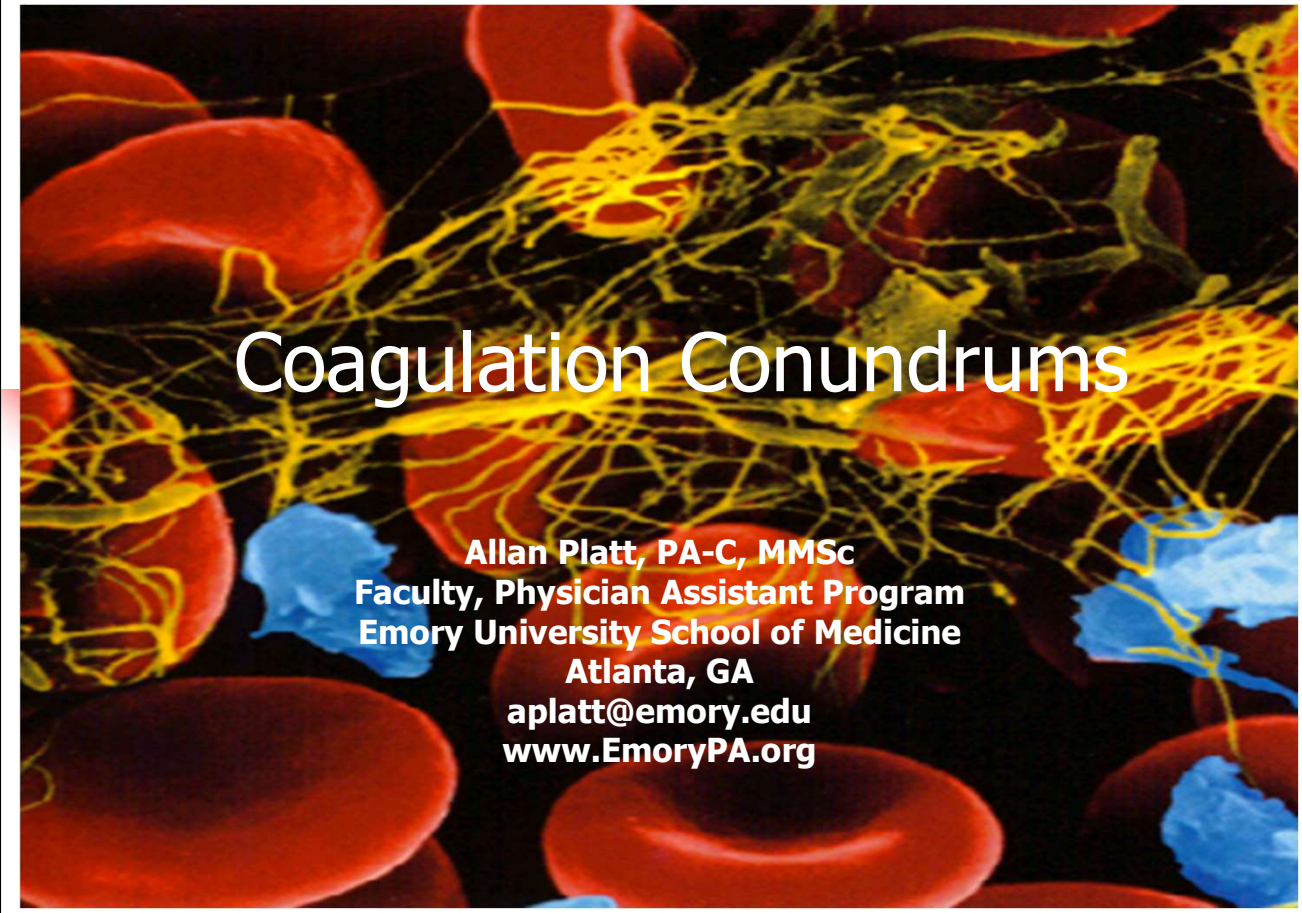


Coagulation Conundrums

Allan Platt, PA-C, MMSc
Faculty, Physician Assistant Program
Emory University School of Medicine
Atlanta, GA
aplatt@emory.edu
www.EmoryPA.org

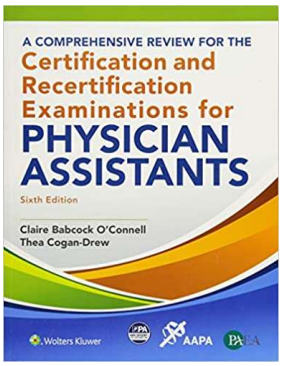
1

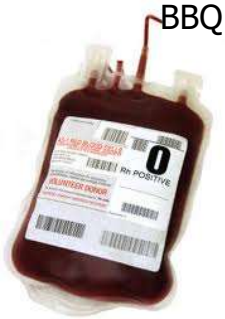
Disclosure

- I have nothing to disclose except
  - I do work for food
  - I promote giving blood
  - I did write chapter 4 in

BBQ ribs are best!

Paid a set fee for Hematology review - no royalties





Give life!

Objectives

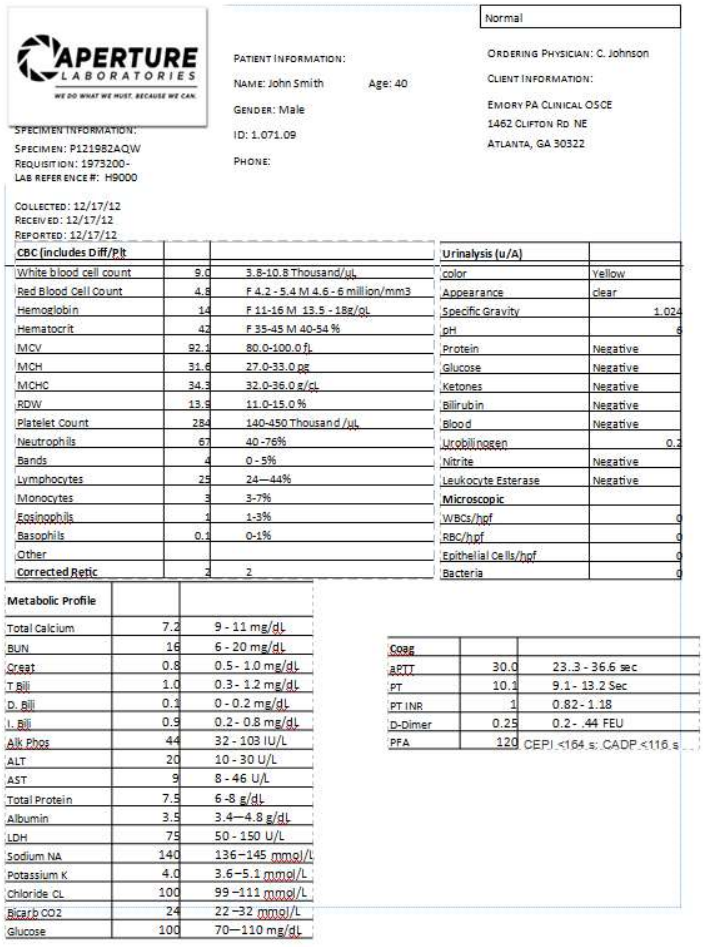
At the end of this session, participants should be able to:

- Recognize common laboratory patterns for common bleeding disorders seen in primary care
- Diagnose common bleeding and clotting disorders
- Formulate a treatment plan or referral for common bleeding and clotting disorders

3

Lab Report

- Most common labs
  - CBC
    - WBC Diff
    - RBC morphology
    - Retic count
  - Complete Metabolic Profile
  - UA with micro
  - Coagulation
    - PT (INR)
    - aPTT
    - d-Dimer
    - PFA



APERTURE LABORATORIES
WE DO WHAT WE MUST, BECAUSE WE CAN.

Normal

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GENDER: Male
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

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RECEIVED: 12/17/12
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CBC (includes Diff/Plt		
White blood cell count	9.0	3.8-10.8 Thousand/uL
Red Blood Cell Count	4.8	F 4.2 - 5.4 M 4.6 - 6 million/mm3
Hemoglobin	14	F 11-16 M 13.5 - 18g/dL
Hematocrit	42	F 35-45 M 40-54 %
MCV	92.1	80.0-100.0 fL
MCH	31.6	27.0-33.0 pg
MCHC	34.3	32.0-36.0 g/dL
RDW	13.9	11.0-15.0 %
Platelet Count	284	140-450 Thousand /uL
Neutrophils	67	40-76%
Bands	4	0 - 5%
Lymphocytes	25	24—44%
Monocytes	3	3-7%
Eosinophils	1	1-3%
Basophils	0.1	0-1%
Other		
Corrected Retic	2	2

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile		
Total Calcium	7.2	9 - 11 mg/dL
BUN	16	6 - 20 mg/dL
Creat	0.8	0.5 - 1.0 mg/dL
T. Bili	1.0	0.3 - 1.2 mg/dL
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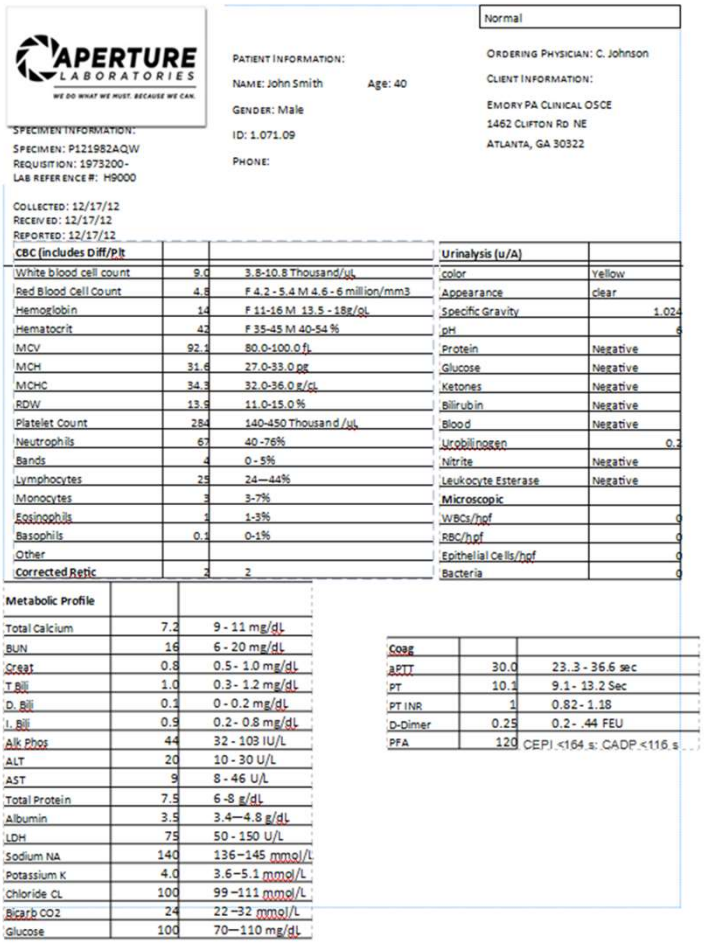
4

Lab - CBC

- ~~Cost $30~~
- WBC count –infection defense
- Platelet count – clot ability
- Red Cells – O2, CO2, CO, NO gas transport, Buffer
  - Hb – Hemoglobin
  - Hct = % red cells/plasma
  - MCV = size of RBCs
  - MCH = Hb inside = Redness
  - RDW – red cell distribution width – higher = cells of different sizes

Cost https://www.health-tests-direct.com/what-tests-are-available



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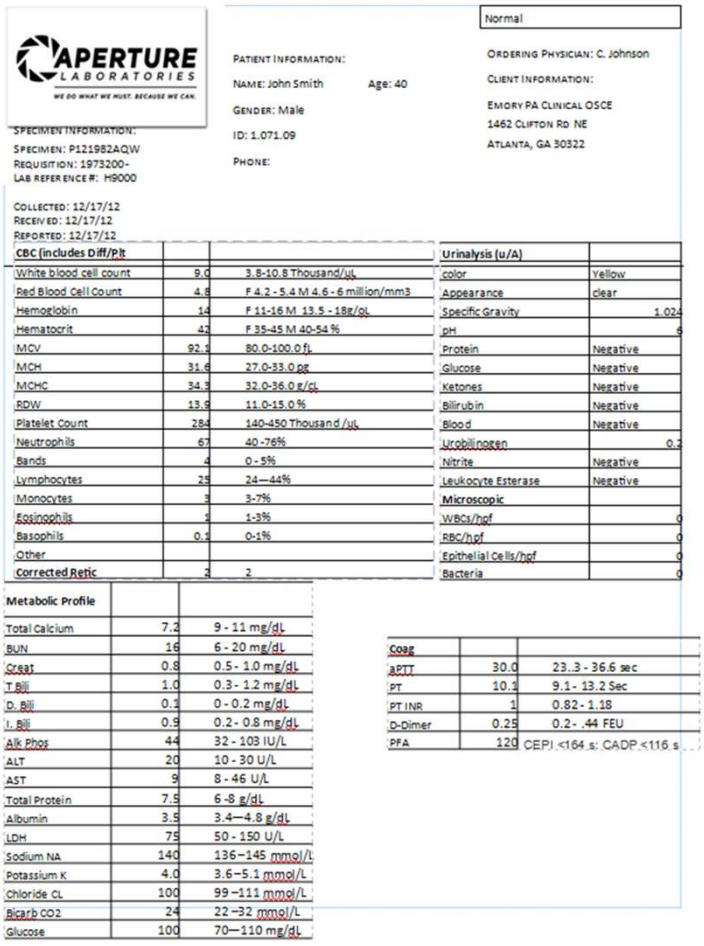
Lab – CBC Diff and Retic

