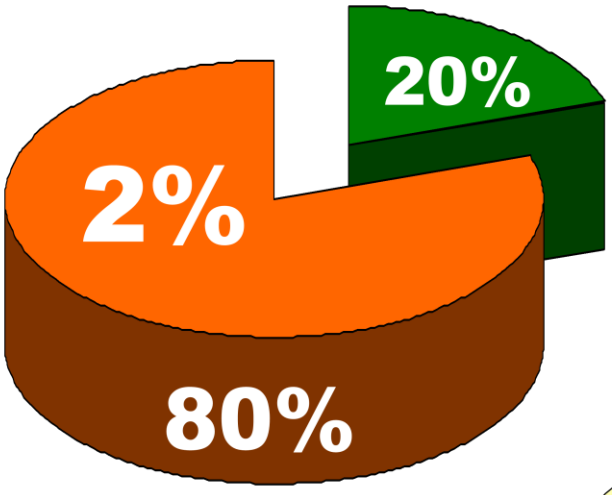
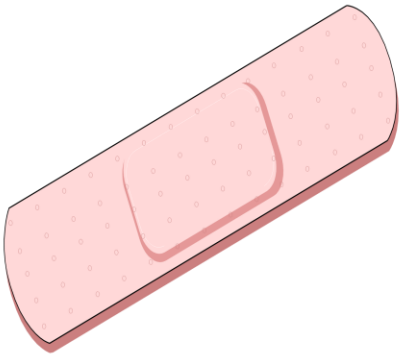
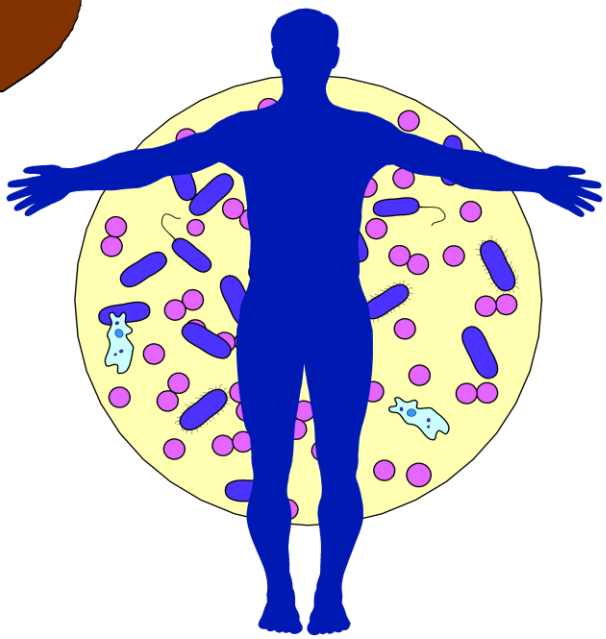
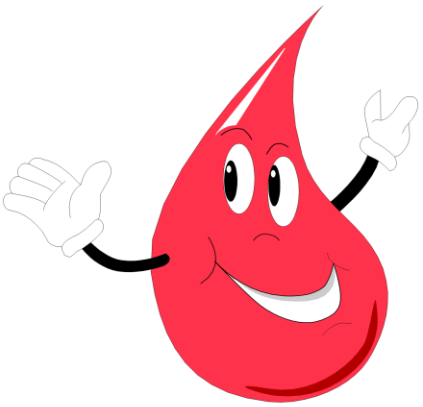
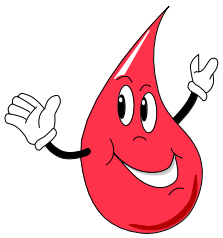
Hematology/ Immunology



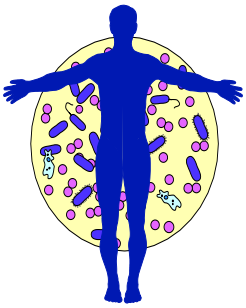








Hematology & Immunology



I. INTRODUCTION

AACN-CCRN/CCRN-E Blueprint 2%

- ✓ Coagulopathies (e.g. ITP, DIC, HIT)

