CMC Certification Review Course:
Handout

Session #: 6
Renal Abnormalities, Endocrine Abnormalities,
Hematologic Abnormalities, Multisystem Abnormalities

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How to use this module:

- CMC Review Course
- Session 6:
  - Renal Abnormalities
  - Endocrine Abnormalities
  - Hematologic Abnormalities
  - Multisystem Abnormalities

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### Sodium

- **Normal value**: 136–145 mEq/L
- **Critical value**:
  - < 120 mEq/L
  - > 160 mEq/L

### Hypernatremia: Etiology

- Decreased water intake
- Hypertonic IV fluids or tube feedings
- Fluid losses
  - Osmotic diuresis
  - Hyperosmolar hyperglycemia state (HHS)
  - Diabetes insipidus

### Hypernatremia: Symptoms

- Extreme thirst
- Tachycardia
- Low-grade fever
- Disorientation
- Lethargy progressing to coma
- Seizures
**Hyponatremia: Etiology**
- Prolonged diuretic therapy
- Diaphoresis
- GI losses
- Hypotonic solutions
- Syndrome of inappropriate antidiuretic hormone (SIADH)

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**Hyponatremia: Symptoms**
- Headache
- Lightheadedness
- Confusion
  - Muscle cramps
  - Convulsions
  - Coma

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**Potassium**
- Normal value
  - 3.5–5.5 mEq/L
- Critical values
  - < 2.5 mEq/L
  - > 6.5 mEq/L
**Hyperkalemia: Etiology**

- Increased intake
- Trauma
- Acidosis
- Kidney failure

**Hyperkalemia: Symptoms**

- **Central nervous system**
  - Hyperactive reflexes
  - Parasthesia
  - Paralysis
- **Cardiovascular**
  - Tall, peaked T waves
  - Bradycardia
  - Escape beats
  - Prolonged PR interval
  - Asystole
  - Ventricular fibrillation
- **GI**
  - Abdominal cramps
  - Diarrhea
  - Intestinal ileus
- **Neuromuscular**
  - Weakness
  - Cramps
  - Twitching

**Hypokalemia: Etiology**

- Decreased intake
- Intracellular shift
- Increased GI loss
- Increased urinary loss
- Aldosterone excess
Hypokalemia: Symptoms

- CNS
  - Hypoactive reflexes
  - Paresthesia
- CV
  - Flattened T waves
  - Prominent U waves
  - Peaked P waves
  - Prolonged PR interval
  - Ventricular asystole or fibrillation
  - Hypotension
- GI
  - Abdominal distention
  - Ileus
  - Nausea and vomiting
- Neuromuscular
  - Weakness
  - Fatigue
  - Cramps
- Other
  - Respiratory arrest
  - Digitalis toxicity

Renal Abnormalities

Calcium

- Normal values
  - 8.5–10.5 mg/dL
  - Ionized: 4.5–5.6 mg/dL
- Critical value
  - < 7.0 mg/dL
  - > 14.0 mg/dL

Renal Abnormalities

Hypercalcemia: Etiology

- Hyperparathyroidism
- Bone release
  - Immobilization
  - Multiple fractures
- Acidosis
  - Albumin
- Excessive vitamin D
- Decreased renal excretion

Renal Abnormalities
**Hypercalcemia: Symptoms**

- CNS
  - Lethargy
- Coma
- CV
  - Shortened QT interval
  - Bradycardia
  - Heart blocks
- GI
  - Constipation
  - Nausea
  - Vomiting
- Neuromuscular
  - Hypoactive deep tendon reflexes
  - Weakness
- Renal
  - Polyuria
  - Renal calculi
  - Flank pain
  - Thirst
  - Dehydration
- Skeletal
  - Deep bone pain
  - Pathological fractures

**Hypocalcemia: Etiology**

- Hypoparathyroidism
- Chronic renal failure
- Decreased intestinal absorption
- Increased binding
- Alkalosis

**Hypocalcemia: Symptoms**

- CV
  - Prolonged QT interval
- GI
  - Diarrhea
  - Nausea and vomiting
- Hematologic
  - Bleeding
- Other
  - Bronchospasm
  - Seizures
- Neuromuscular
  - Irritability
  - Convulsions
  - Hyperactive deep tendon reflexes
  - Tetany
  - + Chvostek
  - + Trousseau

**Renal Abnormalities**
MAGNESIUM

Normal values
- 1.2–2.5 mEq/L

Critical values
- < 1.0 mEq/L
- > 8.0 mEq/L

Hypermagnesemia: Etiology

- Increased intake/absorption
  - Parenteral administration
- Decreased excretion
  - Oliguric renal failure

Hypermagnesemia: Symptoms

- Neuromuscular
  - Loss of deep tendon reflexes
  - Decreased neuromuscular activity
- CV
  - Tachycardia → bradycardia → cardiac arrest
  - Prolonged PR interval
- CV (continued)
  - Prolonged QRS
  - Increased T wave amplitude
- Other
  - Flushing
  - Decreased respiratory rate
  - Lethargy
  - Respiratory arrest

Renal Abnormalities
Hypomagnesemia: Etiology
- Decreased intake/absorption
- Increased excretion
- Alcoholism
  - Hyperaldosteronism
  - Hyperparathyroidism

Hypomagnesemia: Symptoms
- CNS
  - Confusion
  - Coma
  - Dizziness
- Neuromuscular
  - Twitches
  - Muscle cramps
  - Tetany
  - Muscle weakness
- Other
  - Anorexia
  - Nausea

