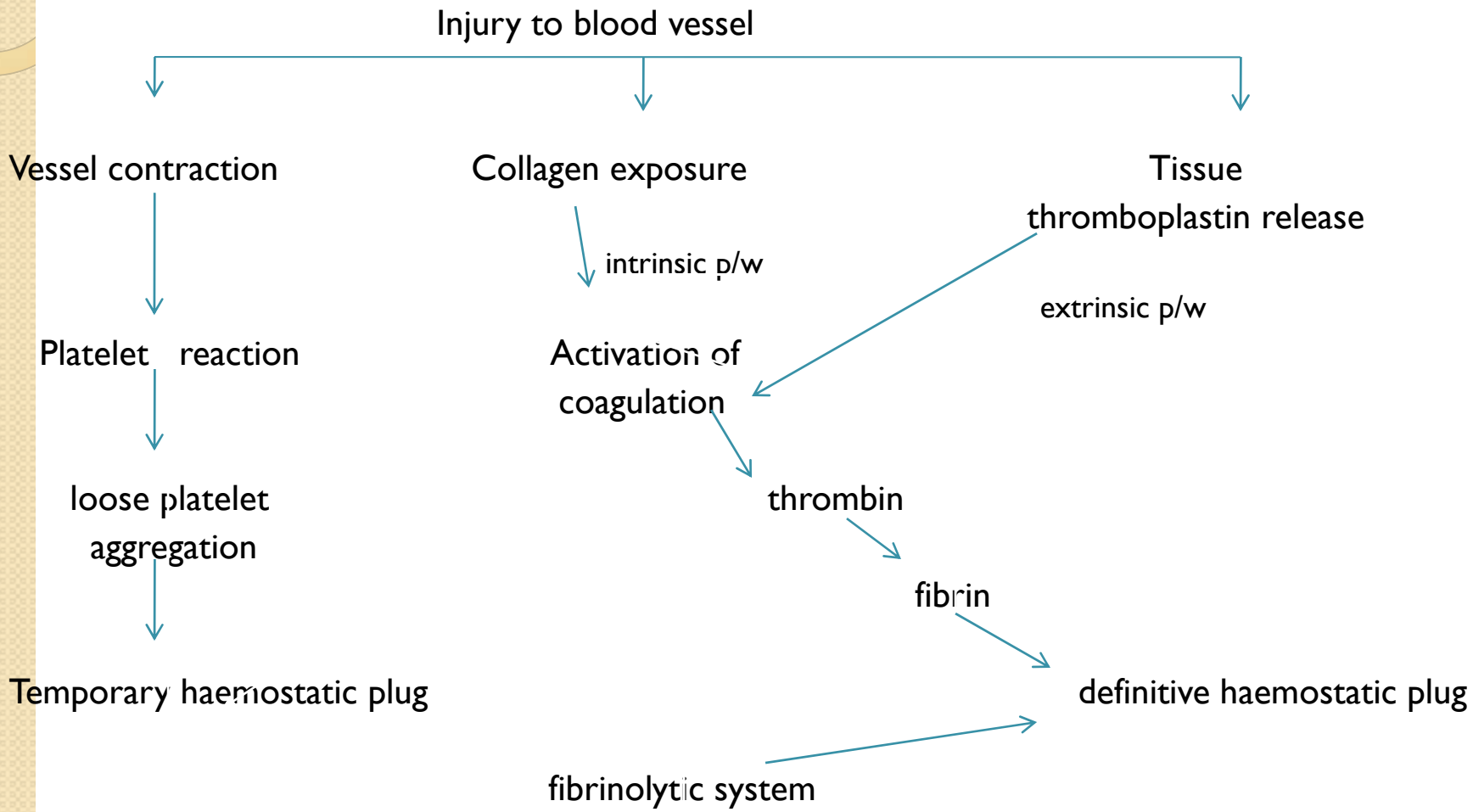
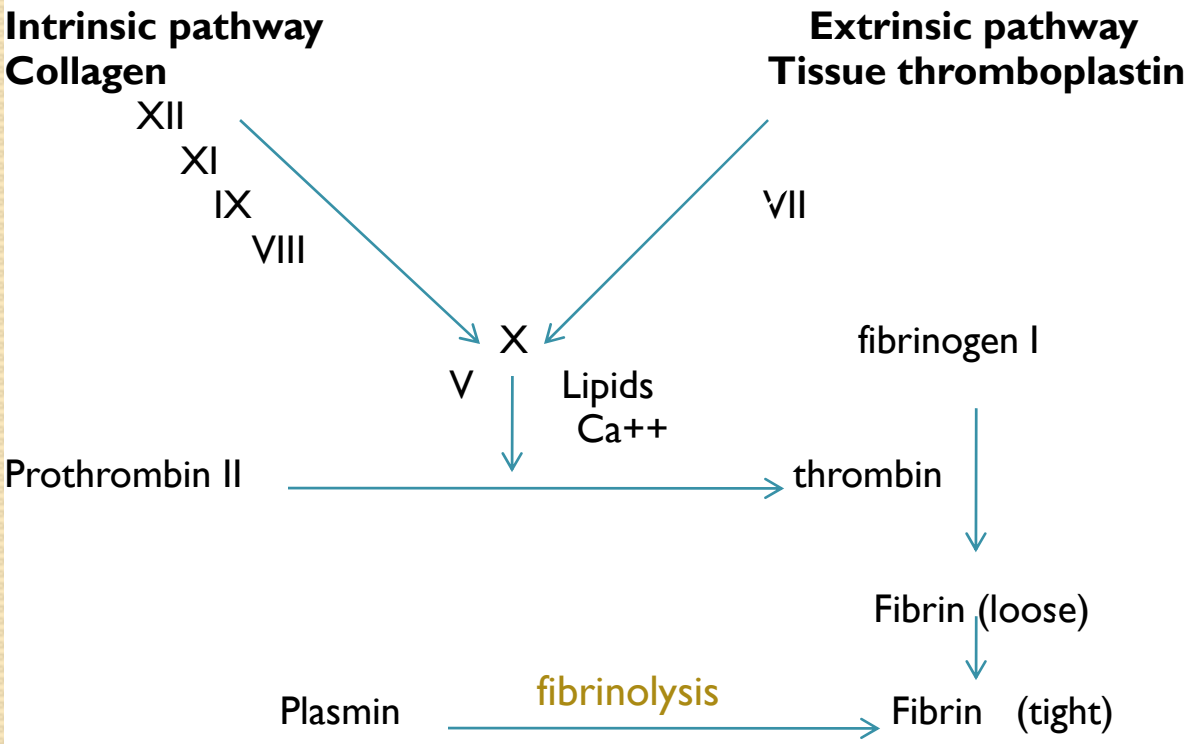
Dental Management of Bleeding Disorder Patients

