Clotting Disorder

Greenlane Summer GP Symposium 2020

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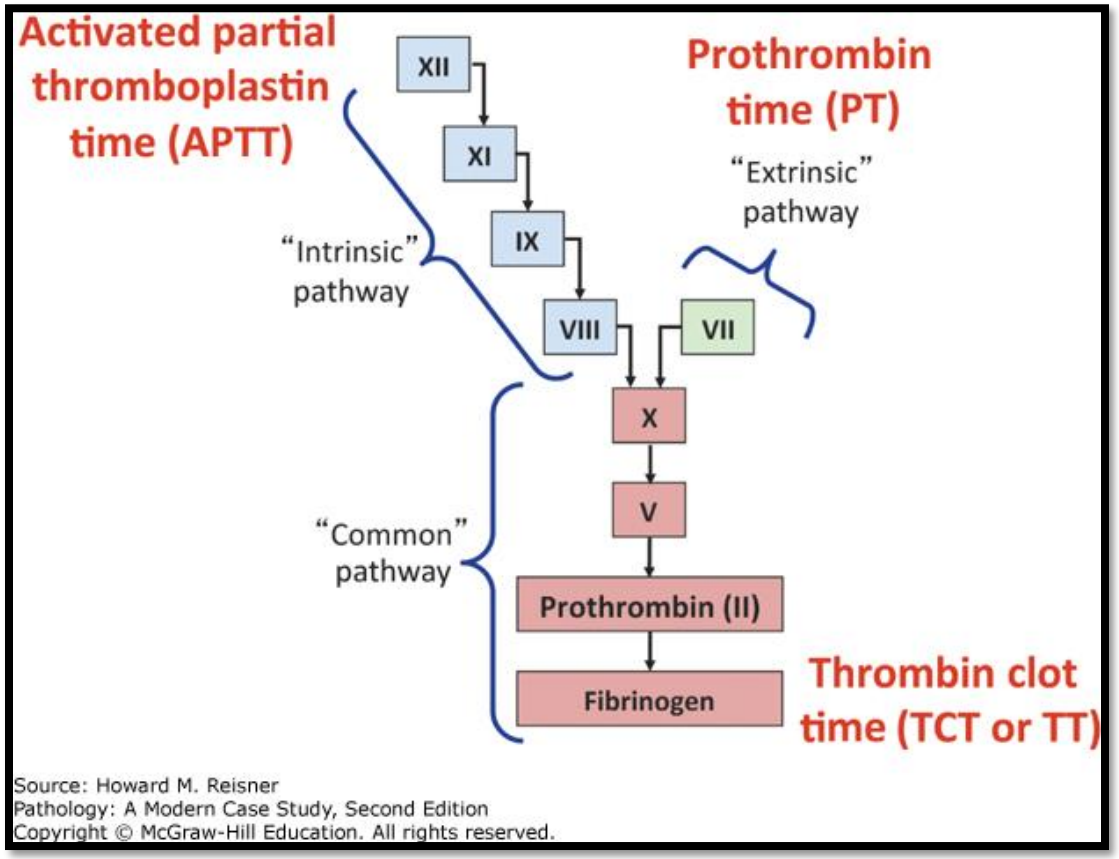
Warm Up Question



		Ref. Range
APTT	49	(25 – 40)
PR	1.5	(0.8 – 1.2)
Fibrinogen	2.5	(1.5 – 4.0)
dTCT	17	(12 – 20)
Platelet	235	(150 – 400)

