Project: Ghana Emergency Medicine Collaborative

Document Title: Hemostasis: Platelet and Coagulation Disorders

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Hemostasis:
Platelet and Coagulation Disorders

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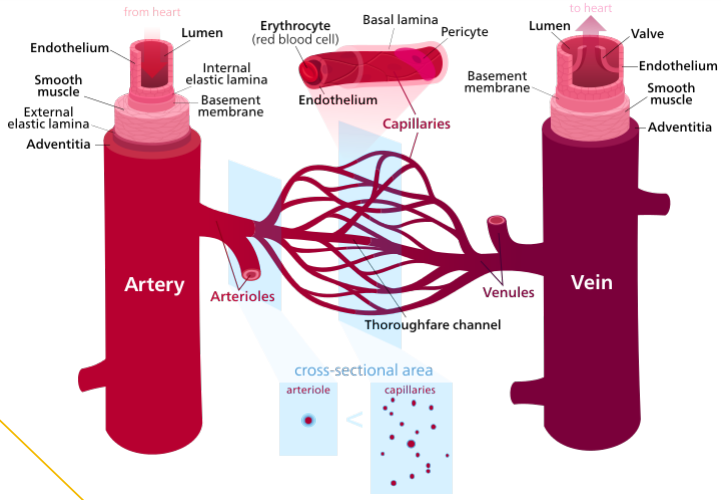
EMERGENCY MEDICINE

Normal Hemostasis

vasculature



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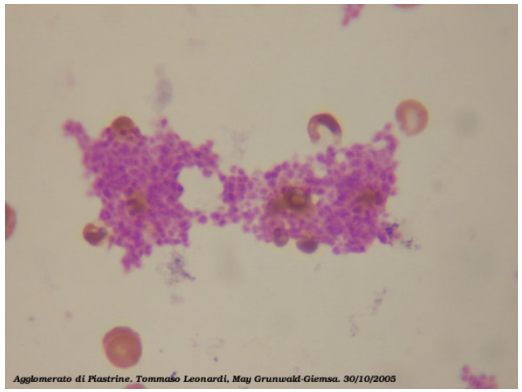
platelets



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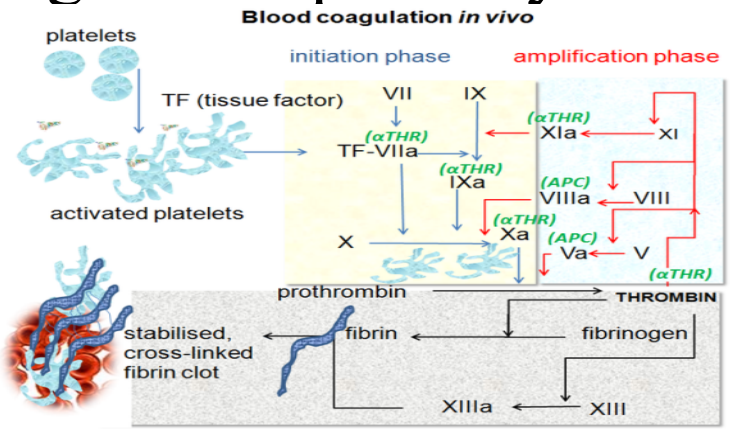
coagulation pathway