Bleeding disorders

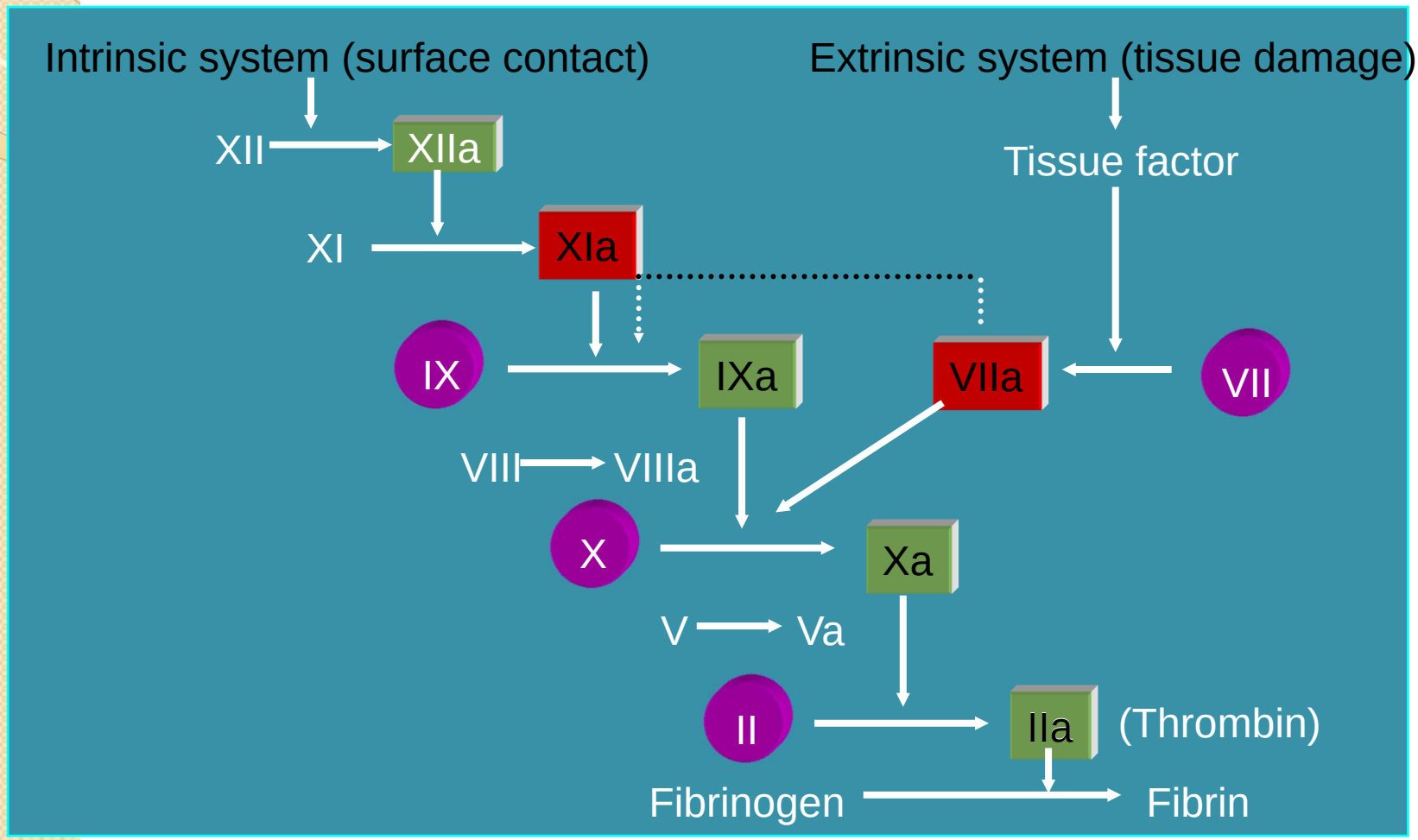
Summary of mechanisms of coagulation following tissue injury