- Do diff when WBC is high or low, chemo/drug monitoring
  - Bands = early Neutrophils
  - Neutrophils – Bacteria
  - Lymphs – (B, T, NK)Viral
  - Mono – TB, HIV, Mono
  - Eos – Allergy, parasites
  - Baso – Mast cell, allergy
- Retic count – when suspect anemia or monitor therapy. Must be corrected



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CBC Patterns

- Pancytopenia – Marrow failure
- Thrombocytopenia – Liver/ Marrow/ Autoimmune/Infection
- Leukocytosis – Infection or leukemias

Lab -CMP Metabolic

Cost $30for CMP

Electrolytes

- Sodium (Na^+) – maintains osmotic pressure, acid/base, nerve impulse transmission
- Chloride (Cl-) – acid/base and water balance
- Potassium (K^+) – nerve conduction, muscle function, acid/base, osmotic pressure
- Calcium (Ca^{2+}) - muscle, nerve, cardiac function, clotting
- Bicarb (CO2) – Renal acid buffer to maintain pH

- Other
  - Glucose (Glu)
  - Blood Urea Nitrogen (BUN)
  - Creatinine (Creat)
  - Albumin (Alb)
  - Bilirubin (T Bili or D Bili)
  - Aspartate transaminase / aminotransferase (AST)
  - Alanine transaminase / aminotransferase (ALT)
  - Alkaline Phosphatase (Alk Phos)
  - Creatine phosphokinase (CPK)
  - Lactate dehydrogenase (LDH)
  - Total Protein (Prot)
  - Uric Acid (Uric)

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CMP Patterns

- Renal disease – BUN/Creat/Albumin
- Liver Disease – AST/ALT/Alk Phos/ Albumin/Total Protein/Direct Bili
- Hemolysis – LDH/ Indirect Bili

Lab - Urine

- Cost - $35
  - Specific Gravity (1.005-1.030) – how concentrated?
  - pH (4.6-8) – acid/base balance
  - Blood (-) – infection? trauma? MP? Other?
  - Protein (-) – renal pathology? DM? due to blood in urine?
  - Leukocytes/Leukocyte Esterase (-) - infection?
  - Nitrite (-) – bacterial infection?
  - Albumin (-) – renal pathology? DM? due to blood in urine?
  - Glucose (-) – DM? renal pathology?
  - Ketones (-) – Diabetic Ketoacidosis? Diet?
  - Bilirubin (-) – Liver or biliary tract damage? Hemolysis?
  - Urobilinogen + unobstructed bile ducts
  - RBCs – stones, CA, bleed
  - WBC – infection
  - Casts – Kidney origin

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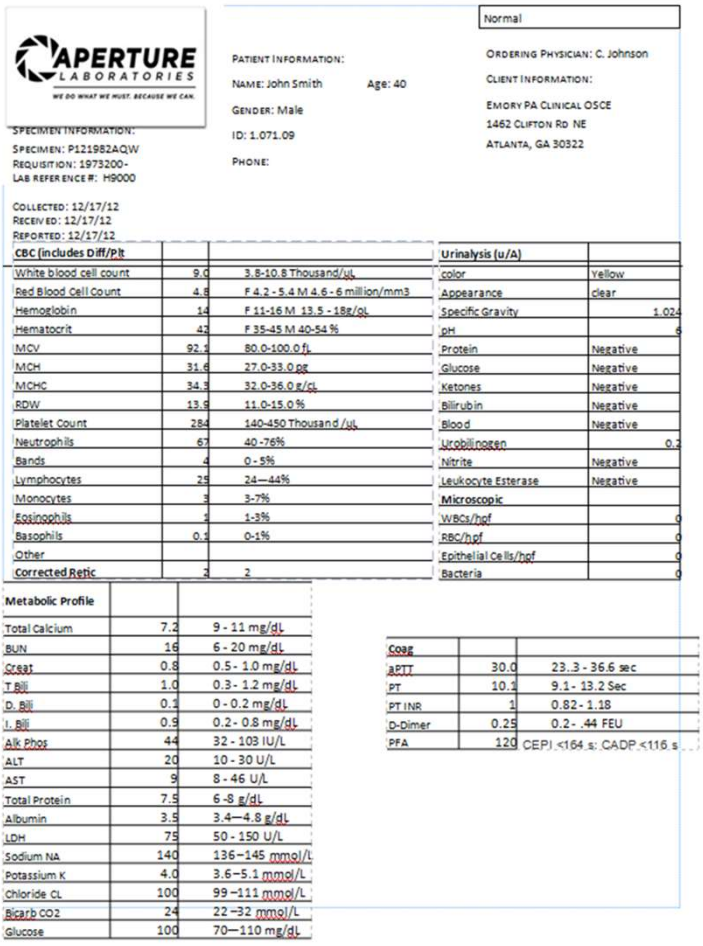
Lab - Coag

- PT /aPTT $41
- D-Dimer/PFA $30
- PT= Prothrombin Time = INR = extrinsic vitamin K clotting system (Coumadin)
- aPTT= activated Partial Thromboplastin Time = Intrinsic clotting system (Heparin)
- D-Dimer = Clot breakdown < or =250 ng/mL D-Dimer Units (DDU)
- < or =0.5 mcg/mL Fibrinogen Equivalent Units (FEU)
- PFA = Platelet Function Analysis = Platelet functioning



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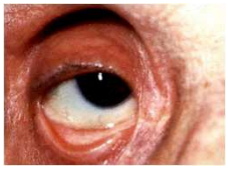
Case #1

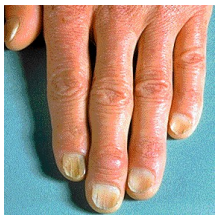
Hx - A 40-year-old truck driver presents with 1 month history of increasing fatigue, dyspnea on exertion, and increasing mid epigastric pain. No melena, hematemesis or PUD. His only medication use is daily “Goodys” powders for his chronic low back pain for 4 years. He does not smoke, use recreational drugs, and old drinks a few beers on the weekend.

Physical Exam- BP 126/78 not orthostatic, P 90 R 16 SpO2 96% on room air.

General Inspection – Spoon Nails, pallor, no jaundice. HEENT, Chest, Heart, Abdomen WNL Rectal – Prostate normal and FOB positive

His lab slip is attached. What test would be indicated and the best treatment plan?





Case 1 Lab

Low Retic, Microcytic anemia
- Hb 9 (13.5)
- MCV 75 (80)
- Corrected retic 0.9 (2)

Thrombocytosis – 550 (450)
Normal CMP/ Lipase
Normal UA
Elevated D-Dimer 300
Elevated PFA
Normal PT/aPTT
Positive FOB

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 1

PATIENT INFORMATION:
NAME: John Smith Age: 40
GENDER: Male
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

History: 1 month weakness, taking Goodys powders for chronic Low Back pain. Now mid epigastric pain

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/uL
RED BLOOD CELL COUNT	3.0 LOW	F 4.2 - 5.4 M 4.6 - 6 million/mm3
HEMOGLOBIN	9 LOW	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	27 LOW	F 35-45 M 40-54 %
MCV	75 LOW	80.0-100.0 fL
MCH	31.6	27.0-33.0 pg
MCHC	34.3	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	550 HIGH	140-450 Thousand /uL
Corrected Retic Count	0.9 Low	2
Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	16	6 - 20 mg/dL
Creat	0.8	0.5 - 1.0 mg/dL
T Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	32 - 103 IU/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 -8 g/dL
Albumin	3.5	3.4—4.8 g/dL
LDH	75	50 - 150 U/L
Sodium NA	140	136 –145 mmol/L
Potassium K	4.0	3.6 –5.1 mmol/L
Chloride CL	100	99 –111 mmol/L
Bicarb CO2	24	22 –32 mmol/L
Glucose	100	70—110 mg/dL

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	Normal 0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Coag		
aPTT	27..5	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	**300 High**	< 250 µg/L
PFA	**300 High**	CEPI <164 s; CADP <116 s

Fecal Occult blood— **Positive**

Amylase— 130 (23—140 U/L
Lipase—100 (<160 U/L)

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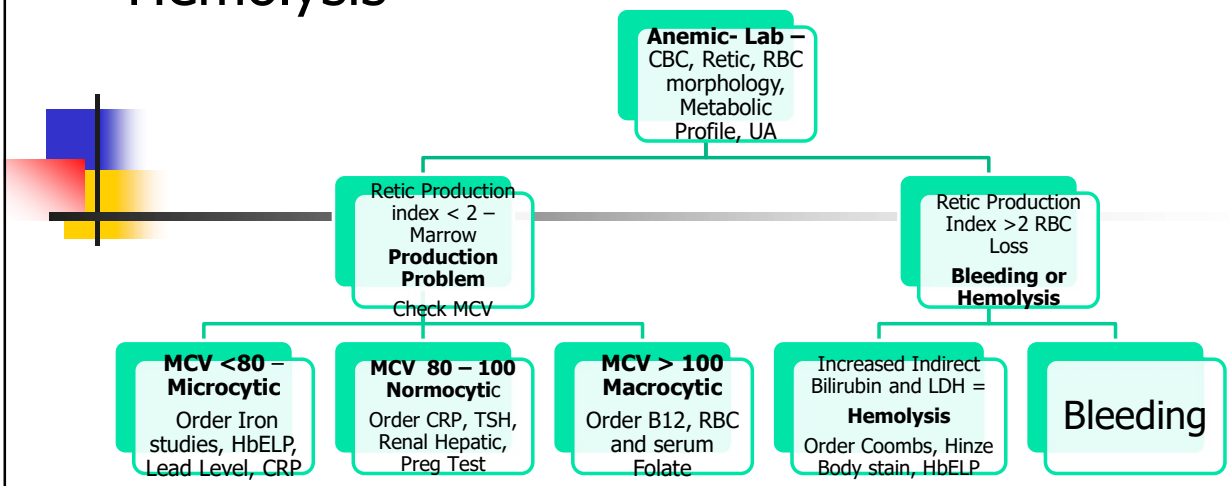
Case 1 Question

A. Order Vitamin B12 and Folate levels, Treat with PPI, change to long acting NSAID, Follow-up 1 month
B. Order Iron studies with Ferritin, Treat with PPI change to acetaminophen for pain
C. Stat Hematology consult for bone marrow biopsy
D. Stat GI consult for upper and lower endoscopy

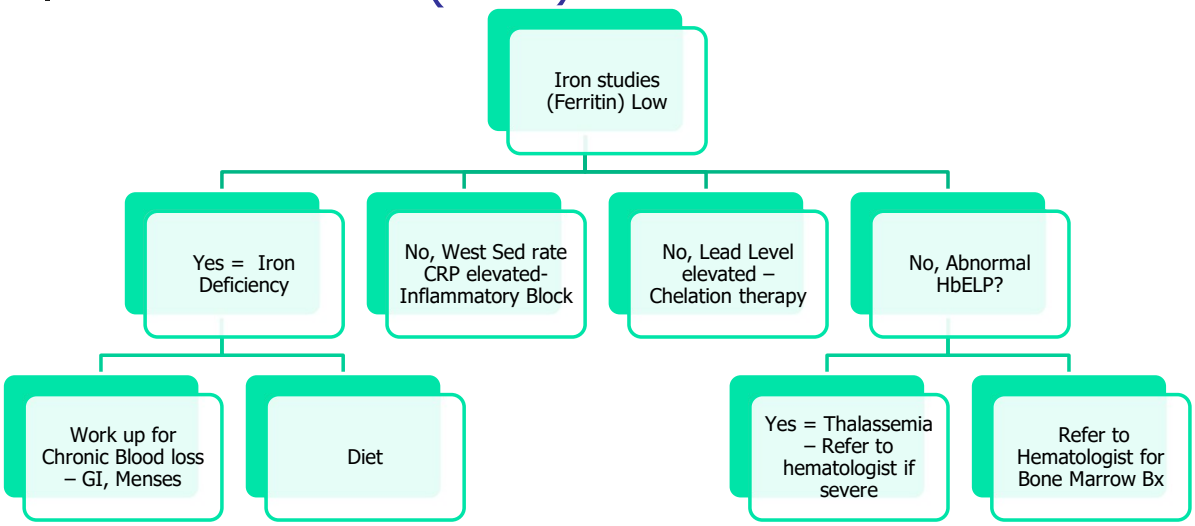
Anemia –Lab work-up
BPH =Bleeding/ Production/ Hemolysis



CRP = C-reactive protein for inflammation
HbELP = hemoglobin electrophoresis
TSH = Thyroid stimulation hormone
UA = urinalysis

Microcytic workup

TICS – Thalassemia, Iron Deficiency, Chronic inflammation, Sideroblastic (Lead)



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Anemia suspect

- Iron Deficiency because
  - Most common microcytic
  - GI bleeding – FOB positive
  - Spoon nails
  - Reactive thrombocytosis

What's in a Goody's???

