



Assessment and treatment of coagulopathy

Lecture 10: Snake Bite Management Course

Introduction

- Bleeding is the major systemic effect of bites by:
 - Malayan pit vipers (*Calloselasma rhodostoma*)
 - Indo-Chinese Russell's vipers (*Daboia siamensis*)
 - Green pit vipers (*Cryptelytrops* spp., *Viridovipera vogeli*)
- The severity of a bleeding disorder can range from mild to very severe
- In many patients bitten by green pit vipers lowered platelet counts do not result in significant bleeding
- At the opposite extreme, severe venom-induced coagulopathy after Malayan pit viper bite can cause catastrophic bleeding from multiple internal and external sites, including intracranial haemorrhage

Species that cause bleeding



Malayan pit viper (*Calloselasma rhodostoma*)



Indo-Chinese Russell's viper (*Daboia siamensis*)



Any 'green pit vipers' including *Cryptelytrops albolabris*, *C. macrops* or *Viridovipera vogeli*

Snake venom effects on blood

- Cleavage of prothrombin to produce thrombin, which activates fibrinogen, produces fibrin, FDP, XDP, and then activates plasminogen, leading to plasmin production: Net effect = incoagulable blood
- 20WBCT will be POSITIVE
- Laboratory tests:
 - Abnormal prothrombin time (PT)
 - Abnormal activated partial thromboplastin time (APTT)
 - Hypofibrinogenaemia
 - Haemoglobin may rise early and then fall due to bleeding
 - Thrombocytopenia
 - WBC: neutrophil leucocytosis

Summary of blood effects

- Factor depletion:
 - II, V, VII, VIII, IX, X, XIIIa
- Hypofibrinogenaemia
 - with increased fibrin, FDP, XDP
- Depletion of activated protein C, antithrombin III and antiplasmin
- Increased fibrinopeptide A
 - due to plasminogen activation by fibrin deposition
- Inhibition of platelet aggregation and increased platelet activation = thrombocytopenia
 - Platelet malformation on microscopy
- RBC structure alteration: spherocytosis

Thrombocytopenia

- The venoms of Cambodian pit vipers affect platelet aggregation and agglutination via direct and indirect mechanisms and also activate platelets
- Net effect = thrombocytopenia
- In combination with consumption coagulopathy and increased endothelial permeability, platelet loss contributes to persistent and potentially fatal bleeding
- It is therefore important to monitor platelet counts at least once a day
- In some cases thrombocytopenia appears before frank bleeding becomes obvious