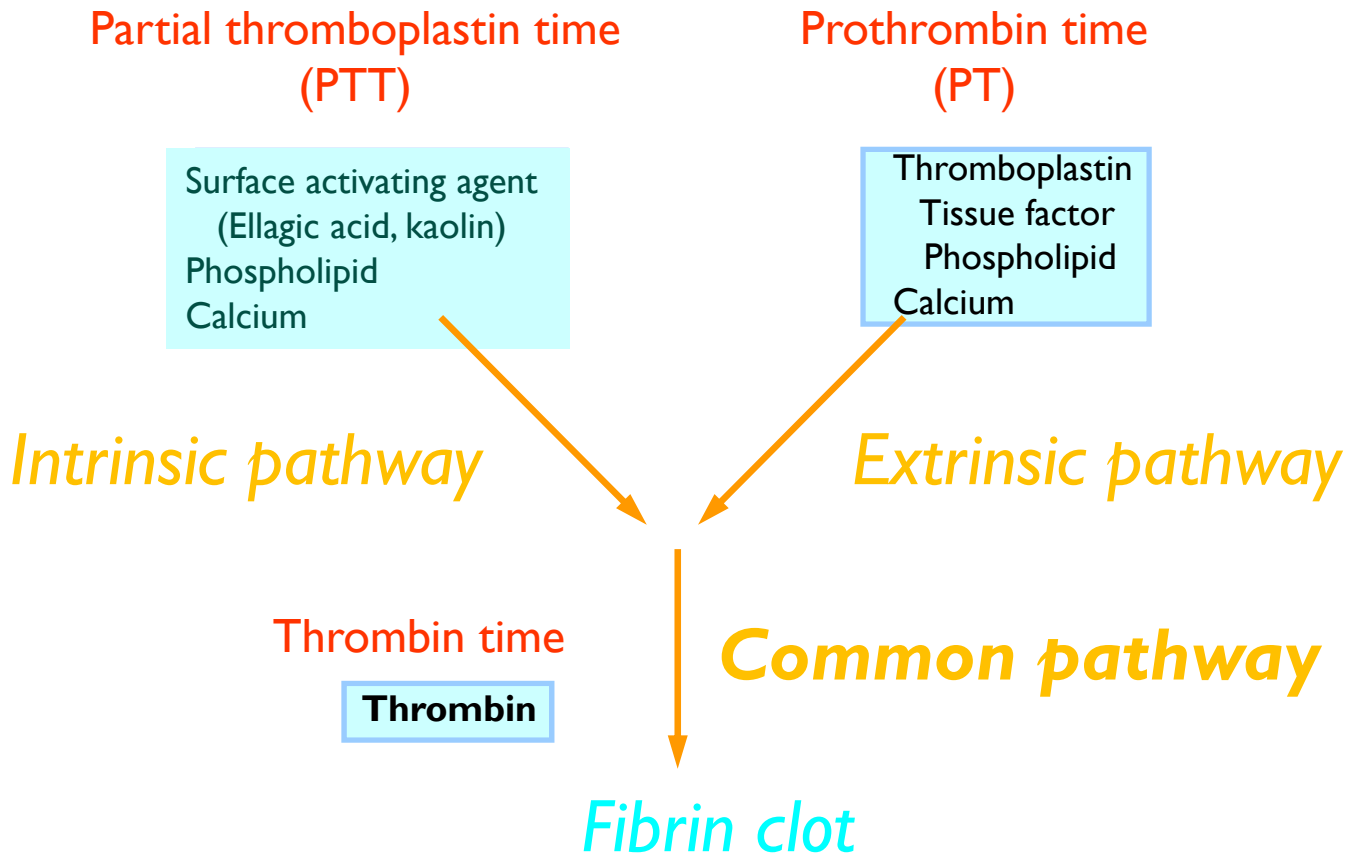
Clotting mechanism



Coagulation cascade



Laboratory Evaluation of the Coagulation Pathways



Protocol for investigation of a clotting disorders

- History
- Take blood
- Laboratory investigation

APTT	Normal APTT
Prolong APTT	Assay factors VIII, IX
PT	
Prolong PT	Assay factor II, V, VII, X and fibrinogen

Contd.