Acute Renal Failure: Definition
- Sudden decline in renal function
- Increase in BUN and creatinine
- Oliguria (< 400 mL/24 hours)
- Hyperkalemia and sodium retention
### RIFLE Criteria

<table>
<thead>
<tr>
<th>RIFLE Class</th>
<th>Definition</th>
<th>Frequency</th>
<th>Need for RRT</th>
<th>90-day Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>↓ Scr x 1.5 or ↓ glomerular filtration rate (GFR) &gt; 25%</td>
<td>30-50%</td>
<td>3%</td>
<td>8%</td>
</tr>
<tr>
<td>Injury</td>
<td>↑ Scr x 2 or ↓ GFR &gt; 50%</td>
<td>5-7%</td>
<td>7%</td>
<td>21%</td>
</tr>
<tr>
<td>Failure</td>
<td>↓ Scr or ↓ GFR &gt; 75%</td>
<td>1-3%</td>
<td>55%</td>
<td>33%</td>
</tr>
<tr>
<td>Loss</td>
<td>AKI with complete loss of kidney function &gt; 4 weeks</td>
<td>1%</td>
<td>100%</td>
<td>40-50%</td>
</tr>
<tr>
<td>ESRD</td>
<td>ESRD &gt; 3 months</td>
<td>1%</td>
<td>100%</td>
<td>&gt;50%</td>
</tr>
</tbody>
</table>

### Acute Renal Failure: Pathophysiology

#### Prerenal
- Reduced circulating volume
- Diminished pump function
- Vasoconstrictor use

#### Intrarenal
- Intrarenal ischemia
- Nephrotoxins
- Immunologic processes
- Rhabdomyolysis

#### Postrenal
- Renal calculi
- Urinary tract infection
- Enlarged prostate
- Trauma to plumbing

### Acute Renal Failure: Clinical Presentation

#### Prerenal
- Decreased skin turgor
- Dry mucus membranes
- Weight loss
- Oliguria
- Hypotension
- Flat neck veins
- Tachycardia

#### Intrarenal
- Usually edema

#### Postrenal
- Often anuria
Acute Renal Failure: Diagnostics

Prerenal
- Urinalysis
  - No abnormal casts
  - Occasional hyaline casts
  - BUN/Creatinine ratio
    - > 20:1
  - Fractional excretion of sodium (FENa), renal failure index (RFI)
    - < 1%

Acute Renal Failure: Diagnostics

Intrarenal
- Urinalysis
  - Abnormal casts
  - BUN/Creatinine ratio
    - 10–15:1
  - FENa, RFI
    - > 1%

Acute Renal Failure: Management

Preventive
- Patients at risk
- Adequate hydration
- Avoid nephrotoxins
Contrast-induced nephropathy

Risk factors:
- SBP < 80
- Heart failure
- NYHA III/IV
- IABP
- Diabetes
- Age ≥ 75
- Preexisting renal disease
  - Serum creatinine (Scr) > 1.5 mg/dL
  - Creatinine clearance (CrC) < 60 mL/min
- Concomitant use of nephrotoxins

Low risk (no risk factors)
- No additional interventions required

Moderate risk (1 risk factor)
- Check for decompensated heart failure, pulmonary edema, or hyponatremia

High risk (> 2 risk factors or Scr > 2.0 or CrC < 40)
- Check for decompensated heart failure, pulmonary edema, or hyponatremia

Preventive
- Prevent and treat shock
- Monitor suspected patients
- Avoid infections
- Corrective and supportive
- Correct reversible causes
- Correct fluid excess or deficit
- Monitor for electrolyte imbalance
- Restore/maintain BP
- Maintain nutrition
- Assist with renal replacement therapy
Acute Renal Failure: Management

- Pharmacological Strategies
  - Loop diuretics
  - Dopamine
  - Fenoldopam
  - N-Acetylcysteine
  - Natriuretic peptides

Acute Renal Failure: Complications

- Infection
- Dysrhythmias
- GI bleed
  - Multiple organ failure
  - Electrolyte abnormalities

Practice Exam Questions
Question #1 - Answer

The antihypertensive medication recommended initially for treatment of high BP in patients with renal failure is:

A. Beta-blocker to maintain BP below 140/90 mm Hg
B. ACE inhibitor to maintain BP at 125/75 mm Hg. The target BP is 125/75 mm Hg, and ACE inhibitors reduce the glomerular pressure and proteinuria.
C. Potassium-sparing diuretic to maintain BP below 110/60 mm Hg
D. Calcium channel blocker to maintain BP at 125/75 mm Hg

Question #2 - Answer

The pharmacological strategy associated with a decreased use of dialysis is:

A. Loop diuretics
B. Dopamine
C. N-Acetylcysteine
D. Natriuretic peptides. Continuous infusion of natriuretic peptides is associated with decreased use of dialysis and improved dialysis-free survival.

Question #3 - Answer

An advantage of peritoneal dialysis over hemodialysis is that it:

A. Lowers serum triglycerides quickly
B. Removes fluid rapidly
C. Causes fewer CV problems. Peritoneal dialysis increases the risk of hyperlipidemia, allows increased protein wasting, removes fluid slowly, and causes fewer CV problems.
D. Allows less protein wasting
The condition consistent with a diagnosis of postrenal failure is:

A. Urinary tract infection. Postrenal causes of renal failure include renal stones, prostatic hypertrophy, trauma to ureters or urethra.