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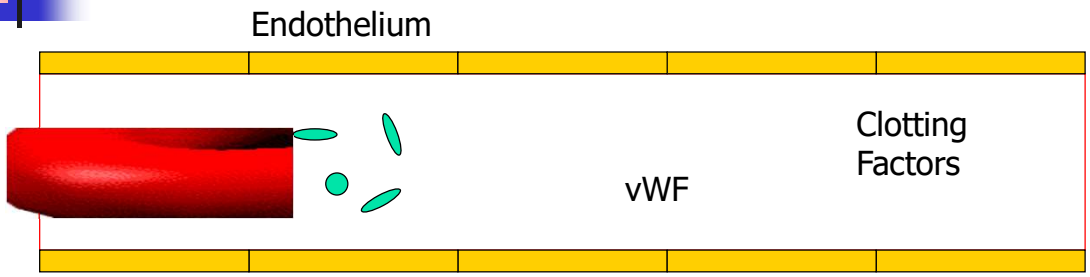
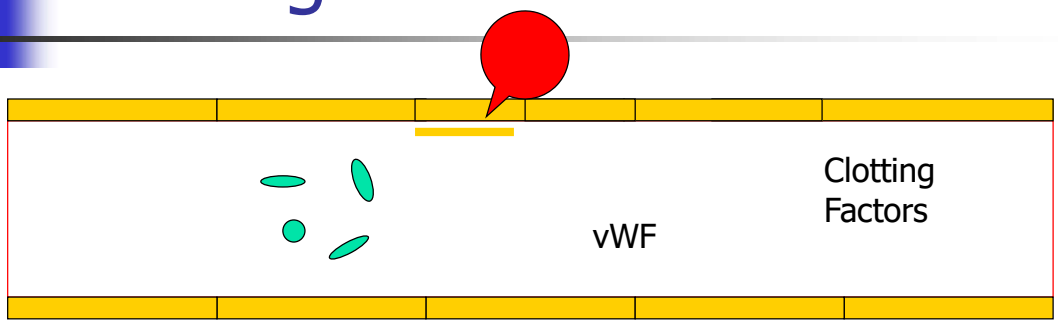
Blood in the Tubing
PVC-pipes



- Platelets Adequate number that work right
- Von Willebrand Factor (vWF)
- Clotting Factors
- Pipes - Intact and healthy endothelium

Clotting Process



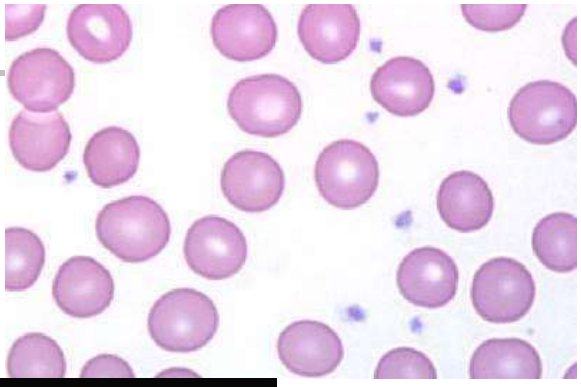
- Break in vessel wall – smooth muscle contracts
- Platelets with (vWF) stick to collagen and Activate
- More platelets are attracted
- Clotting Factors activate to form Fibrin
- Clot contracts

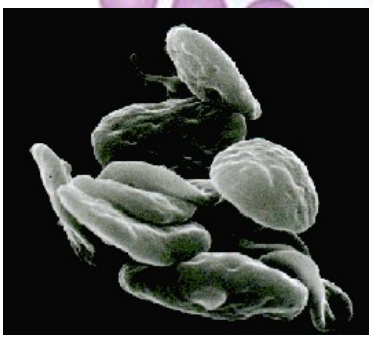
Von Willebrand Factor - vWF

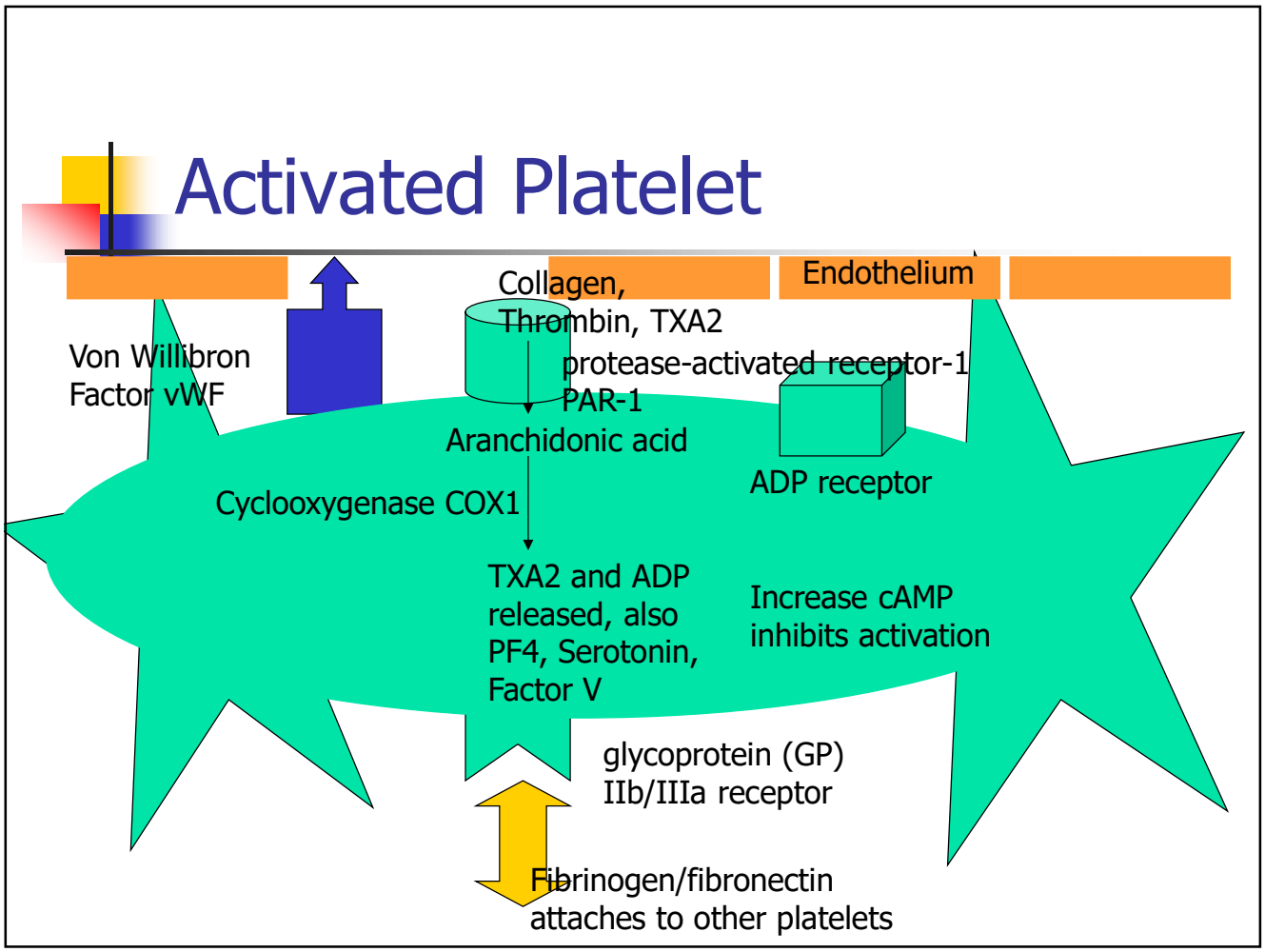
- Super glue of platelets to stick to damaged walls
- Stabilizes and transports Factor VIII
- Made by Endothelial Cells
- Most common genetic bleeding disorder

Platelets

- Made in the bone marrow
- Thrombopoeitin made in liver stimulates production
- Fragments of megacaryocytes
- No nucleus
- 67% in circulation
- 33% in spleen storage
- Life 8 – 10 days






Activated Platelet
Endothelium
Collagen,
Thrombin, TXA2
Von Willibron
Factor vWF
protease-activated receptor-1
PAR-1
Aranchidonic acid
ADP receptor
Cyclooxygenase COX1
TXA2 and ADP
released, also
PF4, Serotonin,
Factor V
Increase cAMP
inhibits activation
glycoprotein (GP)
IIb/IIIa receptor
Fibrinogen/fibronectin
attaches to other platelets

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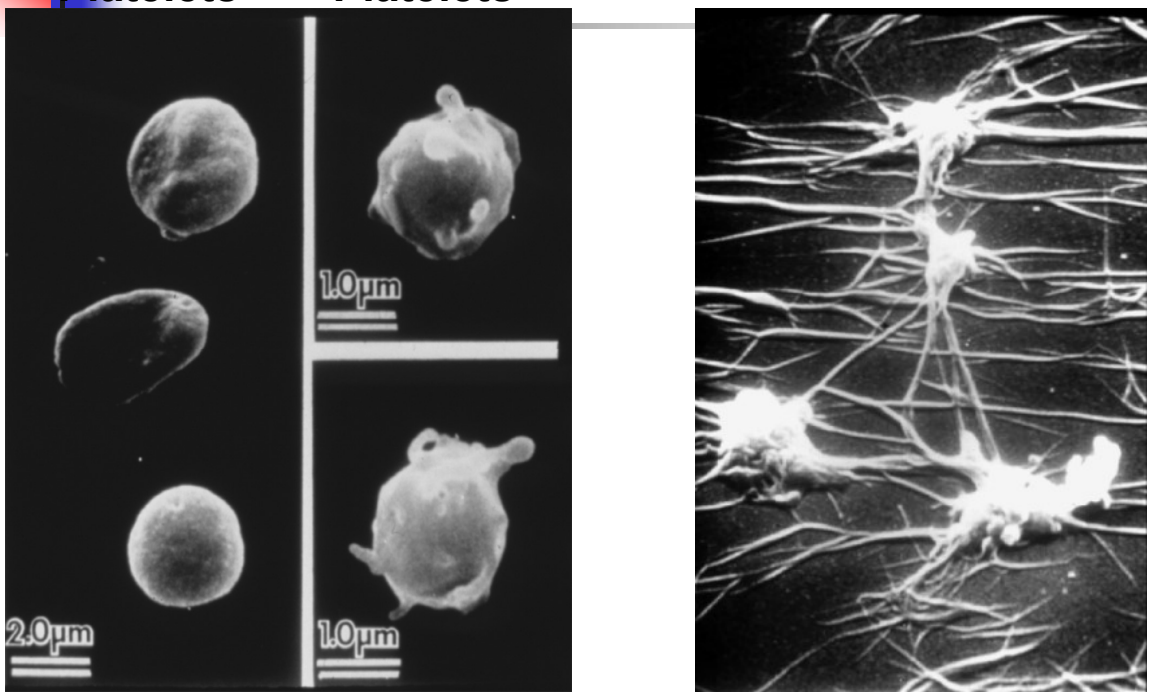
The Shape of Platelets

Flowing Platelets

Activated Platelets

Aggregated - Active Platelets



Courtesy of Helena Diagnostics

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Case 1 Answer

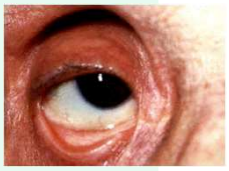
A. Order Vitamin B12 and Folate levels, Treat with PPI, change to long acting NSAID, Follow-up 1 month
B. Order Iron studies with Ferritin, Treat with PPI change to acetaminophen for pain
C. Stat Hematology consult for bone marrow biopsy
D. Stat GI consult for upper and lower endoscopy

Case 1 – NSAID (High PFA) induced gastric ulcer with bleeding (FOB +, High d-dimer from clotting) causing Fe deficient anemia (Microcytic with reactive thrombocytosis) Would check Ferritin, Stop NSAIDs, Give PPIs and F/U. Would do consult GI consult for endoscopy if still bleeding.
http://www.aafp.org/afp/2012/0301/p469.html

Case #2

Hx - A 50 year old factory worker presents with 2 days right calf tenderness and swelling. He has 1 month of feeling weak and non-vertigo dizziness. He has not had any injury, prolonged travel, or unusual exercise. He has a past history of hypertension diagnosed 20 years ago, but stopped medication after 1 year. He smokes 1 pack per day for 30 years, He does not use recreational drugs, and drinks a few beers on the weekend.

Physical Exam – BP is 178/104, P 90, R 16, SpO2 97%
General – Pallor and Lindsay's nails
HEENT – Funduscopic + A/V nicking, No thyromegally
Heart – No JVD, S1 S2 normal no Murmurs or Gallops
Abdomen – No bruits or organomegaly
Ext – R calf swelling and tenderness
His lab slip is attached. What is the most likely diagnosis?