Laboratory tests

Essential tests included:

- Bleeding time (5-10 min.)
- Platelet count (100,000-400,000/mm^3
- APTT (25-40 sec.)
- Prothrombin time (10-15 sec.)
- Serum for blood grouping and cross matching

Laboratory findings in clotting disorders

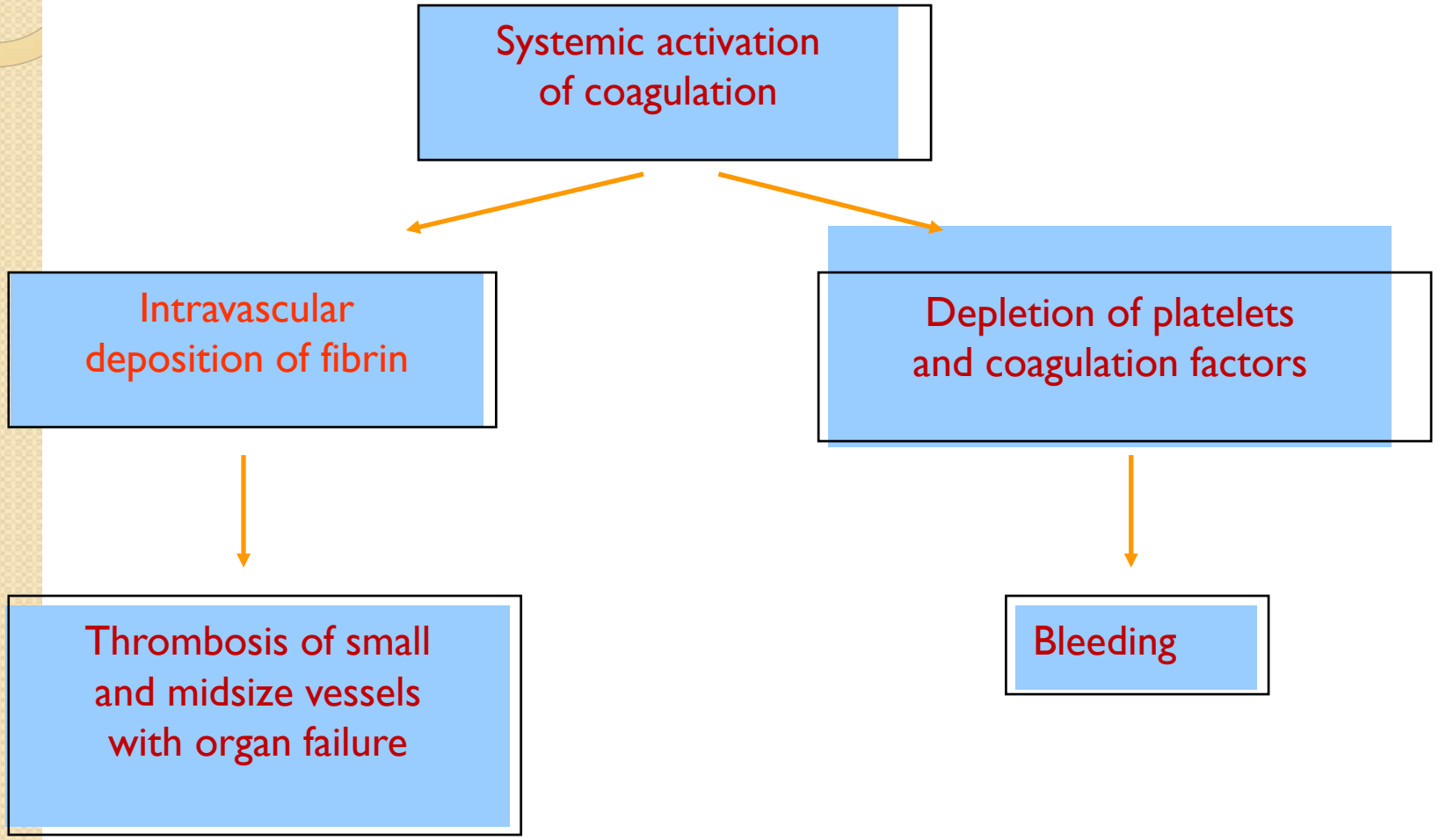
- Haemiphilia A,B, factor XI, XII deficiency APTT
- Anticoagulant therapy, obstructive jaundice, vit.K deficiency, PT,APTT Factor V, X deficiency
- Heparin therapy PT, APTT
- DIC, liver disease PT, APTT
- Factor VII deficiency PT