1. What does the results mean?
2. What is the differential?
3. What further tests would you order?

Continue

Additional Tests

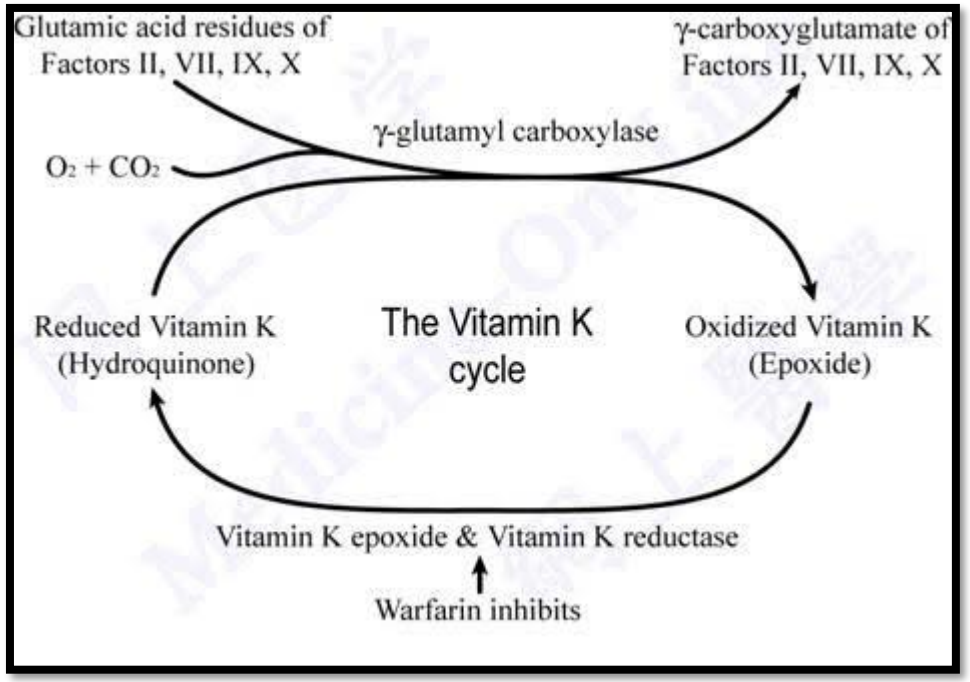
		Ref. Range
APTT	49	(25 – 40)
APTT 1+1	34	(25 – 40)
PR	1.5	(0.8 – 1.2)
PR (+ N plasma)	1.0	(0.8 – 1.2)
Fibrinogen	2.5	(1.5 – 4.0)
dTCT	17	(12 – 20)
Platelet	235	(150 – 400)
Echis Ratio	1.0	(0.8 – 1.2)

Questions

1. What is APTT 1+1 and PR (+ N plasma)?
2. What does the results mean?
3. For bonus mark what is Echis ratio?
4. What is the conclusion?

Quantitative vs Qualitative

Vitamin K



Answer

- Vitamin K deficient (warfarin) patient has reduced “active” factor 2, 7, 9 and 10.
  - However, they have normal amount of factor 2, 7, 9 and 10 (active + inactive)
- Echis (snake venom) activate clotting factor regardless if they are “activated” or not.
  - Normal in vitamin K or warfarin patient
  - Abnormal in liver patient
- Consistent with patient either on warfarin or vitamin K deficient

Question 2

Initial Tests

		Ref. Range
APTT	64	(25 – 40)
APTT 1+1	53	(25 – 40)
PR	1.1	(0.8 – 1.2)
Fibrinogen	4.5	(1.5 – 4.0)
Platelet	420	(150 – 400)