B. Impaired CV function

C. Reduced circulating volume

D. Use of nephrotoxins

Ipsilateral facial muscle contraction caused by tapping the facial nerve just anterior to the ear is a positive:

A. Kernig sign

B. Chvostek sign. Facial muscle contraction is related to hypocalcemia.

C. Brudzinski sign

D. Trousseau sign

Hypercalcemia can be caused by:

A. Multiple fractures. The most common cause is hyperparathyroidism. Other causes are hyperthyroidism, excessive vitamin D, hypophosphatemia, thiazide diuretic and lithium use, and multiple fractures.

B. Vitamin D deficiency

C. Hypoparathyroidism

D. Hyperphosphatemia
Endocrine Abnormalities

Diabetes Mellitus: Definition
- Metabolic disorder
- Hyperglycemia
- Defective insulin
  - Production, secretion, or utilization

Diabetes Mellitus: Pathophysiology
- Type I
  - Absolute or relative lack of insulin
- Type II
  - Defect at cell level
  - Impaired response to insulin
Diabetes Mellitus: Etiology

- Type I
  - Viral
  - Autoimmune
- Type II
  - Heredity
  - Obesity

Diabetes Mellitus: Clinical Presentation

- Hyperglycemia
  - Weight loss
  - Fatigue
  - Polyuria, polydipsia, polyphagia
  - Blurred vision
  - Altered tissue response
  - Delayed wound healing
  - Recurrent infections (skin)

Diabetes Mellitus: Diagnostics

- Fasting blood glucose ≥ 126 mg/dL
- Random blood glucose ≥ 200 mg/dL with classic symptoms
- Hgb A1c levels
Diabetes Mellitus: Management
- Dietary control
- Exercise
- Medications

Diabetes Mellitus: Complications
- Hypoglycemia
- Diabetic ketoacidosis (DKA)
- HHS

Hypoglycemia: Definition
- Serum glucose < 50 mg/dL
- Most common endocrine emergency
- < 35 mg/dL, brain is unable to extract O2 adequately
Hypoglycemia: Etiology
- Very old or very young
- Alcohol ingestion
- Diabetes
- Adrenal insufficiency
- Liver disease
- Drugs
  - Propranolol
  - Salicylates
  - Sedatives

Hypoglycemia: Clinical Presentation
- Cool, diaphoretic skin
- Pale appearance
- Dilated pupils
- Confusion
- Combative behavior or coma
- Seizures

Hypoglycemia: Management
- Supplemental O₂
- Monitor respiratory rate, breath sounds, and signs of adequate oxygenation
- Determine blood glucose level
- 10–15 grams of fast-acting carbohydrate
  - 1 amp dextrose 50% in water (D50W)
- Glucagon
  - 0.5–2 mg IV
  - Not effective in patients who have alcoholism
Hypoglycemia: Treatment
- Peak insulin levels
  - Regular: 3–4 hours
  - NPH/lente: 4–18 hours
  - Protamine zinc/ultralente: 18–30 hours

DKA: Defining Characteristics
- Uncontrolled hyperglycemia
- Profound dehydration
- Electrolyte disturbances
- Acid-base abnormalities

DKA: Signs and Symptoms
- Coma
- Abdominal pain
- Polydipsia, polyuria
- Kussmaul respirations
- Fruity breath
- Nausea and vomiting
- Weakness
- Weight loss
- Hypotension
- Ketonuria
- Tachycardia

Endocrine Abnormalities
**DKA: Treatment**
- **Airway, breathing, circulation (ABCs)**
- **Restore fluid balance**
  - Normal saline
  - D5 0.45% NS
- **Restore metabolism**
  - Regular insulin
- **Correct acidosis**
  - Possibly administer sodium bicarbonate
- **Restore electrolyte balance**
  - Potassium
  - Phosphate
  - Sodium

**HHS: Defining Characteristics**
- Type II diabetes
- Mortality 40%–60%
- Severe dehydration
  - Profound hyperglycemia
  - Sodium abnormality

**HHS: Signs and Symptoms**
- Nausea and vomiting
- Weight loss
- Hypotension
- Tachycardia
- Coma
  - Poor skin turgor
  - Seizures
  - Hyperreflexia
  - Disorientation
HHS: Treatment

ABCs
- Restore fluid balance
  - Normal saline
- Restore metabolism
  - Insulin
  - Treat cause
- Restore electrolytes
  - Potassium
  - Phosphate
- Monitor for cerebral edema

Hypothyroidism: Introduction

- Thyroid gland does not make enough thyroid hormone
- Iodine deficiency is most common cause
- 0.3% of the general American population have overt hypothyroidism
- 4.3% have subclinical hypothyroidism

Hypothyroidism: Types

<table>
<thead>
<tr>
<th>Type</th>
<th>Origin</th>
<th>Description</th>
</tr>
</thead>
</table>
| Primary  | Thyroid      | • Hashimoto's thyroiditis  
• Radioiodine therapy for hyperthyroidism |
| Secondary| Pituitary    | • Does not create enough Thyroid Stimulating Hormone (TSH)  
• Damage to the pituitary gland such as tumor, radiation, or surgery |
| Tertiary | Hypothalamus | • Fails to produce enough TSH  
• Accounts for < 5% of cases |
Hypothyroidism: Signs and Symptoms

Early
- Cold intolerance
- Constipation
- Weight gain and water retention
- Bradycardia
- Decreased sweating
- Muscle cramps and joint pain
- Dry, itchy skin
- Thin, brittle fingernails
- Poor muscle tone
- Depression
- Elevated serum cholesterol

Late
- Goiter
- Slow speech and a hoarse, breaking voice
- Dry puffy skin, especially face
- Low basal body temperature
- Thyroid-related depression

