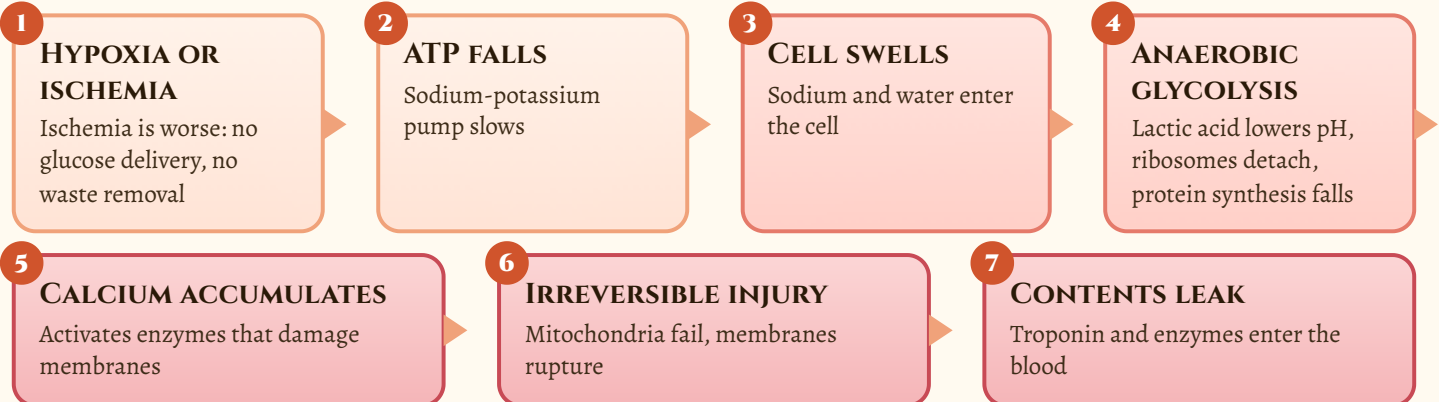


# HOLLOWMERE: CELLS, INFLAMMATION, HEALING AND PAIN

## 1 CELL INJURY AND HYPOXIA

### ◆ HYPOXIC CELL INJURY CASCADE



### ◆ MARKERS OF CELL INJURY

#### TROPONIN I

Normal Below 0.04 ng/mL

**Elevated**

Myocyte death: myocardial infarction

#### LACTATE

Normal 0.5 to 2.0 mmol/L

**Above 2.0**

Anaerobic metabolism from tissue hypoxia

#### ALT

Normal 7 to 56 units/L

**Markedly elevated**

Hepatocyte injury, such as acetaminophen toxicity

#### SERUM CALCIUM

Normal 8.5 to 10.5 mg/dL

**Normal**

Dystrophic calcification still occurs in damaged tissue



*No oxygen, no ATP: the pump fails, sodium and water rush in, and the cell swells.*

### WRITTEN NOTES: CELL INJURY AND HYPOXIA

- Hypoxia is the most common cause of cell injury; ischemia (reduced blood flow) is worse because it also stops glucose delivery and waste removal.
- First event: ATP falls, the sodium-potassium pump slows, sodium and water enter and the cell swells.
- Next: anaerobic glycolysis lowers pH, ribosomes detach, protein synthesis falls and calcium accumulates.

- Irreversible injury: severe mitochondrial damage and membrane rupture; cell contents such as troponin leak into blood.
- Other causes: free radicals and reperfusion, chemicals (acetaminophen depletes glutathione), infection, physical and immune injury.
- Reversible accumulations include fatty change in the liver; dystrophic calcification occurs in damaged tissue with normal serum calcium.

## 2 CELLULAR ADAPTATIONS

### ◆ CHANGES IN SIZE AND NUMBER

| FEATURE | ATROPHY                                                     | HYPERTROPHY                                  | HYPERPLASIA                                           |
|---------|-------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------|
| CHANGE  | Smaller cells                                               | Larger cells                                 | More cells                                            |
| CAUSE   | Disuse, denervation, ischemia, poor nutrition, hormone loss | Increased workload                           | Hormones or growth signals                            |
| EXAMPLE | Casted limb muscle                                          | Left ventricle in hypertension               | Uterus in pregnancy, endometrium with excess estrogen |
| TISSUE  | Any tissue                                                  | Includes nondividing cells like heart muscle | Only tissues that can divide                          |

### ◆ CHANGES IN CELL TYPE

| FEATURE     | METAPLASIA                               | DYSPLASIA                               |
|-------------|------------------------------------------|-----------------------------------------|
| DEFINITION  | One mature cell type replaced by another | Disordered size, shape and organization |
| EXAMPLE     | Barrett esophagus, smoker's bronchi      | Cervical changes on a Pap test          |
| REVERSIBLE  | Yes, if the irritant is removed          | Early stages may regress                |
| CANCER RISK | Can progress to dysplasia                | Precancerous                            |



*Atrophy shrinks cells, hypertrophy enlarges them, hyperplasia adds cells, metaplasia swaps type, dysplasia disorders them.*

### WRITTEN NOTES: CELLULAR ADAPTATIONS

- Atrophy: smaller cells from disuse, denervation, ischemia, poor nutrition or loss of hormones.
- Hypertrophy: larger cells from increased workload, as in the left ventricle with hypertension.
- Hyperplasia: more cells in tissues that can divide; physiologic in pregnancy, pathologic with excess estrogen.
- Metaplasia: one mature cell type replaced by another, such as Barrett esophagus or smoker's bronchi; reversible.

- Dysplasia: disordered size, shape and organization; precancerous, as found on Pap tests.

### 3 NECROSIS AND APOPTOSIS

#### ◆ APOPTOSIS VERSUS NECROSIS

| FEATURE      | APOPTOSIS             | NECROSIS              |
|--------------|-----------------------|-----------------------|
| CONTROL      | Programmed            | Uncontrolled          |
| ENERGY       | Requires ATP          | Follows ATP loss      |
| CELL         | Shrinks and fragments | Swells and ruptures   |
| INFLAMMATION | None                  | Triggers inflammation |
| EXAMPLE      | Normal cell turnover  | Infarction, toxins    |

#### ◆ NECROSIS PATTERNS AND GANGRENE

##### COAGULATIVE

- Ischemic heart and kidney
- Cell outlines preserved

##### LIQUEFACTIVE

- Brain infarcts
- Abscesses

##### CASEOUS AND FAT

- Caseous: tuberculosis
- Fat: pancreatitis

##### GANGRENE

- Dry: arterial, mummified
- Wet: infected and moist
- Gas: Clostridium, crepitus, emergency



*Apoptosis is a quiet exit; necrosis is a messy explosion that calls in inflammation.*

#### WRITTEN NOTES: NECROSIS AND APOPTOSIS

- Apoptosis is programmed, energy dependent and quiet, with no inflammation.
- Necrosis is uncontrolled swelling and rupture that triggers inflammation.
- Coagulative necrosis: ischemic heart and kidney, outlines preserved.
- Liquefactive necrosis: brain infarcts and abscesses. Caseous necrosis: tuberculosis. Fat necrosis: pancreatitis.
- Dry gangrene is arterial and mummified; wet gangrene is infected and moist; gas gangrene (Clostridium) causes crepitus and is an emergency.

## 4 ACUTE INFLAMMATION

### ◆ CARDINAL SIGNS OF INFLAMMATION

**R** **RUBOR**  
Redness from  
vasodilation

**C** **CALOR**  
Heat from increased  
blood flow

**T** **TUMOR**  
Swelling from  
increased  
permeability

**D** **DOLOR**  
Pain from mediators  
and pressure

**F** **FUNCTIO LAESA**  
Loss of function

### ◆ ACUTE INFLAMMATORY RESPONSE

**1** **BRIEF  
VASOCONSTRICTION**  
Seconds after injury

**2** **VASODILATION  
AND LEAK**  
Histamine,  
prostaglandins,  
bradykinin; protein-rich  
exudate forms

**3** **MARGINATION  
AND ADHESION**  
Leukocytes line up and  
stick to endothelium

**4** **DIAPYDEDESIS**  
Neutrophils squeeze out  
of vessels first

**5** **CHEMOTAXIS**  
Cells follow chemical signals to the  
site

**6** **PHAGOCYTOSIS**  
Microbes and debris engulfed

**7** **SYSTEMIC SIGNS**  
Fever, leukocytosis with left shift,  
rising CRP and ESR



*Neutrophils arrive first; vasodilation brings redness and heat, leaky vessels bring swelling.*

### WRITTEN NOTES: ACUTE INFLAMMATION

- Cardinal signs: redness and heat (vasodilation), swelling (permeability), pain (mediators and pressure), loss of function.
- Vascular stage: brief vasoconstriction, then vasodilation and leakage of protein-rich exudate.
- Cellular stage: margination, adhesion, diapedesis, chemotaxis, phagocytosis; neutrophils arrive first.
- Mediators: histamine (mast cells), prostaglandins (blocked by NSAIDs), leukotrienes, bradykinin, complement, cytokines.
- Exudates: serous (clear), serosanguineous (pink), fibrinous (sticky), purulent (pus).
- Systemic signs: fever, leukocytosis with left shift, rising CRP and ESR.

## 5 CHRONIC INFLAMMATION

### ◆ ACUTE VERSUS CHRONIC INFLAMMATION

| FEATURE    | ACUTE                   | CHRONIC                                              |
|------------|-------------------------|------------------------------------------------------|
| DURATION   | Days                    | Weeks to years                                       |
| MAIN CELLS | Neutrophils             | Macrophages and lymphocytes                          |
| CAUSE      | Injury or new infection | Persistent infection, autoimmunity, foreign material |
| HALLMARK   | Exudate and swelling    | Destruction with fibrosis; granulomas                |
| OUTCOME    | Resolution or healing   | Scarring, loss of function                           |
| EXAMPLE    | Cellulitis, sprain      | Tuberculosis, rheumatoid arthritis                   |

### ◆ INFLAMMATION MARKERS

#### WBC

Normal 4,500 to 11,000/mm<sup>3</sup>

**Above 11,000**

Leukocytosis: infection or inflammation

#### BANDS

Normal 0 to 5% of WBC

**Increased**

Left shift: acute bacterial infection

#### CRP

Normal Below 1.0 mg/dL

**Elevated**

Rises within hours, falls quickly with resolution

#### ESR

Normal Men 0 to 15, women 0 to 20 mm/hr

**Elevated**

Slow, nonspecific; tracks chronic disease activity



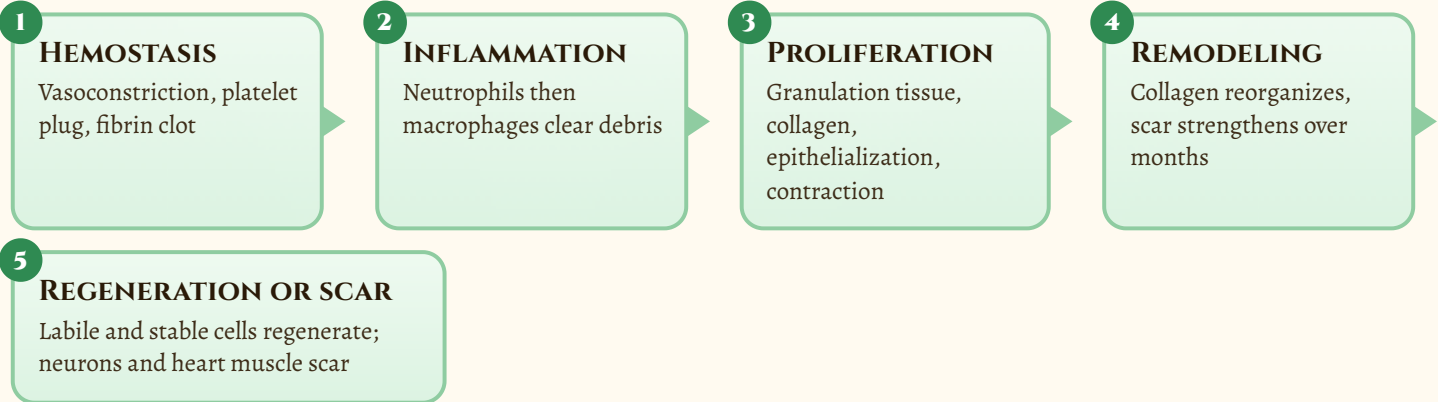
*When the cause never leaves, macrophages and lymphocytes take over and the tissue scars.*

### WRITTEN NOTES: CHRONIC INFLAMMATION

- Develops when the cause persists, such as chronic infection, autoimmunity or foreign material.
- Macrophages and lymphocytes dominate; tissue destruction and fibrosis happen together.
- Granulomas wall off agents that cannot be destroyed, such as tuberculosis.
- Outcome is often scarring with loss of function, as in rheumatoid arthritis joints.

## 6 WOUND HEALING AND REPAIR

### ◆ PHASES OF WOUND HEALING



### ◆ HEALING DELAYS AND COMPLICATIONS

#### DELAYS HEALING

- Diabetes
- Corticosteroids
- Poor perfusion or smoking
- Infection
- Low protein, vitamin C, zinc
- Older age

#### PRIMARY VS SECONDARY

- Primary: edges closed, small scar
- Secondary: open, more granulation, larger scar

#### COMPLICATIONS

- Dehiscence: edges separate
- Evisceration: organs protrude
- Cover with sterile saline-moist dressing
- Keloid and contracture



*Healing needs blood flow, protein, vitamin C and zinc; diabetes, steroids and smoking slow it.*

### WRITTEN NOTES: WOUND HEALING AND REPAIR

- Phases: hemostasis, inflammation, proliferation (granulation, collagen, epithelialization, contraction), remodeling.
- Labile and stable cells can regenerate; permanent cells such as neurons and cardiac muscle heal by scar.
- Primary intention: edges closed, small scar. Secondary intention: open wound, more granulation and contraction, larger scar.
- Delays: diabetes, corticosteroids, poor perfusion, infection, smoking, malnutrition (protein, vitamin C, zinc), older age.
- Complications: dehiscence, evisceration (cover with sterile saline-moistened dressing, call surgeon), keloid, contracture.

## ◆ TYPES OF PAIN

| FEATURE      | SOMATIC                        | VISCERAL                          | NEUROPATHIC                          |
|--------------|--------------------------------|-----------------------------------|--------------------------------------|
| SOURCE       | Skin, muscle, bone, joints     | Organs                            | Damaged nerves                       |
| QUALITY      | Sharp or aching                | Vague, cramping, pressure         | Burning, shooting, tingling          |
| LOCATION     | Well localized                 | Poorly localized, may be referred | Follows nerve distribution           |
| FIBERS       | A-delta fast, C slow           | Mostly C fibers                   | Abnormal nerve firing                |
| BEST OPTIONS | NSAIDs, acetaminophen, opioids | Opioids, treat the cause          | Gabapentinoids, some antidepressants |

## ◆ ANALGESIC LADDER ESSENTIALS

**IBUPROFEN***Advil, Motrin***NSAID****USED FOR** Inflammatory and musculoskeletal pain, fever**WATCH** GI bleeding, kidney injury; give with food**ACETAMINOPHEN***Tylenol***NON-OPIOID ANALGESIC****USED FOR** Mild to moderate pain, fever**WATCH** Hepatotoxic; count hidden doses in combinations**MORPHINE***Duramorph (IV), MS Contin (oral ER)***OPIOID AGONIST****USED FOR** Severe acute pain**WATCH** Check sedation and respirations; keep naloxone ready**NALOXONE***Narcan***OPIOID ANTAGONIST****USED FOR** Opioid respiratory depression**WATCH** Short acting; sedation may return, pain returns**GABAPENTIN***Neurontin***GABAPENTINOID****USED FOR** Neuropathic pain**WATCH** Dizziness, falls; taper, adjust for kidney function*Pain is whatever the client says it is; burning, shooting pain points to nerves.*

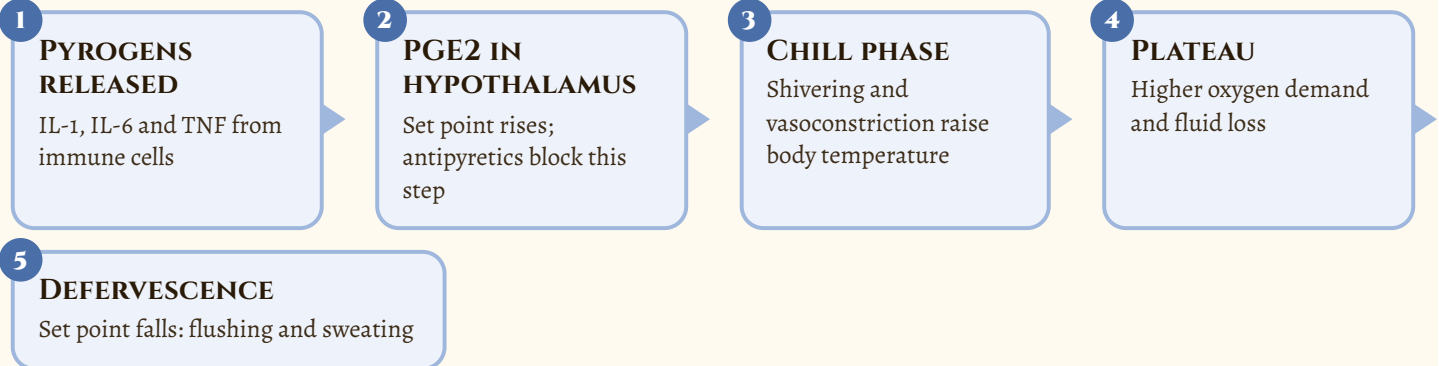
## WRITTEN NOTES: PAIN

- Nociception steps: transduction, transmission, modulation and perception.
- A-delta fibers carry fast, sharp pain; C fibers carry slow, dull, burning pain.
- Somatic pain is localized; visceral pain is vague and may be referred; neuropathic pain burns and shoots.

- Gate control: touch fibers can close the spinal gate; endorphins inhibit substance P release.
- Chronic pain outlasts healing, is no longer protective and often involves sensitization (allodynia, hyperalgesia).
- Self report is the best measure; use nonverbal scales when clients cannot report.

## 8 FEVER AND HYPERTHERMIA

### ◆ HOW FEVER DEVELOPS



### ◆ FEVER VERSUS HYPERTHERMIA

| FEATURE      | FEVER                              | HYPERTHERMIA                  |
|--------------|------------------------------------|-------------------------------|
| SET POINT    | Raised by pyrogens                 | Normal, overwhelmed by heat   |
| CAUSE        | Infection, inflammation            | Heat stroke, exertion in heat |
| ANTIPYRETICS | Effective                          | Do not work                   |
| TREATMENT    | Treat cause, antipyretics, fluids  | Active cooling                |
| OLDER ADULTS | May be absent; watch for confusion | High risk                     |



*Fever raises the set point so antipyretics work; heat stroke overwhelms a normal set point, so cool.*

### WRITTEN NOTES: FEVER AND HYPERTHERMIA

- Pyrogens (IL-1, IL-6, TNF) induce PGE<sub>2</sub>, which raises the hypothalamic set point.
- Chill phase: shivering and vasoconstriction; defervescence: flushing and sweating.
- Benefits: slows some microbes and boosts immune activity; costs: higher oxygen demand and fluid loss.
- Older adults may have little fever with serious infection; watch for confusion.
- Hyperthermia (heat stroke) has a normal set point; cool the body, because antipyretics do not work.



## CLINICAL PEARLS

- ATP falls first: when a cell loses oxygen, think pump failure, sodium in, water in, cell swells.
- Size versus number: hyperTROPHY means bigger cells, hyperPLASIA means more cells, METApLasia means a swapped cell type, DYSpLasia means disordered and precancerous.
- Necrosis by organ: heart and kidney coagulative, brain liquefactive, TB caseous, pancreas fat.
- Neutrophils first, macrophages second, lymphocytes when it lingers: the cell type tells you acute versus chronic.
- Fever is a raised set point (antipyretics work); hyperthermia is a normal set point overwhelmed (cool the body).



## KEY MEDICATIONS

### ◆ MEDICATIONS FOR CELLS, INFLAMMATION, HEALING AND PAIN



#### IBUPROFEN

*Advil, Motrin*

##### NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

**USED FOR** Acute inflammation, musculoskeletal pain and fever

**WATCH** Can cause GI bleeding and kidney injury; give with food and avoid in clients with ulcers, kidney disease or bleeding risk.



#### ACETAMINOPHEN

*Tylenol*

##### NON-OPIOID ANALGESIC AND ANTIPYRETIC

**USED FOR** Fever and mild to moderate pain

**WATCH** Hepatotoxic in overdose; keep within the daily maximum (commonly 3 to 4 g for adults) and check combination products for hidden acetaminophen.