Venom-induced coagulopathy

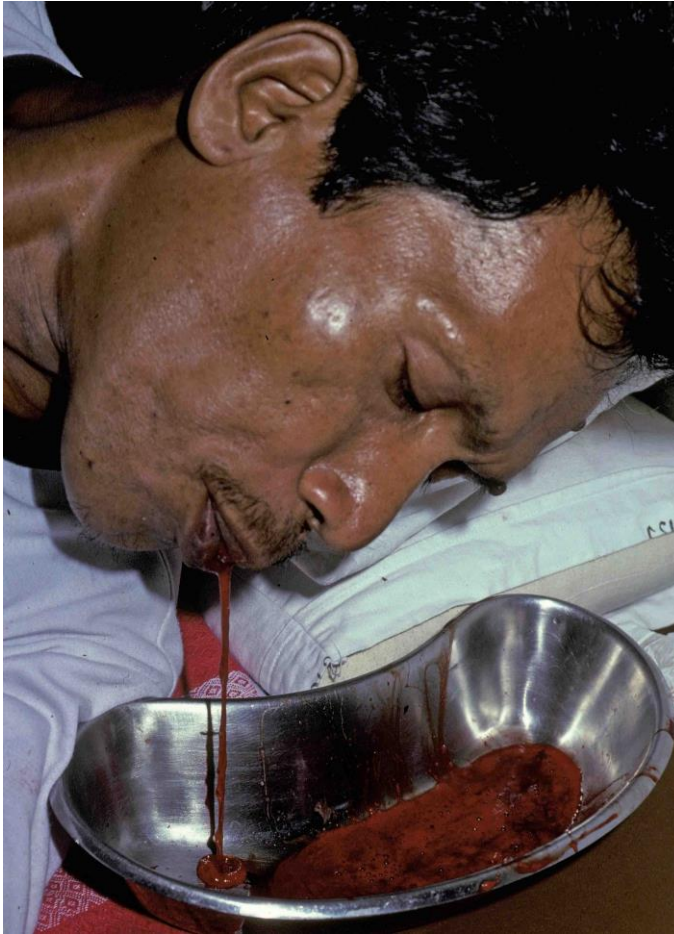


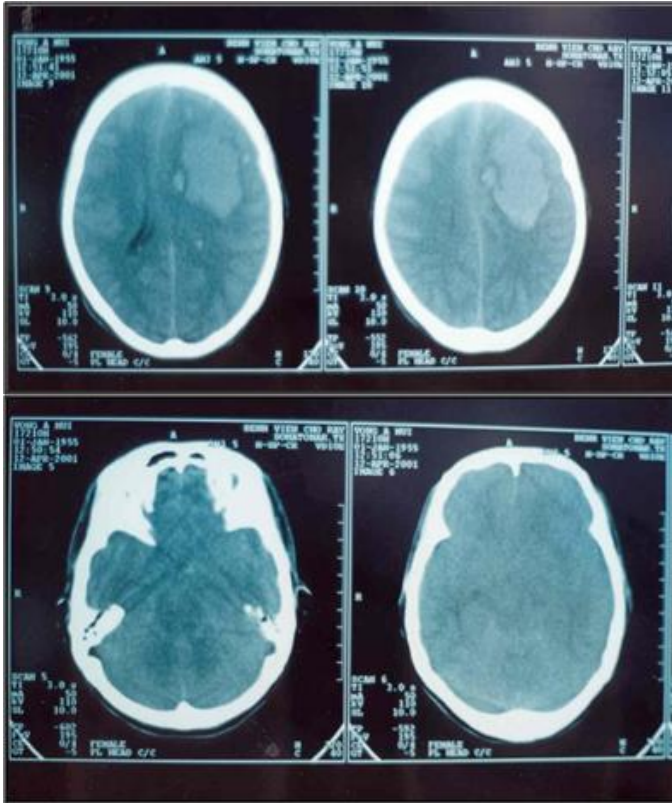
Photo: Prof. D.A. Warrell



Photos: Dr Trinh Xuan Kiem



Venom-induced coagulopathy



Photos: Dr Trinh Xuan Kiem

Intracranial haemorrhage
after Malayan pit viper bite in
South Viet Nam

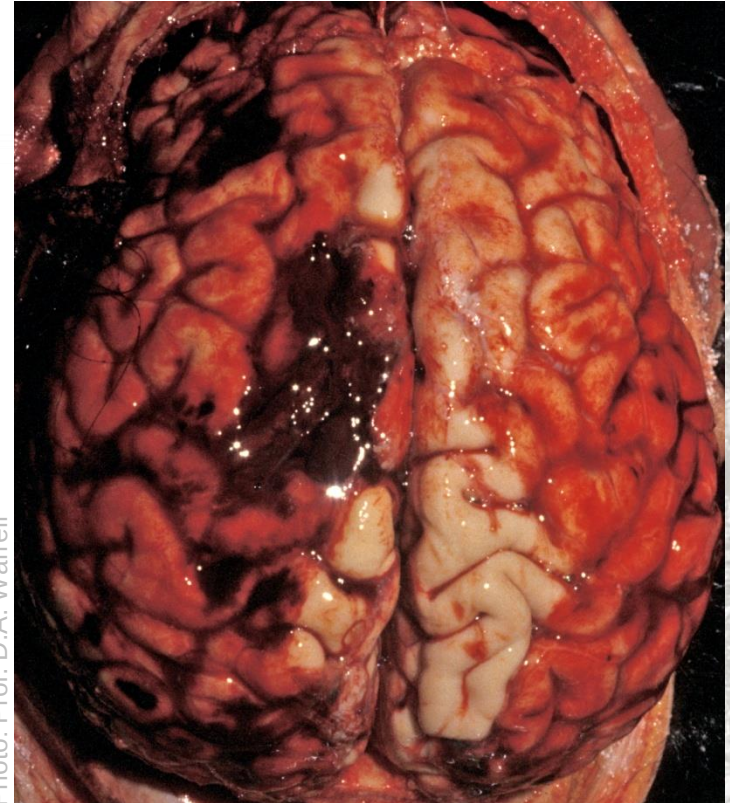


Photo: Prof. D.A. Warrell

Intracranial haemorrhage
after Indo-Chinese Russell's
viper bite in Myanmar

Venom-induced coagulopathy



Photo: Dr Lucineide Porto



Photos: Dr Trinh Xuan Kiem



Photos: Dr Trinh Xuan Kiem

Mechanisms of haemostatic disruption

- Consumptive coagulopathy
 - Often due to procoagulant cleavage of prothrombin which leads to activation of the coagulation cascade resulting in depletion (consumption) of clotting factors and collapse of normal haemostasis
- Anticoagulant coagulopathy
 - Inhibit prothrombinase complex, thrombin inhibition or protein C activation
- Endothelial activation and integrity loss
 - Act by promoting release of plasminogen activator from endothelial cells, or release of urokinase and plasminogen activation inhibitor