Hypothyroidism: Diagnosis

Primary
- TSH
- Free thyroxine (T4)

Secondary and tertiary
- Free triiodothyronine (T3)
- Free T4
- Total T3
- Total T4
Hypothyroidism: Additional Diagnostics
- Free T3 from 24-hour urine
- Antithyroid antibiotics
- Serum cholesterol
  - Prolactin
  - Anemia testing, including ferritin

Hypothyroidism: Treatment
- Levothyroxine (Synthroid)

Hyperthyroidism: Introduction
- Overactive thyroid
  - Produces too much T4
  - Accelerates the body’s metabolism
  - Can mimic other health problems, making diagnosis difficult
Hyperthyroidism: Causes
- Conditions causing too much T4
- Graves’ disease
- Hyperfunctioning thyroid nodules
- Thyroiditis

Hyperthyroidism: Signs and Symptoms
- Sudden weight loss
- Tachycardia
- Increased appetite
- Nervousness, anxiety, irritability
- Tremor
- Sweating
- Sensitivity to heat
- Change in bowel patterns
- Fatigue, muscle weakness
- Difficulty sleeping
- Enlarged thyroid (goiter)

Hyperthyroidism: Graves’ Ophthalmopathy
- Tissue and muscles behind the eyes swell
- Causes eyes to protrude
  - Protruding eyeballs
  - Red or swollen eyes
  - Excessive tearing or discomfort
  - Light sensitivity, blurry or double vision
  - Inflammation or reduced eye movements
Hyperthyroidism: Diagnosis
- TSH levels
- T4 levels
- Radioactive iodine uptake test
- Thyroid scan

Hyperthyroidism: Treatment
- Radioactive iodine
- Antithyroid medications
  - Beta-blockers
  - Thyroidectomy

Hyperthyroidism: Complications
- Heart problems
- Brittle bones
- Graves’ ophthalmopathy
- Graves’ dermopathy
- Thyrotoxic crisis
**Metabolic Syndrome: Introduction**

Combination of medical disorders that increase risk of developing cardiovascular disease and diabetes

- 25% of population
- Prevalence increases with age

**Metabolic Syndrome: Definition**

International Diabetes Foundation

- Raised triglycerides: > 150 mg/dL or treatment for lipid abnormality
- Reduced high-density lipoprotein (HDL): < 40 mg/dL (male)
  < 50 mg/dL (female) or treatment for lipid abnormality
- Elevated blood pressure (BP): systolic BP (SBP) > 130 mm Hg, or diastolic BP (DBP) > 85 mm Hg, or treatment of BP
- Elevated fasting glucose: > 100 mg/dL or previously diagnosed with type 2 diabetes
- Central obesity: waist: hip ratio > 0.9 (male);
  > 0.85 (female) or body mass index > 30 kg/m²

**Metabolic Syndrome: Etiology**

- Obesity
- Older age
- Sedentary lifestyle
- Degree of insulin resistance
- Stress
Metabolic Syndrome

**Signs and Symptoms**
- Fasting hyperglycemia
- Hypertension
- Central obesity
- Decreased HDL
- Elevated triglycerides

**Treatment**
- Lifestyle changes
- Manage underlying causes
- Manage cardiovascular risk

Practice Exam Questions

**Question #1 - Answer**

The cornerstone of therapy in the management of DKA is administering:

A. Sodium bicarbonate to correct acid-base imbalance
B. Insulin to correct metabolic abnormality. The priority therapy is insulin replacement. If the pH is 7 or less, 1 amp of sodium bicarbonate is suggested. When the potassium level reaches 4, potassium and phosphate should be started. Fluid will be replaced hourly in response to loss.
C. Normal saline to correct dehydration
D. Potassium phosphate to correct electrolyte imbalance
The priority in the management of HHS is administering:

A. Sodium bicarbonate to correct acid-base imbalance
B. Insulin to correct metabolic abnormality
C. Normal saline to correct dehydration. Dehydration is the priority problem in HHS. Since the patient has an insulin resistance, insulin is used but only to slowly lower the glucose. These patients are generally not profoundly acidic and usually stabilize with fluid administration.
D. Potassium phosphate to correct electrolyte imbalance

The key criteria for identification of metabolic syndrome is:

A. Elevated HDL
B. Hypoglycemia
C. Normal blood pressure
D. Central obesity. The criteria for metabolic syndrome is low HDL, elevated fasting glucose, hypertension, elevated triglycerides, and central obesity.

The most common cause of hypothyroidism is:

A. Iodine deficiency. Iodine deficiency causes primary hypothyroidism. This can also be caused by acute stress and lithium use. Other etiologies of hypothyroidism include pituitary and hypothalamus abnormalities.
B. A pituitary tumor
C. Acute stress
D. Lithium use
The most significant complication of antithyroid medications is:

A. Osteoporosis
B. Congestive heart disease
C. Severe liver disease. Liver dysfunction is a limiting factor in administration of antithyroid drugs (tapazole and propylthiouracil). Osteoporosis and congestive heart failure are complications of hyperthyroidism. Renal dysfunction is not seen with these drugs.
D. Nephropathy

**Hematologic Abnormalities**

**Thrombocytopenia: Definition**

- Platelet (PLT) count < 100,000 per microliter (µL)
- Most common cause of bleeding disorders
**Thrombocytopenia: Clinical Presentation**

- Usually asymptomatic
- PLTs < 20,000/µL
  - Petechiae
  - Ecchymosis
  - GI/GU bleed
  - CNS bleed