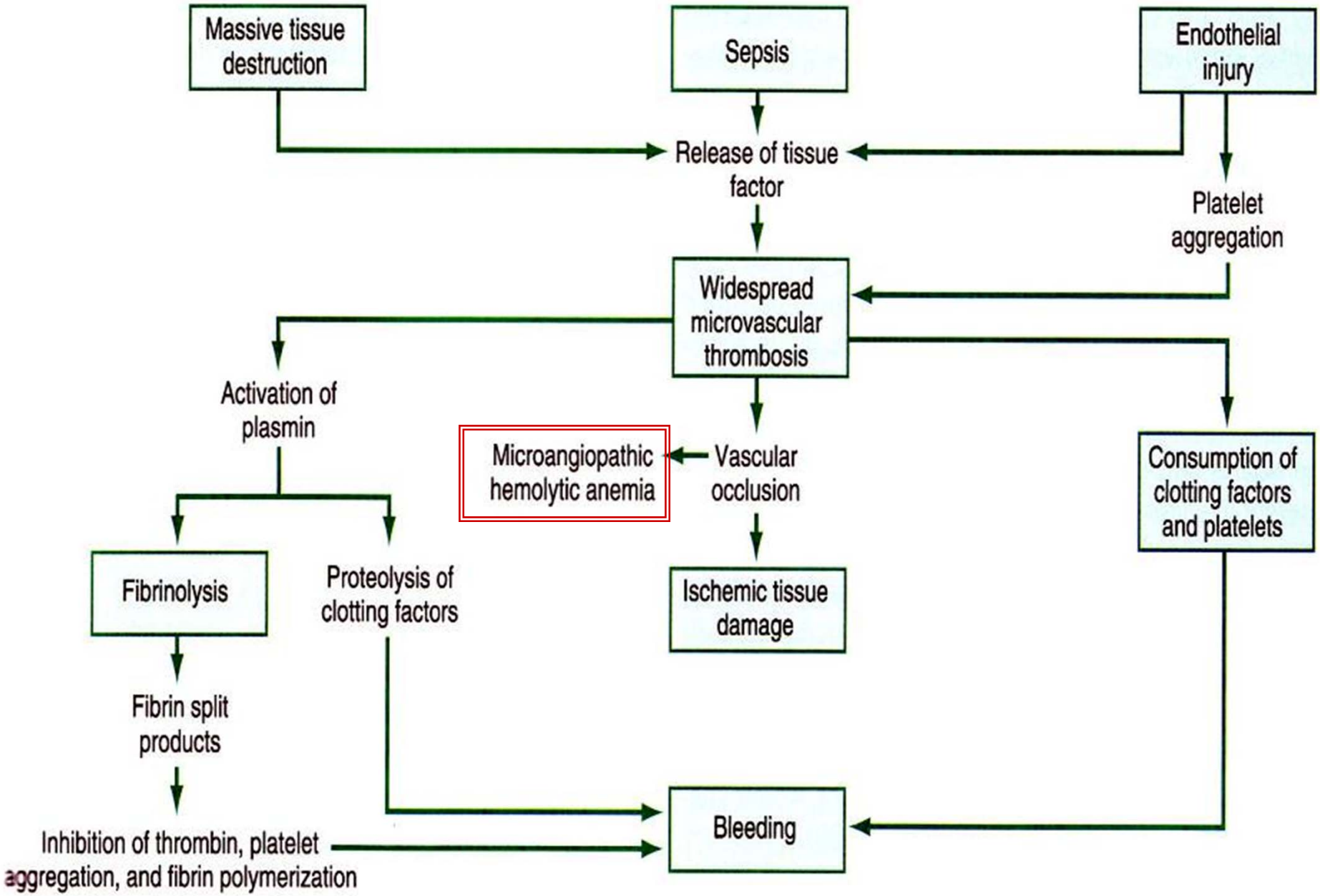
*INR = International Normalized Ratio

INR = $(PTR)^{ISI}$, ISI= International Sensitivity Index

PTR= patient prothrombin time/reference control plasma

Disseminated Intravascular Coagulation (DIC) Mechanism





Robbins

Pathophysiology of disseminated intravascular coagulation - (DIC)

Common clinical conditions associated with DIC

- Sepsis
- Trauma
  - Head injury
  - Fat embolism
- Malignancy
- Obstetrical complications
  - Amniotic fluid embolism
  - Abruptio placentae
- Vascular disorders
- Reaction to toxin (e.g. snake venom, drugs)
- Immunologic disorders
  - Severe allergic reaction
  - Transplant rejection

DIC
Treatment approaches

- Treatment of underlying disorder
- Anticoagulation with heparin
- Platelet transfusion
- Fresh frozen plasma

Hematological problems

Management of patient with a coagulopathy

- Defer surgery until a hematologist is consulted about the patient's management
- Obtain baseline coagulation tests as indicated (prothrombin time, partial thromboplastin time, bleeding time, platelet count and a hepatitis screen
- Schedule the patients in a manner that allows surgery soon after any coagulation correcting measures have been taken (after platelet transfusion, factor replacement, or aminocaproic acid administration)

Contd.

