D	D
Rist Cof	D	D	D or N	D
Rist Aggr	D or N	D	I	D
Multimer	N	A	A	A