 - Loss of integrity causes leakage and increased blood losses

Mechanisms of haemostatic disruption

- Platelet aggregation inhibition
 - Several mechanisms involved
 - Toxins prevent platelet aggregation resulting in reduction in fibrin clot integrity and quality and this contributes to bleeding
- Platelet activation
 - Multiple mechanisms and sites of action
 - Platelet clumping can contribute to thrombosis, and to obstruction of kidney nephrules which leads to renal necrosis and acute renal failure
- Thrombocytopenia
 - Platelet depletion contributes to bleeding disorder and to spontaneous haemorrhage

Assessment of haemostasis

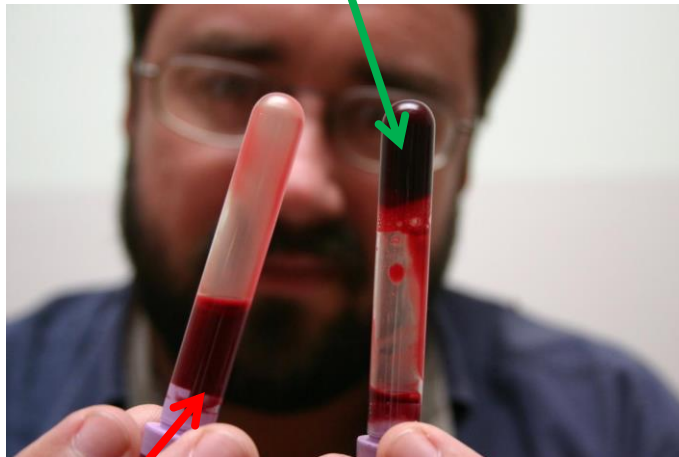
- Visual examination - is the patient bleeding abnormally?
 - From bite site/fang marks/recent wounds, cuts or abrasions
 - Into subcutaneous tissues, blisters/bullae, deeper tissues & muscle
 - From venepuncture sites
 - From gums, nose, subconjunctival, or tear ducts
 - Vomiting blood or blood in stool (malaena)
 - Are they coughing blood (haemoptysis)
 - From renal tract (especially after IDC insertion)
 - Vaginal in both menstruating or non-menstruating women