PHYYSIOLOGY OF HEMATOPOIETIC SYSTEM

A. **Purpose**

- ✓ Circulate
- ✓ Provide Nutrition
- ✓ Provide Oxygen
- ✓ Remove Waste Products (carbon dioxide and metabolic wastes)
- ✓ Maintain Hemostasis

B. Location

✓ Veins & Venules	66%
✓ Pulmonary Loop	12%
✓ Arteries & Arterioles	11%
✓ Heart	6%
✓ Capillaries	5%

C. Composition 4-6 liters of blood

- ✓ Plasma 55%
- ✓ Cellular Components 45%
  - ⇒ Erythrocytes (red blood cells)
  - ⇒ Leukocytes (white blood cells)
  - ⇒ Thrombocytes (platelets)

D. Function & Assessment (see review information at end of this section)

II. BLEEDING DISORDERS

A. **Causes for Bleeding**

1. Vessel Integrity Disruption
   - ⇒ Surgical
   - ⇒ Trauma

2. Platelet Disorders
   ⇒ Quantitative
   ⇒ Qualitative

3. Coagulation Disorders
   ⇒ Acquired
   ⇒ Congenital

B. **Coagulation Disorders**

1. Acquired
   ⇒ Malnutrition
   ⇒ Liver Dysfunction (decrease synthesis of factors)
   ⇒ Vitamin K Deficiency
   ⇒ GI Dysfunction (unable to absorb Vit K)
   ⇒ Uremia
   ⇒ Medications (heparin, Coumadin)
   ⇒ Massive Transfusions
   ⇒ Consumptive Coagulopathies (DIC)

2. Congenital
   ⇒ Abnormal Structure or Function of Blood Vessels
      Rendu-Osler-Weber Disease
   ⇒ Platelet Coagulation Abnormality
      Kasabach-Merrit Syndrome
      vonWillebrand's Disease
      Hemophilia A or B
      Afibrinogenemia
   ⇒ Hyper-Coagulable Disorders
      Protein C or S Deficiency

C. DIC - Disseminated Intravascular Coagulation

Definition - DIC is a secondary disorder resulting from a primary pathophysiologic state or disease. It is complex because it presents as an over stimulation of both bleeding and thrombosis. The victim has microvascular thrombi and bleeding occurring simultaneously. The disorder can be life-threatening, acute or chronic and has a mortality rate of 50%-80%. When DIC is a complication of sepsis or shock the mortality rate can be as high as 90%. It

frequently is associated with MODS.

Risk Factors - There does not appear to be one common risk factor for this acquired coagulation disorder

General Classifications	**Primary Event/Disorder**	**Primary Event/Disorder**
Tissue Damage	Major Surgery Major Trauma Heat Stroke Head Injury	Burns Transplant Rejection Extracorporeal Circulation Snake Bites
Obstetric Complications	HELLP Amniotic Emboli Abruptio Placenta Fetal Demise	NS Abortion Eclampsia Placenta Accreta Placenta Previa
Shock States	Cardiogenic Shock Septic Shock (severe infection or inflammation) Hemorrhagic Shock Dissecting Aneurysm	Massive blood and volume resuscitation Drowning Anaphylaxis
Neoplasms	Acute & Chronic Leukemia Acute & Chronic Lymphoma	Solid Tumors
Hematologic Disorders	Thrombotic Thrombocytopenic Purpura (TTP)	Collagen Vascular Disorders Thrombocythemia Sickle Cell Crisis
Specific System Dysfunction	Acute & Chronic Renal Dis Ulcerative Colitis DKA, Acid Ingestion HIV Disease Cirrhosis	Acute Pancreatitis Liver Dysfunction/Failure SIRS & MODS Pulmonary Embolism Fat Embolism

Common Physiologic Response

⇒ Tissue damage
⇒ Platelet damage
⇒ Endothelial damage

Pathophysiology

⇒ Tissue Damage Occurs
⇒ Healing is Stimulated (Clotting)

⇒ Hemopoietic Chaos
⇒ Fibrinolytic Mediators Released
⇒ Initially Microvascular Thrombi
⇒ Consumption Exceeds Synthesis
⇒ Ability to Clot is Lost
⇒ Fibrinolytic Mediators "Run a Muck"
⇒ Lyse all Clots
⇒ Bleeding State
⇒ Consumption Coagulopathy

Physical Assessment and Findings: the primary problem and pre-existing condition certainly play a major role in the presentation. All systems are at risk for dysfunction. The most common problems occur in the pulmonary, renal and hematopoietic systems. Any bleeding patient who does not have a history of or "reason" for to bleed should be suspected of DIC.