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Case #2 Labs

Low Retic, Normocytic anemia
- Hb 9 (13.5)
- MCV 90 (80)
- Corrected-retic 0.9 (2)

BUN/Creat elevated (33/2.1)
UA - Proteinuria 3+
Elevated D-Dimer
Elevated PFA
Normal PT/aPTT

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

PATIENT INFORMATION:
NAME: John SmithAge: 50
GENDER: Male
ID: 1.071.09
PHONE:

Case 2

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

History: 1 month weak and dizzy, Has hypertension not treated well. Now right calf swelling and tender

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	3.0 LOW	F 4.2 - 5.4 M 4.6 - 6 mil-
HEMOGLOBIN	9 LOW	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	27 LOW	F 35-45 M 40-54 %
MCV	90	80.0-100.0 fL
MCH	31.6	27.0-33.0 pg
MCHC	34.3	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	284	140-450 Thousand /uL
Corrected Retic Count	0.9 Low	2
RBC Morphology	Normal	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	3+
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	33 High	6 - 20 mg/dL
Creat	2.1 High	0.5 - 1.0 mg/dL
T Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 -8 g/dL
LDH	75	50 - 150 U/L

Coag		
aPTT	30.0	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	0.88 High	0.2 - .44 FEU
PFA	240 High	CEPI <164 s; CADP <116 s

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Case #2 Question

- A. DVT and low epo anemia secondary to hypertension induced chronic renal failure
- B. DVT secondary to smoking and anemia from aplastic bone marrow
- C. Ruptured baker's cyst and anemia secondary to bleeding
- D. DVT and anemia from multiple myeloma

Renal Failure and clotting

- Early stages of CKD - Low protein C and antithrombin III, (anticlotting system) Increased fibrinogen, von Willebrand factor, factor VIII (pro thrombotic) Increased plasminogen activator inhibitor-1 (PAI-1), low tissue plasminogen activator (t-PA) So Clots stay
- End stage CKD - accumulating uremic toxins decrease platelet function, inhibiting their adhesion, aggregation and releasing platelet factors, such as serotonin or thromboxane A_2
- Damage to endothelial cells produce large amounts of prostacyclin (PGI_2) and nitric oxide (NO) inhibitor of platelet aggregation platelet adhesion.

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Built in Clot Blockers and Busters

Intrinsic Pathway – Inside the cut Endothelial Injury

Test = aPTT

XII to XII active

XI to XI active

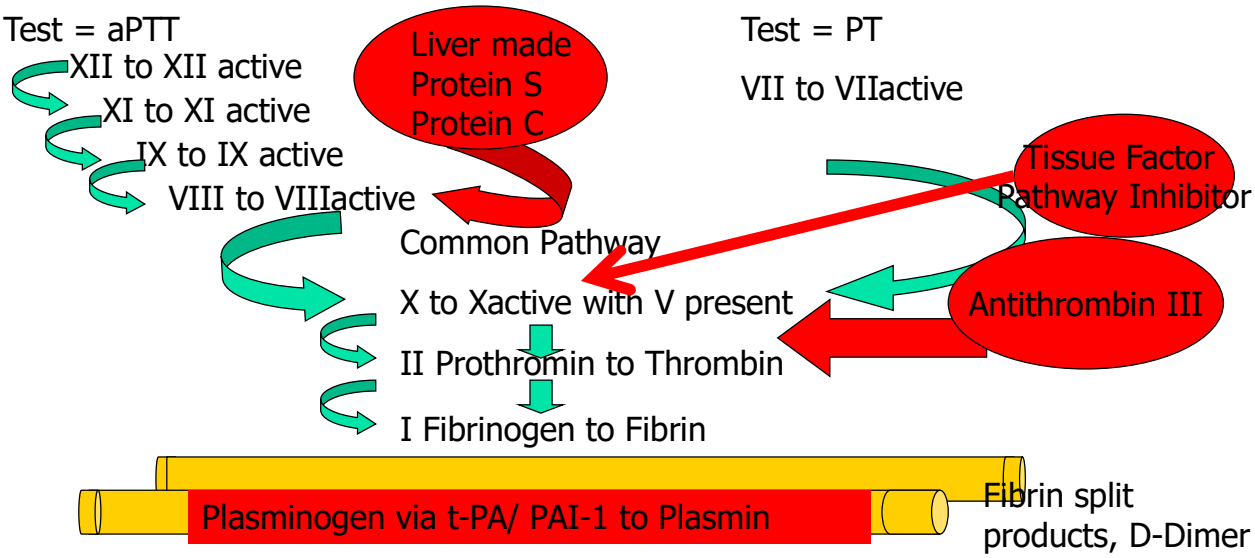
IX to IX active

VIII to VIIIactive

Extrinsic Pathway – outside the cut in the plasma – Tissue Factor

Test = PT

VII to VIIactive



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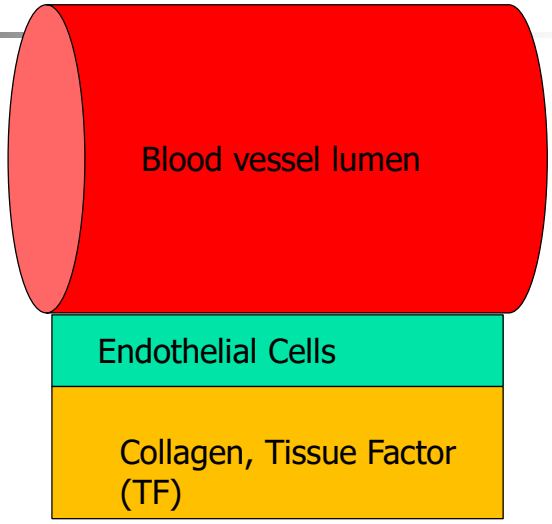
Endothelium

- Covers collagen, Tissue Factor (TF)
- vWF
- tPA
- Nitric Oxide (NO)
- Prostacyclin –Cox2 mediated
- ADPase
- TF Pathway Inhibitor (TFPI)
- Heparin
- Thrombomodulin – Binds free thrombin



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Case #2 Answer

- A. DVT and low epo anemia secondary to hypertension induced chronic renal failure
- B. DVT secondary to smoking and anemia from aplastic bone marrow
- C. Ruptured baker's cyst and anemia secondary to bleeding
- D. DVT and anemia from multiple myeloma

Case 2 - Chronic renal failure (BUN/Creat, proteinuria) Anemia due to low epo, DVT due to hypercoagulable state and elevated PFA from platelet dysfunction. http://ndt.oxfordjournals.org/content/29/1/29.long

Case #3

- A 18 year old male high school student with Hemopillia A presents with 2 hour right knee swelling and pain. He has tried taking ibuprofen for pain relief. There was no injury. His lab slip is attached. What is the best treatment plan?

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Case 3 Labs

Normal CBC
Normal CMP
Normal UA
Normal D-Dimer
Elevated PFA
Prolonged aPTT
Normal PT/INR
Mixing study does not Correct the aPTT

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 3

PATIENT INFORMATION:
NAME: John SmithAge: 18
GENDER: Male
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

History: Hemophillia A with new joint effusion and pain taking NSAID for the pain

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	4.4	F 4.2 - 5.4 M 4.6 - 6 million/mm3
HEMOGLOBIN	14	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	43	F 35-45 M 40-54 %
MCV	85	80.0-100.0 fL
MCH	28	27.0-33.0 pg
MCHC	34	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	284	140-450 Thousand /uL
Corrected Retic Count	2	2
RBC Morphology	Normal	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	10	6 - 20 mg/dL
Creat	0.7	0.5 - 1.0 mg/dL
T Bili	1,0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 -8 g/dL
LDH	100	50 - 150 U/L

Coag		
aPTT	47.5High	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	0.25	0.2 - .44 FEU
PFA	240 High	CEPI <164 s; CADP <116 s

Mixing study—aPTT does not correct 47.5

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Case 3 Questions

A. Recombinant Factor IX infusion

B. Fresh Frozen Plasma transfusion

C. Recombinant Factor VIII infusion

D. Activated Factor VII infusion

Clotting Cascade - Factors

Intrinsic Pathway – Inside the cut Endothelial Injury

Test = aPTT

XII to XII active

XI to XI active

IX to IX active

VIII to VIIIactive

vWF stabilizes Factor VIII

Calcium needed as co-factor

Extrinsic Pathway – outside the cut in the plasma

Vitamin K - Liver dependant

Test = PT

VII to VIIactive + Tissue factor

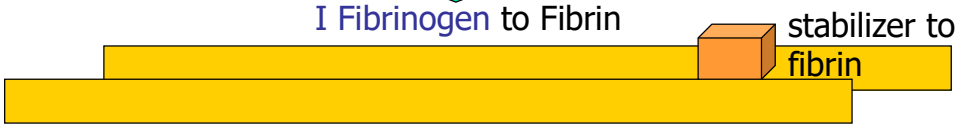
Common Pathway

X to Xactive with V present

II Prothrombin to Thrombin

I Fibrinogen to Fibrin

XIII to XIIIactive stabilizer to crosslink fibrin



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Hemophilia

- US 13,320 cases of hemophilia A (VIII) and 3,640 cases of hemophilia B (IX).
- prolonged aPTT with a normal PT
- Bleeding into joints
- Treat with Recombinant Factor replacement (No longer plasma exposure)
- Three types of Hemophilia A – Genetic, vWD, Inhibitor to factor VIII acquired or developed

Clotting Tests

Intrinsic Pathway –
Inside the cut
Endothelial Injury

Test = aPTT

XII to XII active

XI to XI active

IX to IX active

VIII to VIIIactive

Extrinsic Pathway –
outside the cut in the
plasma – Tissue Factor

Test = PT

VII to VIIactive

Common Pathway Test = TT

X to Xactive with V present

II Prothrombin to Thrombin

I Fibrinogen to Fibrin

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Tests to Order – Screen for Clotting ability

- **--PT** -Prothrombin Time - +/- 2 of control = 11 - 16 sec. Extrinsic system monitor for coumadin therapy. INR is International Normalization Ratio, 1 is normal, 2- 3 for Coumadin Therapy, 2.5 - 3.5 if heart valve
- -**aPTT** - activated Partial Thromboplastin Time- 25 - 38 sec. Intrinsic system. Used to monitor Heparin therapy (if abnormal do Factor analysis and consider vWD)
- **Mixing Study** (add normal plasma to patient plasma re do PT and aPTT) – if PT or aPTT do not correct then there is a inhibitor present and not a factor deficiency.
- **TT** – Thrombin Time measures the common pathway

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Coag Test Summary

PT	aPTT	Differential diagnosis
Prolonged	Normal	Factor VII deficiency or inhibitor, vitamin k deficiency, liver disease, warfarin therapy
Normal	Prolonged	Factor VIII, IX, XI, XII deficiency or inhibitor; von Willebrand disease; lupus anticoagulant; heparin therapy
Prolonged	Prolonged	Prothrombin, fibrinogen, Factor V or X deficiency; liver disease; disseminated intravascular coagulation; combined heparin and warfarin therapy Need TT Thrombin Time

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Case 3 Answer

A. Recombinant Factor IX infusion

B. Fresh Frozen Plasma transfusion

C. Recombinant Factor VIII infusion

D. Activated Factor VII infusion

Case 3 – Prolonged aPTT that does not correct with a mixing study- most likely inhibitors to Factor VIII
https://emedicine.medscape.com/article/779322-treatment
https://www.cdc.gov/ncbddd/hemophilia/inhibitors.html

Case #4

- A 40 year old homeless alcoholic male presents with 1 week increasing jaundice, 3 days nausea and vomiting, 1 day vomiting blood. He smokes about 1 pack per week for 20 years, He does not use recreational drugs, and old drinks a fifth of whiskey a day. His lab slip is attached. What is the cause of the abnormal coagulation studies?

Case 4 Labs

Normal Retic Macrocytic anemia
- Hb 10 (13.5)
- MCV 106 (80)
- C-retic 2 (2)

Thrombocytopenia – 110 (140)
ETOH hepatitis AST/ALT ½
UA – Ketones, Bili, Urobilinogen
Elevated D-Dimer
Normal PFA
Prolonged PT/aPTT
Positive FOB
Normal Amylase/Lipase

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 4

PATIENT INFORMATION:
NAME: John SmithAge: 40
GENDER: Male
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

History: 3 days nausea , 1 day vomiting blood, 1 week jaundice, admits to excessive ETOH

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	3.2LOW	F 4.2 - 5.4 M 4.6 - 6 million/mm3
HEMOGLOBIN	10LOW	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	30 LOW	F 35-45 M 40-54 %
MCV	106 HIGH	80.0-100.0 fL
MCH	31.6	27.0-33.0 pg
MCHC	34.3	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	110 LOW	140-450 Thousand /uL
Corrected Retic Count	2	2
Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	16	6 - 20 mg/dL
Creat	0.8	0.5 - 1.0 mg/dL
T Bili	5.0 H	0.3 - 1.2 mg/dL
D. Bili	4.1 H	0 - 0.2 mg/dL
I. Bili	0.9 H	0.2 - 0.8 mg/dL
Alk Phos	100	32 - 103 IU/L
ALT	300 H	10 - 30 U/L
AST	620 H	8 - 46 U/L
Total Protein	5.5 L	6 -8 g/dL
Albumin	3.2 L	3.4—4.8 g/dL
LDH	175 H	50 - 150 U/L
Sodium NA	140	136 –145 mmol/L
Potassium K	4.0	3.6 –5.1 mmol/L
Chloride105	90 L	99 –111 mmol/L
Bicarb CO2	38 H	22 –32 mmol/L
Glucose	100	70—110 mg/dL

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Positive
Bilirubin	3+Positive
Blood	Negative
Urobilinogen	3+Positive
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Coag		
aPTT	37..5 H	23..3 - 36.6 sec
PT	14 H	9.1 - 13.2 Sec
PT INR	1.22 H	0.82 - 1.18
D-Dimer	400 H	<250 µg/L
PFA	90 norm	CEPI <164 s; CADP <116 s