#### METHYLPREDNISOLONE

*Solu-Medrol, Medrol*

##### CORTICOSTEROIDS

**USED FOR** Severe or chronic inflammatory conditions

**WATCH** Mask infection, raise blood glucose and delay healing; long courses must be tapered, never stopped abruptly.



#### MORPHINE

*Duramorph (IV), MS Contin (oral ER)*

##### OPIOID ANALGESICS

**USED FOR** Severe acute pain

**WATCH** Monitor sedation level and respiratory rate before and after doses, and keep naloxone available.



#### GABAPENTIN

*Neurontin, Gralise*

##### GABAPENTINOIDS

**USED FOR** Neuropathic pain such as diabetic neuropathy and postherpetic neuralgia

**WATCH** Cause dizziness and sedation with fall risk; do not stop abruptly and adjust the dose in kidney impairment.

# TIDEWATER FENS: FLUIDS, ELECTROLYTES AND ACID BASE

Dr. Akash Garg · Dr. Garg Learning

## 1 BODY FLUIDS AND EDEMA

### ◆ FLUID VOLUME DEFICIT VERSUS EXCESS

| FEATURE          | DEFICIT                              | EXCESS                           |
|------------------|--------------------------------------|----------------------------------|
| PULSE AND BP     | Tachycardia, orthostatic hypotension | Bounding pulse, hypertension     |
| NECK VEINS       | Flat                                 | Jugular venous distension        |
| LUNGS AND TISSUE | Dry mucous membranes                 | Crackles, edema                  |
| WEIGHT           | Rapid loss                           | Rapid gain                       |
| URINE            | Low volume, concentrated             | Often dilute                     |
| LABS             | Rising hematocrit and BUN            | Falling hematocrit from dilution |

### ◆ IV FLUID TONICITY

| FEATURE     | ISOTONIC                     | HYPOTONIC                           | HYPERTONIC                         |
|-------------|------------------------------|-------------------------------------|------------------------------------|
| EXAMPLES    | 0.9% saline, lactated Ringer | 0.45% saline, D5W once metabolized  | 3% saline                          |
| WATER MOVES | Stays in vessels             | Into cells                          | Out of cells                       |
| MAIN USE    | Volume replacement           | Cellular dehydration                | Severe symptomatic hyponatremia    |
| CAUTION     | Fluid overload               | Cerebral edema, avoid with high ICP | Overload, overly rapid sodium rise |



*One kilogram gained overnight is about one liter of fluid; weigh daily, same time, same scale.*

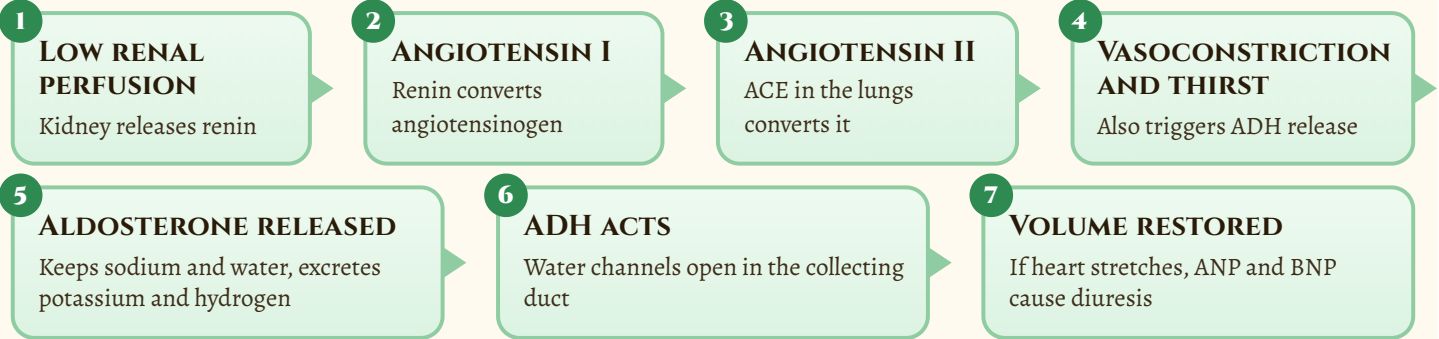
### WRITTEN NOTES: BODY FLUIDS AND EDEMA

- About two thirds of body water is intracellular and one third extracellular (mostly interstitial).
- Edema mechanisms: increased capillary hydrostatic pressure (heart failure), decreased oncotic pressure (low albumin), increased permeability (burns, inflammation) and lymphatic obstruction.
- Fluid deficit: tachycardia, orthostatic hypotension, dry membranes, concentrated urine, rising hematocrit and BUN.
- Fluid excess: weight gain, edema, crackles, jugular venous distension, bounding pulse.
- A rapid weight change of 1 kg equals about 1 liter of fluid; weigh daily at the same time.

- Isotonic (0.9% saline, lactated Ringer) expands volume; hypotonic (0.45% saline, D5W once metabolized) moves water into cells; hypertonic (3% saline) pulls water out of cells.

## 2 VOLUME HORMONES: RAAS, ADH, ANP AND BNP

### ◆ RAAS: SAVING VOLUME



### ◆ DRUGS THAT WORK ON VOLUME



#### FUROSEMIDE

*Lasix*

##### LOOP DIURETIC

**USED FOR** Fluid overload, pulmonary edema

**WATCH** Low potassium, hypotension; slow IV push for ototoxicity



#### SPIRONOLACTONE

*Aldactone*

##### ALDOSTERONE ANTAGONIST

**USED FOR** Heart failure, ascites

**WATCH** Hyperkalemia; avoid salt substitutes



#### LISINOPRIL

*Zestril, Prinivil*

##### ACE INHIBITOR

**USED FOR** Hypertension, heart failure

**WATCH** Angioedema, hyperkalemia, dry cough



#### LOSARTAN

*Cozaar*

##### ANGIOTENSIN II RECEPTOR BLOCKER

**USED FOR** Hypertension, ACE inhibitor cough

**WATCH** Hyperkalemia, avoid in pregnancy



#### POTASSIUM CHLORIDE

*Klor-Con, K-Tab*

##### ELECTROLYTE REPLACEMENT

**USED FOR** Hypokalemia, often with loop diuretics

**WATCH** Never IV push; confirm urine output



*RAAS and ADH save volume; ANP and BNP spend it when a stretched heart cries for relief.*

### WRITTEN NOTES: VOLUME HORMONES: RAAS, ADH, ANP AND BNP

- Low renal perfusion triggers renin; renin forms angiotensin I; ACE forms angiotensin II.
- Angiotensin II causes vasoconstriction, aldosterone release, ADH release and thirst.

- Aldosterone reabsorbs sodium and water and secretes potassium and hydrogen.
- ADH responds to rising osmolality or falling volume and adds water channels in the collecting duct.
- ANP and BNP are released when the heart is stretched and cause natriuresis, diuresis and vasodilation; BNP is a heart failure marker.
- ACE inhibitors and aldosterone antagonists raise potassium; loop diuretics lower it.

### 3 SODIUM

#### ◆ SODIUM AND WATER LABS

##### SODIUM

Normal 135 to 145 mEq/L

**Below 135**

Hyponatremia: brain cells swell, confusion, seizures

##### SODIUM

Normal 135 to 145 mEq/L

**Above 145**

Hypernatremia: brain cells shrink, thirst, restlessness

##### SERUM OSMOLALITY

Normal 275 to 295 mOsm/kg

**Above 295**

Water deficit, triggers thirst and ADH

##### URINE SPECIFIC GRAVITY

Normal 1.005 to 1.030

**Above 1.030**

Concentrated urine: dehydration or excess ADH

#### ◆ HYPONATREMIA VERSUS HYPERNATREMIA

| FEATURE          | HYPONATREMIA                                           | HYPERNATREMIA                             |
|------------------|--------------------------------------------------------|-------------------------------------------|
| BRAIN CELLS      | Swell                                                  | Shrink                                    |
| SIGNS            | Headache, confusion, seizures                          | Thirst, restlessness, seizures            |
| CAUSES           | GI loss replaced with water, heart failure, excess ADH | Poor water intake, water loss             |
| CORRECT TOO FAST | Osmotic demyelination                                  | Cerebral edema                            |
| NURSING FOCUS    | Seizure precautions, fluid restriction if dilutional   | Replace water slowly, seizure precautions |



*Sodium problems are water problems in the brain: low swells cells, high shrinks them.*

#### WRITTEN NOTES: SODIUM

- Normal sodium is about 135 to 145 mEq/L; sodium disorders are mostly water disorders and cause neurologic signs.

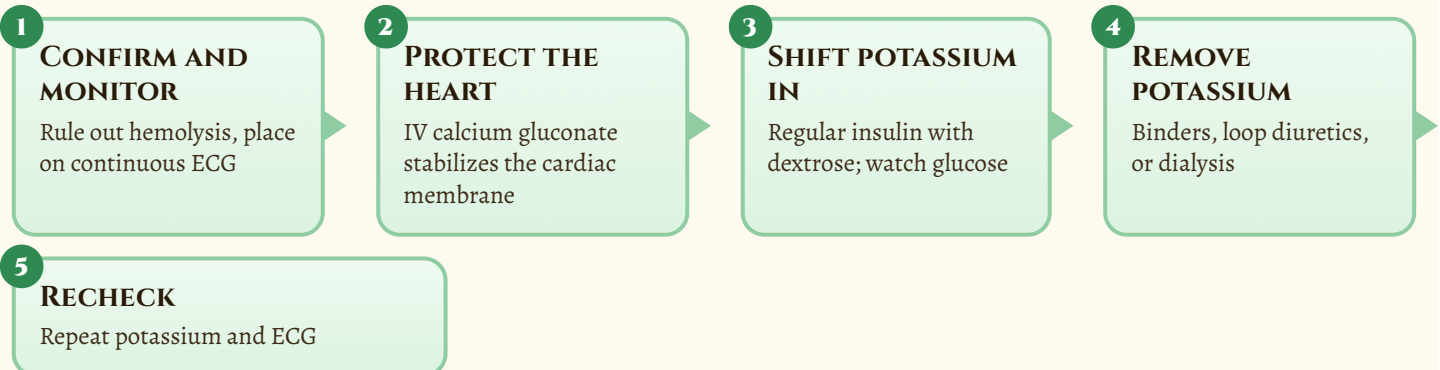
- Hyponatremia: water moves into brain cells; confusion, headache, seizures. Causes include GI loss with water replacement, heart failure and excess ADH.
- Hypernatremia: brain cells shrink; thirst, restlessness, seizures. Causes include poor water intake and water loss.
- Correct chronic sodium disorders slowly: too fast raising risks osmotic demyelination, too fast lowering risks cerebral edema.

## 4 POTASSIUM

### ◆ HYPOKALEMIA VERSUS HYPERKALEMIA

| FEATURE        | HYPOKALEMIA (BELOW 3.5)                                          | HYPERKALEMIA (ABOVE 5.0)                                          |
|----------------|------------------------------------------------------------------|-------------------------------------------------------------------|
| ECG            | Flat T waves, U waves                                            | Peaked T waves, wide QRS                                          |
| MUSCLE AND GUT | Weakness, cramps, ileus                                          | Weakness, paresthesias                                            |
| DANGER         | Dysrhythmias, digoxin toxicity                                   | Cardiac arrest                                                    |
| CAUSES         | Diuretics, vomiting, diarrhea, insulin, alkalosis, low magnesium | Kidney failure, potassium-sparing drugs, acidosis, cell breakdown |
| CHECK FIRST    | Magnesium level                                                  | Hemolyzed sample                                                  |

### ◆ EMERGENCY HYPERKALEMIA TREATMENT



*Potassium is a heart story: protect the heart with calcium, shift with insulin, then remove.*

### WRITTEN NOTES: POTASSIUM

- Normal potassium is about 3.5 to 5.0 mEq/L; most is inside cells.
- Hypokalemia: weakness, ileus, flat T waves, U waves, dysrhythmias, digoxin toxicity. Causes: diuretics, vomiting, diarrhea, insulin, alkalosis, low magnesium.
- Hyperkalemia: weakness, peaked T waves, wide QRS, cardiac arrest. Causes: kidney failure, potassium-sparing drugs, acidosis, cell breakdown.

- Emergency hyperkalemia: calcium gluconate to protect the heart, insulin with dextrose to shift, then remove (binders, diuretics, dialysis).
- Never give IV potassium by push; check urine output first; rule out a hemolyzed sample.

## 5 CALCIUM, MAGNESIUM AND PHOSPHATE

### ◆ CALCIUM AND MAGNESIUM: TWITCHY OR SLUGGISH

#### LOW CALCIUM OR MAGNESIUM

- Tingling and muscle cramps
- Tetany, seizures
- Chvostek and Trousseau signs
- Prolonged QT (low calcium)

#### HIGH CALCIUM OR MAGNESIUM

- Weakness, hyporeflexia
- Constipation
- Confusion
- Respiratory depression (high magnesium)

#### WATCH FOR

- Low magnesium blocks potassium correction
- Kidney failure: high phosphate, low calcium
- Refeeding drops phosphate, potassium, magnesium

### ◆ CALCIUM, MAGNESIUM AND PHOSPHATE LABS

#### TOTAL CALCIUM

Normal 8.5 to 10.5 mg/dL

Low with low albumin

Check ionized calcium before treating

#### IONIZED CALCIUM

Normal 4.5 to 5.3 mg/dL

Below 4.5

True hypocalcemia; alkalosis lowers it

#### MAGNESIUM

Normal 1.7 to 2.2 mg/dL

Below 1.7

Seen with alcohol use, poor intake

#### PHOSPHATE

Normal 2.5 to 4.5 mg/dL

Above 4.5

Kidney failure; calcium falls in opposite direction

#### ALBUMIN

Normal 3.5 to 5.0 g/dL

Below 3.5

Lowers total but not ionized calcium



*Low calcium or magnesium means twitchy nerves; high means sluggish nerves and slow breathing.*

### WRITTEN NOTES: CALCIUM, MAGNESIUM AND PHOSPHATE

- Low calcium or magnesium makes nerves excitable: tingling, cramps, tetany, Chvostek and Trousseau signs, seizures; low calcium prolongs the QT.
- High calcium or magnesium sedates nerves: weakness, hyporeflexia, constipation, confusion; high magnesium depresses breathing.
- About half of calcium is bound to albumin; low albumin lowers total but not ionized calcium; alkalosis lowers ionized calcium.
- Hypomagnesemia (alcohol use, poor intake) blocks correction of potassium and calcium.

- Calcium and phosphate move in opposite directions; kidney failure raises phosphate and lowers calcium.
- Refeeding a starved client can crash phosphate, potassium and magnesium.

## 6 ACID-BASE BASICS AND BUFFERS

### ◆ NORMAL ARTERIAL BLOOD GAS

#### PH

Normal 7.35 to 7.45

**Below 7.35 or above 7.45**

Acidemia or alkalemia

#### PACO<sub>2</sub>

Normal 35 to 45 mm Hg

**Above 45**

Respiratory acid: hypoventilation

#### HCO<sub>3</sub>

Normal 22 to 26 mEq/L

**Below 22**

Metabolic acid: base consumed or lost

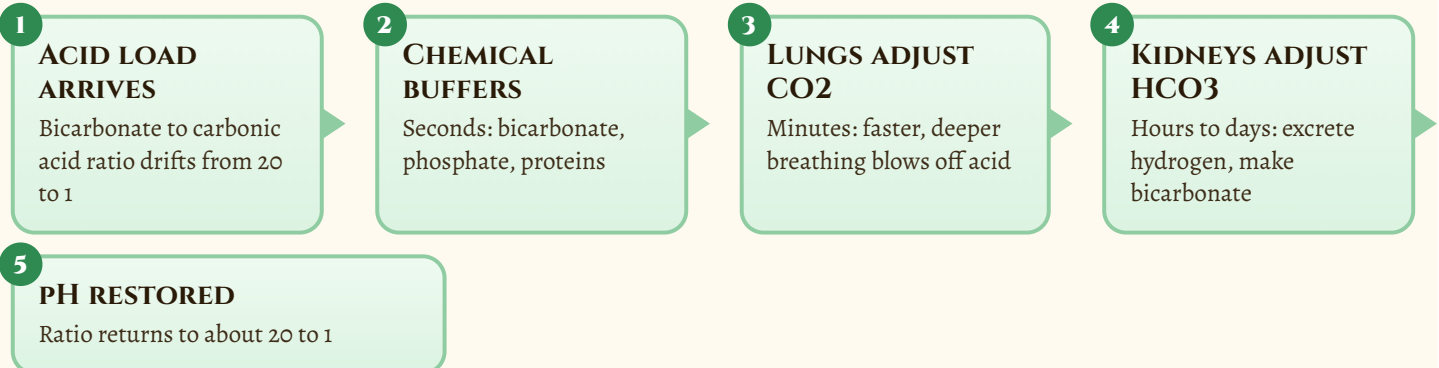
#### PAO<sub>2</sub>

Normal 80 to 100 mm Hg

**Below 80**

Hypoxemia

### ◆ THREE LINES OF PH DEFENSE



*Buffers act in seconds, lungs in minutes, kidneys over days but with the greatest capacity.*

### WRITTEN NOTES: ACID-BASE BASICS AND BUFFERS

- Normal ABG: pH 7.35 to 7.45, PaCO<sub>2</sub> 35 to 45 mm Hg, HCO<sub>3</sub> 22 to 26 mEq/L.
- CO<sub>2</sub> acts as an acid through carbonic acid; bicarbonate is the main base.
- pH stays normal while bicarbonate to carbonic acid stays about 20 to 1.
- Chemical buffers act in seconds, the lungs in minutes, the kidneys over hours to days but with the greatest capacity.
- Kidneys compensate by excreting hydrogen and making or reabsorbing bicarbonate; lungs compensate by changing ventilation.

## 7 ACID-BASE DISORDERS

### ◆ ROME FOR ABG INTERPRETATION

**R** RESPIRATORY  
Look at  $\text{PaCO}_2$

**O** OPPOSITE  
pH and  $\text{PaCO}_2$  move  
in opposite  
directions

**M** METABOLIC  
Look at  $\text{HCO}_3$

**E** EQUAL  
pH and  $\text{HCO}_3$  move  
in the same direction

### ◆ CAUSES OF THE FOUR DISORDERS

#### RESPIRATORY ACIDOSIS

- Hypoventilation
- Opioids, sedatives
- COPD
- Respiratory muscle weakness

#### RESPIRATORY ALKALOSIS

- Hyperventilation
- Anxiety, pain
- High altitude
- Early sepsis

#### METABOLIC ACIDOSIS

- High gap: lactate, ketones, toxins
- Kidney failure
- Normal gap: diarrhea
- Kussmaul breathing compensates

#### METABOLIC ALKALOSIS

- Vomiting, NG suction
- Diuretics
- Treat with saline and potassium



*ROME: respiratory, pH and  $\text{PaCO}_2$  move opposite; metabolic, pH and  $\text{HCO}_3$  move the same way.*

### WRITTEN NOTES: ACID-BASE DISORDERS

- Respiratory acidosis: hypoventilation (opioids, COPD, weakness). Respiratory alkalosis: hyperventilation (anxiety, pain, altitude, early sepsis).
- Metabolic acidosis: lactic acid, ketoacids, kidney failure, diarrhea; Kussmaul breathing compensates.
- High anion gap acidosis means added acids (lactate, ketones, toxins); diarrhea gives a normal gap.
- Metabolic alkalosis: vomiting, NG suction, diuretics; treated with saline and potassium.
- ROME: respiratory opposite (pH and  $\text{PaCO}_2$ ), metabolic equal (pH and  $\text{HCO}_3$ ).
- Compensation: other value moves to correct; partial if pH still abnormal, full if pH back in range.

### + CLINICAL PEARLS

- Starling forces: hydrostatic pressure pushes fluid out, albumin pulls it back in; edema means push too high, pull too low, leaky vessels or blocked lymph.
- Sodium is a brain story, potassium is a heart story, calcium and magnesium are nerve excitability stories (low equals twitchy, high equals sluggish).
- ABGs in three steps: pH acid or base, then which value matches it ( $\text{PaCO}_2$  respiratory,  $\text{HCO}_3$  metabolic), then is the other value moving to compensate.
- Acidosis pushes potassium out of cells (high K); alkalosis pulls it in (low K). Alkalosis also lowers ionized calcium.

- RAAS and ADH save volume; ANP and BNP spend it. Low volume turns on the savers, stretched hearts turn on the spenders.

## RX KEY MEDICATIONS

### ◆ MEDICATIONS FOR FLUIDS, ELECTROLYTES AND ACID BASE



#### FUROSEMIDE

*Lasix*

##### LOOP DIURETICS

**USED FOR** Fluid overload, pulmonary edema and edema from heart failure

**WATCH** Cause hypokalemia and hypotension; monitor potassium, blood pressure and daily weights, and give rapid IV doses slowly to avoid ototoxicity.



#### SPIRONOLACTONE

*Aldactone, CaroSpir*

##### ALDOSTERONE ANTAGONISTS (POTASSIUM-SPARING DIURETICS)

**USED FOR** Heart failure, ascites and hyperaldosteronism

**WATCH** Risk of hyperkalemia; avoid potassium supplements and salt substitutes and monitor potassium, especially with ACE inhibitors.