⇒ **Hematopoietic System**

- ✓ Gross or Subtle Bleeding
- ✓ Ecchymoses
- ✓ Petechiae
- ✓ Hematomas or Hemorrhagic Bullae
- ✓ Scleral or Conjunctival Bleeding
- ✓ Wound and/or Puncture Site Bleeding/Oozing
- ✓ Joint Compartment Bleeding (swollen, hot, painful)
- ✓ Intracranial, Pleural or Pericardial Bleeding
- ✓ Capillary Clotting (cool-cold digits, renal dysfunction/failure, ischemic gut)
- ✓ Acrocyanosis
- ✓ Retroperitoneal Bleed

⇒ **Laboratory Findings**

Test	**Elevated**	**Decreased**
Hgb		
HCT		
Platelet Ct		
PT		
PTT		
Fibrinogen		

FDP/FSP		
D-Dimer		

Treatment: No definitive treatment exists for DIC. The major goal is to treat primary disorder – stopping the hemapoietic chaos. In addition patient and family emotional support is paramount for quality nursing care.

- ✓ Support/Treat the Primary Problem – Eradicate the Cause of DIC
- ✓ Early Recognition
- ✓ Decrease Bleeding Risk
- ✓ Treat Pain
- ✓ Transfusion Therapy – PRBC, FFP, Platelets, Cyro
- ✓ Vit K
- ✓ Anticoagulation Therapy – Heparin
- ✓ General Critical Care Management

D. HELLP Syndrome - Hemolysis, Elevated Liver enzymes & Low Platelets
Atypical variant of severe preeclampsia-eclampsia. Presenting with distinct physical and laboratory abnormalities.

Risk Factors:

- ⇒ Second Trimester → Postpartum
- ⇒ 70% btw 27-37 Weeks Gestation
- ⇒ Pregnancy-Induced Hypertension
- ⇒ Older Multiparas

Pathophysiology:

- ⇒ Preeclampsia: Vasoconstriction, Platelet Aggregation, Altered Thromboxane-to-Prostacyclin Ratio
- ⇒ Microvascular Injury
- ⇒ ? Inflammatory Condition of Hepatocytes
- ⇒ The Physiological Response is Similar to Autoimmune Diseases

Treatment:

- ⇒ Deliver the Baby
- ⇒ Control Blood Pressure
  - Hydralazine, Labetalol, Nipride
  - Post Partum Nifedipine

⇒ Hemotherapy
⇒ Assess Liver
⇒ Prevent Seizures: MgS04
⇒ Dexamethasome
- Antapartum 10mg IV q12
- Postpartum 10mg Q12 X2, 5mg q12 X2

⇒ PP Monitor for S&S of MODS
⇒ Future Pregnancies?

E. Heparin Induced Thrombocytopenia (HIT)

⇒ Acquired Allergy to Heparin
⇒ Antibodies are Produced to Heparin
⇒ With Heparin Admin the Antibodies 'attack' Heparin and Thrombocytes
⇒ Pt's Platelet Count Drops: 50% drop from baseline typically between day 4-10 of Heparin Administration
⇒ Treatment is to Stop all Heparin, Admin a Non-Heparin Anticoagulant & Admin Platelets Only if Needed

F. Thrombotic Thrombocytopenic Purpura (TTP)

⇒ Drop in Platelet Ct
⇒ Hemolytic Anemia
⇒ Classically Presents with Neuro Symptoms or Renal Dysfunction and Fever
⇒ Difficult Diagnosis
⇒ Causes: Drugs or BMT, Autoimmune Dis, AIDS, Depressed Bone Marrow, DIC, HIT, Bleeding, Extracorporeal Cir., Medications, Artificial Heart Valve, Hemodilution
⇒ Treatment
- ✓ Stop Cause
- ✓ Admin Platelets or Neumega
- ✓ Plasmapheresis