Fecal Occult blood— Positive

Amylase— 130 (23—140 U/L

Lipase—100 (<160 U/L)

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Case 4 Question

A. Alcoholic Hepatitis and cirrhosis cause all clotting factors to be inactive

B. Alcoholic Hepatitis and cirrhosis cause all clotting factors to be low in production

C. Whiskey inhibits platelet activation

D. Low platelets cause clotting factor deficiencies

Liver Disease

- The liver is THE site for coagulation factor synthesis (except Factor VIII is liver and endothelium)
- multi-factorial coagulopathy
  - Decreased coagulation factors
  - Decreased anti-coagulation factors
  - Decreased fibrinogen
  - Decreased platelets (liver makes thrombopoietin)
  - Increased D-dimers (interfere with clot formation)
- Bleeding from liver failure is a major cause morbidity and mortality
- Give Vitamin K and/or FFP

Case 4 Answer

A. Alcoholic Hepatitis and cirrhosis cause all clotting factors to be inactive

B. Alcoholic Hepatitis and cirrhosis cause most clotting factors and platelets to be low in production

C. Whiskey inhibits platelet activation

D. Low platelets cause clotting factor deficiencies

Case 4 - Alcoholic Hepatitis AST/ALT ration 2/1, Anemia with low Retic High MCV probably due to folate def. High D/I bili, high PT because of Liver insult (Low clotting factor production low protein/albumin) high d-dimer because of clotting to stop bleeding. Urobilinogen and Bili in urine all high (Urobilinogen is Direct Bili transformed by gut bacteria and reabsorbed- If no Urobilinogen in urine but high Bilirubin – think biliary obstruction. Metabolic alkalosis from vomiting. Low platelets from liver insult-low thrombopoeitin
http://emedicine.medscape.com/article/170539-overview

Case #5

- A 60 year old retired male presents with 1 month increasing weakness, dyspnea on exertion, increasing low back pain and 2 days of left calf swelling with tenderness. He does not smoke, use recreational drugs, or drink alcohol. His lab slip is attached. What is the most likely diagnosis?

Case 5 Labs

CBC- Pancytopenia
WBC 1.9 (3.8)
Hb 9 (15)
Plt 90 (140)
Low Retic 0.9 (2)
Micro: Rouleaux formations
CMP – hypercalcemia 12.2
Elevated protein 9.5
UA Protenuria 2+
Coag – elevated d-dimer

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 5

Patient Information:
Name: John Smith Age: 60
Gender: Male
ID: 1.071.09
Phone:

Ordering Physician: C. Johnson
Client Information:
Emory PA Clinical OSCE
1462 Clifton Rd NE
Atlanta, GA 30322

Specimen Information:
Specimen: P121982AQW
Requisition: 1973200-
Lab reference #: H9000

Collected: 12/17/12
Received: 12/17/12
Reported: 12/17/12

1 month increasing weakness, low back pain, and new DVT

Test Name	Result	Reference Range
Hematology Report		
CBC		
White blood cell count	1.9 Low	3.8-10.8 Thousand/uL
Red Blood Cell Count	3.0 low	F 4.2 - 5.4 M 4.6 - 6 mil-
Hemoglobin	9 Low	F 11-16 M 13.5 - 18g/dL
Hematocrit	27 Low	F 35-45 M 40-54 %
MCV	82	80.0-100.0 fL
MCH	24 Low	27.0-33.0 pg
MCHC	24.3Low	32.0-36.0 g/dL
RDW	13.9	11.0-15.0 %
Platelet Count	90 Low	140-450 Thousand /uL
Corrected Retic Count	0.9 Low	2
RBC Morphology	Rouleax for-mations	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	2+ Positive
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	12.2High	9 - 11 mg/dL
BUN	16	6 - 20 mg/dL
Creat	0.8	0.5 - 1.0 mg/dL
T Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	9.5 High	6 -8 g/dL
LDH	75	50 - 150 U/L

Coag		
aPTT	27.5	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	500 H	< 250 µg/L DDU
PFA	110	CEPI <164 s; CADP <116 s

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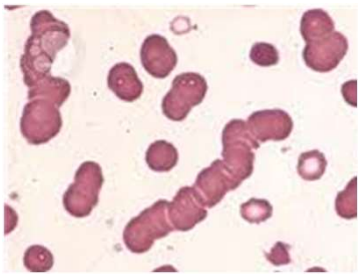
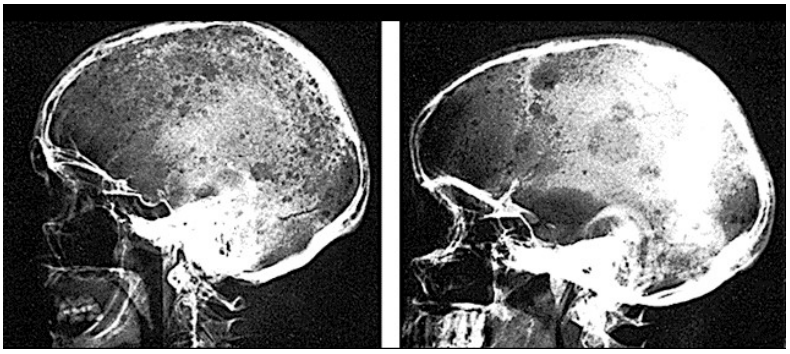
Case 5 Question

A. Chronic Lymphocytic Leukemia with DVT
B. Non Hodgkin's Lymphoma with DVT
C. Multiple Myeloma with DVT
D. Metastatic Lung cancer with DVT

Multiple Myeloma

- Symptoms and Signs - Itching, Bone pain, weakness, anemia, lytic bone lesions, increased protein, M - Spike, Bence Jones protein in urine, renal failure, rouleaux formation





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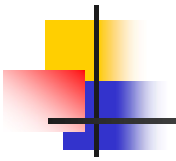
Case 5 Answer

A. Chronic Lymphocytic Leukemia with DVT
B. Non Hodgkin's Lymphoma with DVT
C. Multiple Myeloma with DVT
D. Metastatic Lung cancer with DVT

Case 5 – Multiple Myeloma with increased serum and urine protein – would confirm with SPEP and Urine for Bence Jones protein. Oncology referral for Bone Marrow Bx. Anemia and low platelets from marrow replacement with plasma cells. DVT because MM is a hypercoagulable state.
http://asheducationbook.hematologylibrary.org/content/2007/1/158.full

Case #6



- A 60 year old retired male presents with 3 months increasing weakness, dyspnea on exertion, and gum bleeding after brushing his teeth. He does not smoke, use recreational drugs, or drink alcohol . His lab slip is attached. What is the most likely diagnosis?

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Case 6 Labs

CBC – Leukocytosis 30.9 (10.8)
Low Retic, Microcytic anemia
Hb 9 (13.5)
MCV 70 (80)
C-retic 0.9 (2)
Low Platelets 90 (140)
Mature Lymphocytes on smear
CMP - Normal
UA - Negative
COAG - Normal

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 6

Patient Information:
Name: John Smith Age: 60
Gender: Male
ID: 1.071.09
Phone:

Ordering Physician: C. Johnson
Client Information:
Emory PA Clinical OSCE
1462 Clifton Rd NE
Atlanta, GA 30322

Specimen Information:
Specimen: P121982AQW
Requisition: 1973200-
Lab reference #: H9000

Collected: 12/17/12
Received: 12/17/12
Reported: 12/17/12

3 months progressive weakness and gum bleeding after brushing

Test Name	Result	Reference Range
Hematology Report		
CBC		
White blood cell count	30.9 High	3.8-10.8 Thousand/uL
Red Blood Cell Count	3.0 low	F 4.2 - 5.4 M 4.6 - 6 million/mm3
Hemoglobin	9 Low	F 11-16 M 13.5 - 18g/dL
Hematocrit	27 Low	F 35-45 M 40-54 %
MCV	70 Low	80.0-100.0 fL
MCH	24 Low	27.0-33.0 pg
MCHC	24.3Low	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
Platelet Count	90 Low	140-450 Thousand /uL
Corrected Retic Count	0.9 Low	2
RBC Morphology	Mature Lymphocytes predominate	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	10.0	9 - 11 mg/dL
BUN	16	6 - 20 mg/dL
Creat	0.8	0.5 - 1.0 mg/dL
T.Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	9.5	6 -8 g/dL
LDH	75	50 - 150 U/L

Coag		
aPTT	27.5	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	100	< 250 µg/L DDU
PFA	110	CEPI <164 s; CADP <116 s

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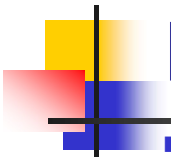
Case 6 Question

A. Chronic Lymphocytic Leukemia
B. Non Hodgkin's Lymphoma
C. Multiple Myeloma
D. Acute Lymphocytic Leukemia

Bleeding: think PVC Pipes



PVC pipes

- **Platelets**
  - Not enough below 50,000 – production, destruction, sequestration
  - Not working –ASA, NSAIDs, Uremia, Congenital
- **Von Willebrands Disease**-Type 1 most common
- **Clotting Factors**
  - Most common: VIII, IX
  - Vitamin K Deficiency, Liver Disease
- **Pipes** - Vasculitis, Scurvy, Ehlers-Danlos, Heritary Hemorrhagic Telangiectasias, Steroids
  - Palpable Purpura – Sepsis, Meningococcemia, Henoch-Schonlein purpura, Drugs

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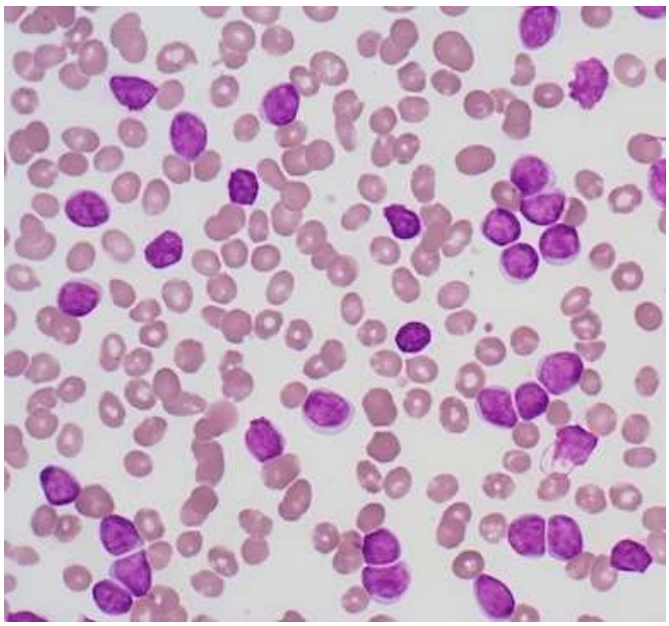
Bleeding Test- PVC- Pipes

- Platelets – CBC platelet count
  - Do they work – PFA (Bleeding time)
- vWF – abnormal PFA and aPTT (Factor VIII depends of vWF) do vWF analysis
- Clotting Factors – PT and aPTT if either abnormal – do Mixing study – if corrects do Factor levels VIII, IX. If both PT and aPTT abnormal do TT Thrombin time
- CMP, UA (Renal or Hepatic causes)
- Pipes – Vasculitis C-Reative Protein, ESR, Biopsy

CLL



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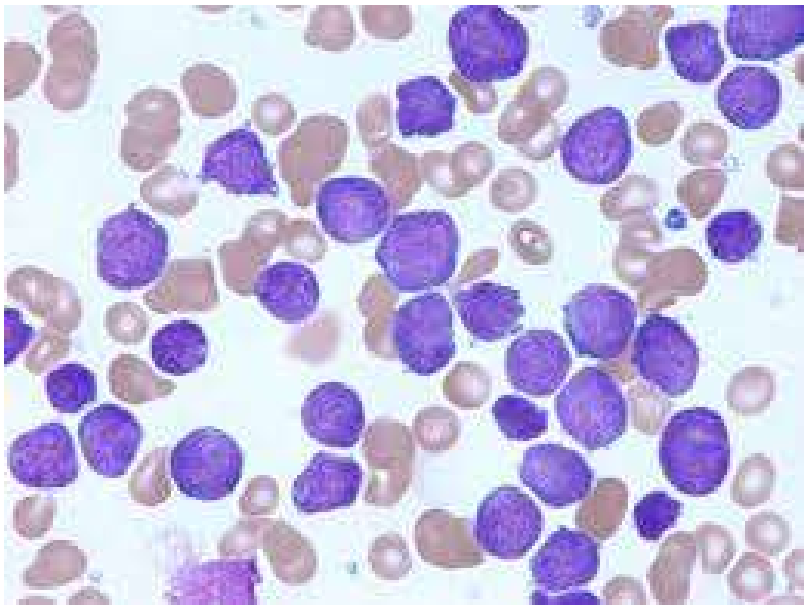
ALL



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Leukemia

- ALL: Acute Lymphocytic Leukemia (Usually in Children)
- AML: Acute Myelogenous Leukemia
- CLL: Chronic Lymphocytic Leukemia (Usually Adults – minimal symptoms)
- CML: Chronic Myelogenous Leukemia

- HX: Fatigue, anorexia, wt loss, fever, bone pain, headaches, lymphadenopathy, non healing infections, thrush, bleeding (Nose, gums, GI, menses)
- PE: Pallor, gingival hyperplasia, Candida infections, lymphadenopathy, hepatosplenomegaly, lung infiltrates, bleeding, bruising
- LAB: CBC: elevated WBC/ low platelets, low Hct, WBC Differential, Chem 18, Bone Marrow Biopsy
- Philadelphia Chromosome seen in CML
- Auer bodies or rods in AML
- CT - MRI chest and abdomen
- CXR - Chest infiltation, pneumonias
- RX: Chemotherapy, Bone Marrow Transplant

Case 6 Answer

A. Chronic Lymphocytic Leukemia

B. Non Hodgkin's Lymphoma

C. Multiple Myeloma

D. Acute Lymphocytic Leukemia

Case 6 – CLL – Low Hb and Platelets with high WBCs mainly mature Lymphs. Refer to oncology for Bone Marrow Biopsy and monitoring
http://emedicine.medscape.com/article/199313-overview

Case #7

- A 28 year old female nurse presents with 1 year of heavy menses, increasing weakness,. She does not smoke, use recreational drugs, or drink alcohol. Her physical exam including pelvic is normal. Her lab slip is attached. What is the most likely cause of her anemia?