#### LISINOPRIL

*Zestril, Prinivil*

##### ACE INHIBITORS

**USED FOR** Hypertension and heart failure

**WATCH** Watch for angioedema, hyperkalemia and a dry cough; angioedema of the lips or tongue is an emergency.



#### POTASSIUM CHLORIDE

*Klor-Con, K-Tab*

##### POTASSIUM SUPPLEMENTS

**USED FOR** Hypokalemia

**WATCH** Never give IV potassium by push; dilute it, use an infusion pump and confirm adequate urine output first.



#### CALCIUM GLUCONATE

*Generic only*

##### CALCIUM SALTS

**USED FOR** Symptomatic hypocalcemia, severe hyperkalemia and magnesium toxicity

**WATCH** Give IV slowly with cardiac monitoring and watch the site, since leakage, especially of calcium chloride, damages tissue.

# WARDENS' BASTION: IMMUNITY, HYPERSENSITIVITY AND INFECTION

Dr. Akash Garg · Dr. Garg Learning

## 1 INNATE IMMUNITY

### ◆ LINES OF INNATE DEFENSE

#### FIRST LINE: BARRIERS

- Skin and mucous membranes
- Cilia
- Stomach acid, tears
- Normal flora

#### SECOND LINE: RESPONDERS

- Neutrophils and macrophages
- NK cells
- Complement
- Inflammation and fever

#### HELPERS

- Opsonins: IgG and C3b
- Interferons: antiviral state
- Eosinophils: parasites, allergy

### ◆ INNATE VERSUS ADAPTIVE IMMUNITY

| FEATURE     | INNATE                           | ADAPTIVE                       |
|-------------|----------------------------------|--------------------------------|
| SPEED       | Minutes to hours                 | Days on first exposure         |
| SPECIFICITY | Nonspecific patterns             | Specific antigens              |
| MEMORY      | None                             | Memory B and T cells           |
| KEY PLAYERS | Phagocytes, NK cells, complement | B cells, plasma cells, T cells |



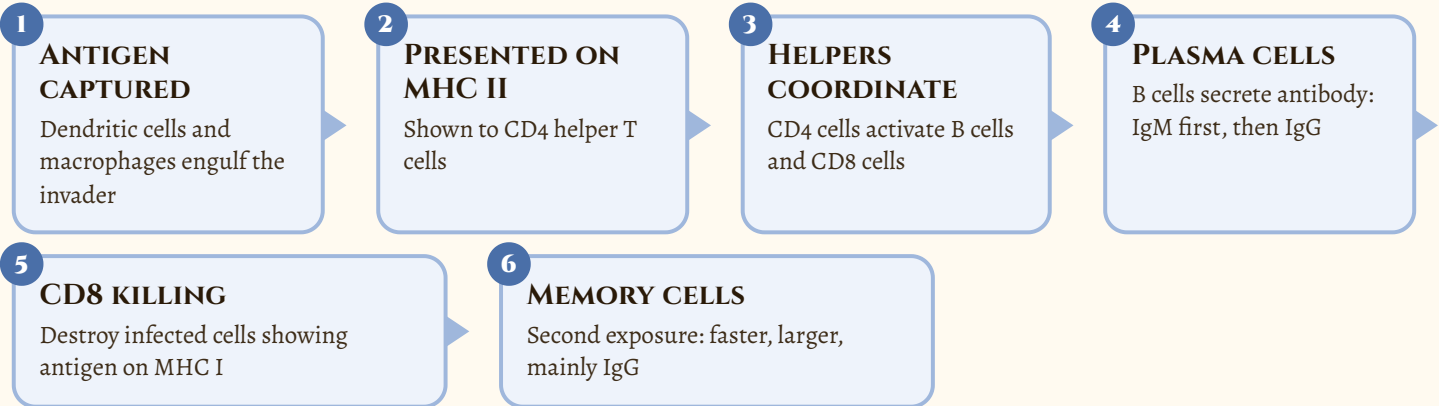
*Innate defenses are fast and nonspecific but never remember; skin is the first wall.*

### WRITTEN NOTES: INNATE IMMUNITY

- First line: skin, mucous membranes, cilia, stomach acid, tears and normal flora.
- Second line: phagocytes (neutrophils, macrophages), NK cells, complement, inflammation and fever.
- Innate responses are fast and nonspecific and do not form memory.
- Opsonization by IgG and complement C3b helps phagocytes engulf microbes.
- Interferons put neighboring cells into an antiviral state; eosinophils fight parasites and join allergic inflammation.

## 2 ADAPTIVE IMMUNITY

### ◆ ADAPTIVE RESPONSE FROM ANTIGEN TO MEMORY



### ◆ GAMED: ANTIBODY CLASSES



*IgM arrives first, IgG remembers and crosses the placenta; vaccines build memory, borrowed antibodies fade.*

### WRITTEN NOTES: ADAPTIVE IMMUNITY

- B cells become plasma cells that secrete antibodies (humoral immunity).
- CD4 helper T cells coordinate responses; CD8 cytotoxic T cells kill infected cells.
- Dendritic cells and macrophages present antigen on MHC class II to CD4 cells; all nucleated cells use MHC class I for CD8 cells.
- Primary response is slow and IgM first; secondary response is fast, large and mainly IgG because of memory cells.
- Antibodies: IgM first, IgG crosses the placenta, IgA in secretions, IgE in allergy, IgD on B cells.
- Active immunity (infection, vaccine) forms memory; passive immunity (placenta, milk, immune globulin) is temporary.

### 3 HYPERSENSITIVITY TYPES I TO IV

#### ◆ ACID: HYPERSENSITIVITY TYPES

##### ANAPHYLACTIC (TYPE I)

**A** IgE on mast cells, minutes: anaphylaxis, hives, asthma

##### CYTOTOXIC (TYPE II)

**C** Antibody against cells: transfusion reaction, newborn hemolysis

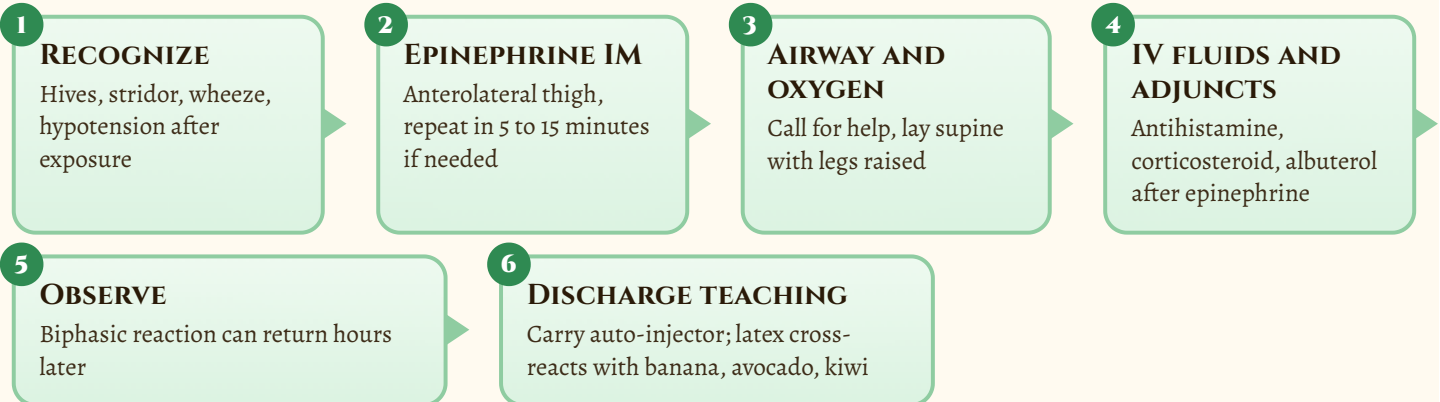
##### IMMUNE COMPLEX (TYPE III)

**I** Deposits in vessels, joints, kidneys: SLE, serum sickness

##### DELAYED (TYPE IV)

**D** T cells, 48 to 72 hours: TB test, contact dermatitis

#### ◆ ANAPHYLAXIS RESPONSE



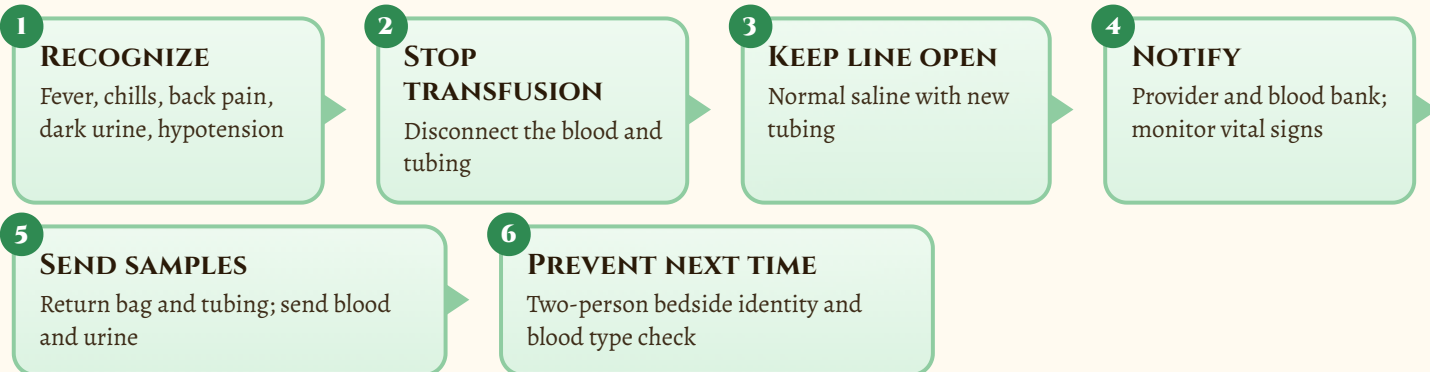
*ACID: Anaphylactic, Cytotoxic, Immune complex, Delayed. In anaphylaxis, epinephrine IM comes first.*

#### WRITTEN NOTES: HYPERSENSITIVITY TYPES I TO IV

- Type I: IgE on mast cells; minutes; anaphylaxis, urticaria, allergic asthma; epinephrine IM first.
- Type II: antibodies against cell surface antigens; transfusion reactions, hemolytic disease of the newborn.
- Type III: immune complexes deposit in vessels, joints and kidneys; SLE, serum sickness, rheumatoid arthritis.
- Type IV: T cell mediated, 48 to 72 hours; TB skin test, contact dermatitis, latex glove dermatitis.
- Anaphylaxis can be biphasic; observe after treatment and send home with an auto-injector.
- Latex allergy cross-reacts with banana, avocado, kiwi and chestnut.

## 4 TRANSFUSION AND TRANSPLANT REACTIONS

### ◆ ACUTE HEMOLYTIC TRANSFUSION REACTION



### ◆ TRANSPLANT REJECTION TIMELINE

| FEATURE   | HYPERACUTE           | ACUTE                                   | CHRONIC                      |
|-----------|----------------------|-----------------------------------------|------------------------------|
| TIMING    | Minutes              | Weeks to months                         | Months to years              |
| MECHANISM | Preformed antibodies | T cells                                 | Slow immune damage, fibrosis |
| OUTCOME   | Graft removed        | Often reversible with immunosuppression | Gradual loss of function     |



*Fever, back pain and dark urine during a transfusion: stop the blood, keep the line open with saline.*

### WRITTEN NOTES: TRANSFUSION AND TRANSPLANT REACTIONS

- Acute hemolytic reaction: fever, chills, back pain, dark urine, hypotension; stop the transfusion, keep the line open with saline, notify provider and blood bank.
- Prevent with two-person bedside verification of identity and blood type.
- Rh-negative mothers receive Rho(D) immune globulin to prevent sensitization.
- Transplant rejection: hyperacute (minutes, preformed antibodies), acute (weeks to months, T cells), chronic (months to years, fibrosis).

## 5 AUTOIMMUNITY AND SLE

### ◆ SLE ACROSS THE BODY

#### SKIN

- Malar butterfly rash
- Photosensitivity: UV triggers flares
- Oral ulcers

#### JOINTS AND BLOOD

- Arthritis
- Fatigue
- Anemia, leukopenia, thrombocytopenia

#### ORGANS

- Lupus nephritis
- Pleuritis, pericarditis

#### WHO AND WHY

- Women of childbearing age
- Triggers: infection, drugs, hormones, genetics

### ◆ LUPUS LABS

#### ANA

Normal Negative Positive

Sensitive screen, not specific for SLE

#### ANTI-DSDNA

Normal Negative Positive

Specific for SLE, tracks nephritis

#### ANTI-SMITH

Normal Negative Positive

Highly specific for SLE

#### COMPLEMENT C3

Normal 90 to 180 mg/dL Low

Consumed by immune complexes during flares

#### URINE PROTEIN

Normal Below 150 mg/day

Elevated

Lupus nephritis



*ANA is sensitive, anti-dsDNA and anti-Smith are specific; low complement signals a lupus flare.*

### WRITTEN NOTES: AUTOIMMUNITY AND SLE

- Autoimmunity is a loss of self tolerance; triggers include infection, drugs, hormones and genetics.
- Molecular mimicry: rheumatic fever after strep throat.
- SLE: autoantibodies to nuclear antigens and immune complexes; malar rash, arthritis, fatigue, cytopenias, nephritis, serositis.
- Labs: ANA sensitive, anti-dsDNA and anti-Smith specific, low complement during flares.
- Most common in women of childbearing age; UV light triggers flares.
- Treatment includes hydroxychloroquine (eye exams), corticosteroids and other immunosuppressants.

## 6 IMMUNODEFICIENCY

### ◆ CAUSES OF IMMUNODEFICIENCY

#### PRIMARY

- DiGeorge: no thymus, low calcium
- SCID
- Selective IgA deficiency

#### SECONDARY

- HIV
- Chemotherapy, corticosteroids
- Diabetes, malnutrition
- Splenectomy
- Older age

#### NURSING SAFETY

- No live vaccines: MMR, varicella
- Asplenia: pneumococcal, meningococcal, Hib vaccines
- Treat any fever promptly

### ◆ IMMUNE STATUS LABS

#### WBC

Normal 4,500 to 11,000/mm<sup>3</sup>

Below 4,500

Leukopenia: infection risk

#### ANC

Normal 1,500 to 8,000/mm<sup>3</sup>

Below 500

Severe neutropenia: neutropenic precautions

#### IGA

Normal 70 to 400 mg/dL

Absent

Selective IgA deficiency: anaphylaxis risk with blood

#### CALCIUM

Normal 8.5 to 10.5 mg/dL

Below 8.5 in infant

Suggests DiGeorge: absent parathyroids



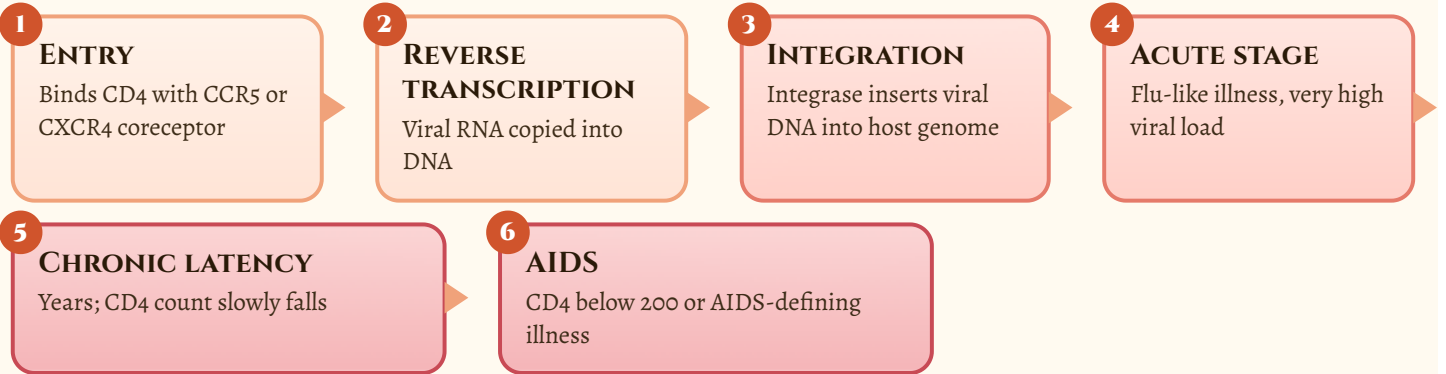
*In neutropenia, fever may be the only sign of infection: treat it as an emergency.*

### WRITTEN NOTES: IMMUNODEFICIENCY

- Primary: DiGeorge (no thymus, low calcium), SCID, selective IgA deficiency (most common; anaphylaxis risk with blood products).
- Secondary: HIV, chemotherapy, corticosteroids, diabetes, splenectomy, malnutrition, older age.
- Neutropenia (ANC below 500 is severe): fever may be the only sign; treat as an emergency.
- No spleen: vaccinate against pneumococcus, meningococcus and Hib; treat fever promptly.
- Avoid live vaccines such as MMR and varicella in severe immunosuppression.

## 7 HIV AND AIDS

### ◆ HIV INFECTION AND PROGRESSION



### ◆ HIV MONITORING

#### CD4 COUNT

Normal 500 to 1,500 cells/mm<sup>3</sup>

**Below 200**

AIDS; start Pneumocystis prophylaxis

#### VIRAL LOAD

Normal Undetectable on therapy

**Rising**

Nonadherence or resistance

#### HIV ANTIGEN/ANTIBODY TEST

Normal Nonreactive

**Reactive**

Confirm with differentiation assay



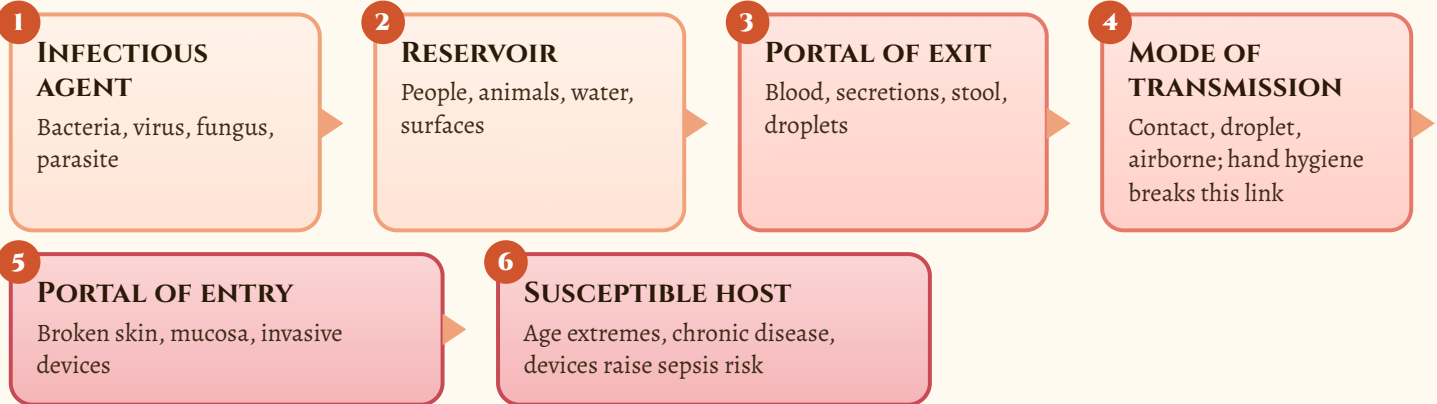
*CD4 tells immune status, viral load tells if therapy works; undetectable equals untransmittable.*

### WRITTEN NOTES: HIV AND AIDS

- Retrovirus that binds CD4 with CCR5 or CXCR4 and uses reverse transcriptase to integrate into host DNA.
- Spread by blood, sexual fluids and breast milk; not by casual contact, saliva or insects.
- Stages: acute (flu-like, very high viral load), chronic latency (years, CD4 slowly falls), AIDS (CD4 below 200 or AIDS-defining illness).
- Viral load measures treatment success; CD4 count measures immune status and guides prophylaxis (Pneumocystis below 200).
- Strict adherence prevents resistance; undetectable equals untransmittable sexually.
- Needlestick: report and start PEP within hours (no later than 72 hours).

## 8 INFECTION, MICROBIOLOGY AND SEPSIS BASICS

### ◆ CHAIN OF INFECTION



### ◆ ANTIMICROBIALS IN SEPSIS AND C. DIFFICILE



#### PIPERACILLIN-TAZOBACTAM

*Zosyn*

**PENICILLIN WITH BETA-LACTAMASE INHIBITOR**

**USED FOR** Broad empiric sepsis coverage

**WATCH** Penicillin allergy; cultures first, no delay



#### CEFTRIAXONE

*Rocephin*

**THIRD-GENERATION CEPHALOSPORIN**

**USED FOR** Pneumonia, meningitis, gram-negative infections

**WATCH** Ask about cephalosporin allergy



#### VANCOMYCIN

*Vancocin*

**GLYCOPEPTIDE**

**USED FOR** MRSA IV; oral for *C. difficile*

**WATCH** Trough levels, kidney function, infuse slowly



#### FIDAXOMICIN

*Dificid*

**MACROLIDE ANTIBIOTIC**

**USED FOR** *C. difficile* infection

**WATCH** Contact precautions, soap and water hand hygiene



*Draw blood cultures, then give antibiotics without delay; soap and water for C. difficile spores.*

### WRITTEN NOTES: INFECTION, MICROBIOLOGY AND SEPSIS BASICS

- Chain of infection: agent, reservoir, portal of exit, mode of transmission, portal of entry, susceptible host; hand hygiene breaks transmission.
- Gram-positive stains purple (thick wall); gram-negative stains pink and has endotoxin in its outer membrane.