**Thrombocytopenia: Diagnosis**

- Decreased hemoglobin, hematocrit, and platelets
- Prolonged bleeding time, PT, activated partial aPTT

**Thrombocytopenia: Admission Screening**

- Identify defects in hemostasis that can be corrected
- Guide the management of hemostatic defects that cannot be corrected
- Help manage the bleeding that cannot be prevented
Thrombocytopenia: History and Physical

- Personal or family history of bleeding
- Abnormal bleeding associated with:
  - Dental extractions
  - Previous surgery
  - Routine childhood trauma

Thrombocytopenia: Admission Screening

- CBC
  - Decreased hemoglobin and hematocrit
  - Decreased PLTs
  - PT/aPTT
  - Bleeding time

- CBC with coagulation studies
  - Check for and correct hypothermia
  - Review the history
  - Review medications
Hematologic Abnormalities

<table>
<thead>
<tr>
<th>Symptom</th>
<th>INR</th>
<th>aPTT</th>
<th>PT Excess</th>
<th>PLT Count</th>
<th>History</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major/ minor bleeding</td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
<td>Normal</td>
<td>Massive intra-abdominal fluid</td>
<td>Shocked Dilutional thrombocytopenia</td>
</tr>
<tr>
<td>Major/ minor bleeding</td>
<td>Normal</td>
<td>Prolonged</td>
<td>Normal</td>
<td>Normal</td>
<td>Negative</td>
<td>Drug-induced heparin</td>
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<tr>
<td>Major/ minor bleeding</td>
<td>Increased</td>
<td>Normal</td>
<td>Normal</td>
<td>N/A</td>
<td>Vitamin K deficiency</td>
<td>Liver disease, warfarin, antibiotics</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Decreased</td>
<td>Normal</td>
<td>DIC</td>
<td></td>
</tr>
</tbody>
</table>

Thrombocytopenia: Etiology

- Decreased PLT production
  - Bone marrow abnormalities
    - Leukemia
    - Aplastic anemia
  - Radiation therapy
    - Abnormal distribution or sequestration in spleen
    - Portal hypertension
- Dilutional after hemorrhage, RBC transfusion
- Increased PLT destruction
  - Infection
  - Drug-induced
    - HIT
    - ITP
    - DIC

Thrombocytopenia: Differential Diagnosis

- PLT count fall that begins 5–10 days after starting heparin in a patient previously exposed to heparin within the past 5–100 days is very suggestive of HIT
**Thrombocytopenia: Heparin-Induced Thrombocytopenia and Thrombosis (HITT)**

**Diagnosis**
- Thrombocytopenia
- > 50% fall in PLTs
- Thrombosis
- 50% VTE
- 25% PE
- ELISA assays
  - Measure presence of antibodies to heparin-PF4 complex
  - Heparin-induced platelet activation
  - Serotonin release assay

**Thrombocytopenia: 4 T System**

<table>
<thead>
<tr>
<th>Category</th>
<th>2 point</th>
<th>1 point</th>
<th>0 point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>&gt; 50% fall</td>
<td>50%-50% fall</td>
<td>&lt; 50% fall</td>
</tr>
<tr>
<td>Timing of decrease in PLT count</td>
<td>Days 5-10 or &lt; 1 day</td>
<td>&lt; 1 day or &lt; 1 day with recent heparin</td>
<td>&lt; 1 day</td>
</tr>
<tr>
<td>Thrombosis or other sequelae</td>
<td>Progressive, recurrent, or silent thrombosis</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Other causes of thrombocytopenia</td>
<td>None evident</td>
<td>Possible</td>
<td>Definite</td>
</tr>
</tbody>
</table>

**HITT: Management**
- Discontinue the drug
- Administer direct thrombin inhibitor
  - Hirudin
  - Lepirudin
  - Argatroban
DIC: Definition
- Serious bleeding disorder
- Thrombosis then hemorrhage

DIC: Pathophysiology

Intrinsic Clotting Cascade
- Endothelial injury
- Assessed by aPTT

Extrinsic Clotting Cascade
- Tissue thromboplastin
- Assessed by PT

DIC: Etiology

Obstetric
- Abruptio placentae
- Amniotic fluid embolus
- Eclampsia
- Hemolytic/Immunologic
  - Anaphylaxis
  - Hemolytic blood reaction
  - Massive blood transfusion

Infectious
- Bacterial
- Fungal
- Viral
- Rickettsial

Vascular
- Shock
- Dissecting aneurysm

Miscellaneous
- Emboli (fat)
- Aspirin poisoning
- GI disturbances
- Pancreatitis
**DIC: Laboratory Findings**

- Decreased PLTs
- Decreased fibrinogen
- Increased PT and/or aPTT
- Increased d-dimer or fibrin split products (FSPs)
- Decreased ATIII

**DIC: Management**

- Treat underlying cause
  - Surgery
  - Antimicrobials
  - Antineoplastics
- Stop thrombosis
  - IV heparin
  - ATIII
  - Plasmapheresis
- Administer blood products
  - PRBCs
  - PLTs
  - FFP
  - Cryoprecipitate

**DIC: Complications**

- Hypovolemic shock
- Acute renal failure
- Infection
- ARDS
Thrombocytopenia: Treatment

- Treat underlying cause
- Administer PLTs

Postoperative Bleeding

- Hyperfibrinolysis
  - Desmopressin (DDAVP®)
  - Antifibrinolytics
    - Aminocaproic acid (Amicar®)