Questions

1. What does the results mean?
2. What is the differential?
3. What further tests would you order?

Continue

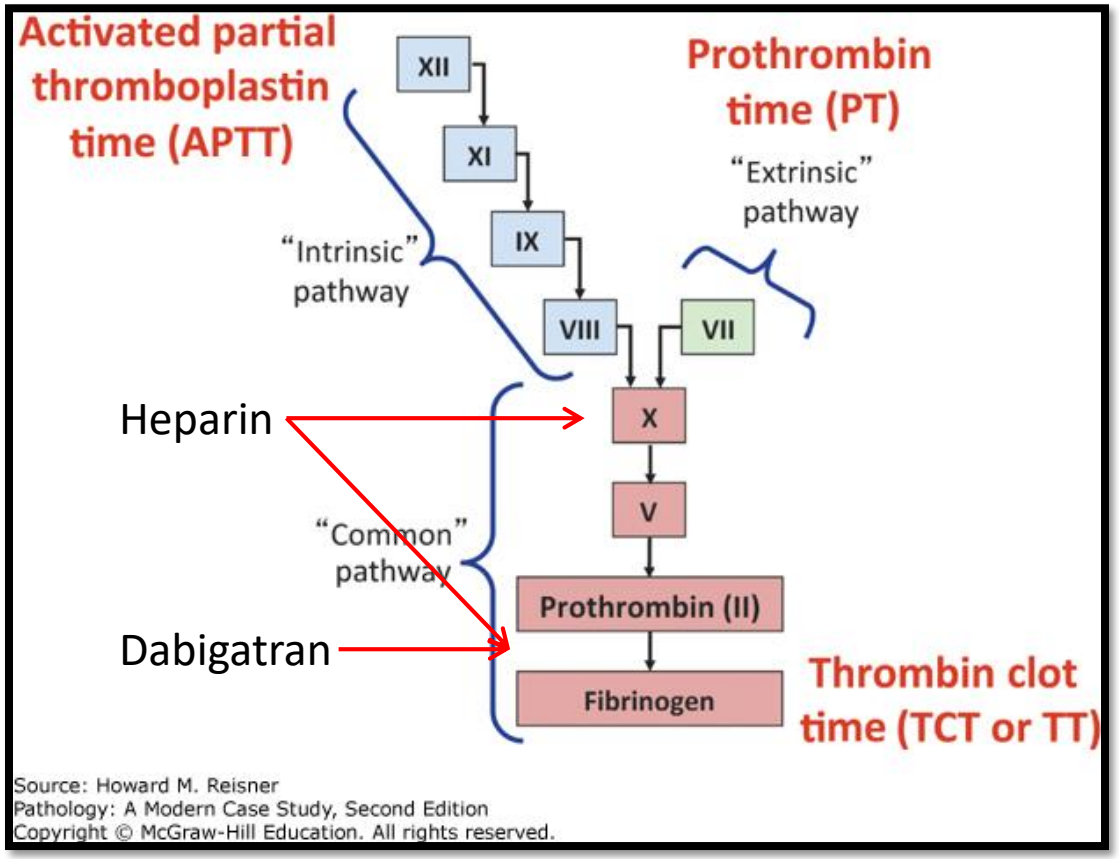
Additional Tests

		Ref. Range
APTT	64	(25 – 40)
APTT 1+1	53	(25 – 40)
PR	1.1	(0.8 – 1.2)
Fibrinogen	4.5	(1.5 – 4.0)
Platelet	420	(150 – 400)
dTCT	>80	(12 – 20)
dTCT + Protamine	>80	(12 – 20)

Questions

1. What causes prolonged dTCT?
2. What does protamine do?
3. What is the conclusion?

dTCT



- Common thrombin inhibitors
  - Dabigatran
  - Heparin
- Protamine reverse heparin but not dabigatran
- Consistent with patient treated on dabigatran
  - Prolonged APTT
    - Not reversed with normal plasma (inhibitor)
  - Prolonged dTCT
    - Not reversed with protamine