- Stages: incubation, prodromal, acute, convalescent, resolution.
- C. difficile follows antibiotic use; spores require soap and water.
- Sepsis is life-threatening organ dysfunction from a dysregulated response to infection; risk is highest at age extremes, with chronic disease and with invasive devices.
- Draw blood cultures, then give antibiotics without delay.



## CLINICAL PEARLS

- ACID for hypersensitivity: Anaphylactic (type I, IgE), Cytotoxic (type II, antibody against cells), Immune complex (type III), Delayed (type IV, T cells).
- Antibody roles: IgM first, IgG long term and crosses the placenta, IgA in secretions, IgE in allergy and parasites.
- Active means you make it (infection or vaccine) and remember it; passive means you borrow it (placenta, milk, immune globulin) and lose it.
- HIV numbers: CD4 below 200 or an AIDS-defining illness means AIDS; viral load shows whether therapy works; undetectable equals untransmittable.
- Precautions: Contact for MRSA and C. diff (soap and water), Droplet for flu and meningococcus, Airborne for measles, chickenpox and TB.

◆ **MEDICATIONS FOR IMMUNITY, HYPERSENSITIVITY AND INFECTION**



**EPINEPHRINE**

*EpiPen, Auvi-Q*

**ADRENERGIC AGONIST**

**USED FOR** Anaphylaxis

**WATCH** Give IM in the anterolateral thigh at the first sign of anaphylaxis; expect tachycardia and observe for a biphasic reaction.



**DIPHENHYDRAMINE**

*Benadryl*

**H1 ANTIHISTAMINES**

**USED FOR** Allergic rhinitis, urticaria and adjunct treatment of anaphylaxis

**WATCH** First-generation agents cause sedation and anticholinergic effects that raise fall risk in older adults; they never replace epinephrine in anaphylaxis.



**BICTEGRAVIR,  
EMTRICITABINE AND  
TENOFIVIR  
ALAFENAMIDE**

*Biktarvy*

**COMBINATION  
ANTIRETROVIRAL THERAPY**

**USED FOR** HIV infection, and some combinations for PrEP and post-exposure prophylaxis

**WATCH** Strict daily adherence prevents resistance; check for drug interactions and monitor kidney function with tenofovir.



**PIPERACILLIN-  
TAZOBACTAM**

*Zosyn*

**BROAD-SPECTRUM BETA-  
LACTAM ANTIBIOTICS**

**USED FOR** Serious bacterial infections and suspected sepsis

**WATCH** Ask about penicillin and cephalosporin allergies and draw blood cultures first, without delaying the first dose.



**HYDROXYCHLOROQUINE**

*Plaquenil*

**ANTIMALARIAL  
IMMUNOMODULATOR**

**USED FOR** Systemic lupus erythematosus and rheumatoid arthritis

**WATCH** Can damage the retina with long-term use, so clients need regular eye examinations.

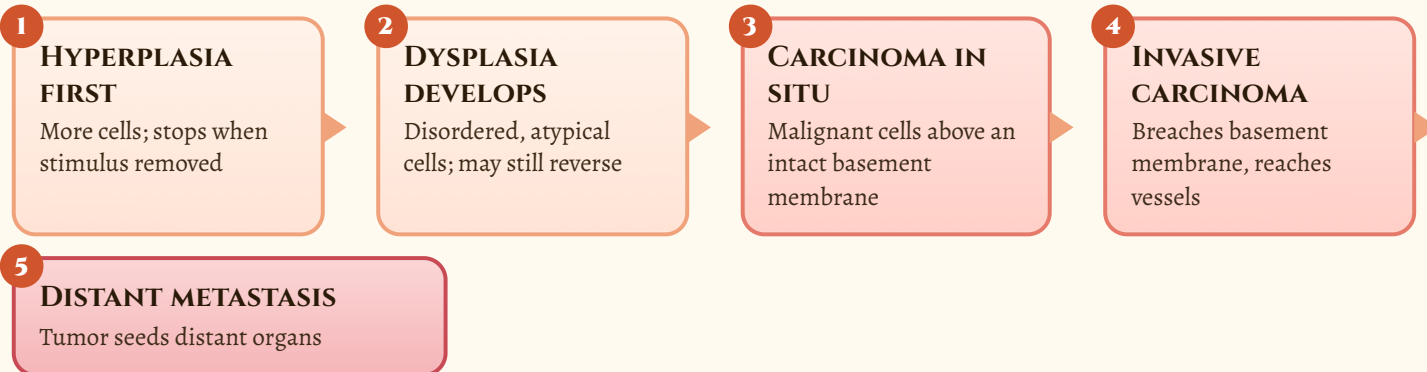
# THE OVERGROWTH: CANCER AND GENETICS

## 1 BENIGN VERSUS MALIGNANT

### ◆ BENIGN VERSUS MALIGNANT

| FEATURE         | BENIGN                          | MALIGNANT                           |
|-----------------|---------------------------------|-------------------------------------|
| GROWTH RATE     | Slow                            | Often rapid                         |
| CAPSULE         | Usually encapsulated            | Not encapsulated, invades           |
| DIFFERENTIATION | Well differentiated             | Poorly differentiated or anaplastic |
| ANGIOGENESIS    | Minimal                         | Induces new vessels                 |
| METASTASIS      | Never                           | Can spread distantly                |
| MAIN DANGER     | Compression, such as meningioma | Invasion, spread, organ failure     |

### ◆ FROM NORMAL CELL TO INVASIVE CANCER



*Benign tumors push; malignant tumors invade, build vessels, and travel. Neoplasms keep growing after the stimulus stops.*

### WRITTEN NOTES: BENIGN VERSUS MALIGNANT

- Benign tumors grow slowly, are usually encapsulated and well differentiated, and do not metastasize.
- Malignant tumors invade, are often poorly differentiated or anaplastic, induce angiogenesis, and metastasize.
- Benign tumors can still be dangerous by compression, such as a meningioma in the skull.
- Carcinoma in situ has not crossed the basement membrane and cannot yet metastasize.
- A neoplasm keeps growing after the stimulus is removed; hyperplasia stops.

### ◆ TUMOR NAMES BY TISSUE

| TISSUE OF ORIGIN     | BENIGN       | MALIGNANT               |
|----------------------|--------------|-------------------------|
| GLANDULAR EPITHELIUM | Adenoma      | Adenocarcinoma          |
| SQUAMOUS EPITHELIUM  | Papilloma    | Squamous cell carcinoma |
| FAT                  | Lipoma       | Liposarcoma             |
| SMOOTH MUSCLE        | Leiomyoma    | Leiomyosarcoma          |
| BONE                 | Osteoma      | Osteosarcoma            |
| MELANOCYTES          | Nevus (mole) | Melanoma                |

### ◆ NAMING TRAPS

#### MALIGNANT DESPITE OMA

- Melanoma
- Lymphoma
- Mesothelioma

#### BLOOD AND LYMPH ORIGIN

- Leukemia: blood forming marrow cells
- Lymphoma: lymphoid tissue

#### METASTASIS KEEPS ORIGIN NAME

- Breast cancer in bone is breast cancer
- Not called bone cancer



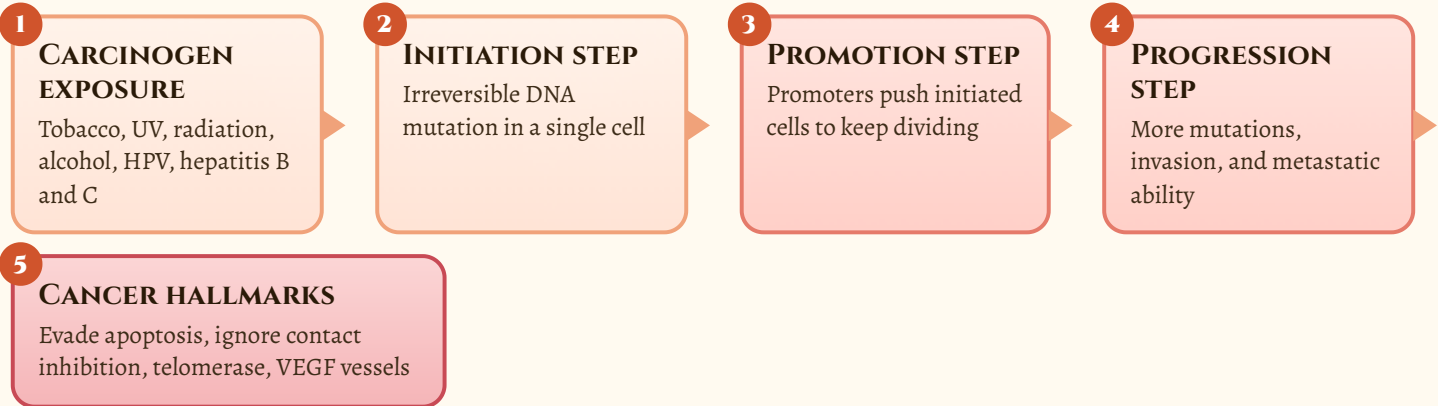
*Oma alone is usually benign; carcinoma is epithelium, sarcoma is connective tissue. Melanoma and lymphoma break the rule.*

### WRITTEN NOTES: NAMING TUMORS

- Oma alone usually means benign: lipoma, adenoma, leiomyoma.
- Carcinoma arises from epithelium; adenocarcinoma from glandular epithelium.
- Sarcoma arises from connective tissue such as bone, fat, or muscle.
- Leukemia arises in blood forming cells; lymphoma in lymphoid tissue.
- Melanoma and lymphoma are malignant despite the oma ending.
- A metastasis keeps the name of its origin, such as breast cancer in bone.

### 3 CARCINOGENESIS

#### ◆ STAGES OF CARCINOGENESIS



#### ◆ CANCER GENES

| FEATURE         | ONCOGENE                     | TUMOR SUPPRESSOR           |
|-----------------|------------------------------|----------------------------|
| NORMAL VERSION  | Proto oncogene drives growth | Brakes growth, repairs DNA |
| TYPE OF CHANGE  | Gain of function             | Loss of function           |
| COPIES AFFECTED | One is enough                | Both lost (two hit)        |
| ANALOGY         | Stuck accelerator            | Failed brakes              |
| EXAMPLES        | RAS, BCR ABL fusion          | p53, Rb, BRCA1, BRCA2      |



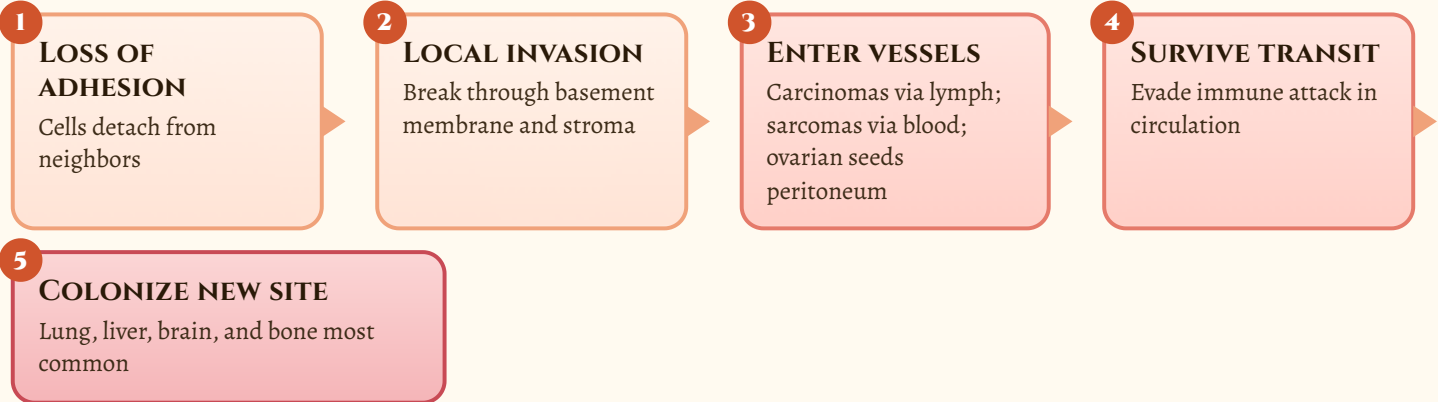
*Oncogenes are a stuck accelerator needing one hit; tumor suppressors are failed brakes needing two hits.*

#### WRITTEN NOTES: CARCINOGENESIS

- Initiation is an irreversible DNA mutation; promotion encourages initiated cells to divide; progression adds mutations and invasion.
- Proto oncogenes become oncogenes by gain of function, such as RAS or the BCR ABL fusion.
- Tumor suppressors such as p53, Rb, and BRCA1 and 2 cause cancer when both copies are lost (two hit hypothesis).
- Carcinogens include tobacco, radiation, UV light, alcohol, processed meats, and viruses such as HPV, hepatitis B and C, and Epstein Barr virus.
- Cancer cells resist apoptosis, ignore contact inhibition, reactivate telomerase, and build blood vessels through VEGF.

## 4 SPREAD, STAGING, AND GRADING

### ◆ THE METASTATIC CASCADE



### ◆ STAGING VERSUS GRADING

| FEATURE           | STAGING                            | GRADING                           |
|-------------------|------------------------------------|-----------------------------------|
| QUESTION ANSWERED | How far has it spread?             | How abnormal are the cells?       |
| TOOL              | Imaging, exam, node biopsy         | Microscope, histology             |
| SYSTEM            | TNM: tumor, nodes, metastasis      | Degree of differentiation         |
| WORSE RESULT      | Distant spread, M1 equals stage IV | Poorly differentiated, high grade |



*Stage says where it spread (scans); grade says how wild the cells look (microscope). Any M1 is stage IV.*

### WRITTEN NOTES: SPREAD, STAGING, AND GRADING

- Metastasis requires loss of adhesion, invasion through the basement membrane, entry into vessels, and survival at a new site.
- Carcinomas often spread by lymphatics first; sarcomas often by blood; ovarian cancer by seeding the peritoneum.
- Common metastatic sites are lung, liver, brain, and bone.
- TNM: T for tumor size, N for regional nodes, M for distant metastasis; any M1 is stage IV.
- Grade reflects differentiation; well differentiated tumors are lower grade and less aggressive.

### ◆ CLINICAL EFFECTS OF CANCER

#### WARNING SIGNS

- Unexplained weight loss
- Fatigue
- Fevers and night sweats
- New pain
- Unusual bleeding

#### CACHEXIA

- Cytokine driven muscle wasting
- Fat loss despite intake

#### MARROW INVOLVEMENT

- Anemia: fatigue, pallor
- Neutropenia: infections
- Thrombocytopenia: bleeding

### ◆ PARANEOPLASTIC LABS

#### SODIUM

Normal 135 to 145 mEq/L

**Below 135**

SIADH from small cell lung cancer

#### CALCIUM

Normal 8.5 to 10.5 mg/dL

**Above 10.5**

PTHrP from squamous cell cancer

#### HEMOGLOBIN

Normal Men 13.5 to 17.5, women 12 to 15.5 g/dL

**Low**

Marrow infiltration or chronic disease

#### PLATELETS

Normal 150,000 to 400,000/mm<sup>3</sup>

**Low**

Marrow failure, bleeding risk



*Small cell secretes ADH (low sodium); squamous cell secretes PTHrP (high calcium). Cachexia is cytokine driven wasting.*

### WRITTEN NOTES: CLINICAL EFFECTS AND PARANEOPLASTIC SYNDROMES

- Warning signs include unexplained weight loss, fatigue, fevers, night sweats, new pain, and unusual bleeding.
- Cachexia is cytokine driven muscle and fat wasting, not simply poor intake.
- Small cell lung cancer can secrete ADH, causing hyponatremia.
- Squamous cell cancers can secrete PTHrP, causing hypercalcemia.
- Marrow involvement causes anemia, infection, and bleeding.

## 6 ONCOLOGIC EMERGENCIES

### ◆ ONCOLOGIC EMERGENCY LABS

#### POTASSIUM

Normal 3.5 to 5.0 mEq/L

High

Tumor lysis: dysrhythmia risk

#### PHOSPHATE

Normal 2.5 to 4.5 mg/dL

High

Tumor lysis: binds calcium, kidney injury

#### URIC ACID

Normal 3.5 to 7.2 mg/dL

High

Tumor lysis: crystal kidney injury

#### CALCIUM

Normal 8.5 to 10.5 mg/dL

Low in TLS, high in malignancy

Low: tetany. High: confusion, short QT

#### ANC

Normal 1,500 to 8,000/mm<sup>3</sup>

Below 500 with fever

Febrile neutropenia: cultures, IV antibiotics within 1 hour

### ◆ EMERGENCY TREATMENT DRUGS



#### ALLOPURINOL

*Zyloprim*

**XANTHINE OXIDASE INHIBITOR**

**USED FOR** Prevent tumor lysis hyperuricemia

**WATCH** Rash, give with hydration



#### RASBURICASE

*Elitek*

**URATE OXIDASE**

**USED FOR** Rapidly lower uric acid in TLS

**WATCH** Avoid in G6PD deficiency: hemolysis



#### ZOLEDRONIC ACID

*Zometa*

**BISPHOSPHONATE**

**USED FOR** Hypercalcemia of malignancy after IV saline

**WATCH** Check creatinine, jaw osteonecrosis



#### DEXAMETHASONE

*Generic now (formerly Decadron)*

**CORTICOSTEROID**

**USED FOR** Spinal cord compression edema

**WATCH** Hyperglycemia, infection risk



#### CEFEPIME

*Maxipime*

**FOURTH GENERATION CEPHALOSPORIN**

**USED FOR** Empiric febrile neutropenia coverage

**WATCH** Draw cultures first, then give fast



*Tumor lysis spills the cell: potassium, phosphate, uric acid up, calcium down. Hydrate first.*

### WRITTEN NOTES: ONCOLOGIC EMERGENCIES

- Febrile neutropenia: ANC below 500 with fever needs cultures and IV antibiotics within about an hour.

- Tumor lysis syndrome: high potassium, phosphate, and uric acid with low calcium; prevent with hydration and allopurinol or rasburicase.
- Hypercalcemia of malignancy: confusion, constipation, polyuria, short QT; treat with IV saline then bisphosphonates or calcitonin.
- Superior vena cava syndrome: facial and arm swelling, distended neck veins, dyspnea; watch the airway.
- Spinal cord compression: back pain first, then weakness and bladder or bowel changes; urgent MRI and corticosteroids.

## 7 HEMATOLOGIC CANCERS

### ◆ LEUKEMIAS AT A GLANCE

| FEATURE     | ALL                          | CML                             | CLL                      |
|-------------|------------------------------|---------------------------------|--------------------------|
| TYPICAL AGE | Children                     | Middle aged adults              | Older adults             |
| CELL TYPE   | Immature lymphoblasts        | Myeloid cells                   | Mature B lymphocytes     |
| HALLMARK    | Most common childhood cancer | Philadelphia chromosome t(9;22) | Often found incidentally |
| KEY POINT   | Often curable                | Responds to imatinib            | Slow, indolent course    |

### ◆ MULTIPLE MYELOMA: CRAB

|                                                                     |                                                             |                                                         |                                                                     |
|---------------------------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------------|---------------------------------------------------------------------|
| <b>C</b> <b>CALCIUM ELEVATED</b><br>Bone breakdown releases calcium | <b>R</b> <b>RENAL INJURY</b><br>Light chains damage tubules | <b>A</b> <b>ANEMIA</b><br>Plasma cells crowd out marrow | <b>B</b> <b>BONE LESIONS</b><br>Lytic lesions, fractures, bone pain |
|---------------------------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------------|---------------------------------------------------------------------|



*CML has the Philadelphia chromosome and answers to imatinib; myeloma means CRAB.*

### WRITTEN NOTES: HEMATOLOGIC CANCERS

- ALL is the most common childhood cancer and is often curable.
- CML carries the Philadelphia chromosome, t(9;22), and responds to imatinib.
- CLL affects older adults and is often found incidentally.
- Hodgkin lymphoma has Reed Sternberg cells, affects young adults, and spreads to neighboring nodes in order.
- Multiple myeloma: CRAB, meaning hypercalcemia, renal injury, anemia, and bone lesions.