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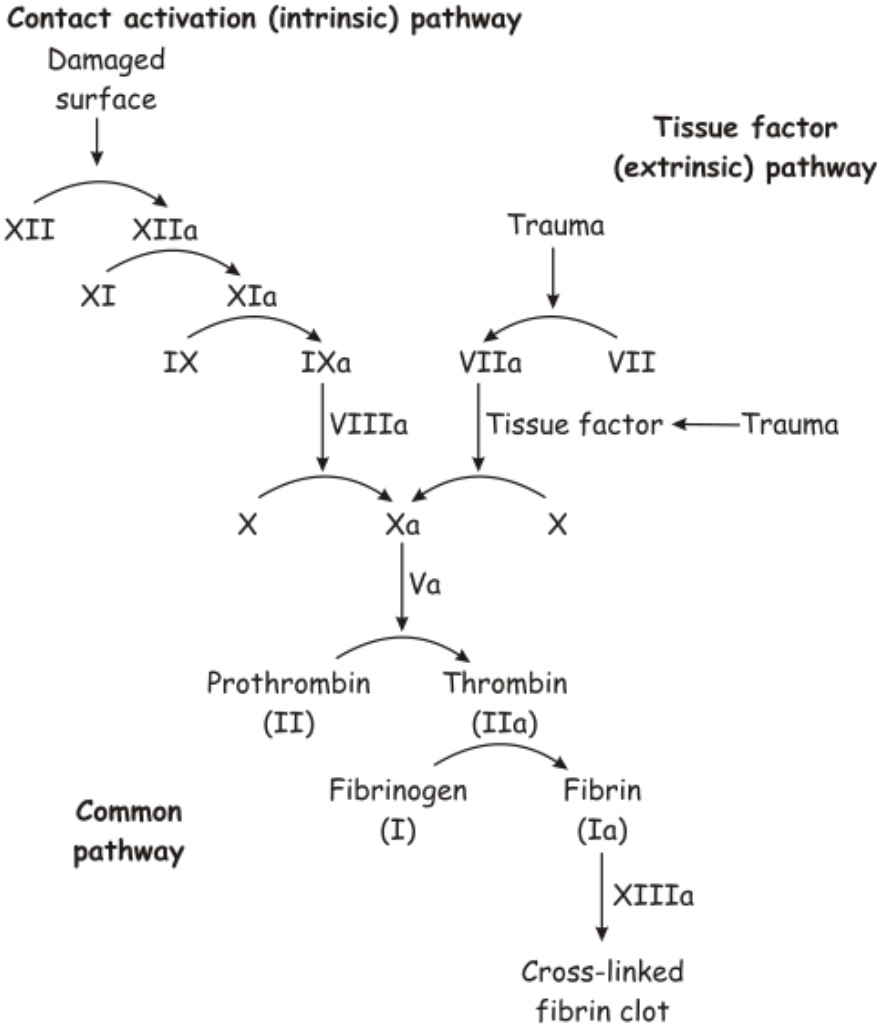
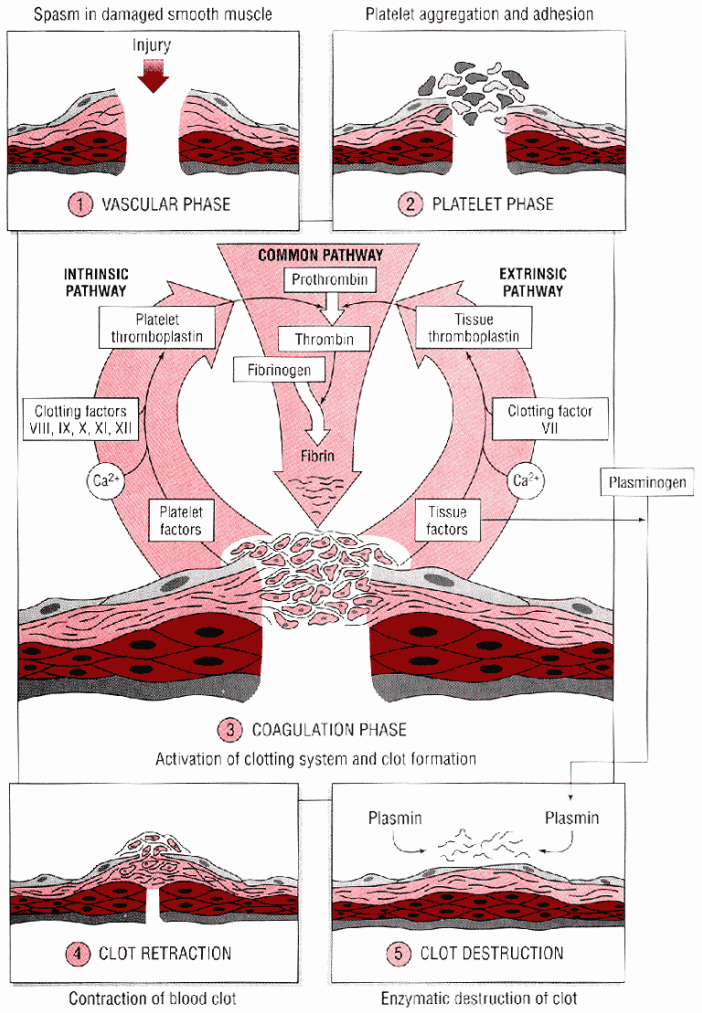
Coagulation Cascade



Coagulation Cascade



Extrinsic Pathway

- Mediated by tissue factors
- Affords a rapid response
- Prolonged prothrombin time (PT)
- Involves factors II, VII, IX, and X
  - Vitamin K dependent (coenzyme)
- Inhibition of vitamin K with warfarin