Question 3

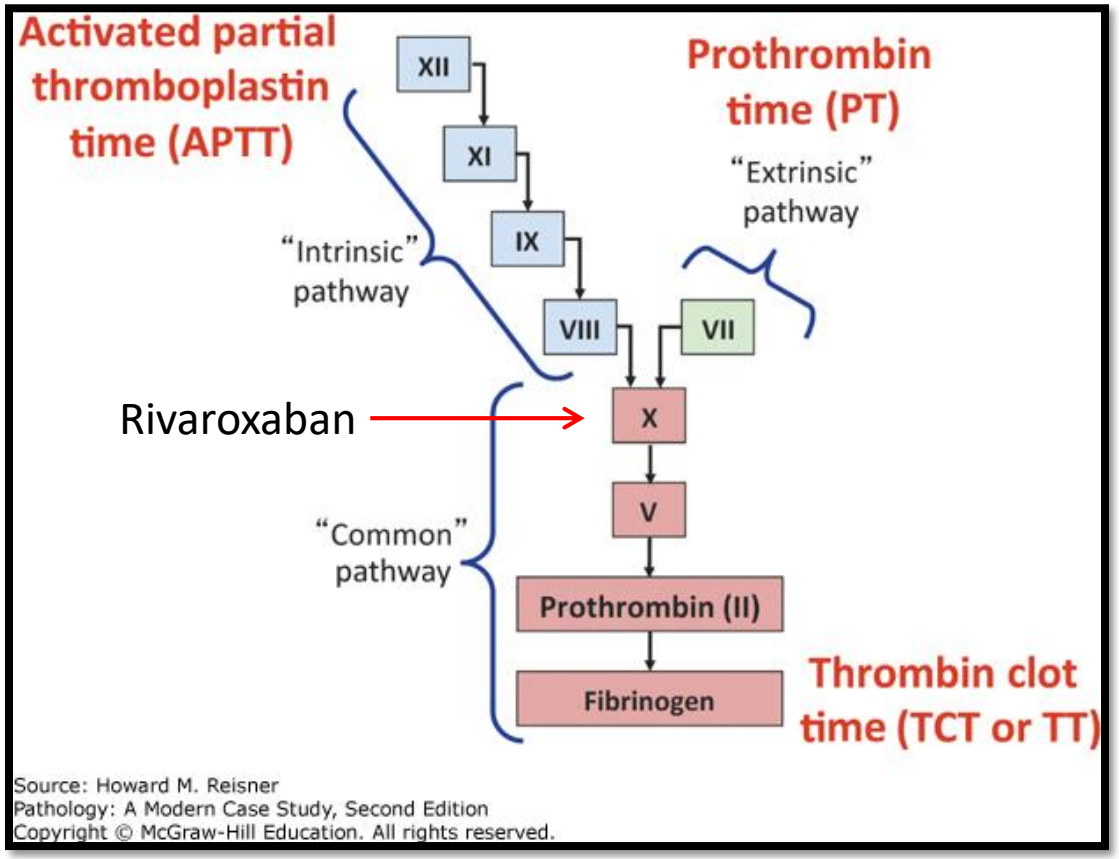
Initial Tests

		Ref. Range
APTT	36	(25 – 40)
PR	1.6	(0.8 – 1.2)
PR (+ N plasma)	1.7	(0.8 – 1.2)
Fibrinogen	3.7	(1.5 – 4.0)
Platelet	215	(150 – 400)

Questions

1. What does the results mean?
2. What is the commonest cause for this presentation?

Rivaroxaban/Apixaban



- Common Xa inhibitor
  - Rivaroxaban
  - Apixaban
- Prolongs PR interval in some laboratory.
  - Depend on the reagent used.
- Consistent with patient treated on rivaroxaban

Anticoagulant 101

Direct Oral Anticoagulants (DOAC) vs Warfarin

- Rapid onset
- Dosing is standardized
  - INR testing is not required (no monitoring)
- Fewer significant interactions with other medications and foods compared with warfarin but **if there are interactions efficacy and safety is unknown**
  - Anticoagulants and anti-platelet agents (solely due to additional blood-thinning effect)
  - P-glycoprotein inhibitors (e.g. amiodarone, verapamil, quinidine, ticagrelor and clarithromycin) and inducers (e.g. rifampicin).
  - Rivaroxaban can be affected by CYP3A4 inducer and inhibitors.