## 8 INHERITANCE PATTERNS

### ◆ SINGLE GENE INHERITANCE

| FEATURE         | AUTOSOMAL DOMINANT                    | AUTOSOMAL RECESSIVE                          | X LINKED RECESSIVE                 |
|-----------------|---------------------------------------|----------------------------------------------|------------------------------------|
| COPIES NEEDED   | One                                   | Two                                          | One X in males                     |
| RISK PER CHILD  | 50 percent from affected parent       | 25 percent, carrier by carrier               | 50 percent of sons, carrier mother |
| WHO IS AFFECTED | Males and females equally             | Males and females equally                    | Mostly males                       |
| EXAMPLES        | Huntington, Marfan, polycystic kidney | Cystic fibrosis, sickle cell, PKU, Tay Sachs | Hemophilia A, Duchenne             |

### ◆ PEDIGREE CLUES

#### AUTOSOMAL DOMINANT

- Appears every generation
- Affected parent in each case

#### AUTOSOMAL RECESSIVE

- Skips generations
- Unaffected carrier parents

#### X LINKED RECESSIVE

- Mostly affected males
- No father to son transmission
- Affected father: all daughters carriers

#### OTHER PATTERNS

- Mitochondrial: mother only
- Multifactorial: genes plus environment
- Penetrance: appears or not
- Expressivity: how strongly



*Dominant Aa by aa: 50 percent affected. Carrier by carrier: 25 percent affected. Carrier mother: each son 50 percent.*

### WRITTEN NOTES: INHERITANCE PATTERNS

- Autosomal dominant: one copy causes disease, 50 percent risk per child of an affected heterozygote; Huntington disease, Marfan syndrome, polycystic kidney disease.
- Autosomal recessive: two copies needed, carrier by carrier gives 25 percent affected; cystic fibrosis, sickle cell disease, PKU, Tay Sachs disease.
- X linked recessive: mostly males; a carrier mother gives each son a 50 percent risk, and an affected father makes all daughters carriers.
- Mitochondrial disorders pass only through the mother.
- Multifactorial conditions such as type 2 diabetes and neural tube defects combine many genes with environment.

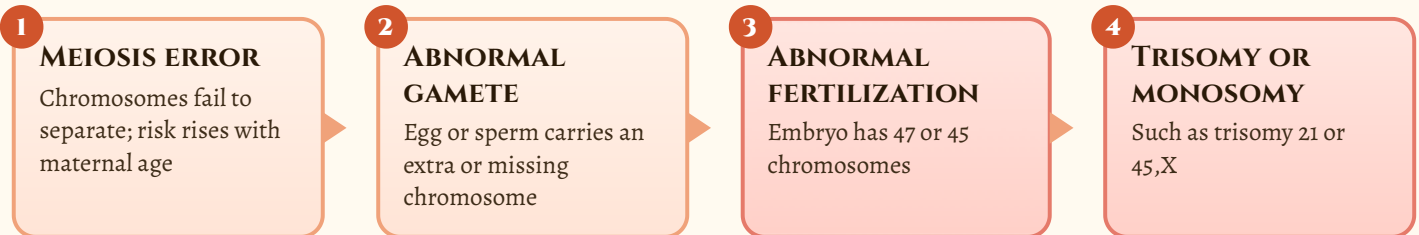
- Penetrance is whether a trait appears; expressivity is how strongly it appears.

## 9 CHROMOSOMES AND TERATOGENS

### ◆ CHROMOSOME DISORDERS

| FEATURE        | DOWN SYNDROME                          | TURNER SYNDROME                   | KLINFELTER SYNDROME              |
|----------------|----------------------------------------|-----------------------------------|----------------------------------|
| KARYOTYPE      | Trisomy 21                             | 45,X                              | 47,XXY                           |
| SEX            | Either                                 | Female                            | Male                             |
| BODY FEATURES  | Hypotonia, single palmar crease        | Short stature, webbed neck        | Tall, small testes, gynecomastia |
| HEART OR OTHER | Heart defects, intellectual disability | Coarctation of aorta, infertility | Infertility                      |

### ◆ NONDISJUNCTION



*Trisomy 21, 45,X, and 47,XXY come from nondisjunction; organs are most vulnerable at weeks 3 to 8.*

### WRITTEN NOTES: CHROMOSOMES AND TERATOGENS

- Nondisjunction causes trisomies and monosomies; risk rises with maternal age.
- Down syndrome is trisomy 21: hypotonia, single palmar crease, heart defects, intellectual disability.
- Turner syndrome is 45,X: short stature, webbed neck, coarctation, infertility.
- Klinefelter syndrome is 47,XXY: tall male, small testes, infertility, gynecomastia.
- Fetal organs are most vulnerable to teratogens during weeks 3 to 8 after conception.

### + CLINICAL PEARLS

- Benign tumors are polite guests: slow, encapsulated, and they stay put. Malignant ones invade, ignore borders, and travel.
- Staging is about spread (where), grading is about appearance (how ugly). Stage uses scans, grade uses the microscope.
- Oncogenes are a stuck accelerator (one hit is enough); tumor suppressors are failed brakes (both copies must go).
- Tumor lysis means everything inside the cell spills out: potassium, phosphate, and uric acid go up, calcium comes down.
- Punnett quick math: dominant Aa by aa is 50 percent affected, recessive carrier by carrier is 25 percent affected, and an X linked carrier mother gives each son a 50 percent risk.

◆ **MEDICATIONS FOR CANCER AND GENETICS**



**CYCLOPHOSPHAMIDE**

*Cytosan*

**ALKYLATING AGENTS**

**USED FOR** Leukemias, lymphomas, and many solid tumors

**WATCH** Watch for bone marrow suppression; with cyclophosphamide push fluids and void often to prevent hemorrhagic cystitis, and with cisplatin monitor kidney function



**METHOTREXATE**

*Trexall, Otrexup*

**ANTIMETABOLITES**

**USED FOR** Leukemias, breast and colorectal cancers

**WATCH** Expect mucositis and myelosuppression; leucovorin rescue may follow high dose methotrexate, and folic acid supplements are not given unless ordered



**IMATINIB**

*Gleevec*

**TYROSINE KINASE INHIBITORS**

**USED FOR** Chronic myeloid leukemia and some lung cancers

**WATCH** Monitor for fluid retention, liver toxicity, and rash; many interact with other drugs and grapefruit



**PEMBROLIZUMAB**

*Keytruda*

**IMMUNE CHECKPOINT INHIBITORS**

**USED FOR** Melanoma, lung, and several other cancers

**WATCH** Report new diarrhea, cough, rash, or fatigue promptly because immune related colitis, pneumonitis, hepatitis, or endocrine failure can occur



**ALLOPURINOL**

*Zyloprim*

**XANTHINE OXIDASE INHIBITOR AND URATE OXIDASE**

**USED FOR** Prevention and treatment of tumor lysis syndrome

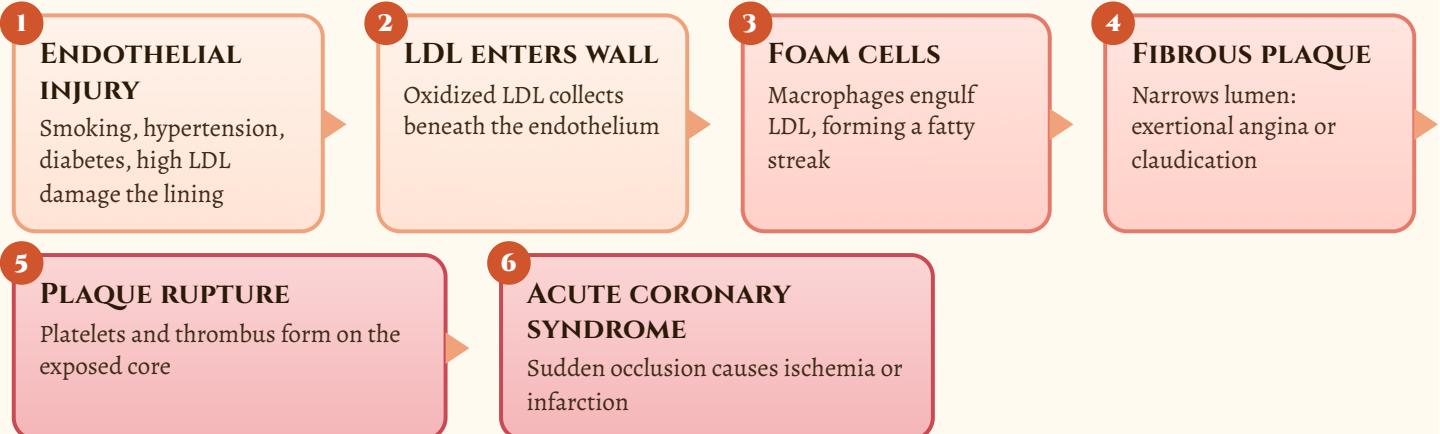
**WATCH** Give with aggressive hydration and monitor potassium, phosphate, calcium, and creatinine; rasburicase is avoided in G6PD deficiency

# PUMPWORKS: HEART, VESSELS AND BLOOD

Dr. Akash Garg · Dr. Garg Learning

## 1 ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE

### ◆ HOW PLAQUE FORMS AND RUPTURES



### ◆ LIPID PANEL TARGETS

#### TOTAL CHOLESTEROL

Normal Below 200 mg/dL

240 or above

High cardiovascular risk

#### LDL

Normal Below 100 mg/dL

160 or above

Drives plaque formation

#### HDL

Normal 40 or above men, 50 or above women mg/dL

Low

Less protection from plaque

#### TRIGLYCERIDES

Normal Below 150 mg/dL

200 or above

Added risk, often with diabetes



LDL builds plaque, HDL protects. Stable plaque causes angina; ruptured plaque causes clot and ACS.

### WRITTEN NOTES: ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE

- Endothelial injury lets LDL into the vessel wall, macrophages form foam cells, and a fibrous plaque develops.
- Modifiable risks: smoking, high LDL, hypertension, diabetes, inactivity, and obesity.
- Stable plaques cause predictable exertional angina; ruptured plaques cause thrombus and acute coronary syndrome.

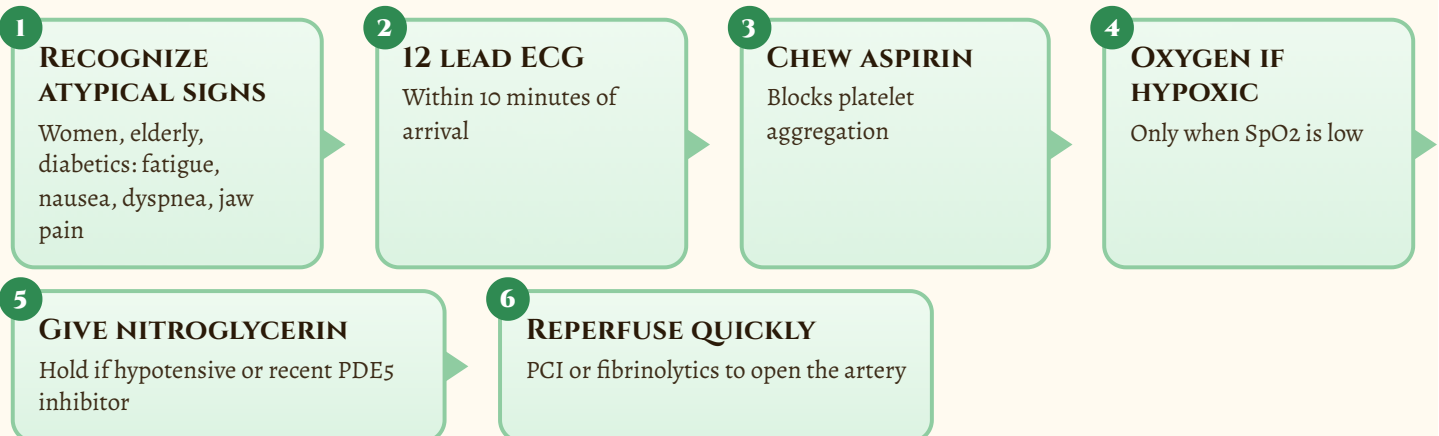
- Peripheral artery disease causes claudication, cool pale skin, and weak pulses.
- HDL is protective; LDL drives plaque.

## 2 ACUTE CORONARY SYNDROME

### ◆ THE ACUTE CORONARY SYNDROMES

| FEATURE  | UNSTABLE ANGINA         | NSTEMI                     | STEMI                              |
|----------|-------------------------|----------------------------|------------------------------------|
| PAIN     | At rest or worsening    | At rest, persistent        | At rest, persistent                |
| ECG      | Normal or ST depression | Normal or ST depression    | ST elevation                       |
| TROPONIN | Normal                  | Elevated                   | Elevated                           |
| DAMAGE   | No necrosis             | Partial thickness necrosis | Full thickness, complete occlusion |
| PRIORITY | Admit, anticoagulate    | Anticoagulate, early cath  | Reperfusion within 90 minutes      |

### ◆ EARLY ACS CARE



*Troponin means dead cells; ST elevation means full occlusion. STEMI needs reperfusion within 90 minutes.*

### WRITTEN NOTES: ACUTE CORONARY SYNDROME

- Stable angina: exertional, relieved by rest or nitroglycerin, normal troponin.
- Unstable angina: rest or worsening pain, ST depression possible, normal troponin.
- NSTEMI: same pattern plus elevated troponin (partial thickness necrosis).
- STEMI: ST elevation plus troponin; complete occlusion; reperfusion within 90 minutes.
- Women, older adults, and people with diabetes may have fatigue, nausea, dyspnea, or jaw pain instead of crushing chest pain.

- Early care: aspirin chewed, oxygen if hypoxic, nitroglycerin unless hypotensive or on PDE5 inhibitors, and reperfusion.

### 3 HEART FAILURE

#### ◆ LEFT VERSUS RIGHT HEART FAILURE

| FEATURE          | LEFT SIDED                              | RIGHT SIDED                        |
|------------------|-----------------------------------------|------------------------------------|
| FLUID BACKS INTO | Lungs                                   | Systemic veins                     |
| KEY SIGNS        | Crackles, orthopnea, pink frothy sputum | JVD, dependent edema, hepatomegaly |
| BREATHING        | Dyspnea, PND, cough                     | Often less dyspnea                 |
| COMMON CAUSE     | MI, hypertension, valve disease         | Left failure, COPD (cor pulmonale) |
| BNP              | Elevated from ventricular stretch       | Elevated from ventricular stretch  |

#### ◆ HEART FAILURE DRUGS BLOCK THE COMPENSATION



##### LISINOPRIL

*Zestril, Prinivil*

**ACE INHIBITOR**

**USED FOR** Lower afterload, slow remodeling

**WATCH** Cough, high potassium, angioedema



##### SACUBITRIL AND VALSARTAN

*Entresto*

**ARNI**

**USED FOR** HFrEF, replaces ACE inhibitor or ARB

**WATCH** Wait 36 hours after last ACE inhibitor



##### CARVEDILOL

*Coreg*

**BETA BLOCKER**

**USED FOR** HFrEF, blocks sympathetic drive

**WATCH** Bradycardia, hypotension, start low



##### SPIRONOLACTONE

*Aldactone*

**ALDOSTERONE ANTAGONIST**

**USED FOR** HFrEF, blocks aldosterone remodeling

**WATCH** Hyperkalemia, gynecomastia



##### FUROSEMIDE

*Lasix*

**LOOP DIURETIC**

**USED FOR** Congestion, pulmonary edema

**WATCH** Low potassium, daily weights



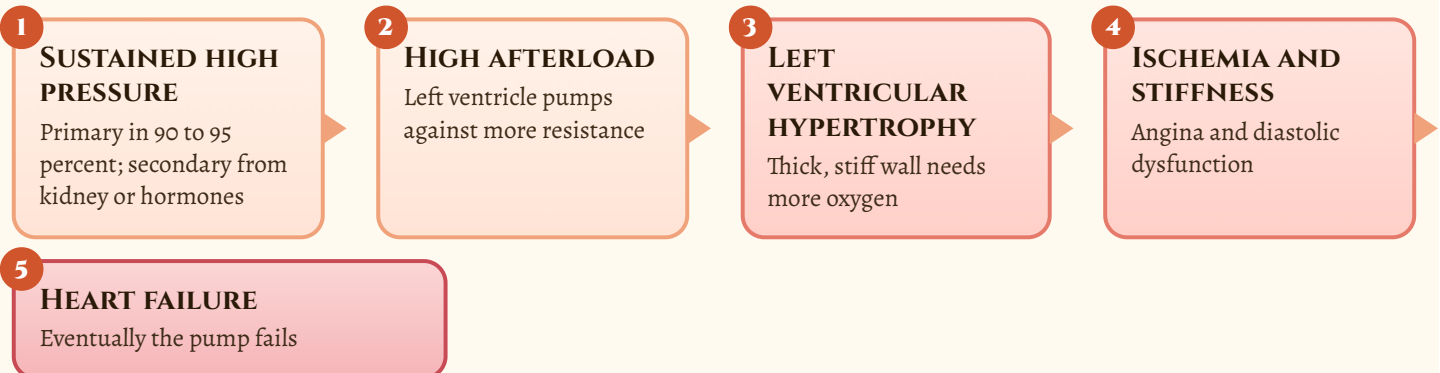
*Left failure floods the lungs; right failure floods the body. Report 2 to 3 pounds in a day.*

WRITTEN NOTES: HEART FAILURE

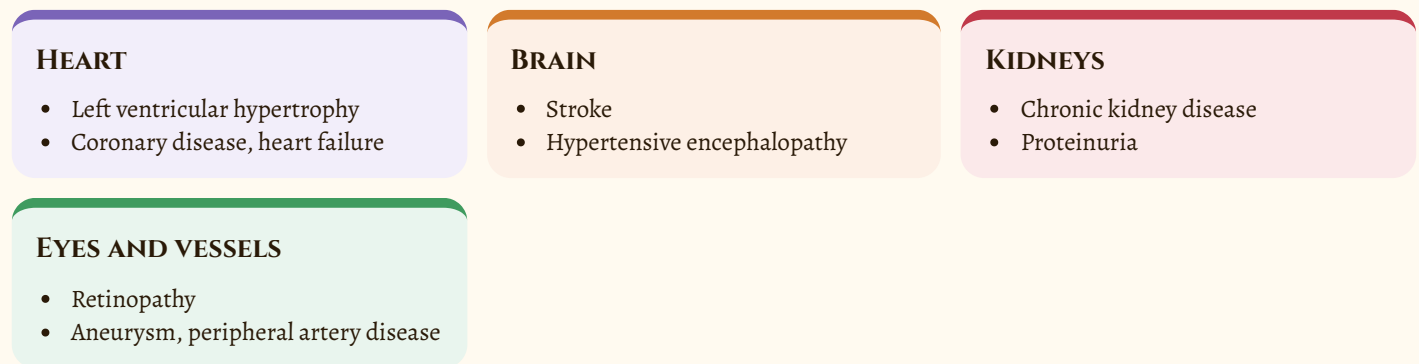
- HFrEF: EF 40 percent or less, weak dilated ventricle. HFpEF: EF 50 percent or more, stiff ventricle.
- Left sided failure causes pulmonary congestion; right sided failure causes systemic venous congestion.
- Compensation through the sympathetic system and RAAS helps short term but causes remodeling long term.
- BNP rises with ventricular stretch and supports the diagnosis.
- Daily weights: report about 2 to 3 pounds in a day or 5 pounds in a week.
- Therapy targets the compensation: ACE inhibitors or ARBs or ARNIs, beta blockers, aldosterone antagonists, and diuretics.

## 4 HYPERTENSION

### ◆ HYPERTENSION DAMAGES THE HEART



### ◆ TARGET ORGAN DAMAGE



*Hypertension is silent until organs fail. In emergency, lower by no more than about 25 percent in the first hour.*

### WRITTEN NOTES: HYPERTENSION

- Primary hypertension (90 to 95 percent) has no single cause; secondary hypertension has a specific cause such as kidney disease or hormone excess.
- It is usually silent until target organs are damaged: heart, brain, kidneys, eyes, and vessels.
- High afterload causes left ventricular hypertrophy.

- Hypertensive emergency means severe elevation with new organ damage; lower by no more than about 25 percent in the first hour.

## 5 DYSRHYTHMIAS

### ◆ KEY RHYTHMS

| FEATURE     | ATRIAL FIBRILLATION                          | VF OR PULSELESS VT               | THIRD DEGREE BLOCK        |
|-------------|----------------------------------------------|----------------------------------|---------------------------|
| ECG         | Irregularly irregular, no P waves            | Chaotic or wide rapid complexes  | P waves and QRS unrelated |
| PULSE       | Irregular                                    | None                             | Slow, regular             |
| MAIN DANGER | Stroke from atrial clot                      | Cardiac arrest                   | Low output, syncope       |
| ACTION      | Rate control, anticoagulate per CHA2DS2 VASc | CPR and immediate defibrillation | Pacing                    |

### ◆ RHYTHM AND STROKE PREVENTION DRUGS



#### APIXABAN

*Eliquis*

##### FACTOR XA INHIBITOR

**USED FOR** Stroke prevention in A fib

**WATCH** Bleeding; do not stop abruptly



#### WARFARIN

*Jantoven*

##### VITAMIN K ANTAGONIST

**USED FOR** A fib, mechanical valves

**WATCH** INR goal 2 to 3, steady vitamin K



#### DILTIAZEM

*Cardizem*

##### CALCIUM CHANNEL BLOCKER

**USED FOR** A fib or flutter rate control

**WATCH** Hypotension, bradycardia



#### AMIODARONE

*Pacerone, Nexterone*

##### CLASS III ANTIARRHYTHMIC

**USED FOR** A fib, VT, VF

**WATCH** Lung, thyroid, liver toxicity



#### ATROPINE

*Generic only*

##### ANTICHOLINERGIC

**USED FOR** Symptomatic bradycardia

**WATCH** Prepare pacing if no response



*A fib is irregularly irregular with no P waves; the danger is a left atrial clot and stroke.*

### WRITTEN NOTES: DYSRHYTHMIAS

- Atrial fibrillation: irregularly irregular, no P waves, stroke risk from left atrial clot; anticoagulate based on CHA2DS2 VASc.