Thrombocytopenia: Complications

- Life-threatening hemorrhage
Anemia

Definition
- Reduction in RBC concentration

Causes
- Iron deficiency
- Thalassemia
- Anemia of chronic disease

Anemia: Etiology

Defects in production
- Increased destruction
- Increased loss of erythrocytes

Anemia: Microcytic

- Mean corpuscular volume (MCV) < 80 femtoliter (fL)
- Mean corpuscular hemoglobin concentration (MCHC) < 32 gm/dL

Examples
- Iron deficiency anemia
- Thalassemia
- Chronic lead poisoning
**Anemia: Normocytic**

- **MCV**
  - 80–100 fL
- **MCHC**
  - 32–36 gm/dL
- **Examples**
  - Acute blood loss
  - Chronic disease
  - Hemolytic

**Anemia: Macrocytic**

- **MCV > 130 fL and MCHC > 36 gm/dL**
  - Vitamin B₁₂ deficiency
  - Folate deficiency
- **MCV 101–120 fL and MCHC > 36 gm/dL**
  - Liver disease

<table>
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<tr>
<th>Test</th>
<th>Iron Deficiency</th>
<th>Chronic Disease</th>
<th>Folic Acid Deficiency</th>
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<tr>
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<tr>
<td>Transferrin</td>
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**Anemia**

- Hematologic Abnormalities
Anemia: Treatment
- Search for treatable disorders
  - Deficiencies of iron, B₁₂, folic acid
  - Underlying infection, renal disease, inflammation, or malignancy
  - Other: bleeding disorder, alcohol abuse, hypothyroidism
- Symptomatic anemia
  - RBC transfusion
  - Erythropoiesis-stimulating agent

Hypercoagulable State
- Abnormality of blood coagulation
- Increases risk of thrombosis
  - Found in 50% of people who have:
    - DVT
    - PE

Hypercoagulable State: Etiology
- Congenital
  - Type I defects
    - ATIII deficiency
    - Protein C deficiency
    - Protein S deficiency
  - Type II defects
    - V Leiden
    - Prothrombin G20210A
- Acquired
  - Autoimmune disease
  - HIT
  - Sickle cell anemia
  - Metastatic cancer
  - Nephrotic syndrome
  - Pregnancy
  - Obesity
Hypercoagulable State: Diagnosis of Thrombophilia

- CBC
- PT
  - aPTT
  - Thrombin time
  - Fibrinogen levels

Hypercoagulable State: Management

- Treat underlying cause
- Anticoagulant administration
  - Warfarin (Coumadin®)

Practice Exam Questions
The most common type of anemia in the United States is:

A. Anemia of chronic disease  
B. Folic-acid-deficiency anemia  
C. Iron-deficiency anemia. Iron-deficiency anemia is most often found in children and nonpregnant women and is the most common anemia worldwide.  
D. Pernicious anemia

In iron-deficiency anemia, lab parameters should reveal:

A. Decreased MCV and increased TIBC. The lab values associated with iron deficiency anemia are decreased MCV, decreased iron, increased TIBC, decreased ferritin, and increased transferrin.  
B. Increased MCV and decreased ferritin  
C. Increased transferrin and decreased serum iron  
D. Decreased MCV and increased ferritin level

The lab data consistent with a diagnosis of DIC is:

A. Platelet count < 110,000  
B. Fibrinogen < 100. The DIC panel shows a platelet count < 80,000, D-dimer > 2.5, prolonged PT and/or aPTT, and fibrinogen < 100.  
C. D-dimer < 2  
D. Normal PT and aPTT
Hematologic Abnormalities

**HIT** may occur as rapidly as within 24 hours of heparin therapy in patients:

A. Previously treated with heparin. HIT usually occurs 5–14 days after initiation of heparin therapy. If the patient previously received heparin, HIT can occur as rapidly as within 24 hours.

B. With DIC
C. With platelet dilution after resuscitation
D. Receiving continuous renal replacement therapy

---

**Question #4 - Answer**

HIT may occur as rapidly as within 24 hours of heparin therapy in patients:

A. Previously treated with heparin. HIT usually occurs 5–14 days after initiation of heparin therapy. If the patient previously received heparin, HIT can occur as rapidly as within 24 hours.

B. With DIC
C. With platelet dilution after resuscitation
D. Receiving continuous renal replacement therapy

---

**Question #5 - Answer**

The clotting that occurs with HIT begins when heparin binds to:

A. Fragment crystallizable receptors on activated platelets
B. Immunoglobulin G (IgG) antibodies
C. Activated platelets
D. Platelet factor 4. Heparin binds to platelet factor 4, which is released from an activated platelet. IgG antibodies recognize and bind to this complex. This complex binds to the Fc receptor on other platelets, leading to platelet activation.

---

**Question #6 - Answer**

A risk for antiphospholipid syndrome is:

A. Heparin therapy
B. Smoking
C. Systemic lupus erythematosus. Antibodies are developed against the cell membrane. It is found in patients with autoimmune diseases, and risk increases during pregnancy.
D. Obesity
Hematologic Abnormalities

The lab finding consistent with DIC is:

A. Low fibrinogen level. In DIC the platelet count will be < 80,000, the ATIII level will be decreased, the FSP between 10–100, and the fibrinogen level will be < 100.
B. Elevated platelet level
C. Normal ATIII level
D. FSP > 100

Question #7 - Answer

Multisystem Abnormalities

Progressive, cumulative organ dysfunction
Secondary to inadequate substrate/O₂
Altered host homeostasis

Multiple Organ Dysfunction Syndrome (MODS): Definition
MODS: Etiology
- Shock
- SIRS → Septic shock
- ARDS
  - DIC
  - Acute tubular necrosis