  - For a complete list of interactions or the management of interactions, please contact a clinical pharmacist.
- DOAC are associated with **less risk of intracranial haemorrhage but more gastrointestinal bleeding**
  - Overall, similar major bleeding event
- Extreme weight (<40kg and >120kg)

Dabigatran vs Rivaroxaban

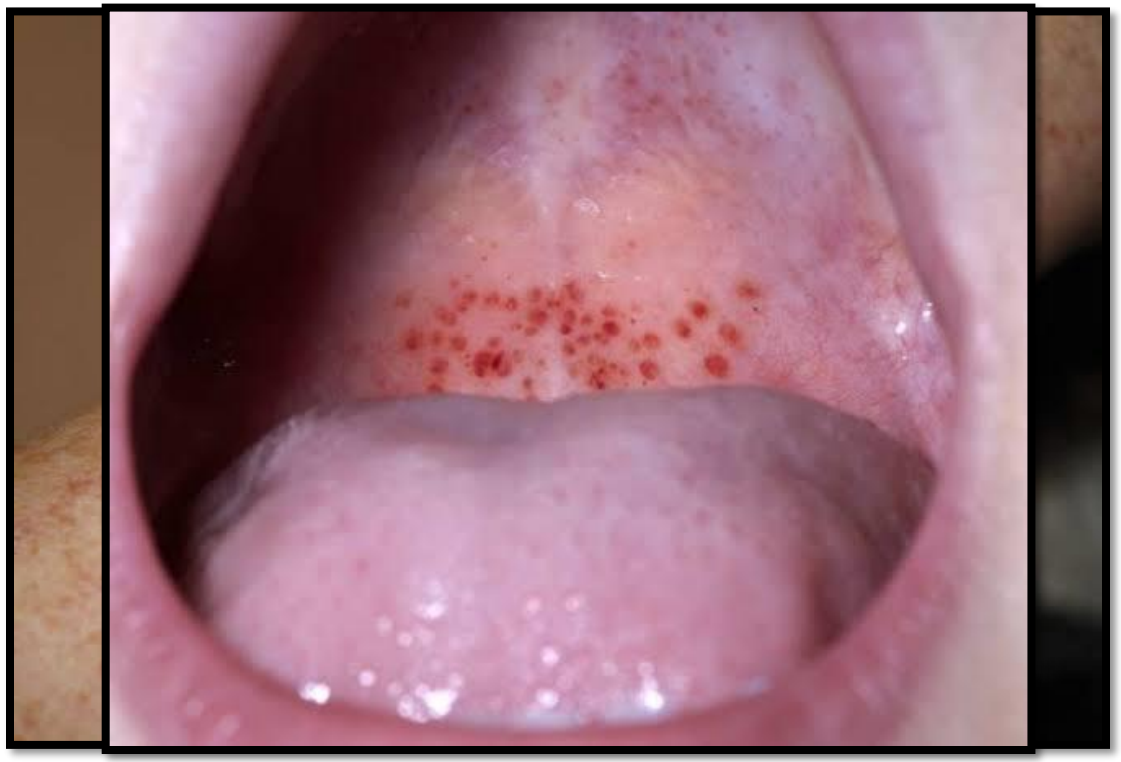
- Bleeding Profile
  - Dabigatran has been associated with a lower risk of major bleeding compared to rivaroxaban in observational study.
  - Reversal agent for dabigatran (**idarucizumab**) has been approved and used in NZ whilst reversal agent for rivaroxaban (**andexanet alfa**) currently not available in NZ.
- Rivaroxaban generally requires once daily dosing.
- Rivaroxaban may be preferred in mild to moderate renal dysfunction (CrCl 30-49mL/min) due to reduce renal clearance.
  - No age adjusted dosing is required.
- Rivaroxaban may be better tolerated by patient with a history of upper GI symptoms.
- Rivaroxaban can be delivered via NGT and blister packed.
- Rivaroxaban doesn't require low molecular weight heparin in treatment of VTE.