G. Idiopathic Thrombocytopenic Purpura (ITP)

⇒ Thrombocytopenia < 150,000
⇒ Unable to Determine Cause

III. SUMMARY

Hematology: Assessment & Function

Components

Hematopoiesis – blood cells from stem cells in the bone marrow

Erythrocytes: (red blood cells)

⇒ Development: Erythropoiesis takes place in the bone marrow from stem cell differentiation. Vit B12, folic acid and iron are essential for erythropoiesis

⇒ Function: Exchange of oxygen and carbon dioxide between lungs and tissues – respiration. Globin, a simple protein, attaches to heme creating hemoglobin which has the ability to carry oxygen and carbon dioxide. The affinity of oxygen and hemoglobin is dynamic and dependent on the environment of the blood: acid base balance – pH, temperature, 2,3 DPG & partial pressure of oxygen.

⇒ Stimulation: Erythropoietin, a hormone released from the kidneys (95%), communicates to the bone marrow to make more erythrocytes. The mechanism is stimulated by cellular hypoxia, hemorrhage, pulmonary disease & anemia. Renal failure with decrease production of RBCs secondary to decrease levels of erythropoietin.

⇒ Amount: 5 million/mm^3

⇒ Life Spain: 120 days

⇒ Excretion: Recycled. The cell ruptures, 90% ends up n the spleen. The iron portion returns to the iron pool and hemoglobin is converted to bilirubin and secreted by the liver as bile.

Leukocytes: (white blood cells)

⇒ Development: from stem cells in bone marrow. Amino acids and B vitamins as well as adequate nutrition are essential . Six types,

granulocytes: neutrophils, eosinphils & basophils, nongranulocytes: lymphocytes (B&T) & monocytes.

⇒ Function: Defend the body against infection. Phagocytic activity, nonspecific immunity, specific immunity – hormonal and cellular.

⇒ Stimulation: Stored in bone marrow and stimulated and released by activation of the immune system. There are as many as three times more granulocytes stored in the marrow than are circulating (a six day supply).

⇒ Amount: 4,500-11,000/mm^3

⇒ Life Span: Granulcytes – 4-8 hours in blood, 4-5 days in tissues
Monocytes – few hours in blood, months → years in the tissues as macrophages
Lymphocytes – few hours in blood, 100-300 days in the tissues

⇒ Excretion: Die or become inactivated when performing function of defense.

Thrombocytes (Platelets)

⇒ Development: From stem cells in the bone marrow by the cytoplasmic division of megakaryocytes – platelets are the smallest cellular component in the blood. Also formed in the lungs.

⇒ Function: Key role in Hemostasis, provide integrity to vessel by forming clots and preventing blood loss. At least 40 different substances are released from the platelet when it is stimulated.

⇒ Stimulation: Thrombopoietin (humoral hormone-like substance from unknown origin) stimulates the production of platelets and is stimulated by thrombocytopenia.

⇒ Amount: 150,000-400,000/mm^3

⇒ Life Span: 9-12 days

⇒ Excretion: Removed by the liver & spleen if not consumed by clotting reactions.

Plasma: (Coagulation Factors)

⇒ Development: Produced primarily in the liver, also by endothelial cells and platelets. Vitamin K, functioning liver and adequate nutrition are essential for coagulation factor development. The vitamin K dependent factors are II, VII, IX, X.

⇒ Function: Promote hemostasis through coagulation process.

⇒ Stimulation: Activation of the intrinsic of extrinsic clotting cascade.

⇒ Amount: Twelve different factors (13 numbers, 6 is not assigned) all with different active and inactivated levels.