Assessment of haemostasis

- Non-visual indications from history or examination:
 - Intracranial haemorrhage may be indicated by history of headache, sudden collapse, confusion, impaired conscious state or lateralising neurological signs
 - Abnormal abdominal tension or tenderness
 - Auscultation of chest sounds
- Bedside investigations
 - 20 Minute Whole Blood Clotting Test (20WBCT) is the most important test in snake bite as it directly tests haemostasis and is a sensitive indicator of blood factor consumption
- Laboratory investigations
 - Prothrombin time (PT), activated partial thromboplastin time (APTT) fibrinogen, platelets, FBC, factor assays

20 Minute Whole Blood Clotting Test

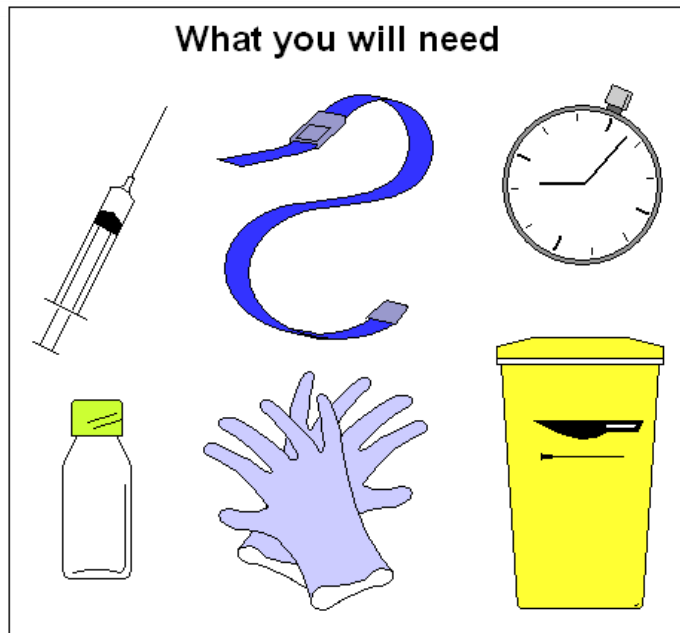
Negative test: clotting blood



Positive test: non-clotting blood

- Known as 20WBCT
- Result recorded as either a positive or negative test finding
- ‘positive test’: non-clotting (incoagulable) blood
- ‘negative test’: normally clotting (coagulable) blood
- A positive test diagnoses pit viper envenoming
- A positive test is an absolute indication for antivenom

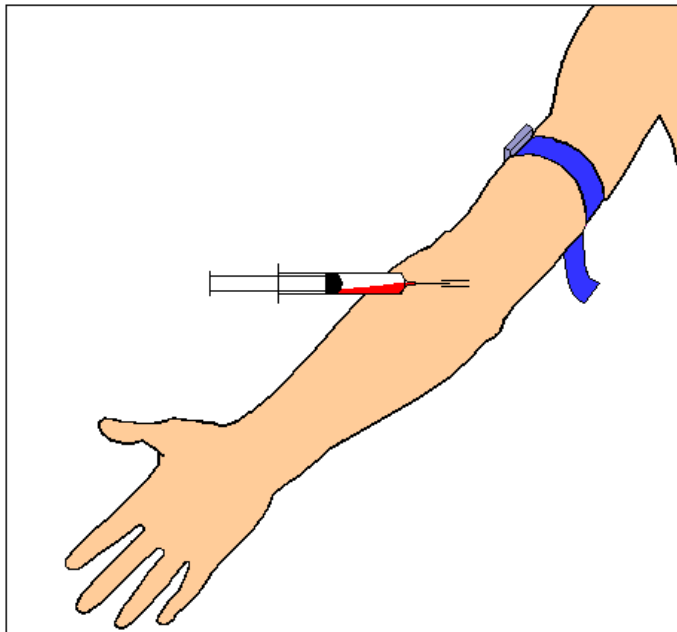
20 Minute Whole Blood Clotting Test



- Equipment needed:
 - Needle and syringe
 - Alcohol swabs
 - Tourniquet
 - Clean, dry **GLASS** bottle or test tube
 - Gloves
 - Sharps disposal container
 - Watch or clock
- It is absolutely essential that **GLASS** be used, plastic tubes or bottles will give the wrong result