Questions?

Case Presentation

Master CG

- 5 year old active boy
  - Mother brought him because of rash over his body (new)
  - Gum bleeding when brushing
  - No PMHx and no FHx
    - Not on any medication
  - No recent travel history
  - Had uneventful birth
    - No problem after circumcision



Diagnosis?

Most likely ITP/Immune mediated

		Ref. Range
Haemoglobin	125	(113 – 145)
MCV	80	(74 – 87)
MCH	27	(24.0 – 29.0)
Platelets	7	(150 – 475)
WBC	10.5	(4.5 – 12.0)
Neutrophils	6.5	(1.5 – 8.0)
Lymphocytes	3.7	(1.4 – 5.7)
Monocytes	0.2	(0.3 – 1.00)
Eosinophils	0.1	(<1.0)

Infection vs Badness

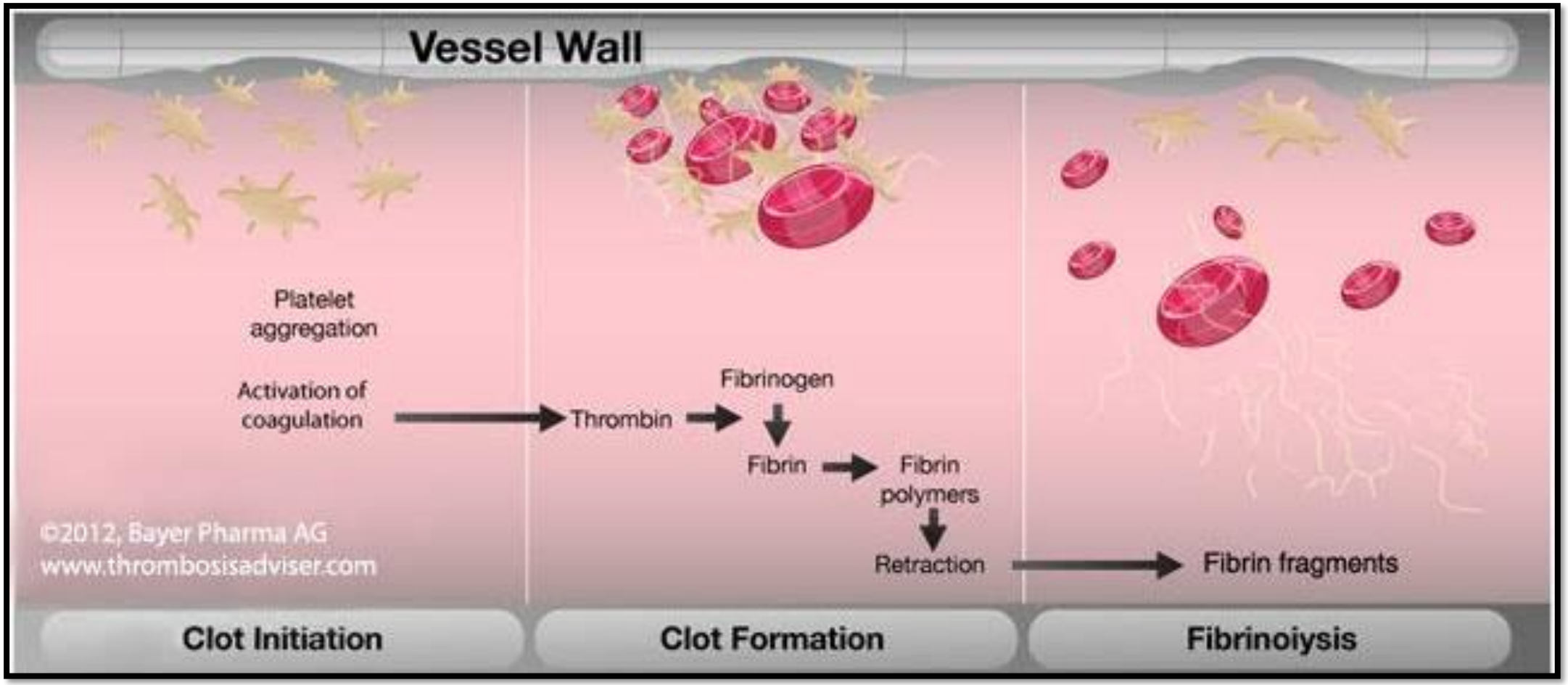
		Ref. Range
Haemoglobin	102	(113 – 145)
MCV	80	(74 – 87)
MCH	27	(24.0 – 29.0)
Platelets	25	(150 – 475)
WBC	3.5	(4.5 – 12.0)
Neutrophils	0.8	(1.5 – 8.0)
Lymphocytes	2.4	(1.4 – 5.7)
Monocytes	0.2	(0.3 – 1.00)
Eosinophils	0.1	(<1.0)

Ms RS

- 25 year old woman
  - Known recurrent iron deficiency anaemia
  - Due to increased PV blood loss
    - Not heavy but seems to go on forever (start & stop)
- Wisdom tooth extraction is complicated by bleeding 2 to 3 days afterwards
- Mother also had similar problem and treated with hysterectomy
- Nil regular medication
  - NKDA
- Social Hx:
  - Smoker 20/day
  - ETOH within guideline

		Ref. Range
Haemoglobin	102	(115 – 155)
MCV	76	(80 – 99)
MCH	23.4	(27.0 – 33.0)
Platelets	412	(150 – 400)
WBC	5.2	(4.0 – 11.0)
Neutrophils	2.7	(1.90 – 7.50)
Lymphocytes	1.7	(1.00 – 4.00)
APTT	32	(25 – 40)
PR	0.9	(0.8 – 1.2)
Fibrinogen	3.2	(1.5 – 4.0)