Intrinsic Pathway

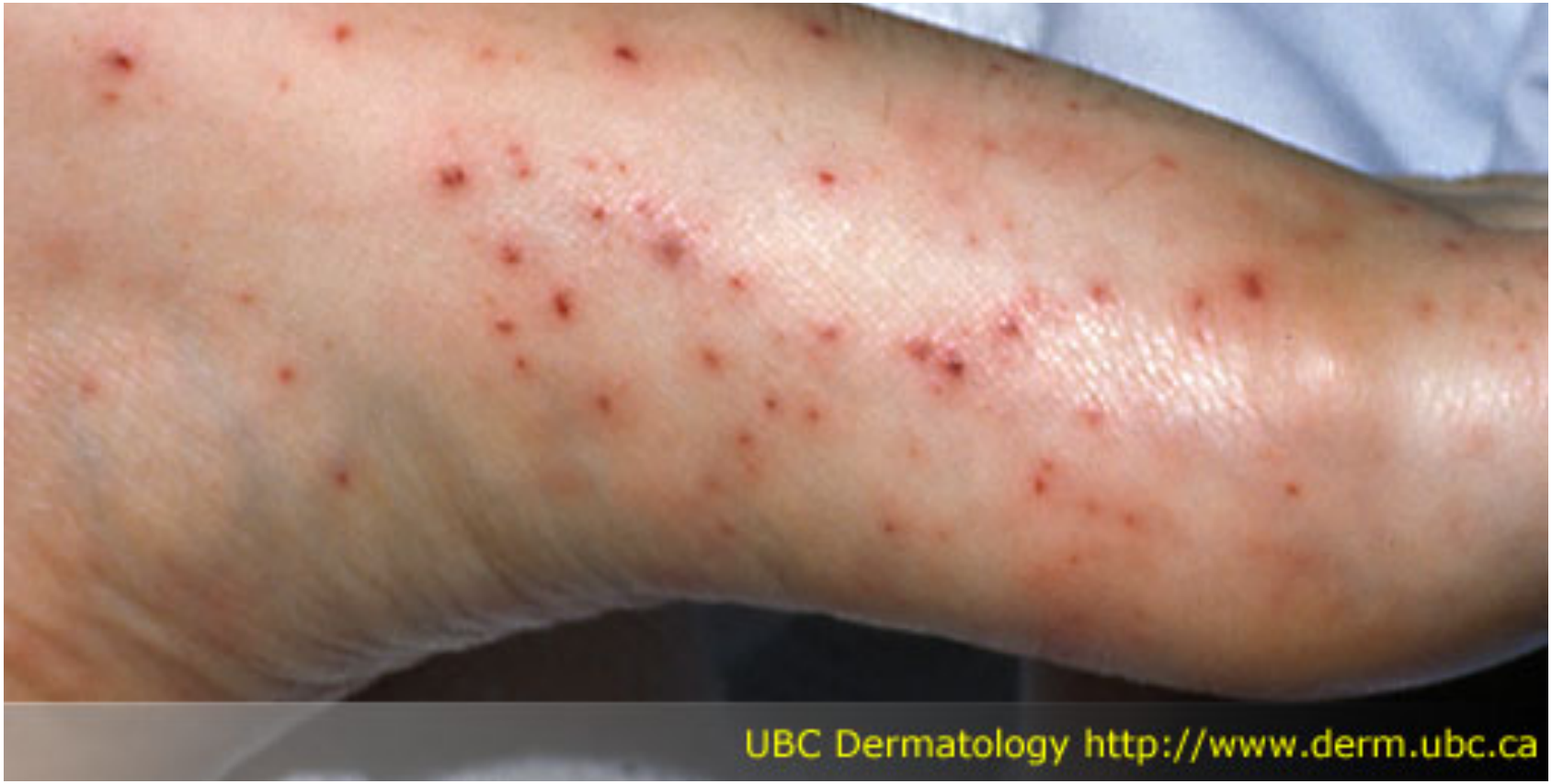
- Mediated by surface contact factors
- Slower responder
- Prolonged partial thromboplastin time (aPTT)
- Involves factors VIII, IX, and XI
  - Accounts for 99% of inherited bleeding disorders
    - Hemophilia A – factor VIII
    - Hemophilia B – factor IX
    - Hemophilia C – factor XI

Common Pathway

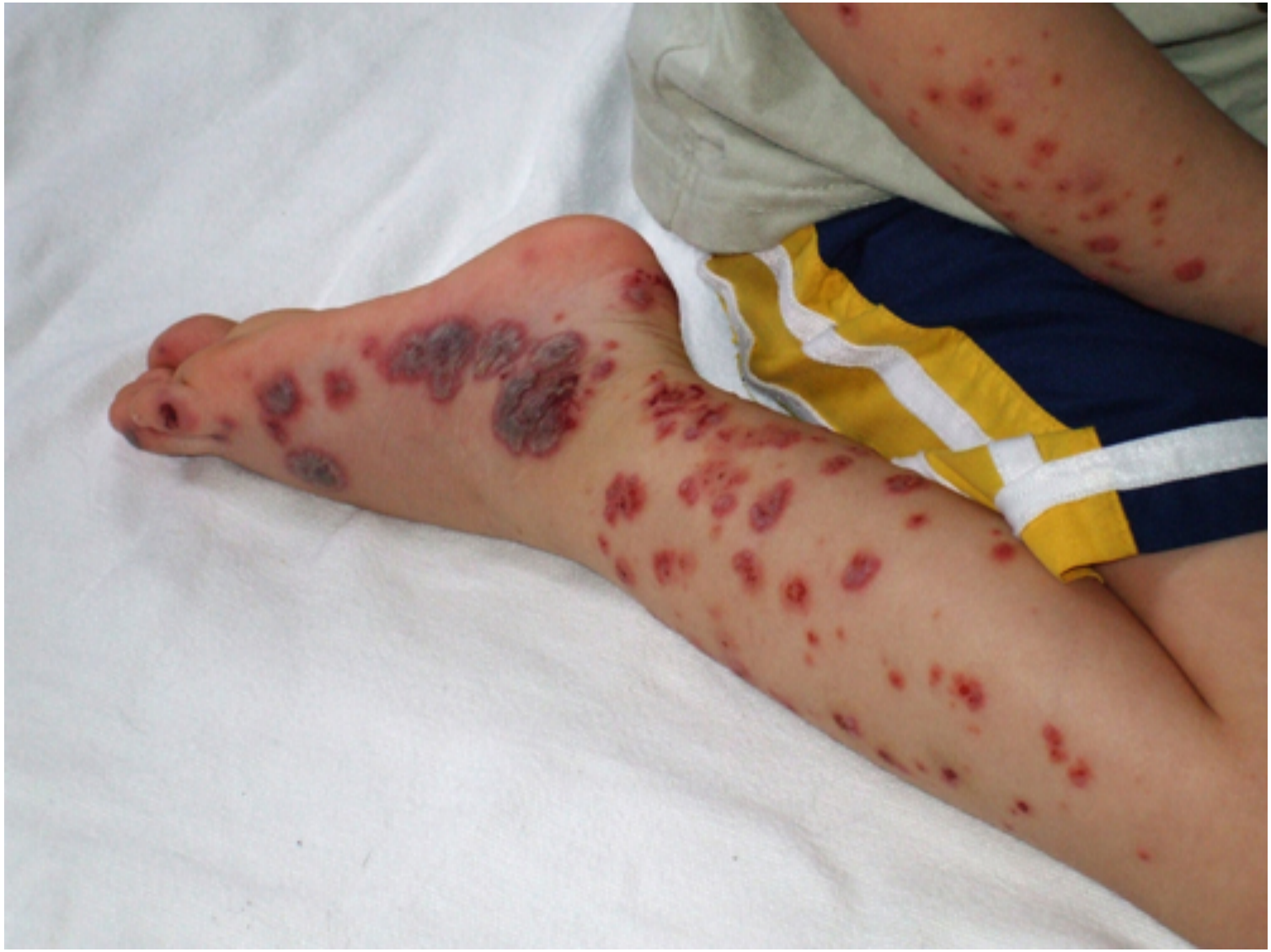
- Prolonged PT and aPTT
- Thrombin and fibrinogen form insoluble clot