20 Minute Whole Blood Clotting Test

Draw 2 millilitres of venous blood after cleaning the venepuncture site with a sterile, alcohol swab. Follow appropriate sharps protocols

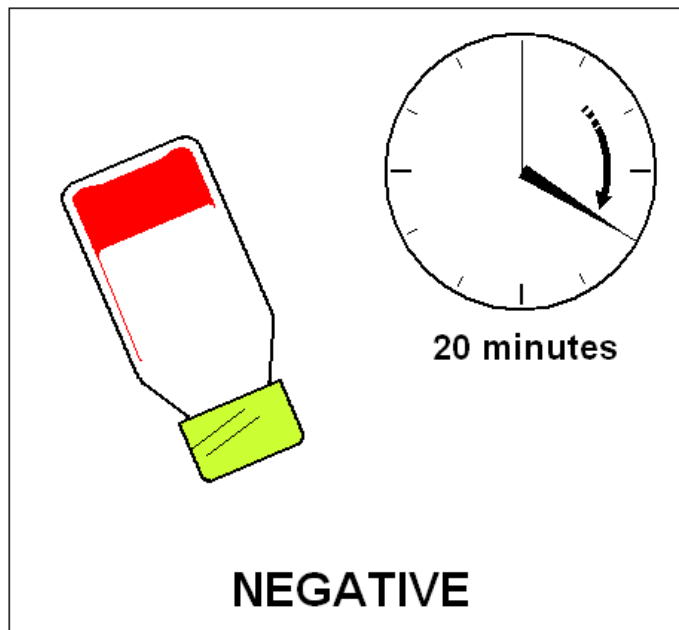


Place the blood in a clean, dry **GLASS** tube or bottle, and let stand undisturbed for 20 minutes at room temperature, away from sunlight

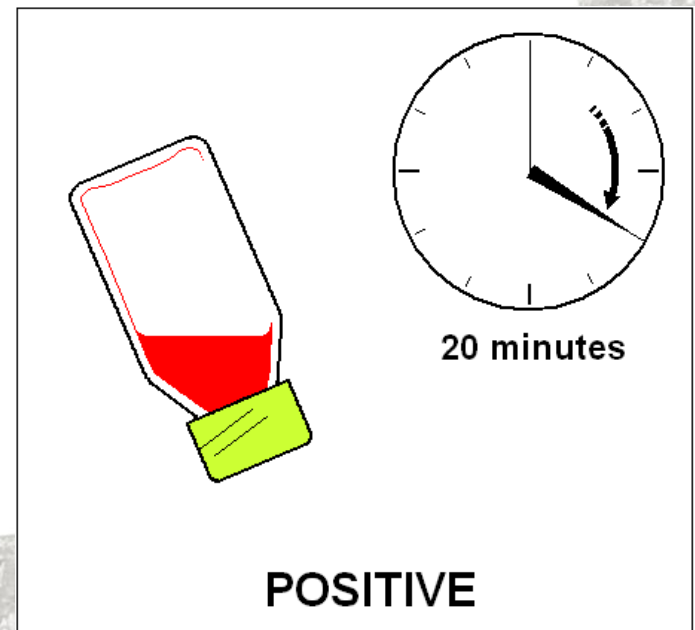


20 Minute Whole Blood Clotting Test

After 20 minutes has passed tilt the bottle/tube over ONCE. If the blood has clotted it will appear as a solid clot in the bottom of the container, indicating a NEGATIVE result