Case 7 Labs

CBC
Low Retic, Microocytic anemia
Hb 9 (13.5)
MCV 70 (80)
C-retic 0.9 (2)
Normal Platelets 284 (140)
CMP - Normal
UA - Negative
Coag - Elevated PFA
Prolonged aPTT that corrects with mixing study

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 7

Patient Information:
Name: Sally Jones Age: 28
Gender: Female
ID: 1.071.09
Phone:

Ordering Physician: C. Johnson
Client Information:
Emory PA Clinical OSCE
1462 Clifton Rd NE
Atlanta, GA 30322

Specimen Information:
Specimen: P121982ACW
Requisition: 1975200-
Lab reference #: H9000

History: Heavy menses,

Collected: 12/17/13
Received: 12/17/13
Reported: 12/17/13

Test Name	Result	Reference Range
Hematology Report		
CBC		
White blood cell count	9	3.8-10.8 Thousand/uL
Red Blood Cell Count	3.0 low	F 4.2 - 5.4 M 4.6 - 6 mil-
Hemoglobin	9 Low	F 11-16 M 13.5 - 18g/dL
Hematocrit	27 Low	F 35-45 M 40-54 %
MCV	70 Low	80.0-100.0 fL
MCH	24 Low	27.0-33.0 pg
MCHC	24.3Low	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
Platelet Count	284	140-450 Thousand /uL
Corrected Retic Count	0.9 Low	2
RBC Morphology	Microcytes,	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	10	6 - 20 mg/dL
Creat	0.7	0.5 - 1.0 mg/dL
T Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 - 8 g/dL
LDH	100	50 - 150 U/L

Coag		
aPTT	47..5High	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	0.25	0.2 - .44 FEU
PFA	240 High	CEPI <164 s; CADP <116 s

Mixing study—aPTT corrects to 30.0 sec

Case 7 Question

A. Iron Deficiency secondary to fibroids

B. Thalassemia minor

C. Iron deficiency and Von Willebrand Disease

D. Lead toxicity

Clotting Tests for bleeding

Test/Disease	PT	aPTT	PFA	Platelet Ct
vWD	Normal	Increased	Abnormal	Normal
Hemophilia A/B heparin, lupus	Normal	Increased	Normal	Normal
DIC	Increased	Increased	Abnormal	Low
Uremia	Normal	Normal	Abnormal	Normal
Aspirin NSAIDs	Normal	Normal	Abnormal	Normal
Early: Liver Dz Vit K def, F VII coumadin	Increased	Normal	Normal	Normal
Late Liver Dz	Increased	Increased	Normal	Low
ITP, TTP, HUS, HIT	Normal	Normal	Normal	Low

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Von Willebrand Disease

- Most common inherited bleeding disorder
- Found in approximately 1% of the population
- Most individuals are asymptomatic unless a significant bleeding event occurs
- Blood Group O individuals have significantly lower vWF than other groups (30% lower)
- vWF stabilizes Factor VIII so any decrease in vWF will increase aPTT and platelet function analysis will be abnormal

Von Willebrand Disease

- Measure vWF antigen (vWF:Ag)
  - How much protein is present?
- Measure vWF activity (Ristocetin Cofactor)
  - How well is the protein working?
- Measure Factor VIII activity
  - How well is vWF stabilizing Factor VIII?
- Evaluate pattern of von Willebrand multimers by electrophoresis
  - Important for classification of disease (6 types) and therapeutic management
- Treat most common cause with DDAVP

Case 7 Answer

A. Iron Deficiency secondary to fibroids

B. Thalassemia minor

C. Iron deficiency and Von Willebrand Disease

D. Lead toxicity

Case 7 – Menorrhagia from Von Willebrand disease (VWD) with elevated aPTT (not stabilizing Factor VIII and abnormal PFA (super glue of Platelets) Iron def anemia (Microcytic low retic)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4874860/

Case #8

- A 13-year-old healthy male presents with 2 days of recurrent gum bleeding and nosebleeds. He had a viral syndrome over 1 week ago that resolved. No other positives in his medical history. On PE he has petechea and purpura on his chest and legs. His lab slip is attached. What is the most likely cause of his symptoms?

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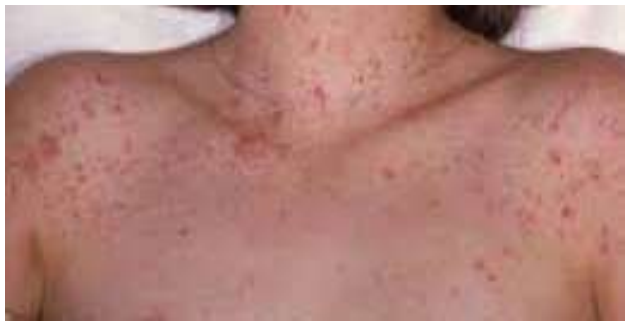
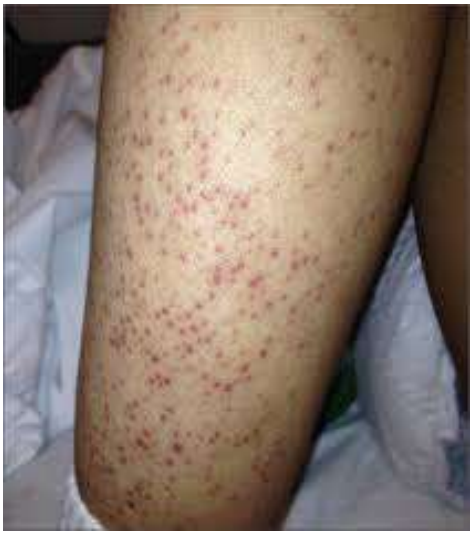
Petechea and Purpura





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Case 8 Labs

CBC – Thrombocytopenia 20 (140)
CMP - Normal
UA - Negative
Coag – Normal PFA
Normal PT/aPTT

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 8

Patient Information:
Name: John Smith Age: 13
Gender: Male
ID: 1.071.09
Phone:

Ordering Physician: C. Johnson
Client Information:
Emory PA Clinical OSCE
1462 Clifton Rd NE
Atlanta, GA 30322

Specimen Information:
Specimen: P121982AQW
Requisition: 1973200-
Lab reference #: H9000

Collected: 12/17/12
Received: 12/17/12
Reported: 12/17/12

History: Bleeding gums and nose post viral infection 1 week ago

Test Name	Result	Reference Range
Hematology Report		
CBC		
White blood cell count	9	3.8-10.8 Thousand/uL
Red Blood Cell Count	4.4	F 4.2 - 5.4 M 4.6 - 6 mil-
Hemoglobin	14	F 11-16 M 13.5 - 18g/dL
Hematocrit	43	F 35-45 M 40-54 %
MCV	85	80.0-100.0 fL
MCH	28	27.0-33.0 pg
MCHC	34	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
Platelet Count	20 Low	140-450 Thousand /uL
Corrected Retic Count	2	2
RBC Morphology	Normal	

Urinalysis (u/A)	
color	Yellow
Appearence	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	10	6 - 20 mg/dL
Creat	0.7	0.5 - 1.0 mg/dL
T Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 - 8 g/dL
LDH	100	50 - 150 U/L

Coag		
aPTT	27.5	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	0.25	0.2 - .44 FEU
PFA	90 norm	CEPI <164 s; CADP <116 s

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Case 8 Question

A. Chronic Lypmphocytic Leukemia
B. Non Hodgkins Lymphoma
C. Mononucleosis
D. Immune Thrombocytopenic Purpura

Thrombocytopenia

- Production
  - Nutritional B12 or Folate Deficiency
  - Congenital – Alports syndrome, Fanconi anemia, Wiscott-Aldrich syndrome
  - Marrow damage – aplastic anemia, chemotherapy, drugs, maligancy – myeloma or leukemia, radiation, mylodysplasia
- Destruction
  - Immune – (Positive Platelet Associated Antibody test or HIT assay) ITP, Drug, HIV, SLE, HIT
  - Non-Immune- DIC, TTP, Preeclampsia, HELLP syndrome Anti-phospholipid syndrome
- Sequestration- Liver, spleen, marrow -myelofibrosis, cancer

Platelets - How Low Can you go?

- 150,000 - 350,000 cu/mm Normal
- 80 – 100 – need for surgery
- 40 – 50 for procedures like LP
- 10 – 40 –At risk if trauma or surgery
- < 10,000 spontaneous bleeding
- if > 1 million - Clotting too much

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Thrombocytopenia Testing

- Liver Spleen size – Ultrasound or CT
- Bone Marrow Biopsy
- Platelet antibodies (direct and indirect)
- HIT assay if on heparin
- ADAMTS 13 (TTP)
- Blood smear (morphology)
- Antibody response to *Escherichia coli O157:H7*

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ITP - Immune Thrombocytopenic Purpura

- In children linked to viral infection
  - platelet-associated antibodies
  - 80% rapid remission, and does not recur
    - Treatment: steroids and IVIG
  - 10% to 20% develop chronic ITP
    - splenectomy works in 70%
- Adults linked to HIV and Hep C
  - 50% develop chronic ITP
  - Same treatments

There is a song for that

Friends With Low Platelets | Garth Brooks Parody | ZDoggMD.com

https://www.youtube.com/watch?v=-rwcIRfHcAE

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Case 8 Answer

A. Chronic Lypmphocytic Leukemia

B. Non Hodgkins Lymphoma

C. Mononucleosis

D. Immune Thrombocytopenic Purpura

Case 8 - ITP post viral syndrome. Can watch and wait with frequent CBC follow-ups. The American Society of Hematology (ASH) recommends that children who have no bleeding or minor bleeding (eg, cutaneous manifestations such as bruising and petechiae) be managed with observation alone regardless of platelet count. [8
http://emedicine.medscape.com/article/202158-overview
https://ashpublications.org/bloodadvances/article/3/23/3829/429213

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Case #9

- A 25 year old male graduate student is admitted for his second unprovoked DVT and is now being treated day 2 with unfractionated heparin by IV pump. His lab slip is attached. What lab test would be most likely positive?

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Case 9 Labs

CBC
Normal Platelets 284 (140)
CMP - Normal
UA - Negative
Coag - Elevated PFA
Prolonged aPTT that corrects with mixing study
Elevated D-Dimer

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

PATIENT INFORMATION:
NAME: John SmithAge: 25
GENDER: Male
ID: 1.071.09
PHONE:

Case 9

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

History: admitted for second unprovoked DVT on UFH and NSAID

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	4.4	F 4.2 - 5.4 M 4.6 - 6 million/mm3
HEMOGLOBIN	14	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	43	F 35-45 M 40-54 %
MCV	85	80.0-100.0 fL
MCH	28	27.0-33.0 pg
MCHC	34	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	284	140-450 Thousand /uL
Corrected Retic Count	2	2
RBC Morphology	Normal	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	10	6 - 20 mg/dL
Creat	0.7	0.5 - 1.0 mg/dL
T Bili	1,0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 -8 g/dL
LDH	100	50 - 150 U/L

Coag		
aPTT	47.5High	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	400 H	< 250 µg/L
PFA	240 High	CEPI <164 s; CADP <116 s

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Case 9 Question

A. Elevated homocysteine level
B. Positive Factor V Leiden
C. Low antithrombin III
D. Antiphospholipid (anticardiolipin) antibody

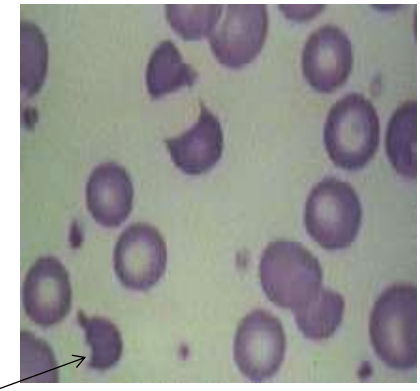
Best screening test for hypercoagulability?

- There is none!!
- Unprovoked clot is the fist clue
- More than one clot suggests a genetic issue
- Start testing for most common

82

Tests – Is Clotting going on?