Platelet Disorders

- Thrombocytopenia = platelet count < 100,000 cu mm
- Platelet count < 50,000 variable risk
- Platelet count < 20,000 transfusion appropriate
- Platelet count < 10,000 spontaneous hemorrhage
- Platelet dysfunction = mucus membrane bleeding
  - Epistaxis
  - Gingival
  - Vaginal bleeding
  - Petechiae, purpura



UBC Dermatology



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Platelet Disorders

- Immune (Idiopathic) Thrombocytopenic Purpura (ITP)
- Thrombotic Thrombocytopenic Purpura (TTP)
- Hemolytic-Uremic Syndrome (HUS)
- Heparin –Induced Thrombocytopenia (HIT)
- Drug-Induced Inactivation of Platelets

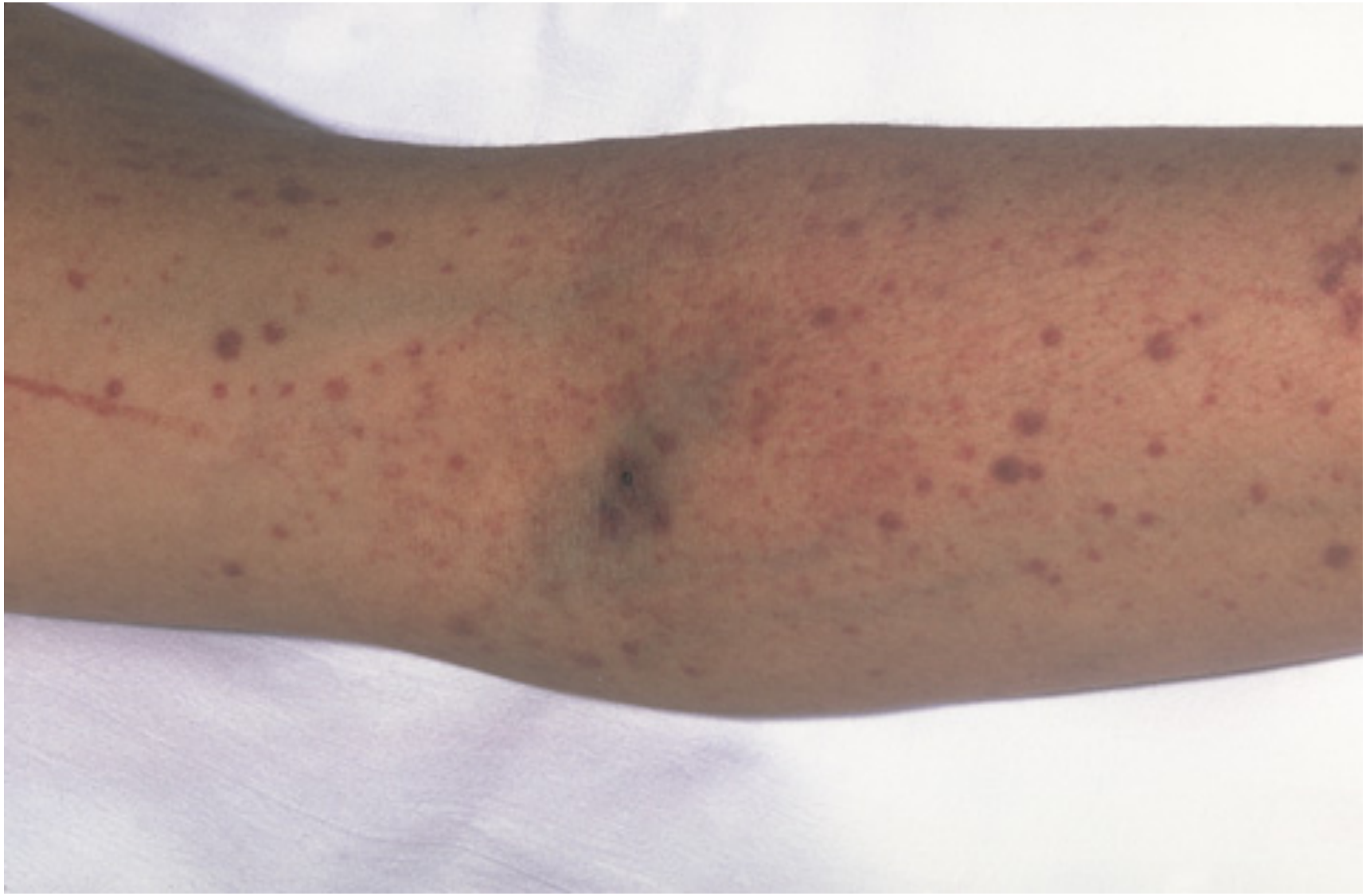
Immune Thrombocytopenic Purpura