- Augment clotting during surgery with the use of topical coagulation promoting substance, sutures, and well place pressure packs
- Monitor the wound for 2 hours to ensure that good initial clot forms
- Instruct patient in ways to prevent dislodgement of the clot and in what to do should bleeding restarts
- Avoid prescribing NSAIDs
- Take hepatitis precautions during surgery

Management of patient who is therapeutically anticoagulated

Patients receiving aspirin or other platelet inhibiting drugs

- Consult the patient's physician to determine the safety of stopping the anticoagulant drug for several days
- Defer surgery until the platelet inhibiting drugs have been stopped for 5 days
- Take extra measures during and after surgery to help promote clot formation and retention
- Restart drug therapy on the day after surgery if no bleeding is present

Contd.

Patients receiving warfarin (coumadin)

- Consult the patient physician to determine the safety of allowing the PT to fall to 1.5 INR for few days
- Obtain baseline PT
- If PT is 1 to 1.5 INR , proceed with surgery

Contd.

- If the PT is more than 1.5 INR, stop warfarin approximately 2 days before surgery
- Check the PT daily and proceed with the surgery on the day when the PT falls to 1.5 INR
- Take extra measures during and after surgery, to help promote clot formation and retention
- Restart warfarin on the day of surgery

Contd.

Antibiotics which are safe with Coumadin

- Prolong courses of any antibiotic can effect the intestinal flora, alter vitamin K synthesis and prolong INR.
- Make a course of antibiotic administration as short as possible.

Contd.

Among the antibiotics commonly prescribed for treatment of dental infection:

- **Tetracycline is contraindicated.**
- **Erythromycin, clarithromycin, metronidazole, ciprofloxacin, ofloxacin and levofloxacin interact with coumadin and should be avoided.**
- **Safer antibiotics include penicillins, cephalosporins, clindamycin and azithromycin.**

Contd.

- **Azithromycin** is an interesting macrolide that does not interfere with cytochrome p450 and less effect on anticoagulation therapy.

Contd.

Safer analgesics:

- Aspirin and NSAIDs should be avoided.
- Acetaminophen can interact with Coumadin to a finite extent. Several doses of acetaminophen can increase the INR of patients on stable doses of Coumadin.
- Safer analgesics include codeine(methylmorphine) and codeine derivatives, lower doses of acetaminophen component, meperidine (pethidine) or meperidine plus promethazine (phenergan, long lasting hyponotic).

Contd.

Patients receiving heparin

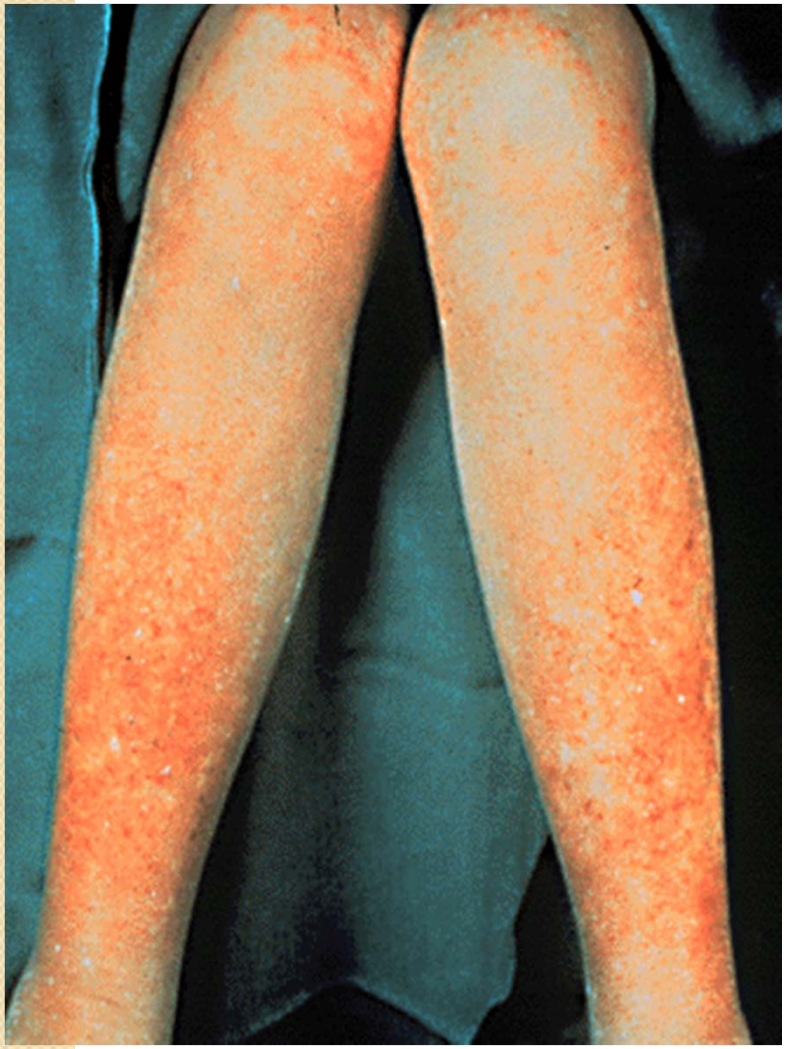
- Consult patient's physician to determine the safety of stopping heparin for the perioperative period
- Defer surgery until at least 6 hours after the heparin is stopped
- Restart heparin once a good clot has formed