MODS: Theories
- "One-hit" model
  - Massive insult
  - Severe SIRS
- "Two-hit" model
  - Moderate insult
  - Moderate SIRS
  - Second insult
  - Late MODS
- "Persistent-hit" model
  - Insult → recovery → insult → sepsis/inflammation → MODS → late mortality

MODS: Mortality Rates
- 30% overall in tertiary ICUs
  - 1 organ = 1%
  - 2 organs = 11%
  - 3 organs = 50%
  - 4 organs = 75%

"One-hit" model
- Massive insult
- Severe SIRS
- Early MODS

"Two-hit" model
- Moderate insult
- Moderate SIRS
- Second insult
- Late MODS

"Persistent-hit" model
- Insult → recovery → insult → sepsis/inflammation → MODS → late mortality
MODS: Assessing System Failure

Cardiovascular (1 or more)
- SBP < 60 mm Hg
- HR < 40 or > 200 bpm
- MAP < 50 mm Hg
- Cardiac arrest
- Continuous IV infusion of inotropic agent to maintain BP or CI

Pulmonary (1 or more)
- RR > 70
- Mechanical ventilation
- pH < 7.2 with normal PaCO$_2$
- PaO$_2$ < 40; PaCO$_2$ > 65
- P/F ratio < 200 mm Hg

MODS: Assessing System Failure

Neurological
- GCS < 5 with no sedation
- Fixed, dilated pupils
- ICP > 20 mm Hg for > 20 minutes

Renal (1 or more)
- Urine output < 0.5 mL/kg/h x 4 hours or 300 mL/24 h
- BUN > 100 mg/dL
- Serum creatinine > 1.2
- Requires renal replacement therapy

Hepatic (presence of 3 or more)
- PT
- AST > 100 µ/L
- Serum albumin < 30 g/L
- Conjugated bilirubin > 10 mmol/L

Hematologic (2 or more)
- Hgb < 5 g/dL
- WBCs < 3,000 cell/mm$^3$
- PLTs < 20,000 mm$^3$
- DIC
  - Prolonged PT or aPTT
  - FSPs > 10
  - D-dimer > 2
  - Fibrinogen < 100

MODS: Assessing System Failure

Multisystem Abnormalities
MODS: Identification of High-Risk Patient

**SIRS**
- Infection
- Trauma
- Ischemic or reperfusion injury
- Single lactate > 4 or more at initial presentation
- Failure to clear lactate levels during first 6 hours associated with increased morbidity and mortality
- C-reactive protein (CRP)
- Brain natriuretic peptide (BNP)

**MODS: Identification of High-Risk Patient**
- Procalcitonin
- Interleukin-6
- Protein C
- Altered mental status
- Band count > 5%
- Infection of lower respiratory tract
- Residence in nursing home

**Sepsis**
- Ninth leading cause of death
- 50% develop due to hospital-associated infection
- Activation of immune/inflammatory response
**SIRS**
- Immune cellular interactions
  - Endotoxin
  - Arachidonic acid metabolites
  - Tumor necrosis factor
  - Complement
- Early systemic effects
  - Alteration in myocardia function
  - Maldistribution of blood flow
  - Alteration in $O_2$ delivery and utilization

**SIRS: Criteria**
- Temperature
  - $> 100.4^\circ F$ or $< 96.8^\circ F$ ($> 38^\circ C$ or $< 36^\circ C$)
- HR
  - $> 90$ bpm
- RR
  - $> 20$
  - $PaCO_2 < 32$ mm Hg
- WBC
  - $> 12,000$ or $< 4,000$
  - $> 10\%$ bands

**Early Sepsis: Septicemia**
- Onset: minutes to hours
- Clinical signs of infection
- Improved CI
  - Decreased afterload and increased HR
- Peripheral vasodilation
- Systemic edema
- Relative hypovolemia
Early Sepsis: Signs and Symptoms

- Tachycardia
- Widened pulse pressure
- Tachypnea
- Decreased level of consciousness
- Thrombocytopenia

Transition From Early Sepsis to Severe Sepsis

- Occurs most often during first 24 hours of hospitalization
- Increase in mortality of 20%–46%
- Decreased O₂ delivery and CV insufficiency accompanies transition
- Usually not detected by vital signs or SIRS criteria

O₂ Transport and Utilization

- Global tissue hypoxia resulting from innate immune response
- Hypoxia stimulates further inflammation
- O₂ delivery is insufficient to meet demands at cellular level
- Results in increased lactate levels
- SvO₂ < 65% ScvO₂ < 70%
  - Results in increased lactate
  - Suggests presence of global tissue hypoxia
  - Greater extraction by tissues
**O₂ Transport and Utilization**

- Normal SvO₂, ScvO₂, and lactate levels suggest O₂ supply meets demands.
- High SvO₂, ScvO₂, and lactate levels indicate that despite adequate global systemic O₂ delivery, tissues are unable to extract O₂.
  - Tissue hypoxia further activates endothelial mediators:
    - Loss of vascular integrity
    - Inflammatory cytokines
    - Procoagulants
    - Reduced fibrinolysis

**Early Septic Shock**

- Hypotension
- Metabolic acidosis
  - Increased capillary permeability
    - Systemic and pulmonary edema
  - Hypoxemia

**Late: Cardiogenic Septic Shock**

- Severe LV dysfunction → decreased CI
- Increased peripheral vasoconstriction
- Cold extremities
  - Hypotension
  - Severe acidosis
**Septic Shock: Treatment**
- Support airway and ventilation
- Support CV function
- Prevent infection
- Provide nutritional support