- Atrial flutter: sawtooth waves, similar stroke risk.
- Ventricular fibrillation and pulseless VT: CPR and immediate defibrillation.
- Symptomatic bradycardia: atropine, then pacing.
- Third degree block: P waves and QRS unrelated; pacing needed.

## 6 VALVES, PERICARDIUM, AND CONGENITAL DEFECTS

### ◆ PERICARDITIS VERSUS TAMPONADE

| FEATURE        | PERICARDITIS                    | CARDIAC TAMPONADE             |
|----------------|---------------------------------|-------------------------------|
| PAIN           | Sharp, eased by leaning forward | May be absent                 |
| HEART SOUNDS   | Friction rub                    | Muffled                       |
| BLOOD PRESSURE | Usually normal                  | Hypotension, pulsus paradoxus |
| NECK VEINS     | Normal                          | Distended (JVD)               |
| ACTION         | NSAIDs, colchicine              | Emergency pericardiocentesis  |

### ◆ VALVE AND CONGENITAL CLUES

#### AORTIC STENOSIS

- Angina
- Syncope
- Heart failure

#### AORTIC REGURGITATION

- Wide pulse pressure
- Leaky valve, backflow

#### ACYANOTIC LEFT TO RIGHT

- VSD
- ASD
- PDA

#### CYANOTIC OR COARCTATION

- Tetralogy of Fallot: right to left
- Coarctation: arm BP above leg BP
- Weak femoral pulses



*Tamponade is Beck triad: hypotension, JVD, muffled heart sounds. Aortic stenosis brings angina, syncope, heart failure.*

### WRITTEN NOTES: VALVES, PERICARDIUM, AND CONGENITAL DEFECTS

- Stenosis is a narrowed valve that obstructs flow; regurgitation is a leaky valve.
- Aortic stenosis: angina, syncope, heart failure. Aortic regurgitation: wide pulse pressure.
- Rheumatic heart disease follows untreated strep infection and most often damages the mitral valve.
- Pericarditis: positional pain, friction rub. Tamponade: hypotension, JVD, muffled sounds.
- Left to right shunts (VSD, ASD, PDA) are acyanotic at first; tetralogy of Fallot is a right to left cyanotic defect.

- Coarctation: higher pressure in the arms than the legs, weak femoral pulses.

## 7 SHOCK

### ◆ FOUR TYPES OF SHOCK

#### HYPOVOLEMIC: NO VOLUME

- Bleeding
- Vomiting or diarrhea
- Burns

#### CARDIOGENIC: NO PUMP

- Large MI
- Pulmonary congestion, crackles

#### DISTRIBUTIVE: NO TONE

- Septic
- Anaphylactic
- Neurogenic: bradycardia, warm skin

#### OBSTRUCTIVE: NO PATH

- Cardiac tamponade
- Tension pneumothorax
- Massive PE

### ◆ PERFUSION TARGETS

#### LACTATE

Normal 0.5 to 2.0 mmol/L

**Above 2, rising**

Worsening tissue hypoperfusion

#### MAP

Normal 70 to 100 mmHg

**Below 65**

Organs underperfused, needs fluids or pressors

#### URINE OUTPUT

Normal 0.5 mL/kg/hr or more

**Below 0.5**

Kidneys underperfused



*No volume, no pump, no tone, no path. Aim for MAP 65 or more and urine 0.5 mL/kg/hr.*

### WRITTEN NOTES: SHOCK

- Hypovolemic: lost volume from bleeding, vomiting, or burns.
- Cardiogenic: pump failure, with pulmonary congestion.
- Distributive: septic, anaphylactic, or neurogenic vasodilation.
- Obstructive: tamponade, tension pneumothorax, or massive PE.
- Rising lactate signals worsening hypoperfusion; aim for MAP of at least 65 and urine output of at least 0.5 mL/kg/hr.

## ◆ SORTING THE ANEMIAS

| FEATURE     | IRON DEFICIENCY      | THALASSEMIA              | B12 DEFICIENCY                         |
|-------------|----------------------|--------------------------|----------------------------------------|
| CELL SIZE   | Microcytic           | Microcytic               | Macrocytic                             |
| FERRITIN    | Low                  | Normal or high           | Normal                                 |
| CAUSE       | Chronic blood loss   | Reduced globin chains    | Pernicious anemia, no intrinsic factor |
| NEURO SIGNS | No                   | No                       | Yes: numbness, ataxia                  |
| TREATMENT   | Iron, find the bleed | No iron unless deficient | B12 injections                         |

## ◆ ANEMIA WORKUP

## HEMOGLOBIN

Normal Men 13.5 to 17.5, women 12 to 15.5 g/dL

Low

Anemia

## MCV

Normal 80 to 100 fL

Below 80 or above 100

Microcytic or macrocytic

## FERRITIN

Normal Men 12 to 300, women 10 to 150 ng/mL

Low

Iron stores depleted

## RETICULOCYTES

Normal 0.5 to 2.5 percent

High

Hemolysis or bleeding; marrow responding

## INDIRECT BILIRUBIN

Normal 0.2 to 0.8 mg/dL

High

Hemolysis, jaundice



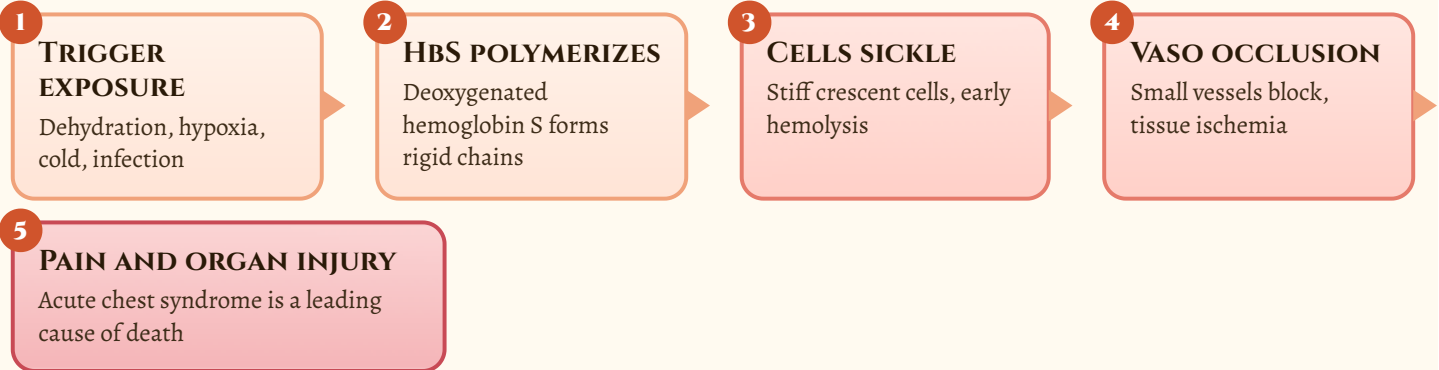
*Microcytic: iron or thalassemia. Macrocytic: B12 with nerve signs, folate without.*

## WRITTEN NOTES: ANEMIAS

- Iron deficiency: microcytic, low ferritin; most often from chronic blood loss.
- Thalassemia: microcytic from reduced globin chains, normal or high ferritin; do not give iron unless deficient.
- B12 deficiency: macrocytic with neurologic signs; pernicious anemia lacks intrinsic factor.
- Folate deficiency: macrocytic without neurologic signs.
- Aplastic anemia: pancytopenia from marrow failure.
- Hemolytic anemia: jaundice, high indirect bilirubin, high reticulocytes.

## 9 SICKLE CELL DISEASE AND BLEEDING AND CLOTTING DISORDERS

### ◆ SICKLE CELL CRISIS



### ◆ BLEEDING AND CLOTTING LABS

#### APTT

Normal 30 to 40 seconds

1.5 to 2.5 times control

Therapeutic on heparin; antidote protamine

#### INR

Normal 0.8 to 1.1

2 to 3

Therapeutic on warfarin; antidote vitamin K

#### PLATELETS

Normal 150,000 to 400,000/mm<sup>3</sup>

Drop 50 percent, day 5 to 10

Suspect HIT: stop all heparin

#### FIBRINOGEN

Normal 200 to 400 mg/dL

Low

Consumed in DIC

#### D DIMER

Normal Below 0.5 mcg/mL FEU

High

Clot breakdown: DIC, DVT, PE



Heparin: aPTT and protamine. Warfarin: INR and vitamin K. HIT: stop all heparin.

### WRITTEN NOTES: SICKLE CELL DISEASE AND BLEEDING AND CLOTTING DISORDERS

- Sickle cell: autosomal recessive, HbS polymerizes when deoxygenated; crises triggered by dehydration, hypoxia, cold, and infection.
- Acute chest syndrome is a leading cause of death in sickle cell disease.
- Hemophilia A: factor VIII deficiency, joint and deep bleeds. Von Willebrand disease: mucosal bleeding with a normal platelet count.
- DIC: clotting and bleeding at once, low fibrinogen, high D dimer.
- HIT: platelets fall about 5 to 10 days into heparin with new clots; stop all heparin.
- DVT: unilateral warm swollen limb; Virchow triad is stasis, hypercoagulability, and vessel injury.



## CLINICAL PEARLS

- Troponin means dead cells. ST elevation means full thickness. Unstable angina has neither troponin nor necrosis.
- Left heart failure floods the lungs (crackles, orthopnea); right heart failure floods the body (JVD, edema, liver).
- Heparin: aPTT and protamine. Warfarin: INR and vitamin K.
- Shock types by cause: no volume (hypovolemic), no pump (cardiogenic), no tone (distributive), no path (obstructive).
- Microcytic anemia: think iron or thalassemia. Macrocytic: think B12 (with nerve signs) or folate (without).



## KEY MEDICATIONS

### ♦ MEDICATIONS FOR HEART, VESSELS AND BLOOD



#### NITROGLYCERIN

*Nitrostat, Nitrolingual*

##### NITRATES

**USED FOR** Angina and acute coronary syndrome

**WATCH** Check BP first; hold for systolic pressure below 90 or recent PDE5 inhibitor use, and expect headache



#### METOPROLOL

*Lopressor, Toprol XL*

##### BETA BLOCKERS

**USED FOR** Angina, post MI, HFrEF, atrial fibrillation rate control

**WATCH** Check apical pulse and BP; can mask hypoglycemia signs, and nonselective agents can trigger bronchospasm



#### LISINAPRIL

*Zestril, Prinivil*

##### ACE INHIBITORS

**USED FOR** Hypertension, heart failure, post MI

**WATCH** Monitor potassium and creatinine; dry cough is common, and angioedema of the face or tongue is an emergency



#### WARFARIN

*Jantoven (formerly Coumadin)*

##### ANTICOAGULANTS

**USED FOR** DVT, pulmonary embolism, atrial fibrillation

**WATCH** Watch for bleeding; heparin uses aPTT and protamine, warfarin uses INR and vitamin K, and consistent vitamin K intake matters on warfarin



#### FUROSEMIDE

*Lasix*

##### LOOP DIURETICS

**USED FOR** Heart failure with congestion and pulmonary edema

**WATCH** Monitor potassium (hypokalemia raises digoxin toxicity risk), daily weight, BP, and intake and output

# WINDMILL HEIGHTS: LUNGS AND BREATHING

Dr. Akash Garg · Dr. Garg Learning

## 1 GAS EXCHANGE AND V/Q MISMATCH

### ◆ THREE CAUSES OF POOR GAS EXCHANGE

| FEATURE      | DEAD SPACE                    | SHUNT                         | DIFFUSION DEFECT                |
|--------------|-------------------------------|-------------------------------|---------------------------------|
| PROBLEM      | Ventilation without perfusion | Perfusion without ventilation | Thick or lost alveolar membrane |
| V/Q          | High                          | Low, near zero                | Variable                        |
| EXAMPLES     | Pulmonary embolism            | Pneumonia, ARDS, atelectasis  | Fibrosis, emphysema             |
| EXTRA OXYGEN | Helps                         | Helps little                  | Usually helps                   |

### ◆ HYPOXEMIA: EARLY VERSUS LATE

#### EARLY

- Restlessness, anxiety
- Tachycardia
- Tachypnea

#### LATE

- Cyanosis
- Bradycardia
- Decreased level of consciousness

#### RIGHT SHIFT: OXYGEN RELEASED

- Fever
- Acidosis
- High CO<sub>2</sub>



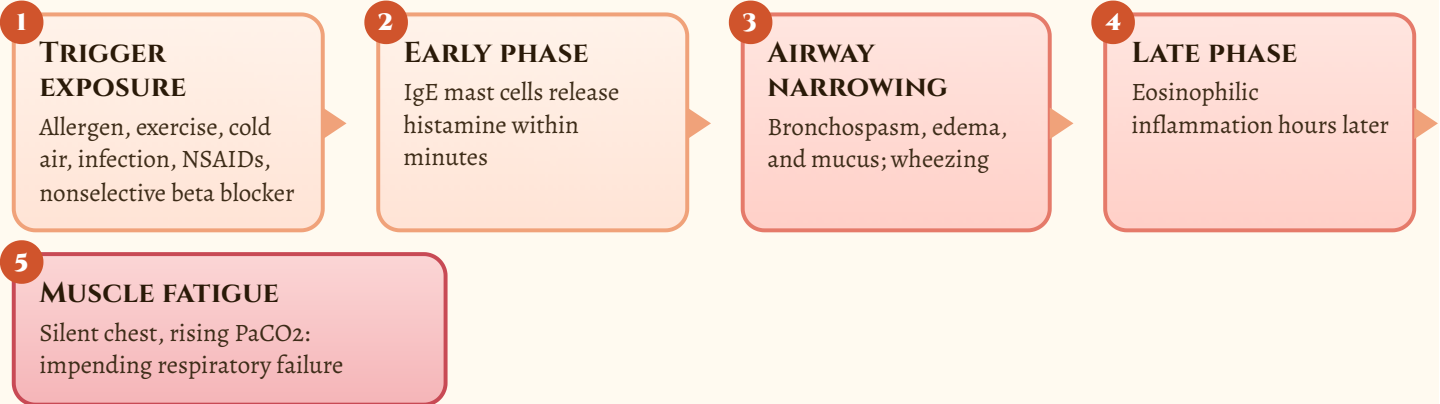
*PE is dead space (air, no blood); pneumonia is shunt (blood, no air). Shunt resists extra oxygen.*

### WRITTEN NOTES: GAS EXCHANGE AND V/Q MISMATCH

- Dead space is ventilation without perfusion, as in pulmonary embolism.
- Shunt is perfusion without ventilation, as in pneumonia, ARDS, and atelectasis; extra oxygen helps little.
- Diffusion problems come from thickened or lost alveolar membranes, as in fibrosis and emphysema.
- Early hypoxemia causes restlessness and tachycardia; cyanosis and bradycardia are late.
- A right shift of the oxyhemoglobin curve (fever, acidosis, high CO<sub>2</sub>) releases oxygen to tissues more easily.

## 2 ASTHMA

### ◆ AN ASTHMA ATTACK



### ◆ RESCUE AND CONTROL



#### ALBUTEROL

*Ventolin HFA (ProAir HFA now generic)*

**SHORT ACTING BETA 2 AGONIST**

**USED FOR** Rescue for acute bronchospasm

**WATCH** Tremor, tachycardia; rising use means poor control



#### BUDESONIDE AND FORMOTEROL

*Symbicort*

**ICS PLUS LABA**

**USED FOR** Daily control of persistent asthma

**WATCH** Rinse mouth after use: thrush



#### FLUTICASONE AND SALMETEROL

*Advair Diskus*

**ICS PLUS LABA**

**USED FOR** Maintenance asthma or COPD

**WATCH** Not for rescue; rinse mouth



#### MONTelukAST

*Singulair*

**LEUKOTRIENE RECEPTOR ANTAGONIST**

**USED FOR** Asthma control, exercise induced asthma

**WATCH** Mood changes, suicidal thoughts warning



#### PREDNISONE

*Generic now (formerly Deltasone)*

**SYSTEMIC CORTICOSTEROID**

**USED FOR** Moderate to severe exacerbation

**WATCH** Hyperglycemia; taper long courses



*A silent chest or rising PaCO<sub>2</sub> in a tiring asthmatic is a red flag, not recovery.*

### WRITTEN NOTES: ASTHMA

- Chronic airway inflammation with reversible bronchospasm, edema, and mucus.
- Early phase is IgE mast cell release; late phase is eosinophilic inflammation hours later.

- A silent chest or a rising PaCO<sub>2</sub> in a tiring client signals impending respiratory failure.
- SABA for rescue, inhaled corticosteroid for control; rinse the mouth after ICS.
- Triggers include allergens, exercise, cold air, infection, NSAIDs, and nonselective beta blockers.
- Peak flow zones: green 80 to 100 percent, yellow 50 to 79 percent, red below 50 percent.

### 3 COPD

#### ◆ EMPHYSEMA VERSUS CHRONIC BRONCHITIS

| FEATURE     | EMPHYSEMA                             | CHRONIC BRONCHITIS                      |
|-------------|---------------------------------------|-----------------------------------------|
| MAIN LESION | Destroyed alveolar walls, lost recoil | Inflamed airways, excess mucus          |
| COUGH       | Minimal                               | Productive, 3 months in each of 2 years |
| APPEARANCE  | Thin, barrel chest, pursed lips       | Often edema, cyanosis                   |
| BREATHING   | Tripod position, prolonged expiration | Rhonchi, frequent infections            |
| LATE RESULT | Air trapping, hyperinflation          | Hypoxemia, cor pulmonale                |

#### ◆ COPD NUMBERS

##### FEV<sub>1</sub> TO FVC

Normal 0.70 or higher

**Below 0.70 after bronchodilator**

Confirms airflow obstruction

##### PACO<sub>2</sub>

Normal 35 to 45 mmHg

**Chronically high**

CO<sub>2</sub> retention

##### HCO<sub>3</sub>

Normal 22 to 26 mEq/L

**High**

Renal compensation for chronic acidosis

##### SPO<sub>2</sub>

Normal 95 to 100 percent

**Target 88 to 92 in retainers**

Avoid oxygen induced CO<sub>2</sub> rise

##### HEMATOCRIT

Normal Men 41 to 50, women 36 to 44 percent

**High**

Polycythemia from chronic hypoxemia



*FEV<sub>1</sub> to FVC below 0.70 means obstruction. Titrate oxygen to 88 to 92 percent in CO<sub>2</sub> retainers.*

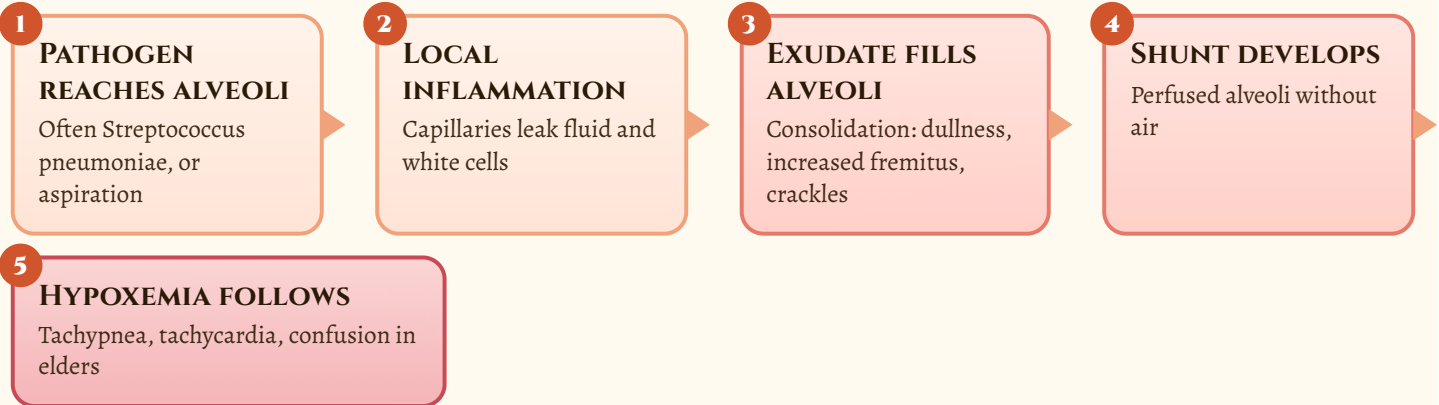
#### WRITTEN NOTES: COPD

- Emphysema destroys alveolar walls and elastic recoil; chronic bronchitis is a productive cough for 3 months in each of 2 years.
- Spirometry shows a post bronchodilator FEV<sub>1</sub> to FVC ratio below 0.70.