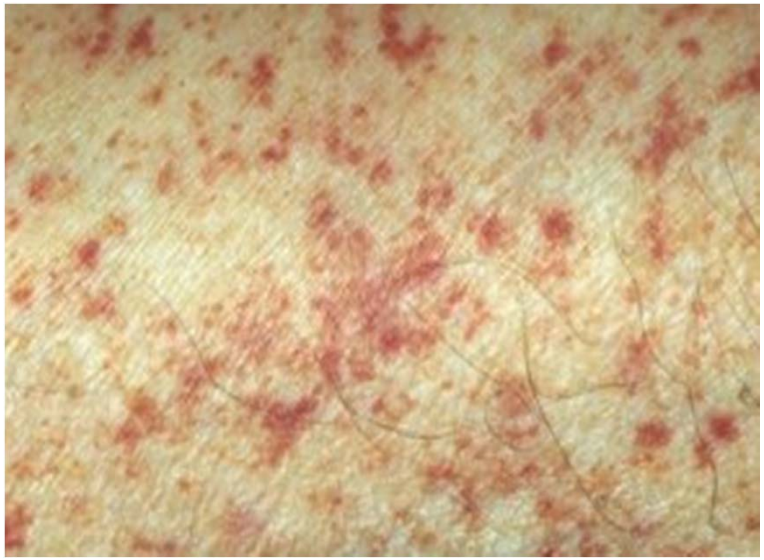
Disorders of Platelets and Platelet Transfusion

Sites of bleeding in thrombocytopenia

- Skin and mucous membranes
  - Petechiae
  - Ecchymosis
  - Hemorrhagic vesicles
  - Gingival bleeding and epistaxis
- Menorrhagia
- Gastrointestinal bleeding
- Intracranial bleeding

Petechiae





Classification of platelet disorders

- Quantitative disorders
  - Abnormal distribution
  - Dilution effect
  - Decreased production
  - Increased destruction
- Qualitative disorders
  - Inherited disorders (rare)
  - Acquired disorders
    - Medications
    - Chronic renal failure
    - Cardiopulmonary bypass

Acquired thrombocytopenia with shortened platelet survival

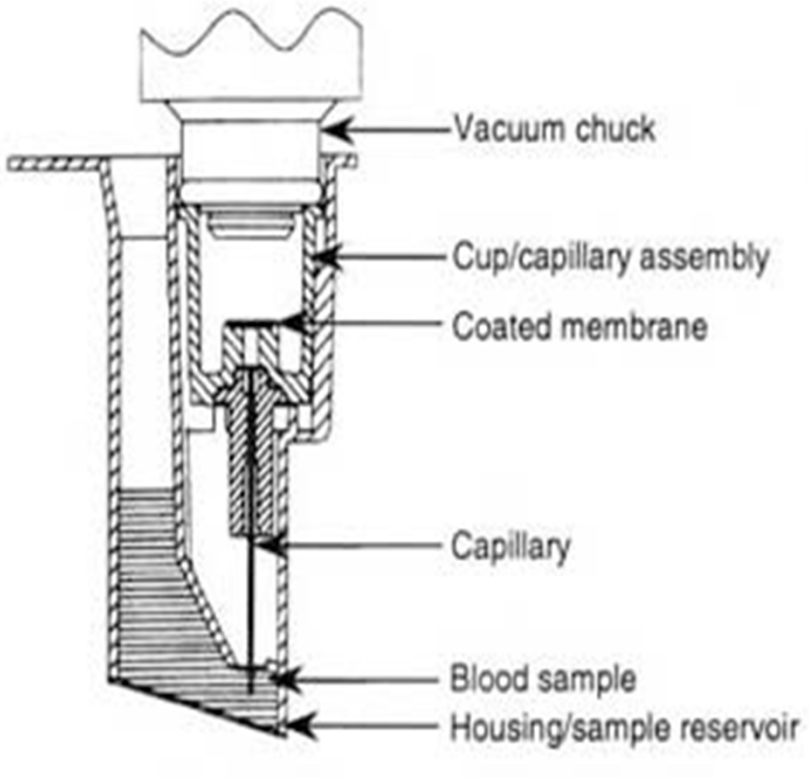
- Associated with bleeding
  - Immune-mediated thrombocytopenia (ITP)
  - Most drug-induced thrombocytopenias
  - Most others
- Associated with thrombosis
  - Thrombotic thrombocytopenic purpura
  - DIC
  - Trousseau's syndrome
  - Heparin-associated thrombocytopenia