- Acquired autoimmune disorder
  - Thrombocytopenia with normal bone marrow

- Acute form
  - Children 2-6 yrs. old
  - Associated with prior viral illness (<3 wk)
  - Resolution > 1-2 months, often quite longer
  - Spontaneous resolution in 90%

Immune Thrombocytopenic Purpura

- Chronic form
  - Adults: women > men or women < men
  - Associated with autoimmune disorder (SLE, HIV)
  - Resolution is rare
  - Thrombocytopenia < 20,000
  - Mucosal bleeding



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Immune Thrombocytopenic Purpura

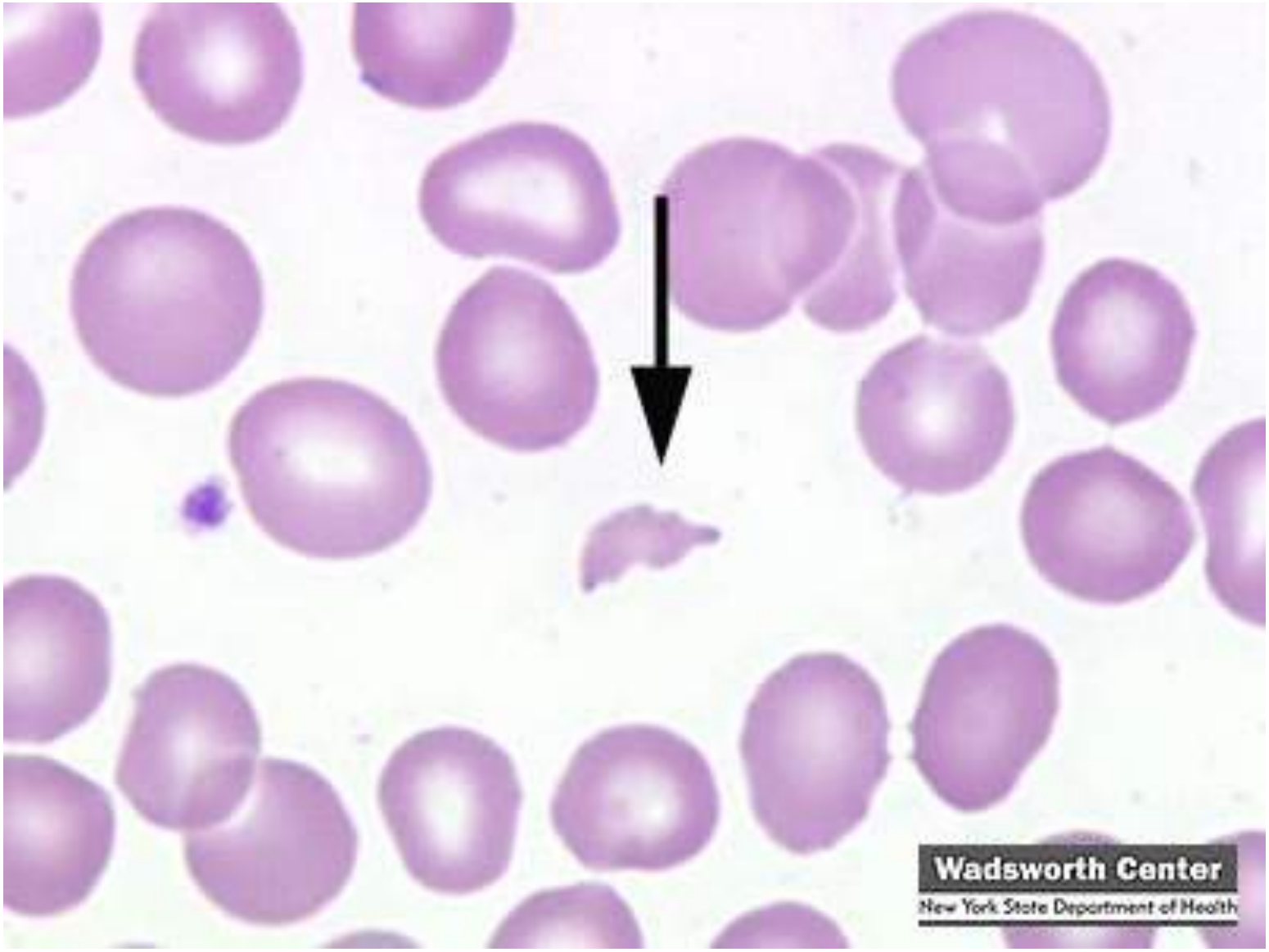
- Management
  - Do not transfuse platelets
  - Steroids
  - Splenectomy
  - Immunoglobulin therapy
  - Plasmapheresis