Haemostasis

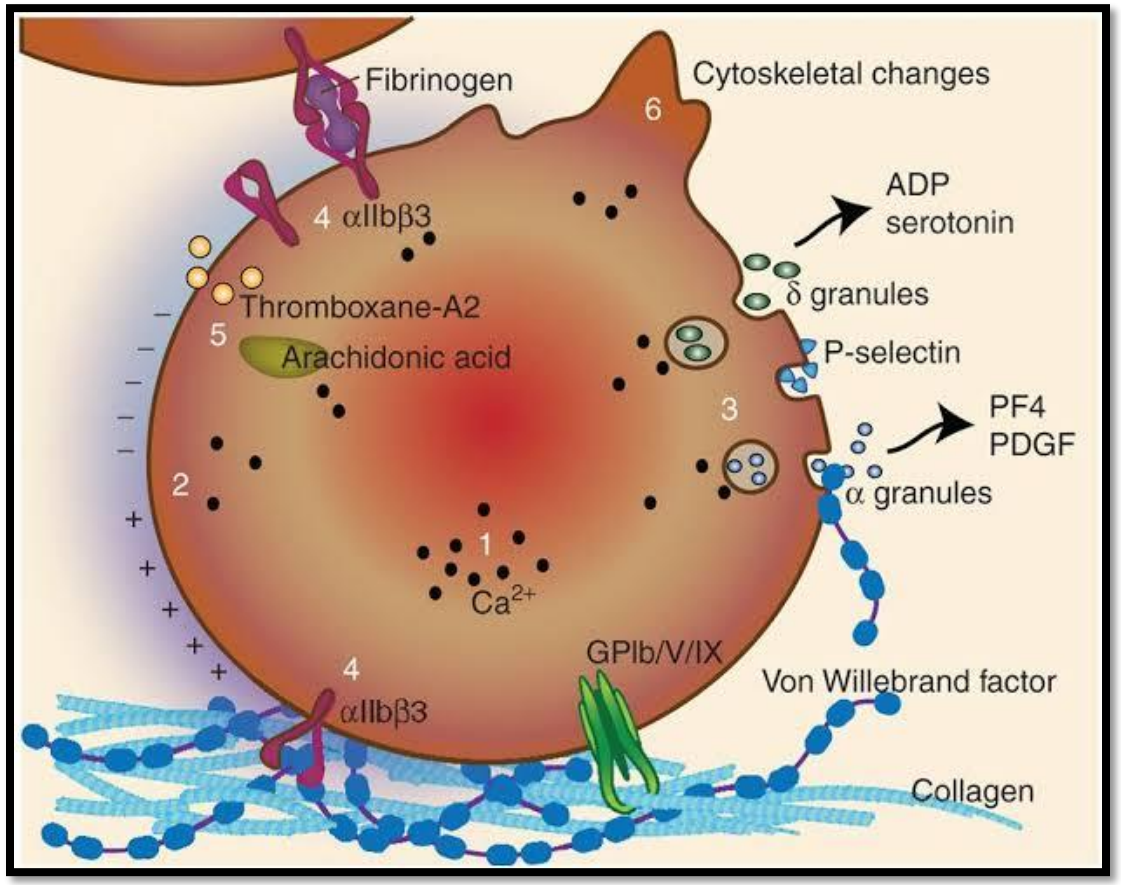


Primary Haemostasis

Secondary Haemostasis

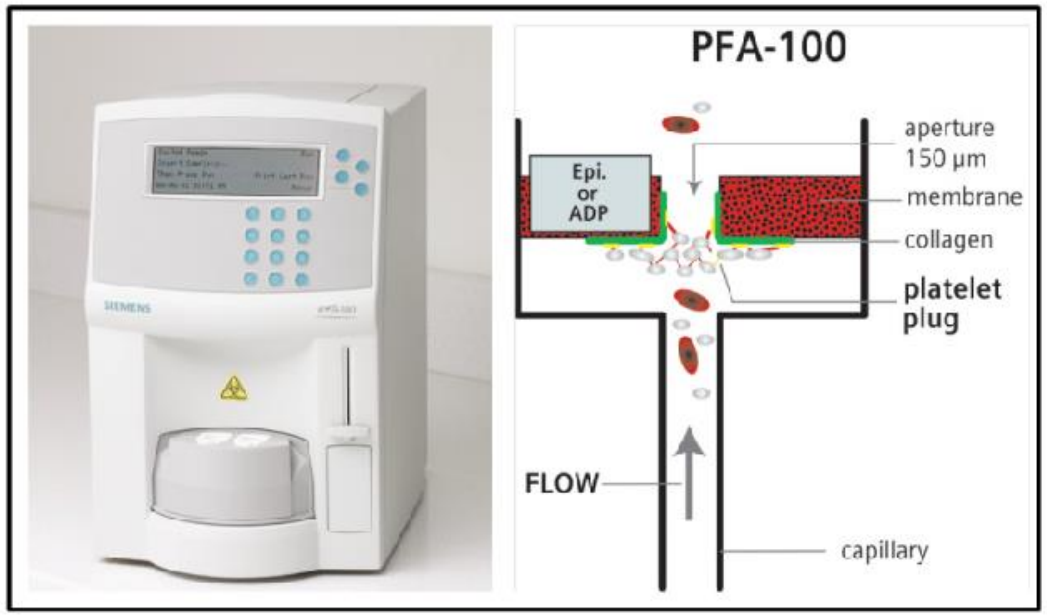
Primary Haemostasis

1. Damage to blood vessel
   - Expose collaged
2. Von Willebrand factor bind to exposed collagen and become “activated”
3. Platelet bind to activated vWF and it trigger secretion of platelet enzyme
   - Platelet aggregation
   - Activation of secondary haemostasis
4. What test do you order to check primary haemostasis?