- D-Dimer elevation – from thrombolysis (break apart)
  - Also used to know when to stop anticoagulant therapy
- Fibrin Split products
- Peripheral smear may show shistocytes (helmet cells)
- https://ashpublications.org/blood/article/124/2/196/32915/D-dimer-to-guide-the-duration-of-anticoagulation



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Tests – Clotting too much recurrent DVT/PE

- Fasting homocysteine level/ MTHFR gene
- Factor V Leiden assay
- Protein S, C, antithrombin III assay
- Lupus anticoagulant
- Anticardiolipin antibodies
- Anti Beta-GPI antibodies
- Prothrombin 20210 mutation test
- Fibrinogen level
- HIT Assay if Heparin exposure

Prevalence and Relative Risk of Clotting problem DVT/PE

- Hyperhomocyteinemia/ MTHFR gene (10% -15%) RR=3
- Factor V Leiden (5% Most common genetic) RR=7-80
- Platelet GPIIb/IIIa Human Platelet Antigen -HPA-1b (2 - 3%) RR = 4
- Prothrombin 20210 mutation (1- 2%) RR=2-5
- Protein C deficiency (0.2 – 0.5%) RR=7
- Protein S deficiency (0.1%) RR= 8.5
- Antithrombin III deficiency (0.2 – 0.5%) RR=8

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5056464/
- https://www.hematology.org/education/clinicians/guidelines-and-quality-care/clinical-practice-guidelines/venous-thromboembolism-guidelines

Case 9 Answer

A. Elevated homocysteine level

B. Positive Factor V Leiden

C. Low antithrombin III

D. Antiphospholipid (anticardiolipin) antibody

Case 9 – Factor V Leiden is the most common genetic cause of hypercoagulable states and may need lifelong anticoagulation
http://emedicine.medscape.com/article/211039-overview

Case #10

- A 30-year-old male had ACL repair on his right knee 5 days ago, developed a DVT post op day 1 and has been in the hospital receiving unfractionated heparin by IV infusion pump. His lab slip is attached for post-op day 6. What is the most appropriate order to write?

Case 10 Labs

CBC – Thrombocytopenia 90 (140)
CMP - Normal
UA - Negative
Coag – Normal PFA
Elevated aPTT
Elevated D-Dimer

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 10

PATIENT INFORMATION:
NAME: John SmithAge: 30
GENDER: Male
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

History: 5 days after Knee surgery Diagnosis of PE treated with Unfractionated Heparin for 4 days

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	4.4	F 4.2 - 5.4 M 4.6 - 6 million/mm3
HEMOGLOBIN	14	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	43	F 35-45 M 40-54 %
MCV	85	80.0-100.0 fL
MCH	28	27.0-33.0 pg
MCHC	34	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	90 LOW	140-450 Thousand /uL
Corrected Retic Count	2	2
RBC Morphology	Normal	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	10	6 - 20 mg/dL
Creat	0.7	0.5 - 1.0 mg/dL
T Bili	1.0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 -8 g/dL
LDH	100	50 - 150 U/L

Coag		
aPTT	47.5High	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	400 H	< 250 µg/L
PFA	100	CEPI <164 s; CADP <116 s

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Case 10 Question

A. Switch to fondaparinux sub q and order a HIT assay
B. Continue Heparin but start Warfarin for home treatment
C. Switch to LMH sub q and start Warfarin for home treatment
D. Start antiplatelet therapy using low dose aspirin

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Heparin-induced thrombocytopenia (HIT)

- Due to an antibody against heparin
- Occurs in 1-3% of adult patients receiving heparin for 1 week or more. heparin binds to platelet factor 4 (PF4), forming a highly reactive antigenic complex on the surface of platelets
- An unexpected fall in platelet count occurring 4-14 days after heparin exposure
- Platelet count usually falls by 50% - Monitor CBCs
- Mean platelet count 60,000 – 100,000/uL
- Platelets become activated and induce clotting
- Associated with thrombosis - 10-30% develop arterial or venous thromboses (usually DVTs or PEs)
- Of those forming a clot, 30% will die or require amputation
- Platelet counts should be monitored while patient is on heparin therapy
- HIT Assay
- STOP all Heparin products (Flush, LMWH, Heparin) and give Direct Thrombin Inhibitor.

Non-Heparin
Fondaprinux

Intrinsic Pathway –
Inside the cut
Endothelial Injury

Test = aPTT

XII to XII active

XI to XI active

IX to IX active

VIII to VIIIactive

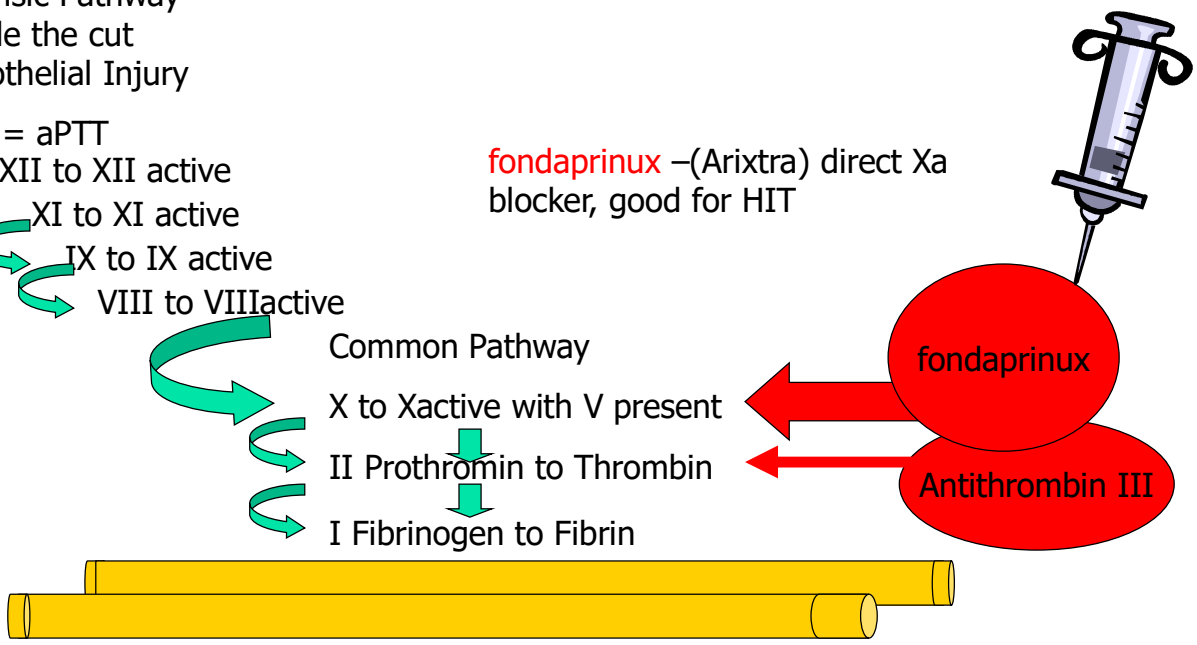
Common Pathway

X to Xactive with V present

II Prothrombin to Thrombin

I Fibrinogen to Fibrin

fondaprinux –(Arixtra) direct Xa blocker, good for HIT



Thrombin Inhibitors

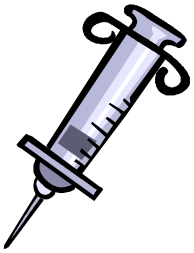
Intrinsic Pathway –
Inside the cut
Endothelial Injury

Test = aPPT

XII to XII active
XI to XI active
IX to IX active
VIII to VIIIactive

Common Pathway

X to Xactive with V present
II Prothrombin to Thrombin
I Fibrinogen to Fibrin



Bivalirudin – Angiomax
Lepirudin- Refludan
Argatroban –
Antithrombin III - ThrombateII

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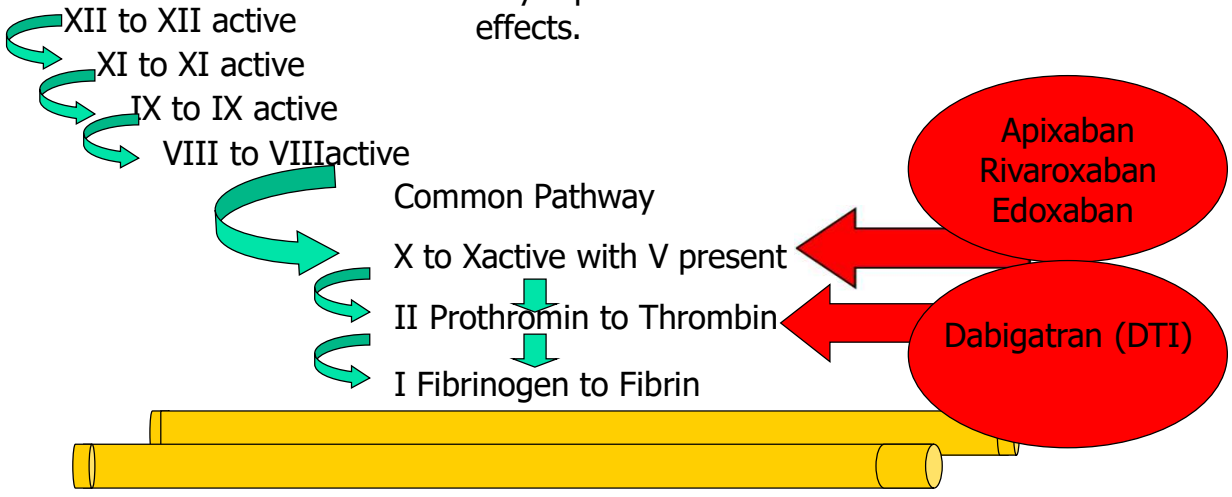
Non Vitamin K antagonist Oral Anticoagulants - NOACs

Intrinsic Pathway –
Inside the cut
Endothelial Injury

Test = aPPT

May replace Coumadin with fewer side effects.



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Case 10 Answer

A. Switch to fondaparinux sub q and order a HIT assay
B. Continue Heparin but start Warfarin for home treatment
C. Switch to LMH sub q and start Warfarin for home treatment
D. Start antiplatelet therapy using low dose aspirin

Case 10 -Heparin-induced thrombocytopenia (HIT)
http://emedicine.medscape.com/article/1357846-overview

Case #11

- A 20-year-old male college student is admitted for his first unprovoked DVT He has a positive history of recurrent headaches, non vertigo dizziness and tinnitus. His lab slip is attached. What lab test would be most likely be positive?

95

Case 11 Labs

CBC –
Leukocytosis 13.0 (10.8)
Erythrocytosis RBC 7 (6)
Thrombocytosis 500 (450)
CMP - Normal
UA - Negative
Coag – Normal PFA
Normal PT/aPTT
Elevated D-Dimer

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

Case 11

PATIENT INFORMATION:
NAME: John SmithAge: 20
GENDER: Male
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

History: Headaches, dizziness and tinnitus presents with DVT

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	13 .0 HIGH	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	7.0 HIGH	F 4.2 - 5.4 M 4.6 - 6 mil-lion/mm3
HEMOGLOBIN	20 .0 HIGH	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	60 HIGH	F 35-45 M 40-54 %
MCV	85	80.0-100.0 fL
MCH	28	27.0-33.0 pg
MCHC	34	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	500 HIGH	140-450 Thousand /uL
Corrected Retic Count	2	2
RBC Morphology	Normal	

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Negative
Bilirubin	Negative
Blood	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	10	6 - 20 mg/dL
Creat	0.7	0.5 - 1.0 mg/dL
T Bili	1,0	0.3 - 1.2 mg/dL
D. Bili	0.1	0 - 0.2 mg/dL
I. Bili	0.9	0.2 - 0.8 mg/dL
Alk Phos	44	20 - 90 U/L
ALT	20	10 - 30 U/L
AST	9	8 - 46 U/L
Total Protein	7.5	6 -8 g/dL
LDH	100	50 - 150 U/L

Coag		
aPTT	30.0	23..3 - 36.6 sec
PT	10.1	9.1 - 13.2 Sec
PT INR	1	0.82 - 1.18
D-Dimer	400 H	< 250 µg/L
PFA	150	CEPI <164 s; CADP <116 s

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Case 11 Question

A. Elevated Erythropoietin level
B. Low Erythropoietin level
C. Low antithrombin III
D. Elevated Antiphospholipid (anticardiolipin) antibody

Primary - Polycythemia vera

- Sx: Pruritis HA, Dizziness, vertigo, visual disturbance, tinnitus
- PE: Rubor, BP increased, splenomegaly or hepatomegally
- Lab: HCT >55 Increased platelets and WBC count
- Low Epo and +JAK2 gene
- RX: Phlebotomy, Hydroxyurea

Secondary Polycythemia

- Increase erythropoietin due to hypoxia (COPD, smokers, high altitude), tumors of kidney, ovary, liver, brain, drugs: steroids, androgen, dehydration, burns
- PE: No hepatospenomegaly unless tumor
- Lab – Only elevated RBC, Hb, Hct

Case 11 Answer

A. Elevated Erythropoietin level

B. Low Erythropoietin level

C. Low antithrombin III

D. Elevated Antiphospholipid (anticardiolipin) antibody

Case 11- Polycythemia Vera - Clue: all cell lines are increased
http://emedicine.medscape.com/article/205114-overview#a1

100

Case #12

- A 24-year-old healthy female, 8 months pregnant presents to the ED with 1 day jaundice, anorexia, weakness and nose bleeds. She does not smoke, use recreational drugs, or drink alcohol. Her lab slip is attached. What is the most likely cause these results?