Thrombotic Thrombocytopenic Purpura

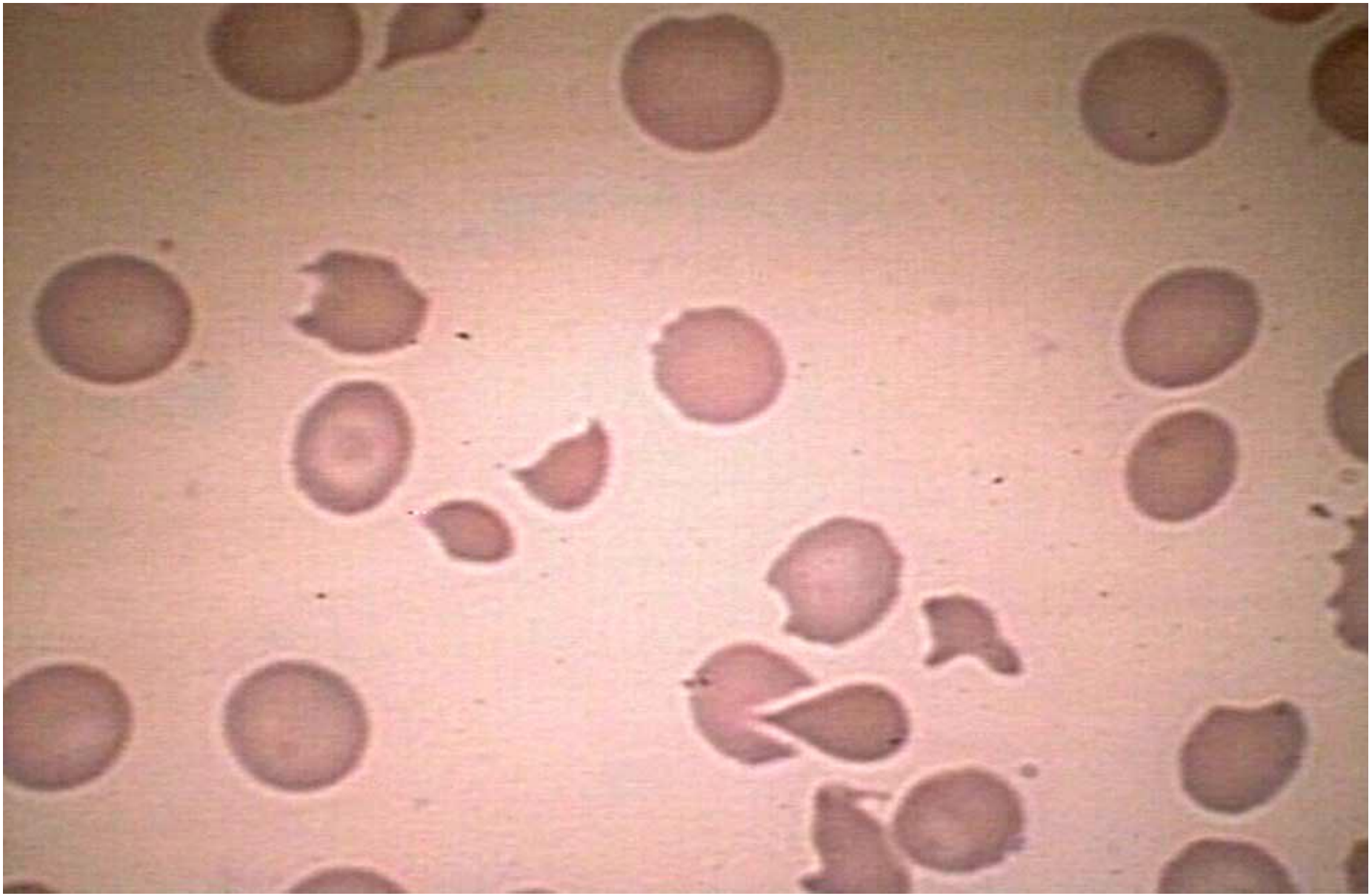
- Thrombocytopenia + microangiopathic hemolytic anemia
- Classic pentad -
  - Fever, anemia, thrombocytopenia, renal failure, neurologic symptoms
- Associations –
  - Autoimmune – AIDS, lupus, scleroderma, Sjogren
  - Pregnancy
  - Rx – cyclosporine, tacrolimus, quinidine