- Findings include barrel chest, pursed lip breathing, prolonged expiration, and tripod positioning.
- Compensation: renal bicarbonate retention, polycythemia, and pulmonary vasoconstriction leading to cor pulmonale.
- Titrate oxygen to 88 to 92 percent in CO<sub>2</sub> retainers; smoking cessation is the most effective intervention.
- Alpha 1 antitrypsin deficiency causes early lower lobe emphysema.

## 4 PNEUMONIA, INFLUENZA, AND ATELECTASIS

### ◆ HOW PNEUMONIA IMPAIRS OXYGENATION



### ◆ INFECTION AND PREVENTION

#### PNEUMONIA

- Fever, productive cough
- Crackles, dullness
- Older adults: confusion only

#### ASPIRATION RISK

- Dysphagia
- Sedation
- Stroke
- Right lower lobe

#### INFLUENZA

- Abrupt fever, myalgia
- Antivirals within 48 hours

#### PREVENT ATELECTASIS

- Incentive spirometry
- Deep breathing
- Early mobility



*Older adults with pneumonia may show confusion without fever. Aspiration favors the right lower lobe.*

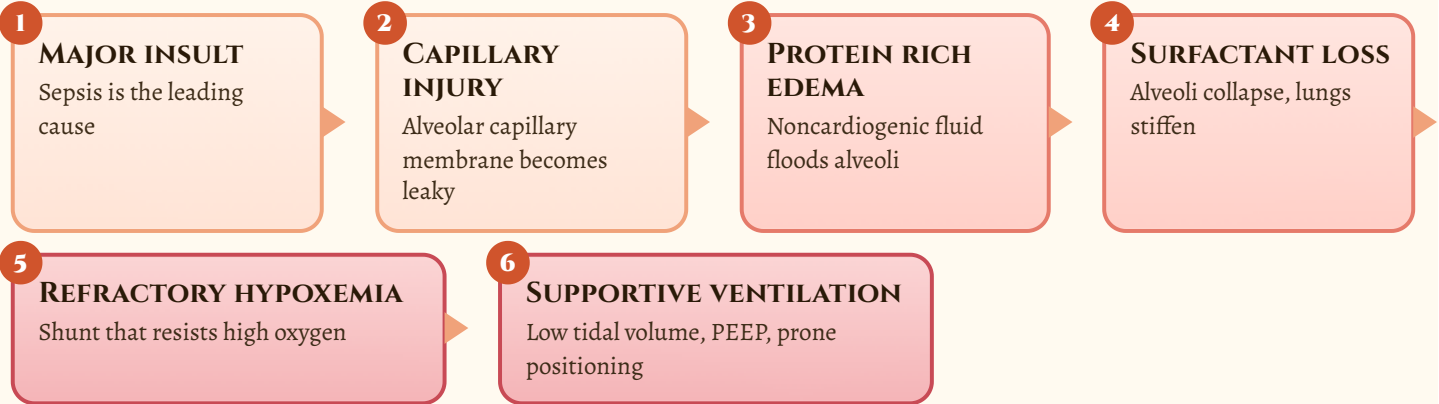
### WRITTEN NOTES: PNEUMONIA, INFLUENZA, AND ATELECTASIS

- Pneumonia fills alveoli with exudate: fever, productive cough, crackles, dullness, increased fremitus.
- Community acquired is often *Streptococcus pneumoniae*; hospital acquired begins 48 hours or more after admission.
- Aspiration risk rises with dysphagia, sedation, and stroke; the right lower lobe is common.
- Older adults may show confusion without fever.

- Influenza starts abruptly with fever and myalgia; antivirals work best within 48 hours.
- Atelectasis is prevented with incentive spirometry, deep breathing, and early mobility.

## 5 ARDS AND RESPIRATORY FAILURE

### ARDS CASCADE



### RESPIRATORY FAILURE VALUES

#### PAO<sub>2</sub>

Normal 80 to 100 mmHg

**Below 60**

Hypoxemic respiratory failure

#### PACO<sub>2</sub>

Normal 35 to 45 mmHg

**Above 50**

Hypercapnic failure if pH below 7.35

#### pH

Normal 7.35 to 7.45

**Below 7.35**

Acidosis

#### PAO<sub>2</sub> TO FiO<sub>2</sub> RATIO

Normal About 400 to 500

**300 or less**

Meets ARDS oxygenation criterion



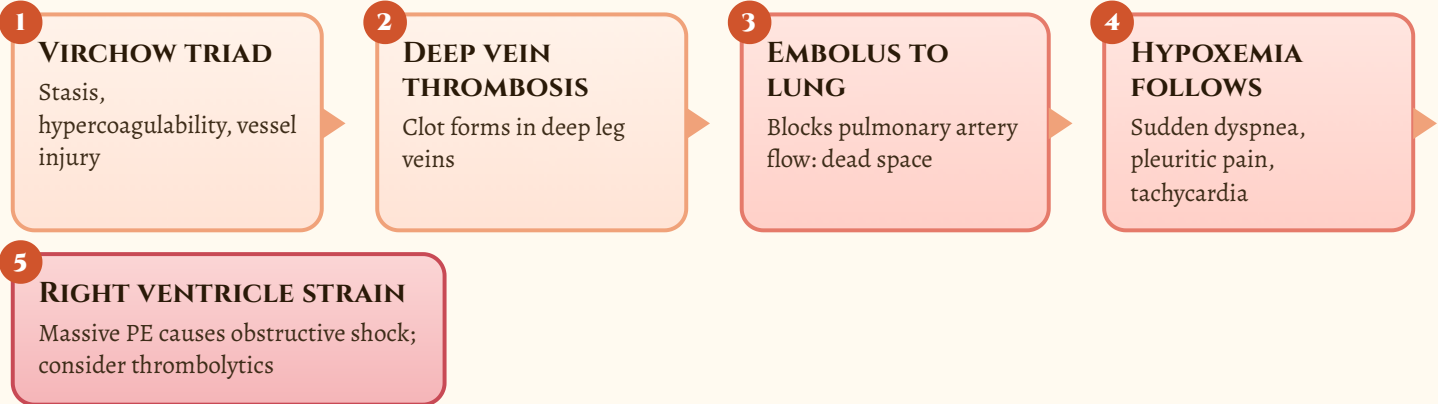
*ARDS is leaky, noncardiogenic edema: bilateral infiltrates, P/F 300 or less, oxygen alone fails.*

### WRITTEN NOTES: ARDS AND RESPIRATORY FAILURE

- ARDS is noncardiogenic pulmonary edema from alveolar capillary injury; sepsis is the leading cause.
- Hallmarks are bilateral infiltrates and a PaO<sub>2</sub> to FiO<sub>2</sub> ratio of 300 or less with refractory hypoxemia.
- Treatment uses low tidal volume ventilation, PEEP, and prone positioning.
- Hypoxemic failure: PaO<sub>2</sub> below 60. Hypercapnic failure: PaCO<sub>2</sub> above 50 with pH below 7.35.
- Neonatal respiratory distress syndrome comes from surfactant deficiency in premature infants.

## 6 PULMONARY EMBOLISM

### ◆ FROM LEG CLOT TO OBSTRUCTIVE SHOCK



### ◆ PE LABS

#### D DIMER

Normal Below 0.5 mcg/mL FEU

**High**

Nonspecific; negative helps rule out low risk PE

#### PAO2

Normal 80 to 100 mmHg

**Low**

Hypoxemia from V/Q mismatch

#### PACO2

Normal 35 to 45 mmHg

**Below 35**

Hyperventilation

#### PH

Normal 7.35 to 7.45

**Above 7.45**

Respiratory alkalosis



*Sudden dyspnea and pleuritic pain after immobility: think PE. CT pulmonary angiography confirms.*

### WRITTEN NOTES: PULMONARY EMBOLISM

- Most emboli come from deep leg veins; Virchow triad is stasis, hypercoagulability, and vessel injury.
- Classic signs: sudden dyspnea, pleuritic chest pain, tachycardia, and hypoxemia with respiratory alkalosis.
- CT pulmonary angiography confirms; a negative D dimer helps rule out low probability cases.
- Massive PE strains the right ventricle and can cause obstructive shock; thrombolytics are considered.
- Prevent with early ambulation, compression devices, and prophylactic anticoagulation.

### ◆ CYSTIC FIBROSIS BY ORGAN

#### LUNGS

- Thick mucus, chronic infection
- Bronchiectasis
- Airway clearance before meals

#### PANCREAS AND GUT

- Steatorrhea
- Poor growth
- Enzymes with meals and snacks
- Vitamins A, D, E, K

#### NEWBORN

- Meconium ileus

#### SWEAT GLANDS

- Salty skin
- High sweat chloride

### ◆ CF DIAGNOSTIC TESTS

#### SWEAT CHLORIDE

Normal Below 30 mmol/L

**60 mmol/L or higher**

Confirms cystic fibrosis

#### FECAL ELASTASE

Normal Above 200 mcg/g stool

**Below 200**

Pancreatic insufficiency



*CF makes every secretion thick. Clear airways before meals; give enzymes with every meal and snack.*

### WRITTEN NOTES: CYSTIC FIBROSIS

- Autosomal recessive CFTR chloride channel defect makes secretions thick.
- Sweat chloride testing confirms the diagnosis.
- Lungs: chronic infection and bronchiectasis; clear airways before meals, often after a bronchodilator.
- Pancreas: steatorrhea and poor growth; enzymes with all meals and snacks plus vitamins A, D, E, and K.
- Newborns may present with meconium ileus; CFTR modulators improve channel function.

## 8 TUBERCULOSIS

### ◆ LATENT VERSUS ACTIVE TB

| FEATURE           | LATENT TB                | ACTIVE TB                                    |
|-------------------|--------------------------|----------------------------------------------|
| BACTERIA          | Walled off in granulomas | Multiplying, causing disease                 |
| SYMPTOMS          | None                     | Cough, hemoptysis, night sweats, weight loss |
| CONTAGIOUS        | No                       | Yes, airborne                                |
| SKIN TEST OR IGRA | Positive                 | Positive                                     |
| PRECAUTIONS       | None needed              | Negative pressure room, N95                  |

### ◆ FIRST LINE TB DRUGS, 6 MONTHS OR MORE



#### ISONIAZID

*Generic only*

**ANTITUBERCULAR**

**USED FOR** Active and latent TB

**WATCH** Hepatotoxicity, give vitamin B6 for neuropathy



#### RIFAMPIN

*Rifadin*

**RIFAMYCIN**

**USED FOR** Active and latent TB

**WATCH** Orange fluids, weakens oral contraceptives



#### PYRAZINAMIDE

*Generic only*

**ANTITUBERCULAR**

**USED FOR** First 2 months of active TB

**WATCH** Hepatotoxicity, raises uric acid



#### ETHAMBUTOL

*Myambutol*

**ANTITUBERCULAR**

**USED FOR** Active TB

**WATCH** Optic neuritis: check vision and color



*TB is airborne: negative pressure room and N95. Positive skin test is 5, 10, or 15 mm by risk.*

### WRITTEN NOTES: TUBERCULOSIS

- Airborne spread: negative pressure room and N95 respirators.
- Latent TB is contained in granulomas, without symptoms or contagion; active TB causes cough, hemoptysis, night sweats, and weight loss.
- Skin test cutoffs: 5 mm for HIV or immunosuppression, 10 mm for moderate risk, 15 mm for no risk factors; IGRA is preferred after BCG.
- Treatment uses isoniazid, rifampin, pyrazinamide, and ethambutol for at least 6 months; adherence prevents resistance.

- Isoniazid needs vitamin B6; rifampin turns fluids orange; both affect the liver.

## 9 PLEURAL PROBLEMS AND OTHER CONDITIONS

### ◆ PLEURAL EMERGENCIES

| FEATURE         | SPONTANEOUS PNEUMOTHORAX    | TENSION PNEUMOTHORAX                  | HEMOTHORAX                  |
|-----------------|-----------------------------|---------------------------------------|-----------------------------|
| TYPICAL PATIENT | Tall, thin young male       | Trauma or ventilated patient          | Chest trauma                |
| PERCUSSION      | Hyperresonant               | Hyperresonant                         | Dull                        |
| TRACHEA         | Midline                     | Shifted away from injured side        | Usually midline             |
| CIRCULATION     | Usually stable              | Hypotension, JVD                      | Hypotension from blood loss |
| ACTION          | Oxygen, chest tube if large | Needle decompression, then chest tube | Chest tube, replace volume  |

### ◆ CHEST TUBES AND OTHER AIRWAY PROBLEMS

#### EXPECTED

- Tidal in water seal
- Gentle bubbling in suction chamber

#### REPORT

- Continuous water seal bubbling: air leak
- Sudden large drainage

#### SUCKING CHEST WOUND

- Occlusive dressing taped three sides

#### OTHER CONDITIONS

- Restrictive: low volumes, normal FEV<sub>1</sub> to FVC
- Sleep apnea: upper airway collapse, CPAP



*Tension pneumothorax pushes the trachea away; decompress first. Continuous water seal bubbling means air leak.*

### WRITTEN NOTES: PLEURAL PROBLEMS AND OTHER CONDITIONS

- Spontaneous pneumothorax: tall thin young males, sudden pain and dyspnea, hyperresonance.
- Tension pneumothorax: tracheal shift away, hypotension, JVD; needle decompression then chest tube.
- Hemothorax: dullness and hypotension after trauma.
- Chest tubes: tidal in is normal; continuous bubbling in the water seal means an air leak.
- Sucking chest wound: occlusive dressing taped on three sides.

- Restrictive diseases such as pneumoconiosis reduce volumes with a normal or high FEV<sub>1</sub> to FVC ratio; obstructive sleep apnea is upper airway collapse treated with CPAP.

## + CLINICAL PEARLS

- V/Q: PE is dead space (air, no blood); pneumonia is shunt (blood, no air). Shunt resists extra oxygen.
- Asthma is reversible bronchospasm; COPD is largely irreversible. A silent chest is a red flag, not a recovery.
- COPD with CO<sub>2</sub> retention: titrate oxygen to 88 to 92 percent, and watch for drowsiness from rising CO<sub>2</sub>.
- Tension pneumothorax pushes the trachea away from the injured side; decompress first, x ray later.
- TB is airborne: negative pressure room, N95, and at least 6 months of multidrug therapy.

## Rx KEY MEDICATIONS

### ♦ MEDICATIONS FOR LUNGS AND BREATHING



#### ALBUTEROL

*Ventolin HFA (ProAir HFA now generic)*

##### SHORT ACTING BETA 2 AGONISTS

**USED FOR** Acute asthma symptoms and COPD exacerbations

**WATCH** Expect tremor and tachycardia; increasing rescue use means poor control and should be reported



#### FLUTICASONE

*Arnuity Ellipta (Flovent HFA now generic)*

##### INHALED CORTICOSTEROIDS

**USED FOR** Persistent asthma and some COPD

**WATCH** Not for rescue; rinse the mouth after each use to prevent oral thrush



#### TIOTROPIUM

*Spiriva HandiHaler, Spiriva Respimat*

##### LONG ACTING MUSCARINIC ANTAGONISTS

**USED FOR** Maintenance therapy in COPD

**WATCH** Watch for dry mouth and urinary retention; use caution with narrow angle glaucoma and keep powder out of the eyes



#### RIFAMPIN

*Rifadin*

##### ANTITUBERCULAR COMBINATION THERAPY

**USED FOR** Active tuberculosis

**WATCH** Monitor liver function and avoid alcohol; rifampin turns fluids orange and weakens oral contraceptives, isoniazid needs vitamin B<sub>6</sub>, and ethambutol needs vision checks



#### ELEXACFTOR, TEZACFTOR, AND IVACFTOR

*Trikafta*

##### CFTR MODULATORS

**USED FOR** Cystic fibrosis with eligible CFTR mutations

**WATCH** Monitor liver enzymes and eye exams in children, and take with fat containing food for absorption

# FILTER FALLS: KIDNEYS AND URINARY TRACT

Dr. Akash Garg · Dr. Garg Learning

## 1 ACUTE KIDNEY INJURY: THREE LOCATIONS

### ◆ THREE LOCATIONS OF AKI

| FEATURE           | PRERENAL                                       | INTRARENAL (ATN)                                         | POSTRENAL                             |
|-------------------|------------------------------------------------|----------------------------------------------------------|---------------------------------------|
| PROBLEM           | Low perfusion to the kidney                    | Damaged tubules and tissue                               | Blocked urine outflow                 |
| CAUSES            | Hypovolemia, hemorrhage, heart failure, sepsis | Prolonged ischemia, contrast, aminoglycosides, myoglobin | BPH, stones, tumors, blocked catheter |
| BUN TO CREATININE | Above 20 to 1                                  | Near 10 to 1                                             | Variable                              |
| URINE SODIUM      | Below 20 mEq/L                                 | Above 40 mEq/L                                           | Variable                              |
| URINE             | Concentrated, bland sediment                   | Muddy brown casts, fixed specific gravity                | Hydronephrosis on ultrasound          |
| FIRST FIX         | Restore volume and perfusion                   | Remove nephrotoxin, support                              | Relieve the obstruction               |

### ◆ LABS THAT DEFINE AND SORT AKI

#### SERUM CREATININE

Normal 0.6 to 1.2 mg/dL

Rise of 0.3 in 48 hours or 1.5 times baseline

Meets AKI definition

#### URINE OUTPUT

Normal At least 0.5 mL/kg/hour

Below 0.5 mL/kg/hour for 6 hours

Oliguria: meets AKI definition

#### BUN

Normal 10 to 20 mg/dL

BUN to creatinine above 20 to 1

Prerenal: tubules still reabsorbing

#### URINE SODIUM

Normal Varies with intake

Below 20 mEq/L

Prerenal; high value suggests ATN

#### URINE SPECIFIC GRAVITY

Normal 1.005 to 1.030

Fixed near 1.010

ATN: tubules cannot concentrate



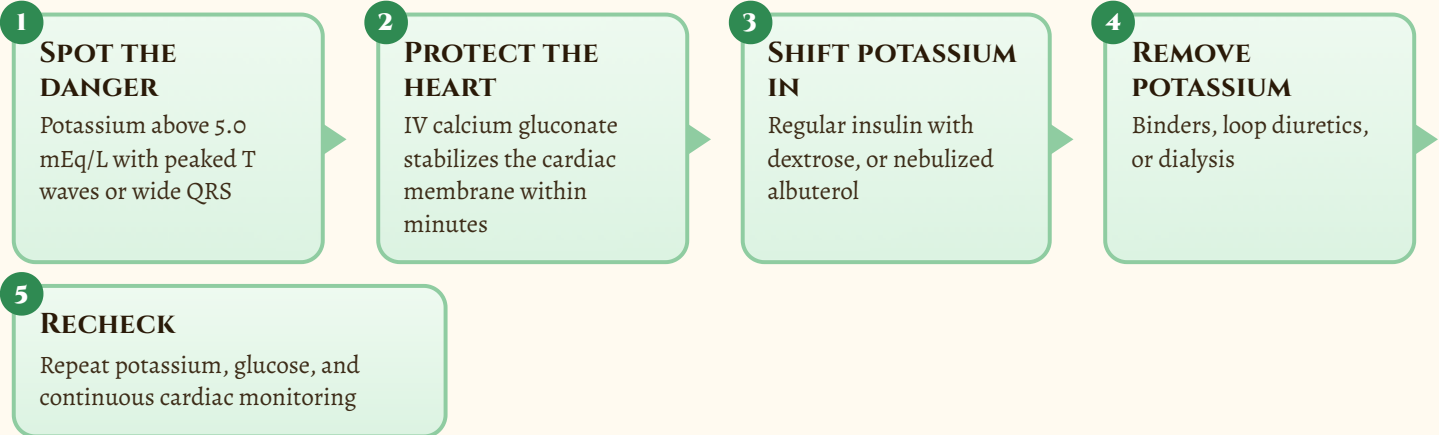
*Ask where the problem sits: before the kidney, in the kidney, or after it.*

WRITTEN NOTES: ACUTE KIDNEY INJURY: THREE LOCATIONS

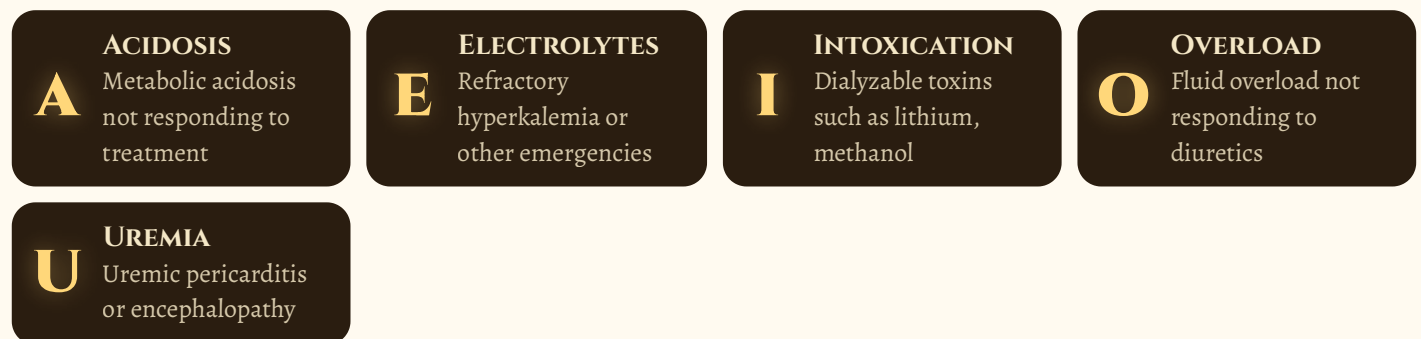
- Prerenal AKI is reduced perfusion from hypovolemia, hemorrhage, heart failure, sepsis, or drugs that lower glomerular pressure.
- Intrarenal AKI is damage to kidney tissue, most often acute tubular necrosis from prolonged ischemia or nephrotoxins such as contrast, aminoglycosides, and myoglobin.
- Postrenal AKI is obstruction of outflow from BPH, stones, tumors, or a blocked catheter, causing hydronephrosis.
- AKI is defined by a creatinine rise of 0.3 mg/dL within 48 hours, a rise to 1.5 times baseline within 7 days, or urine output below 0.5 mL/kg/hour for 6 hours.
- Prerenal clues: BUN to creatinine above 20 to 1, urine sodium below 20 mEq/L, concentrated urine. ATN clues: muddy brown casts, high urine sodium, fixed specific gravity.