Platelet Function Assay (PFA)

			Ref. Range
1	PFA – Epinephrine CT	100	(80 – 160)
2	PFA – Epinephrine CT	220	(80 – 160)
	PFA – ADP CT	90	(60 – 110)
3	PFA – Epinephrine CT	177	(80 – 160)
	PFA – ADP CT	276	(60 – 110)



How to interpret above results?

1. Normal

2. Aspirin/NSAIDs

3. Abnormal (either quantitative or qualitative defect in platelet or vWF)
   - Clopidogrel
   - Platelet <100
   - Other

Question 3

Additional Tests

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Questions

1. What is APTT 1+1 and PR (+ N plasma)?
2. What does the above results mean?
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Von Willebrand Screen

		Ref. Range
Factor VIII Assay	55	(55 – 150)
VWF Antigen	52	(55 – 150)
Ristocetin Cofactor	48	(55 – 150)
Collagen Binding Assay	49	(55 – 150)

		Ref. Range
Factor VIII Assay	60	(55 – 150)
VWF Antigen	72	(55 – 150)
Ristocetin Cofactor	48	(55 – 150)
Collagen Binding Assay	60	(55 – 150)

Interpret with caution (ask a haematologist)

1. Blood Group is important
   - AB should be at upper range of normal
   - O should be near the lower range of normal
2. Timing of test is important
   - 3 to 5 fold increase during inflammation or pregnancy

Types of vWD

1. Type 1 = Mild quantitative reduction
   - Everything mildly low
2. Type 2 = Qualitative defect
   - Low ristocetin or collagen binding relative to vWF antigen
3. Type 3 = Severe quantitative reduction (absent)

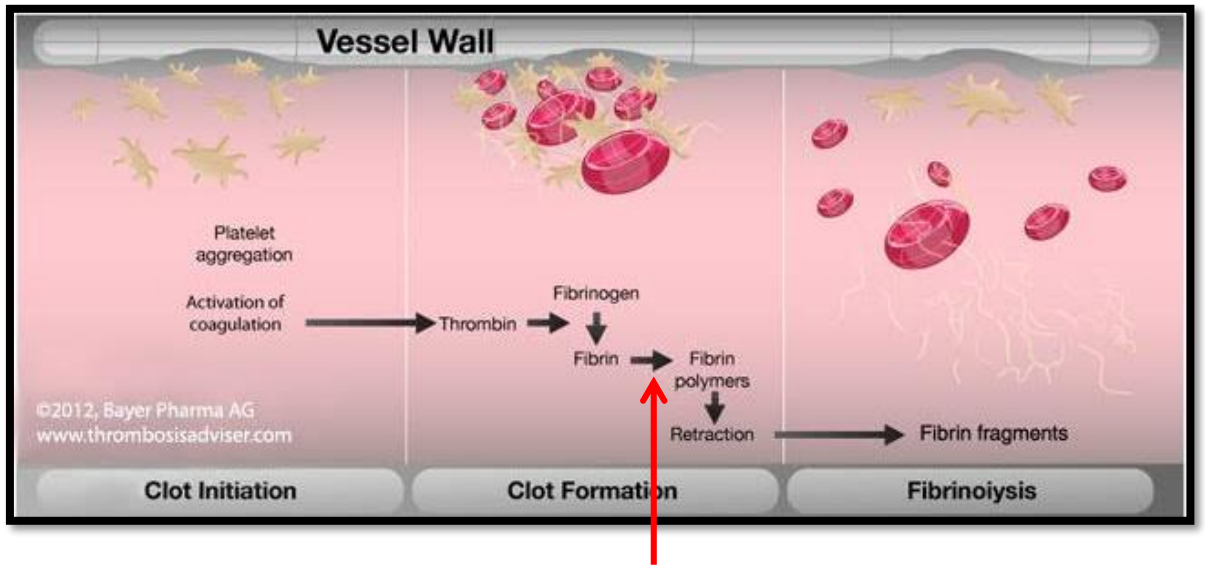
CMDHB

	23/02/17 12:32	13/04/17 10:31	22/03/18 12:14
Factor VIII Assay		**42**	71
Von Willebrand Factor Antigen	63	68	69
Ristocetin Cofactor	**35**	**48**	66
Collagen Binding Assay		60	62
Comment :			
Collagen Binding Assay	**38**		
Comment :			

Platelet Aggregation Study

Back to RS

		Ref. Range
PFA – Epinephrine CT	100	(80 – 160)



Factor 13

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