Thrombotic Thrombocytopenic Purpura

- Laboratory findings
  - Schistocytes (helmet cells)
    - Intravascular hemolysis – peripheral smear
  - Platelets < 20,000
  - Increased reticulocyte count
  - Increased indirect bilirubin
  - Increased LDH
  - Decreased haptoglobin
- Tx: urgent hematology consult, plasmapheresis, steroids



PD-INEL Wadsworth Center



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Hemolytic-Uremic Syndrome

- Thrombocytopenia + microangiopathic hemolytic anemia + acute renal failure
- Primarily in children 6 mo – 4 yr
  - Most common cause of acute renal failure in children
- Associations –
  - *E. coli* H7:0157 → Shiga-like toxin

Hemolytic-Uremic Syndrome

- Presentation – bloody diarrhea and seizure
  - Pentad of TTP
  - TTP – neurologic symptoms more pronounced
  - HUS – renal dysfunction more pronounced

- Laboratory findings
  - SCHISTOCYTES
  - TTP lab findings
  - Worse renal function parameters, i.e. renal failure

Hemolytic-Uremic Syndrome

- Treatment
  - Supportive, dialysis (?), do not administer antibiotics.

Schistocytes + child = HUS
Schistocytes + adult = TTP

Schistocytes + neurologic dysfunction = TTP
Schistocytes + renal dysfunction = HUS

Heparin-Induced Thrombocytopenia

- Type I
  - Platelet count rarely < 100,000
  - Occurs within first few days
  - Benign – not associated with thrombosis
  - Platelet count normalizes regardless of heparin use / disuse

Heparin-Induced Thrombocytopenia

- Type II
  - Autoimmune and consumptive
  - Occurs day 4-14
  - 1/3 of cases associated with thrombosis
  - Must d/c heparin No LMW heparins
  - No platelet transfusions unless life-threatening bleeding
  - Treat with direct thrombin inhibitors
    - Hirudin (Revasc)
    - Lepirudin (Refludan)
    - Argatroban (Novastan)

Drug-Induced Inactivation of Platelets

- Most common
  - Quinidine / quinine, sulfonamides. Phenytoin, ASA
- Less common
  - Chronic EtOH, NSAID's (indomethacin), valproic acid
- Development of antiplatelet antibodies
- Treatment
  - Recovery within one week
  - Steroids
  - DDAVP / platelet transfusions for severe hemorrhage

Coagulation Disorders

- Hemophilia A (classic hemophilia)
- Hemophilia B (Christmas disease)
- Disseminated Intravascular Coagulation
- von Willibrand's Disease
- Medication toxicity

Hemophilia A (Classic Hemophilia)

- X-linked recessive bleeding disorder due to deficiency of factor VIII function
- Spontaneous genetic mutations occur accounting 1/3 of new cases
- Severity of disease dependent on % factor VIII activity function
  - Classified as mild, moderate, severe

Hemophilia A

- Severe – spontaneous bleeding
  - < 1% factor VIII activity
- Moderate – occasional spontaneous bleeding but more commonly follows trauma / surgery
  - 1% - 5% factor VIII activity
- Mild – occasional hemorrhage after dental extractions, menses
  - >5% factor VIII activity

Hemophilia A

- 90% of bleeding events involve
  - Joints – knee involvement > 50%
  - Intramuscular – neuro-vascular compromise possible
- Bleeding manifestations can be delayed for hours – though normally seen within 8 hrs
- Minor lacerations and abrasions not normally problematic
- Head injuries are treated without waiting for CT
- Believe the patient !

Hemophilia A

- Laboratory findings
  - PTT increased *unless* > 30% factor activity present
  - Specific factor assays necessary
  - Inhibitor may be present in 10-25% of patients
    - Antibody against factor VIII

Hemophilia A

- Treatment
  - Recombinant factor VIII – therapy of choice - $$$$$
    - each IU/kg increases factor VIII by 2%
  - Factor VIII concentrate –pooled donors (infection risk)
  - Major life-threatening bleeding 50 IU/kg initially
  - Hemarthrosis / muscle bleeding 25-50 IU/kg
  - Minor bleeding 12.5 – 25 IU/kg
  - Desmopressin (DDAVP) – mild to moderate disease
    - Stimulates increase of functional factor VIII by 3-5 fold
    - Onset 30 min; dose 0.3 microgram/kg IV

Hemophilia A

- Treatment (cont)
  - Fresh frozen plasma contains one IU/ml of factor VIII
    - 250 ml/bag [14 bags = 3500ml]
  - Cryoprecipitate contains 100 IU of factor VIII per bag
    - 80-100 ml bag [35+ bags = 3500ml]
  - FFP and/or cryoprecipitate should be used only as temporizing measures if recombinant or concentrate factor VIII not available
- Get a consulting hematologist on board early to direct treatment choices and dosing.