If the blood is liquid and runs down to the inverted cap of the container, the blood is non-clotting indicating a POSITIVE result. A partially clotted sample is also a POSITIVE result



20 Minute Whole Blood Clotting Test

- The 20WBCT should be performed on all snake bite patients when they first arrive at hospital
- If the initial result is negative, and the bite occurred less than 2 hours previously, repeat after 1 hour
- A test is considered positive, even if a partial clot is present in the sample: indicates reduced factor level
- A positive 20WBCT is an absolute indication for administration of appropriate antivenom, such as **TRC Hemato Polyvalent Snake Antivenin**
- The test should be repeated every 6 hours after the administration of antivenom, and can be used as a guide to the need for further antivenom treatment

Basic supportive treatment

- Strict bed rest with conservative elevation of the bitten limb to assist drainage of fluid from tissue
- Minimise trauma, avoid unnecessary venepuncture
- Maintain BP of at least 90/60 by providing adequate replacement of bleeding losses:
 - Crystalloid or colloid
 - Haemaccel
- Avoid intramuscular injections due to increased risk of bruising
- Give a therapeutic dose of correct antivenom as soon as possible to neutralise toxins
- May need to consider blood products/whole blood

Antivenom for bleeding patients



- TRC Haemato Polyvalent Antivenin is recommended as primary treatment
- Starting dose:
 - 2-5 vials for severe green pit viper bites
 - 10 vials for Malayan pit viper or Indo-Chinese Russell's viper bites
- Review after 6 hours:
 - If **20WBCT positive** AND **active bleeding** = **repeat antivenom**
 - **20WBCT positive** AND there is **NO bleeding** = hold antivenom
 - **20WBCT negative** AND there is **NO bleeding** = hold antivenom

Use of blood products and whole blood

- There are risks associated with the transfusion of blood products and whole blood
- In some cases this may increase the severity of the coagulopathy, and could potentially result in an increased risk of haemorrhage
- Blood products such as fresh frozen plasma and cryoprecipitate are expensive
- Haemaccel for volume expansion in hypovolaemic shock is also expensive
- Transfusion of whole fresh blood may be necessary, especially in the absence of effective neutralisation of circulating venom by an appropriate antivenom

Deciding to give fresh whole blood

- In the absence of effective antivenom, the decision to transfuse should be based on results of regular review of haemostasis (at least 6 hourly)
- If 20WBCT positive AND significant active bleeding:
 - fresh whole blood transfusion and administration of vitamin K (10 mg i.v.i.) with review every 6 hours
- If 20WBCT positive AND there is NO bleeding:
 - consider giving vitamin K (10 mg i.v.i.) with review every 6 hours
- If 20WBCT negative AND there is NO bleeding:
 - haemostasis normal and transfusion may not be required, but continue 6 hourly reassessment

Transfusion of fresh whole blood

- Only consider if 20WBCT is positive **AND** there is evidence of **SIGNIFICANT** active bleeding
- Patients who do not have significant blood losses probably do not need transfusion
 - Assess bleeding you can see and potential bleeding that you cannot see
 - Thrombocytopenia in absence of active bleeding may not require platelet replacement
 - Positive 20WBCT indicates factor depletion, but in the absence of active bleeding, may not require transfusion of blood factors, use of vitamin K may be enough to correct
- Cross-matching absolutely vital
- Think rationally and act on the evidence!

Summary

- Bleeding is caused by pit vipers, not cobras or kraits!
- Results in factor depletion, thrombocytopenia and failure of haemostasis
- Compounded by loss of blood vessel integrity due to increase endothelial permeability and leakage
- 20WBCT is most important test in snake bite
- Platelet counts should be done daily
- Antivenom is the most important drug for treating coagulopathy and loss of endothelial integrity
- Fresh whole blood may be needed if antivenom is not available and 20WBCT ++ with active bleeding
- Vitamin K can help to accelerate factor biosynthesis