Approach to the thrombocytopenic patient

- History
  - Is the patient bleeding?
  - Are there symptoms of a secondary illness? (neoplasm, infection, autoimmune disease)
  - Is there a history of medications, alcohol use, or recent transfusion?
  - Are there risk factors for HIV infection?
  - Is there a family history of thrombocytopenia?
  - Do the sites of bleeding suggest a platelet defect?
- Assess the number and function of platelets
  - CBC with peripheral smear
  - Platelet function study

Platelet function screen

- Replaces the *bleeding time* as a test of platelet function
- PFA-100; ordered as "platelet function screen"
- Blue top tube
- Measures the time it takes for blood to block membrane coated with either collagen/epinephrine or collagen/ADP



Platelet transfusions

- Source
  - Platelet concentrate (Random donor)

    Each donor unit should increase platelet count ~10,000 /µl
  - Pheresis platelets (Single donor)
- Storage
  - Up to 5 days at room temperature
- "Platelet trigger"
  - Bone marrow suppressed patient (>10-20,000/µl)
  - Bleeding/surgical patient (>50,000/µl)

Platelet transfusions - complications

- Transfusion reactions
  - Higher incidence than in RBC transfusions
  - Related to length of storage/leukocytes/RBC mismatch
  - Bacterial contamination
- Platelet transfusion refractoriness
  - Alloimmune destruction of platelets (HLA antigens)
  - Non-immune refractoriness
    - Microangiopathic hemolytic anemia
    - Coagulopathy
    - Splenic sequestration
    - Fever and infection
    - Medications (Amphotericin, vancomycin, ATG, Interferons)

Laboratory Evaluation of Bleeding
Overview

CBC and smear	Platelet count	Thrombocytopenia
	RBC and platelet morphology	TTP, DIC, etc.
Coagulation	Prothrombin time	Extrinsic/common pathways
	Partial thromboplastin time	Intrinsic/common pathways
	Coagulation factor assays	Specific factor deficiencies
	50:50 mix	Inhibitors (e.g., antibodies)
	Fibrinogen assay	Decreased fibrinogen
	Thrombin time	Qualitative/quantitative fibrinogen defects
		Fibrinolysis (DIC)
Platelet function	von Willebrand factor	vWD
	Bleeding time	*In vivo* test (non-specific)
	Platelet function analyzer (PFA)	Qualitative platelet disorder and vWD
	Platelet function tests	Qualitative platelet disorder

Adjunctive therapy for bleeding disorders

Adjunctive drug therapy for bleeding

- Fresh frozen plasma
- Cryoprecipitate
- Epsilon-amino-caproic acid (Amicar)
- DDAVP
- Recombinant human factor VIIa (Novoseven)

Fresh frozen plasma

- Content - plasma (decreased factor V and VIII)
- Indications
  - Multiple coagulation deficiencies (liver disease, trauma)
  - DIC
  - Warfarin reversal
  - Coagulation deficiency (factor XI or VII)
- Dose (225 ml/unit)
  - 10-15 ml/kg
- Note
  - Viral screened product
  - ABO compatible

Cryoprecipitate

- Prepared from FFP
- Content
  - Factor VIII, von Willebrand factor, fibrinogen
- Indications
  - Fibrinogen deficiency
  - Uremia
  - Von Willebrand disease
- Dose (1 unit = 1 bag)
  - 1-2 units/10 kg body weight

Aminocaproic acid (Amicar)

- Mechanism
  - Prevent activation plaminogen -> plasmin
- Dose
  - 50mg/kg po or IV q 4 hr
- Uses
  - Primary menorrhagia
  - Oral bleeding
  - Bleeding in patients with thrombocytopenia
  - Blood loss during cardiac surgery
- Side effects
  - GI toxicity
  - Thrombi formation

Desmopressin (DDAVP)

- Mechanism
  - Increased release of VWF from endothelium
- Dose
  - 0.3µg/kg IV q12 hrs
  - 150mg intranasal q12hrs
- Uses
  - Most patients with von Willebrand disease
  - Mild hemophilia A
- Side effects
  - Facial flushing and headache
  - Water retention and hyponatremia

Recombinant human factor VIIa (rhVIIa; *Novoseven*)

- Mechanism
  - Activates coagulation system through extrinsic pathway
- Approved Use
  - Factor VIII inhibitors in hemophiliacs
- Dose: (1.2 mg/vial)
  - 90 µg/kg q 2 hr
  - "Adjust as clinically indicated"

Recombinant human factor VIIa in non-approved settings

- Surgery or trauma with profuse bleeding
  - Consider in patients with excessive bleeding without apparent surgical source and no response to other components
  - Dose: 50-100ug/kg for 1-2 doses
  - Risk of thrombotic complications not well defined
- Anticoagulation therapy with bleeding
  - 20ug/kg with FFP if life or limb at risk; repeat if needed for bleeding

Approach to bleeding: Summary

- Identify and correct any specific defect of hemostasis
- Use non- transfusional drugs whenever possible
- RBC transfusion for surgical procedures or large blood loss

THANK YOU