Hemophilia B (Christmas disease)

- X-linked recessive bleeding disorder due to deficiency of factor IX function
- Classification is same as Hemophilia A
- Clinical presentation is same as Hemophilia A
- Inhibitor to factor IX found < 2% of patients

Hemophilia B

- Treatment
  - Recombinant factor IX, if available
  - Factor IX concentrate (pooled = infection risk)
  - Both factor products increase factor IX by 1% for each IU/kg
  - Fresh frozen plasma contains 1 IU/ml of factor IX
  - Cryoprecipitate - no factor IX
  - Desmopressin (DDAVP) ineffective

Disseminated Intravascular Coagulation

- Consumptive coagulopathy – hemostasis gone wild
- Simultaneous coagulation and fibrinolytic pathways promoting both bleeding and thrombotic components – one predominates
- Etiology:
  - Infection – most common, esp. gram neg sepsis
  - Carcinoma / leukemia
  - Trauma, hepatic dz, pregnancy, ARDS, viper envenomation, transfusion reaction

Disseminated Intravascular Coagulation

- Laboratory –
  - PT elevated, PTT often elevated
  - Decreased platelets, fibrinogen
  - Increased fibrin split products and d-dimer (more specific, less sensitive)
  - Fragmented RBC's → anemia

Disseminated Intravascular Coagulation

- Treatment
  - Supportive aggressive resuscitation
    - IV fluids and RBC transfusion
  - Fresh frozen plasma to replace coagulation factors
    - Two units at a time
  - Cryoprecipitate for fibrinogen replacement
    - Ten bags
  - Platelet transfusion
  - Heparin if thrombosis predominates
    - Ca, leukemia, pregnancy-related
  - Activated protein C, if septic shock

von Willibrand's Disease

- Most common inherited bleeding disorder
- von Willibrand's factor (vWF) facilitates platelet adhesion to each other and to damaged endothelium
  - Also, a carrier protein for factor VIII
- Three forms of clinical presentation
- Laboratory – usually normal PT and PTT; bleeding time prolonged; vWF activity low

von Willibrand's Disease

- Type I
  - Mild form = 80% of patients
  - Mucosal bleeding – decrease in vWF (quantitative)
- Type II
  - Mild form =10% of patients
  - Mucosal bleeding – dysfunctional vWF (qualitaitve)
- Type III
  - Severe form =10% of patients
  - Bleeding episodes resemble hemophilias – no detectable vWF

von Willibrand's Disease

- Treatment
  - Desmopressin (DDAVP) – stimulates endothelial cells to secrete stored vWF
    - 0.3 microgram / kg IV or SC over 30 min q 12 hr
    - Concentrated intranasal form
      - 1 spray in one nostril (150 micrograms) in children > 5 y/o
      - 1 spray each nostril (300 micrograms) in adolescent / adult
  - Factor VIII concentrates 20-30 IU/kg for nonresponder Type I or Type II and III
  - Cryoprecipitate 1-2 bags / 10 kg

Anticoagulant Toxicity

- Warfarin
  - Vitamin K 1.0-2.5 mg po
    - 10 mg slow IV for severe hemorrhage
  - Fresh frozen plasma 2-4 units
    - 4-6 units for severe hemorrhage
  - Prothrombin complex concentrate
    - 8.8 units/kg IV up to 500 units
  - Recombinant factor VIIa (NovoSeven)
    - 15-20 micrograms / kg IV over 3-5 min

Heparin Toxicity

- Protamine sulfate
  - 1 mg per 100 units of infused heparin in previous 4 hrs IV over 10 min (no more than 50 mg)
- Low molecular weight heparin (partial reversal)
  - 1 mg per 1 mg of enoxaparin
  - 1 mg per 100 anti-Xa units of dalteparin

Fibrinolytic Hemorrhage

- Cryoprecipitate 10 units IV
- Fresh frozen plasma 2 units IV
- Platelet transfusion 6 units IV (?)
- Aminocaproic acid (Amicar) 6 mg IV or po q 4hr
- Recombinant factor VIIa (NovoSeven)
  - 40-160 micrograms / kg IV over 1-2 min

Bleeding in Hepatic Failure

- Vitamin K 10 mg SC or IV
- Fresh frozen plasma 10-25 ml / kg
- Platelet transfusion
- Desmopressin (DDAVP)
  - 0.3 microgram / kg SC or
  - 0.3 microgram / kg in 50 ml NS IVPB over 30 min
- Cryoprecipitate if fibrinogen levels < 100 mg/dl

Bleeding in Renal Failure

- Hemodialysis provides transient benefit to platelet function for 24 – 48 hrs
- Desmopressin (DDAVP)
  - 0.3 micrograms / kg in 50 ml NS IVPB over 30 min
- Platelet transfusion
- Cryoprecipitate

Drug Inactivation of Platelets

- ASA, NSAID's, clopidogrel (Plavix), ticlopidine (Ticlid)
  - All inhibit platelet aggregation
- Discontinue agent
- Platelet transfusion
- Desmopressin (DDAVP)
  - 0.3 micrograms / kg in 50 ml NS IVPB over 30 min