Case 12 Labs

CBC - High Retic Normocytic Anemia
Hb – 10 (11)
C –Retic 4 (2)
Thrombocytopenia 90 (140)
CMP – Tbili 5 (1.2)
Dbili 1.1 (0.2)
Ibili 4.9 (0.8)
ALT 100 (30)
AST 120 (46)
LDH 300 (150)
UA - + Ketones, 3+ Bilirubin 3+ Urobilinogen
Coag – Normal PFA Normal PT/aPTT

APERTURE LABORATORIES
WE DO WHAT WE MUST. BECAUSE WE CAN.

PATIENT INFORMATION:
NAME: Jane Smith Age: 24
GENDER: Female
ID: 1.071.09
PHONE:

ORDERING PHYSICIAN: C. Johnson
CLIENT INFORMATION:
EMORY PA CLINICAL OSCE
1462 CLIFTON RD NE
ATLANTA, GA 30322

SPECIMEN INFORMATION:
SPECIMEN: P121982AQW
REQUISITION: 1973200-
LAB REFERENCE #: H9000

History: 8 months pregnant with jaundice, anorexia, weakness and nosebleeds

Test Name	Result	Reference Range
HEMATOLOGY REPORT		
CBC		
WHITE BLOOD CELL COUNT	9	3.8-10.8 THOUSAND/UL
RED BLOOD CELL COUNT	3.2LOW	F 4.2 - 5.4 M 4.6 - 6 million/mm3
HEMOGLOBIN	10LOW	F 11-16 M 13.5 - 18g/oL
HEMATOCRIT	30 LOW	F 35-45 M 40-54 %
MCV	96	80.0-100.0 fL
MCH	31.6	27.0-33.0 pg
MCHC	34.3	32.0-36.0 g/cL
RDW	13.9	11.0-15.0 %
PLATELET COUNT	90 LOW	140-450 Thousand /uL
Corrected Retic Count	4 High	2
Metabolic Profile BMP		
Total Calcium	7.2	9 - 11 mg/dL
BUN	16	6 - 20 mg/dL
Creat	0.8	0.5 - 1.0 mg/dL
T Bili	5.0 H	0.3 - 1.2 mg/dL
D. Bili	1.1 H	0 - 0.2 mg/dL
I. Bili	4.9 H	0.2 - 0.8 mg/dL
Alk Phos	100	32 - 103 IU/L
ALT	100 H	10 - 30 U/L
AST	120 H	8 - 46 U/L
Total Protein	6.5	6 -8 g/dL
Albumin	4.0	3.4—4.8 g/dL
LDH	300 H	50 - 150 U/L
Sodium NA	140	136 –145 mmol/L
Potassium K	4.0	3.6 –5.1 mmol/L
Chloride105	99	99 –111 mmol/L
Bicarb CO2	20	22 –32 mmol/L
Glucose	100	70—110 mg/dL

Urinalysis (u/A)	
color	Yellow
Appearance	clear
Specific Gravity	1.024
pH	6
Protein	Negative
Glucose	Negative
Ketones	Positive
Bilirubin	3+Positive
Blood	Negative
Urobilinogen	3+Positive
Nitrite	Negative
Leukocyte Esterase	Negative
Microscopic	
WBCs/hpf	0
RBC/hpf	0
Epithelial Cells/hpf	0
Bacteria	0

Coag		
aPTT	35.0	23..3 - 36.6 sec
PT	12.0	9.1 - 13.2 Sec
PT INR	1.0	0.82 - 1.18
D-Dimer	200	< 250 µg/L
PFA	90 norm	CEPI <164 s; CADP <116 s

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Case 12 Question

A. Hemolytic Uremic Syndrome
B. TTP
C. ITP
D. HELLP syndrome

HELLP- Pregnancy

- Hemolysis (high indirect Bilirubin, LDH, high retic anemia)
- Elevated Liver Enzymes (AST, ALT)
- Low Platelets
- Severe preeclampsia (BP increased and proteinuria) increased maternal and fetal mortality
- 1 per 1000 pregnancies up to 20% with preeclampsia/eclampsia at 28 – 36 weeks gestation
- Rx Support and Deliver Baby

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Thrombocytopenia – Not HIT

Issue/ Disease	Acute ITP	Chronic ITP	TTP	HUS	DIC	HELLP
Age	Children	Adults	Adults	Children	Any	Pregnant
Cause	Immune Post viral	Immune HIV Hep C, SLE	ADAMTS-3 and big vWF	Infections E.Coli 0157:h7	Sepsis, Burns trauma	Pre-ecclampsia
PT/PTT	normal	normal	normal	normal	abnorm	+/-
Fever	no	no	yes	yes	depends	+/_
Hemolysis*	no	no	yes	yes	no	yes
Organ failure	no	no	CNS > Renal	Renal > CNS	All possible	Liver
Treatment	None – IVIG, Steroids	Steroids Splenectomy	Plasma Exchange, No Plts	Support, No Plts	FFP, Cryo, platelets	Deliver ($MgSO_4$)

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Case 12 Answer

A. Hemolytic Uremic Syndrome

B. TTP

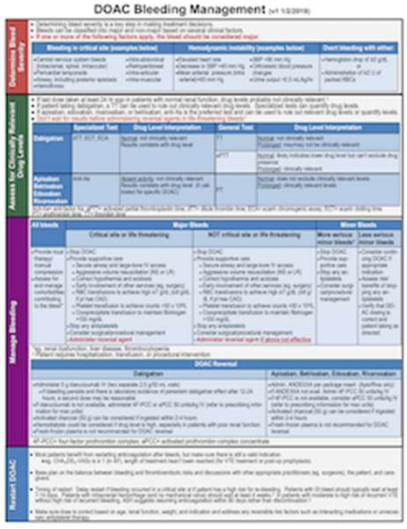
C. ITP

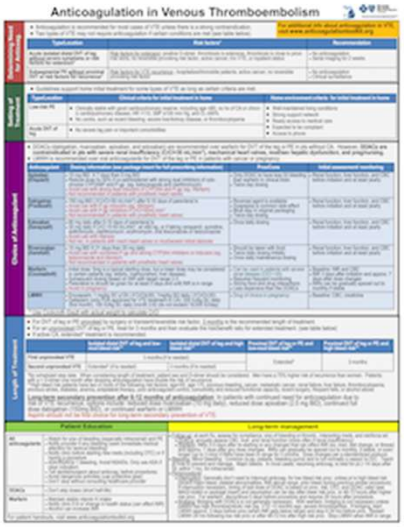
D. HELLP syndrome

Case 12- HELLP syndrome, named for 3 features of the disease (hemolysis, elevated liver enzyme levels, and low platelet levels)
http://emedicine.medscape.com/article/1394126-overview

One Page Guides

- https://anticoagulationtoolkit.org/providers





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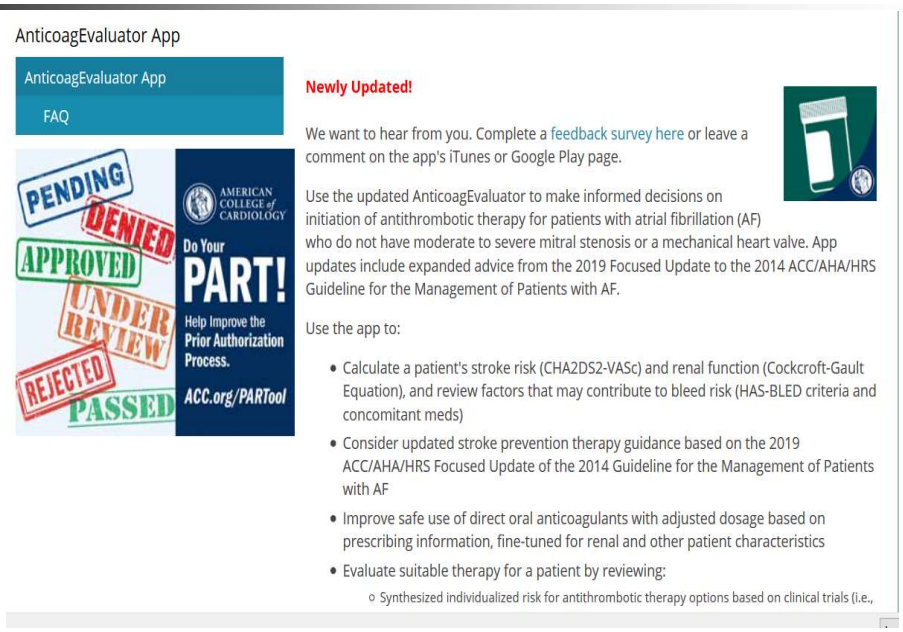
Apps: CDC anticoagulation manager

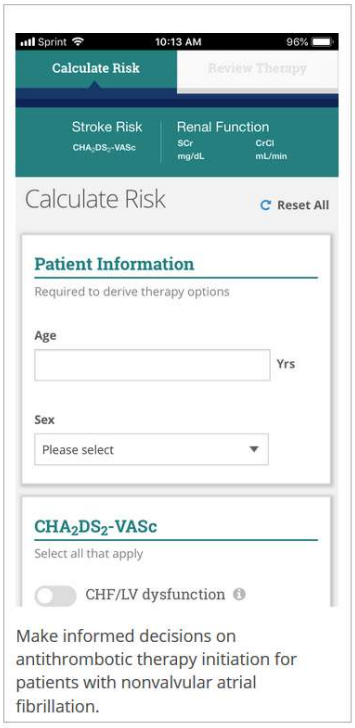
ACC – Anticoag evaluator



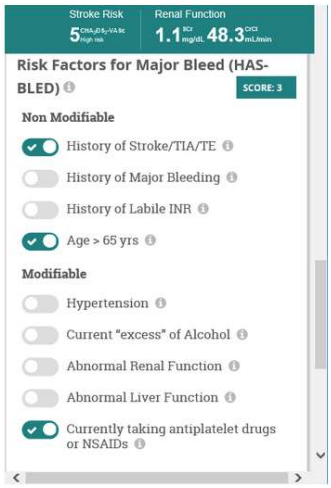
https://www.acc.org/anticoagevaluator

ACC – Anticoag App

App Screenshots



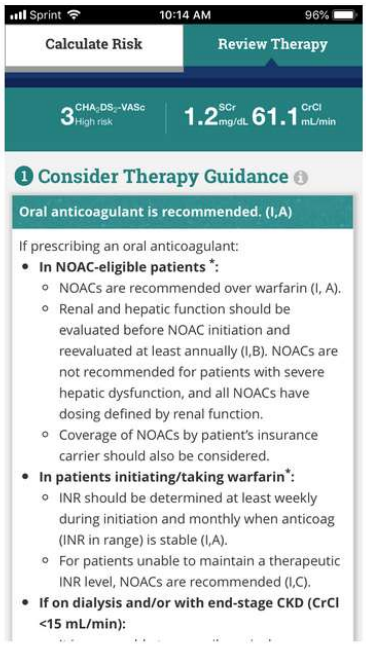
Make informed decisions on antithrombotic therapy initiation for patients with nonvalvular atrial fibrillation.



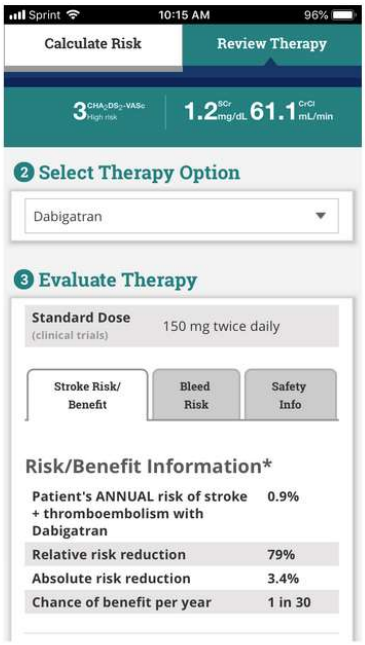
Calculate a patient's stroke risk and renal function and evaluate bleed risk factors.

110

ACC – Anticoag app



Review guidance from ACC/AHA/HRC's 2019 Focused Update of the 2014 Atrial Fibrillation Guideline and select from a full range of therapy options.



Review adjusted dosage based on prescribing information and synthesized risk for antithrombotic therapy options based on clinical trials.

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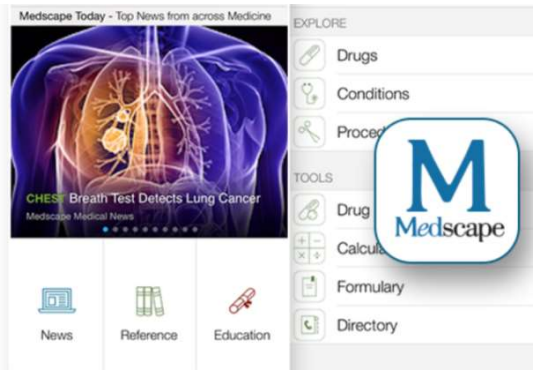
Apps

- Medscape – Free in the App store
- AFP by Topic- Free EBM review articles

American Family Physician



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Clot Prevention

- Healthy diet
- Healthy weight
- Exercise
- No Smoking
- Alcohol in moderation
- Aspirin
- Statins

The **Double Coronary Bypass**.
From Vortex's menu: Beef Topped with two fried eggs, four slices of American cheese, and 5 slices of bacon, with two grilled cheese sandwiches replacing the buns.