⇒ Excretion: Used up in clotting mechanism

Red Blood Cell	Male: 4.6 – 6.0 million/mm^3 Female: 4.0 – 5.0 million/mm^3
Mean Corpuscular Volume (MCV)	Men: 78 – 100 cubic micrometers Female: 78 – 102 cubic micrometers
Mean Corpuscular Hemoglobin (MCH)	25 – 35 pg
Mean Corpuscular Hemoglobin Concentration (MCHC)	31 – 37%
RBC Distribution Width (RDW)	11.5% - 14.5%
Erythrocyte Sedimentation Rate (Sed Rate)	Male: 0 - 17mm/hr Female: 1 – 25mm/hr
Hematocrit (Hct)	Male: 37 – 49% Female:36 – 46%
Hemoglobin (Hgb)	Male: 13 – 18 g/100ml Female:12 – 16 g/100ml
Hemoglobin Electrophoresis	Hgb A_1 = 95-98% Hgb A_2 = 1.5% Hgb F < 2%
Methemoglobin	< 1% of total Hemoglobin
Reticulocyte Count	0.5 – 2.5% of total RBC count
White Blood Cells	4,500 – 11,000/mm^3
Polymorphonuclear (PMN) or Granulocytes Leukocytes	% / Absolute count Neutrophils 45 – 75% 2,000 – 7,000 Eosinophils 0 – 4% 0 - 400 Basophils 0 – 3% 0 – 200
Mononuclear Leukocytes	% / Absolute count Lymphocytes 25 – 40% 1700 – 3500 Monocytes 4 – 6% 200 – 600

TEST	NORMAL RANGE	PARAMETER MEASURED
Platelet Count	150,000-400,000/mm^3	# of Circulating Platelets, Measures Amount not Functional Ability
Prothrombin Time (PT)	11-15 seconds	Extrinsic & Common Coagulation Pathways
International Normalized Ratio (INR)	0.7 – 1.8	Standardized method of reporting the PT
Partial Thromboplastin Time (PTT) Activated Partial Thromboplastin Time (APTT)	APTT 20-35 seconds PTT 60 – 70 seconds	Intrinsic & Common Coagulation Pathways
Bleeding Time	Depends on system Ivy 1-8, Duke 1-3min	Normal Platelet and Tissue Function with Bleeding
Activated Clotting Time (ACT)	70 – 120 seconds	Intrinsic & Common Coagulation Pathways
Fibrinogen	200 - 400mg/dL	Circulating Fibrinogen
Thrombin Time (TT)	14 -16 sec	Common Coagulation Pathway and Quality of the Functional Fibrinogen
Fibrin Degradation (Split) Products	2-10mcg/ml	Degree of Fibrinolysis
D-Dimer	< 2.5mcg/ml	Specific Fibrin Breakdown Product

BLOOD PRODUCTS

A. **Whole Blood**: Has been replaced with component therapy. Had advantage of single donor and therefore less risk of disease transmission. But patient receives more volume and possibly some components they do not need. Storage time can deplete the fragile platelets so the patient may still need platelet transfusion.

B. **Packed Red Blood Cells**: Utilized for symptomatic anemia. Increases volume and oxygen carrying capacity. A transfusion of one unit of RBCs will usually increase the Hgb by 1g and the HCT by 3% - in the none bleeding patient. The actual point at which RBC are necessary is controversial due to risk of disease transmission and hypersensitivity reaction.

Side Effects of Massive Transfusion

- ⇒ Coagulation Disorders
  - ✓ Decrease Platelet Count and Function
  - ✓ Increase Bleeding Time
  - ✓ Increase PT & PTT
  - ✓ Decrease Fibrinogen
- ⇒ Metabolic Derangements
  - ✓ Metabolic Acidosis
  - ✓ Myocardial Dysfunction
  - ✓ Hypothermia
  - ✓ Electrolyte Abnormalities
  - ✓ Drop in 2,3 DPG, Left shift
  - ✓ Citrate Intoxication
- ⇒ Increase Risk of Disease Transmission
- ⇒ Increase Risk of Bacterial Sepsis
- ⇒ Increased Risk of ARDS
- ⇒ Increased Intravascular Viscosity

Transfusion Reactions

Types

- ⇒ Acute Hemolytic
- ⇒ Febrile, NonHemolytic
- ⇒ Mild Allergic
- ⇒ Anaphylactic

Signs & Symptoms

⇒ Fever
⇒ Chills
⇒ Hypotension
⇒ Shock
⇒ Hematuria
⇒ Uticaria
⇒ SOB
⇒ Flank Pain
⇒ Arthralgias
⇒ Rigor