**First 6 Hours**
- Resuscitation
  - Cultures
  - Antibiotics
- Early goal-directed therapy
- Delays in management of sepsis result in high mortality rates and increased utilization of hospital resources

**Early Goal-Directed Therapy**
- CVP 8–12 mm Hg
- MAP > 65 mm Hg
- Urine output > 0.5 mL/kg/hour
- ScvO$_2$ > 70% or SvO$_2$ > 65%
Sepsis: Resuscitation Algorithm

Multisystem Abnormalities

Initial Identification
- Increased serum lactate
- Identifies tissue hypoperfusion in patients who are not hypotensive
- Early antimicrobial therapy
  - Empiric antibiotics within 4–8 hours of hospital presentation
  - Surviving Sepsis Campaign recommends antibiotics within 1 hour

Source of infection and local hospital sensitivity and resistance patterns
- Surgical consultation
- Resistant organisms when patients live in nursing homes or are IV drug users
**Volume Therapy**
- Repletion of intravascular volume
- Rapid repeated 500 mL boluses of either crystalloid or colloid (20 mL/kg)
- CVP 8–12 mm Hg
- 5% albumin or normal saline
- Found no significant difference in mortality between the groups

**Vasoactive Agents**
- Norepinephrine 2–20 mcg/min
- Vasopressin 0.01–0.04 units/min
- Vasopressin and Septic Shock Trial (VASST) study
- Phenylephrine 40–300 mcg/min
- Dopamine 5–20 mcg/kg/min
- Adverse consequences
  - Splanchnic hypoperfusion
  - Excess tachycardia
  - Coronary ischemia

**IIR Management**
- RBC replacement
  - If ScvO2 remains < 70% after optimization of preload, afterload, O2 sat
  - Increase Hct to 30%
  - Optimal erythrocyte transfusion
  - Fresh vs. stored blood
- Inotropic therapy
  - Sepsis may be accompanied by myocardial suppression in 10%–15% of patients
  - Dobutamine titrated at 2.5 mcg/kg/min every 20–30 min to ScvO2 of 70%
  - Milrinone
    - Long half-life
    - Accumulates in renal failure
**IIR Management**

- Decreasing $O_2$ Consumption
  - Intubation
  - Sedation
  - Analgesia
  - Control fever

---

**Steroid Therapy**

- Theoretical benefits
  - Possible inhibition of massive inflammatory cascade
  - Inflammatory cascade leads to:
    - Inadequate release or response to adrenocorticotropic hormone (ACTH)
    - Peripheral steroid resistance at receptor level

- On vasopressors
  - Draw random cortisol
  - < 25 mcg/mL give corticosteroids

- Not on vasopressors
  - Draw baseline random cortisol level
  - Cortisol stimulating test
    - Levels at 30 and 60 min
    - If difference is < 9 give corticosteroids

---

**Steroid Therapy**

- Low doses of hydrocortisone decreased requirement of vasopressors and lowered mortality
  - Hydrocortisone 50 mg IV every 6 hours
  - Dexamethasone 4 mg IV every 8 hours
  - Fludrocortisone 100 mcg (PFT) daily
**Practice Exam Questions**

**Question #1 - Answer**

The parameter required to meet the SIRS criteria is:

A. HR 110 bpm. SIRS criteria: HR > 90; WBC < 4,000 or > 12,000; PaCO₂ < 32; temperature < 36°C or > 38°C.

B. WBC 4,500

C. PaCO₂ 35 mm Hg

D. Temperature 37.4°C
A sign or symptom consistent with alcohol withdrawal is:

The earliest definitive indicator of the development of distributive shock is:

A. Increased HR
B. Widening pulse pressure. Distributive shock is characterized by vasodilation, which results in dropped diastolic pressure and widened pulse pressure. Increased HR occurs in most shock (except neurogenic). Altered LOC is a sign of all shocks as perfusion to the brain decreases.
C. Decreased systolic pressure
D. Altered level of consciousness

The mortality rate associated with 3 organ failures is:

A. 1%
B. 11%
C. 50%. One organ failure is 1% mortality, 2 organs failing is 11% mortality, 3 is 50%, and 4 failing organs results in 75% mortality.
D. 75%

A sign or symptom consistent with CV failure is:

A. HR 180 bpm
B. MAP < 65 mm Hg
C. SBP < 90 mm Hg
D. Continuous use of dobutamine. SBP < 60 mm Hg; HR < 40 or > 200; MAP < 50 mm Hg; cardiac arrest or continuing use of inotropic drugs to maintain CI or BP.
A patient with suspected septicemia had cultures obtained and antibiotics started. The next intervention would be to administer:

A. Normal saline to increase CVP to 8 mm Hg. The priority is giving fluids. Next would be a vasopressor. Later in management consider RBCs and steroids.
B. Packed red blood cells to boost O₂-carrying capacity
C. Norepinephrine to improve BP
D. Corticosteroids to treat adrenal insufficiency

The pathophysiology of distributive shock is:

A. The intravascular compartment fills beyond capacity allowing fluid to leak out, compressing vital organs
B. The circulating volume causes excessive constriction of the vessels, causing blood pooling
C. Widely fluctuating BPs stimulate vascular collapse, causing severe alterations in peripheral perfusion
D. Although the circulating volume is intact, excessive vascular dilation causes drastic drops in BP. The pathophysiology of distributive shock is massive vascular dilation and possible capillary leak leading to a drop in BP.