Treatment

⇒ Stop Transfusion
⇒ Infuse NS
⇒ Collect Urine & Blood Samples
⇒ Medications:
Epinephrine, Diphenhydramine, Acetaminophen

C. **Platelets**: Transfusions are indicated when he patient is thrombocytopenic ad actively bleeding. Platelet count should be > 50,000/mm^3. If bleeding is occurring with a ct >50,000 something other than the thrombocytopenia is contributing to the bleeding. Multiple-donor platelets come from centrifuged whole blood. Single-donor platelets are obtained by hemopheresis. Single-donor are more difficult to get, more expensive but carry less risk of transfusion-transmitted disease. One unit of multiple-donor platelets should increase the platelet ct 5,000-10,000, single donor 30,000-60,000.

D. **Fresh Frozen Plasma (FFP):** FFP contains most coagulation factors (II, VII, IX, X) except those unique to platelets. Plasma is retrieved by centrifugation of whole blood. It given within 6 hours and not frozen it is fresh plasma. If typically has been frozen immediately after collection and can be stored for up to 12 months. FFP is indicated to replace specific factor deficiencies and not prophylactically. It is not recommended as a first line fluid for volume expansion.

E. **Cryoprecipitate**: A white precipitate that forms as FFP is thawed. It is the only form of fibrinogen available. It also contains factor VIII, fibronectin, immunoglobulins, albumin & vonWillebrand factor. No research based recommendations for dosing are published.

F. **Factor Concentrates**: Some of the coagulations factors have been isolated and can be given to deficient patients, such as factor VIII for hemophilia. Factor concentrates (from human blood) carry a high risk of transfusion-transmission diseases.

HEMOSTASIS AND FIBRINOLYSIS

A. Local Vascular Response

Injured Vessel Constriction
⇒ Collagen exposed to subendothelium
⇒ Platelets activate, adhere and aggregate
⇒ Arachidonic acid pathway activated
⇒ Thromboxane A2 (vasoconstrictor) released
⇒ Vasoconstriction = decreased blood flow to area & decreased blood loss

B. Clot Formation

1. Platelet Plug
   ⇒ Endothelium release von Willebrand factor
   ⇒ Platelet adhesion
   ⇒ Platelets change shape promoting more adhesion and activation
   ⇒ More mediators are released which promote more aggregation
   ⇒ Unstable clot or platelet plug formed

2. Blood Clot
   ⇒ Mediators released from activated platelets and damaged endothelium
   ⇒ Activation of intrinsic and extrinsic coagulation pathways
   ⇒ Prothrombin is converted to thrombin on the surface of the platelets
   ⇒ Thrombin detached from platelets and converts fibrinogen to fibrin
   ⇒ Fibrin creates a clot mesh
   ⇒ Red blood cells are caught in mesh and stable clot is formed

D. Fibrinolysis

1. Plasma Fibrinolysis

⇒ Plasma proteins are part of the formed clot, specifically plasminogen
⇒ Tissue plasminogen activating factor (t-PA) is released from vascular endothelium
⇒ Plasminogen is converted to plasmin
⇒ Plasmin hydrolyses fibrin and dissolves clots
⇒ Fibrin degradation products or fibrin split products result from lysed clots
⇒ Serine protease inhibitors (antithrombin III, protein C & S) limit extension of clot beyond injury location

2. Cellular Fibrinolysis
⇒ White blood cells release proteolytic enzymes which break down fibrin
⇒ Endothelium release mediators that stimulate procoagulant response (AA metabolites, Interleukins, PAF, tissue thromboplastin)
⇒ Platelet activating factor also released from neutrophils and macrophages

E. Hemostasis Harmony Factors
⇒ Functioning liver
⇒ Adequate nutritional status
⇒ Functioning bone marrow for platelet source
⇒ Platelets functioning properly
⇒ Healthy immune response
⇒ Normothermic
⇒ No pharmacologic interruptions or inhibitions
⇒ Proper pH
⇒ Proper acid base balance
⇒ Balance between O_2 supply & demand