## 2 AKI COURSE AND COMPLICATIONS

### ◆ TREATING HYPERKALEMIA WITH ECG CHANGES



### ◆ AEIOU: URGENT DIALYSIS INDICATIONS



*Hyperkalemia kills first in AKI: calcium shields the heart, insulin shifts, binders or dialysis remove.*

### WRITTEN NOTES: AKI COURSE AND COMPLICATIONS

- Oliguric phase: retained potassium, phosphate, acid, water, and urea. Hyperkalemia is the most dangerous early threat.

- Hyperkalemia with ECG changes: IV calcium to protect the heart, then insulin with glucose or albuterol to shift potassium, then removal by binders, diuretics, or dialysis.
- Diuretic phase: large volumes of dilute urine with risk of hypovolemia, hyponatremia, and hypokalemia.
- Urgent dialysis indications: refractory acidosis, electrolyte emergencies, certain toxins, refractory fluid overload, uremic pericarditis or encephalopathy.
- Daily weights are the best bedside measure of fluid balance.

### 3 CHRONIC KIDNEY DISEASE

#### ◆ CKD STAGING BY GFR

##### GFR STAGE 1 TO 2

Normal 90 or more mL/min/1.73 m<sup>2</sup>

60 or more plus damage such as albuminuria

CKD only if damage lasts over 3 months

##### GFR STAGE 3

Normal 90 or more mL/min/1.73 m<sup>2</sup>

30 to 59

Moderate loss; complications begin

##### GFR STAGE 4

Normal 90 or more mL/min/1.73 m<sup>2</sup>

15 to 29

Severe loss; plan dialysis access

##### GFR STAGE 5

Normal 90 or more mL/min/1.73 m<sup>2</sup>

Below 15

Kidney failure; dialysis or transplant

##### URINE ALBUMIN TO CREATININE

Normal Below 30 mg/g

30 mg/g or more

Earliest sign of diabetic kidney disease

#### ◆ SLOWING CKD PROGRESSION



##### LISINOPRIL

Zestril, Prinivil

ACE INHIBITOR

**USED FOR** Lowers glomerular pressure and albuminuria

**WATCH** Hyperkalemia, rising creatinine, dry cough, angioedema



##### LOSARTAN

Cozaar

ARB

**USED FOR** Diabetic kidney disease with albuminuria

**WATCH** Hyperkalemia; do not combine with ACE inhibitor



##### DAPAGLIFLOZIN

Farxiga

SGLT2 INHIBITOR

**USED FOR** Slows CKD progression, with or without diabetes

**WATCH** Volume depletion, genital infections

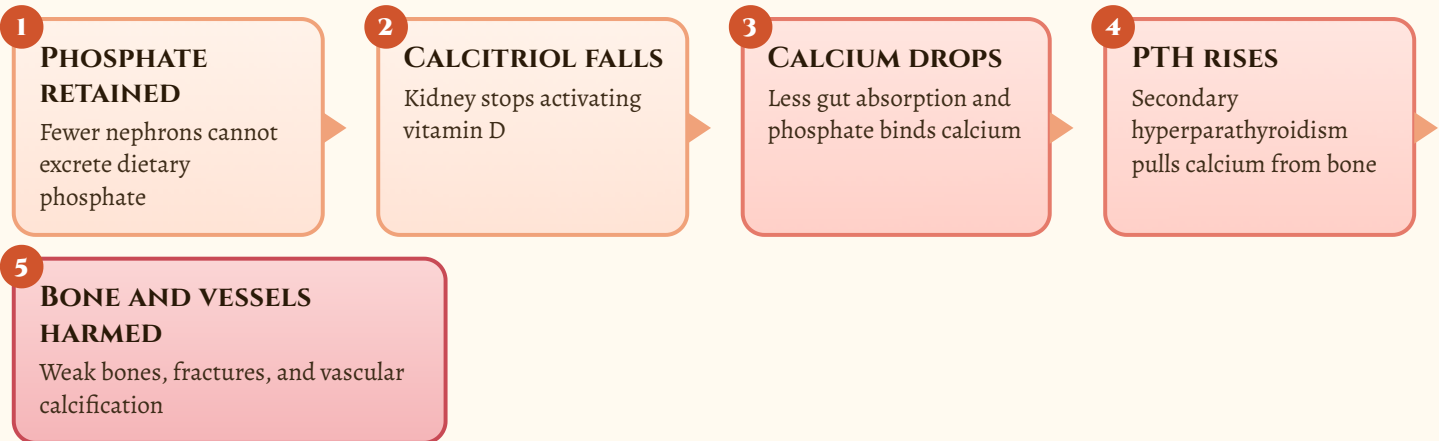


*Diabetes and hypertension cause most CKD; albuminuria comes first, and ACE inhibitors or ARBs slow the slide.*

- Defined as kidney damage or GFR below 60 lasting more than 3 months. Diabetes and hypertension are the leading causes.
- Stages by GFR: stage 3 is 30 to 59, stage 4 is 15 to 29, stage 5 is below 15 (kidney failure).
- Surviving nephrons hyperfilter, which hides early disease but drives further damage.
- Albuminuria is the earliest sign of diabetic kidney disease. ACE inhibitors and ARBs lower glomerular pressure and slow progression.
- Complications: hypertension, fluid overload, hyperkalemia, metabolic acidosis, anemia, mineral and bone disorder, uremia.
- Avoid magnesium antacids and adjust renally cleared drugs.

## 4 CKD COMPLICATIONS IN DEPTH

### ◆ CKD MINERAL AND BONE DISORDER



### ◆ TREATING CKD COMPLICATIONS



#### SEVELAMER

*Renvela*

##### PHOSPHATE BINDER

**USED FOR** Hyperphosphatemia

**WATCH** Give with meals; constipation



#### CALCIUM ACETATE

*Generic now (formerly PhosLo)*

##### CALCIUM BASED PHOSPHATE BINDER

**USED FOR** Hyperphosphatemia

**WATCH** Give with meals; hypercalcemia



#### EPOETIN ALFA

*Epogen, Procrit*

ESA

**USED FOR** Anemia of CKD

**WATCH** Hold if hemoglobin above about 11 g/dL; hypertension, clots



#### CALCITRIOL

*Rocaltrol*

##### ACTIVE VITAMIN D

**USED FOR** Low calcium, high PTH

**WATCH** Hypercalcemia



*Failing kidneys keep phosphate and lose erythropoietin and calcitriol: bones thin, vessels calcify, blood thins.*

#### WRITTEN NOTES: CKD COMPLICATIONS IN DEPTH

- Anemia: low erythropoietin causes normocytic anemia. Treat with ESAs and iron, keeping hemoglobin from rising above about 11 g/dL.
- Mineral and bone disorder: phosphate retention and low calcitriol lower calcium and raise PTH, weakening bone and calcifying vessels.
- Phosphate binders are taken with meals.
- Uremia: pruritus, nausea, metallic taste, fatigue, pericarditis, encephalopathy.
- Diet: limit sodium, potassium, and phosphorus; avoid salt substitutes containing potassium.

## 5 DIALYSIS ESSENTIALS

### ◆ DIALYSIS CHECKPOINTS

#### AV FISTULA CARE

- Palpate thrill, auscultate bruit
- No blood pressures on that arm
- No venipuncture on that arm
- No tight clothing or jewelry

#### DISEQUILIBRIUM SYNDROME

- Headache
- Nausea and vomiting
- Confusion or restlessness
- Cerebral edema from fast urea removal

#### PERITONEAL DIALYSIS

- Cloudy effluent means peritonitis
- Report abdominal pain and fever

#### FLUID TRACKING

- Weigh before and after hemodialysis
- Weight change shows fluid removed



*Feel the thrill, hear the bruit, and protect the fistula arm from cuffs, needles, and tight sleeves.*

#### WRITTEN NOTES: DIALYSIS ESSENTIALS

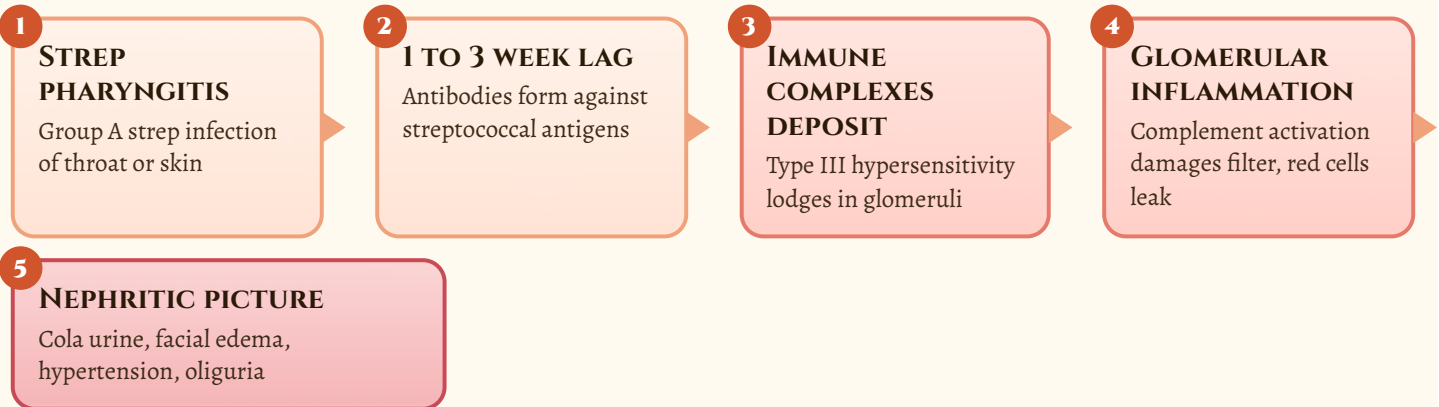
- Arteriovenous fistula: feel the thrill and hear the bruit; no blood pressures, venipunctures, or tight clothing on that arm.
- Dialysis disequilibrium: headache, nausea, and confusion from cerebral edema when urea is removed too quickly.
- Peritoneal dialysis: cloudy effluent signals peritonitis.
- Weigh before and after hemodialysis to judge fluid removal.

## 6 GLOMERULAR DISEASE: NEPHROTIC VERSUS NEPHRITIC

### ◆ NEPHROTIC VERSUS NEPHRITIC

| FEATURE             | NEPHROTIC                                      | NEPHRITIC                             |
|---------------------|------------------------------------------------|---------------------------------------|
| HALLMARK            | Proteinuria above 3.5 g/day                    | Hematuria with red cell casts         |
| URINE LOOK          | Foamy, lipiduria                               | Cola colored, smoky                   |
| BLOOD               | Low albumin, high lipids                       | Rising BUN and creatinine             |
| PRESSURE AND VOLUME | Edema, often anasarca                          | Hypertension, oliguria, facial edema  |
| KEY RISK            | Clots, renal vein thrombosis, infection        | Fluid overload, kidney failure        |
| CLASSIC CAUSE       | Minimal change in children; diabetes in adults | Post streptococcal glomerulonephritis |

### ◆ POST STREPTOCOCCAL GLOMERULONEPHRITIS



*Nephrotic is protein and swelling; nephritic is blood, hypertension, and low urine output.*

### WRITTEN NOTES: GLOMERULAR DISEASE: NEPHROTIC VERSUS NEPHRITIC

- Nephrotic: proteinuria above 3.5 g/day, hypoalbuminemia, edema, hyperlipidemia, lipiduria and foamy urine.
- Nephrotic complications: hypercoagulability with renal vein thrombosis, infections, and hyperlipidemia.
- Minimal change disease is the top cause in children; diabetic kidney disease in adults.
- Nephritic: hematuria with red cell casts, hypertension, oliguria, azotemia, mild proteinuria.
- Post streptococcal glomerulonephritis is a type III immune complex disease 1 to 3 weeks after pharyngitis; cola colored urine and facial edema.

## 7 KIDNEY STONES

### ◆ MAIN KIDNEY STONE TYPES

| FEATURE    | CALCIUM                                 | URIC ACID                | STRUVITE                      |
|------------|-----------------------------------------|--------------------------|-------------------------------|
| FREQUENCY  | Most common                             | Less common              | Less common                   |
| LINKED TO  | Hypercalciuria, hyperparathyroidism     | Gout, high purine intake | Urease producing bacteria     |
| URINE PH   | Variable                                | Acidic                   | Alkaline                      |
| X RAY      | Radiopaque                              | Radiolucent              | Radiopaque, can form staghorn |
| PREVENTION | Fluids; do not restrict dietary calcium | Fluids, alkalinize urine | Fluids, treat infection       |

### ◆ RENAL COLIC AT THE BEDSIDE

#### PRESENTATION

- Sudden colicky flank pain
- Pain radiates to groin
- Hematuria
- Nausea and vomiting
- Restless, cannot get comfortable

#### NURSING ACTIONS

- Strain all urine for analysis
- Analgesia and fluids
- Tamsulosin for small distal stones

#### EMERGENCY

- Fever with obstructing stone
- Needs drainage plus antibiotics



*Push fluids to 2 to 2.5 L of urine daily; fever with an obstructing stone needs drainage now.*

### WRITTEN NOTES: KIDNEY STONES

- Presentation: sudden colicky flank pain radiating to the groin, hematuria, nausea, restlessness.
- Calcium stones are most common and link to hypercalciuria and hyperparathyroidism.
- Uric acid stones form in acidic urine with gout and are radiolucent. Struvite stones form in alkaline urine with urease producing bacteria and can become staghorn stones.
- Prevention for all types: fluids to produce 2 to 2.5 L of urine daily. Do not restrict dietary calcium for calcium oxalate stones.
- Strain urine for analysis; tamsulosin helps small distal stones pass.
- Fever with an obstructing stone is an emergency needing drainage plus antibiotics.

## ◆ CYSTITIS VERSUS PYELONEPHRITIS

| FEATURE      | CYSTITIS                                     | PYELONEPHRITIS                  |
|--------------|----------------------------------------------|---------------------------------|
| SITE         | Bladder                                      | Kidney and renal pelvis         |
| SYMPTOMS     | Dysuria, frequency, urgency, suprapubic pain | Fever, chills, flank pain       |
| EXAM         | No systemic signs                            | Costovertebral angle tenderness |
| URINE        | Leukocyte esterase, nitrites                 | Same, plus white cell casts     |
| OLDER ADULTS | May show confusion or falls                  | Confusion, falls, sepsis risk   |

## ◆ URINALYSIS FOR INFECTION

## LEUKOCYTE ESTERASE

Normal Negative

Positive

White cells present: pyuria

## NITRITES

Normal Negative

Positive

Gram negative bacteria such as E. coli

## URINE WBC

Normal 0 to 5 per hpf

Above 5 per hpf

Inflammation or infection

## WHITE CELL CASTS

Normal None

Present

Kidney involvement: pyelonephritis

## URINE CULTURE

Normal No growth

Significant colony count

Confirms organism and sensitivities



*Fever and flank pain move a UTI up to the kidney; older adults may only show confusion.*

## WRITTEN NOTES: URINARY TRACT INFECTION AND PYELONEPHRITIS

- Most uncomplicated UTIs are caused by E. coli; women are at higher risk because of a short urethra.
- Cystitis: dysuria, frequency, urgency, suprapubic discomfort, no systemic signs.
- Pyelonephritis: fever, chills, flank pain, costovertebral angle tenderness, possible white cell casts.
- Urinalysis: positive leukocyte esterase and nitrites support bacterial infection.
- Older adults may present with confusion or falls rather than urinary symptoms.
- Remove indwelling catheters as soon as they are not needed to prevent CAUTI.

## 9 BPH AND INCONTINENCE

### ◆ BPH MEDICATIONS



#### TAMSULOSIN

*Flomax*

##### ALPHA 1 BLOCKER

**USED FOR** BPH symptoms, distal ureteral stones

**WATCH** Orthostatic hypotension; rise slowly



#### ALFUZOSIN

*Uroxatral*

##### ALPHA 1 BLOCKER

**USED FOR** BPH symptoms

**WATCH** Orthostatic hypotension, dizziness



#### FINASTERIDE

*Proscar*

##### 5 ALPHA REDUCTASE INHIBITOR

**USED FOR** Enlarged prostate

**WATCH** Months to work; halves PSA; pregnancy handling



#### DUTASTERIDE

*Avodart*

##### 5 ALPHA REDUCTASE INHIBITOR

**USED FOR** Enlarged prostate

**WATCH** Lowers PSA; pregnant people avoid contact

### ◆ FOUR TYPES OF INCONTINENCE

#### STRESS

- Leak with cough, sneeze, lifting
- Pelvic floor weakness

#### URGE

- Sudden strong urge, then leak
- Detrusor overactivity

#### OVERFLOW

- Constant dribbling, full bladder
- Obstruction or weak detrusor

#### FUNCTIONAL

- Cannot reach the toilet in time
- Mobility or cognitive limits



*Alpha blockers work in days, 5 alpha reductase inhibitors in months; avoid decongestants and anticholinergics in BPH.*

### WRITTEN NOTES: BPH AND INCONTINENCE

- BPH is DHT driven hyperplasia of the periurethral transition zone, causing hesitancy, weak stream, nocturia, and retention.
- Alpha 1 blockers work in days but cause orthostatic hypotension. 5 alpha reductase inhibitors shrink the gland over months and halve PSA.
- Decongestants and anticholinergics can trigger acute retention.
- TUR syndrome: dilutional hyponatremia from absorbed irrigation fluid.

- Incontinence types: stress (pelvic floor weakness), urge (detrusor overactivity), overflow (obstruction or weak detrusor), functional (cannot reach the toilet).

## CLINICAL PEARLS

- Where is the blockage? Before the kidney is prerenal (perfusion), in the kidney is intrarenal (tissue), after the kidney is postrenal (outflow).
- BUN to creatinine above 20 to 1 and low urine sodium mean the tubules still work: think prerenal and give volume.
- Nephrotic is protein: foamy urine, low albumin, edema, high lipids. Nephritic is blood and pressure: red cell casts, hypertension, oliguria.
- Kidney failure keeps what it should lose: potassium, phosphate, acid, water, and urea. It loses what it should keep making: erythropoietin and active vitamin D.
- Fever plus flank pain moves a UTI up to the kidney. Fever plus an obstructing stone is an emergency.

## RX KEY MEDICATIONS

### ♦ MEDICATIONS FOR KIDNEYS AND URINARY TRACT



#### FUROSEMIDE

*Lasix*

##### LOOP DIURETICS

**USED FOR** Fluid overload in kidney disease and heart failure

**WATCH** Monitor potassium, blood pressure, and daily weight; rapid IV doses can cause hearing damage.



#### SEVELAMER

*Renvela*

##### PHOSPHATE BINDERS

**USED FOR** Hyperphosphatemia in CKD

**WATCH** Give with meals; calcium based binders can cause hypercalcemia.



#### EPOETIN ALFA

*Epogen, Procrit, Retacrit*

##### ERYTHROPOIESIS STIMULATING AGENTS

**USED FOR** Anemia of CKD

**WATCH** Monitor blood pressure and hemoglobin; hold when hemoglobin is above target because of stroke and clot risk.



#### TAMSULOSIN

*Flomax*

##### ALPHA 1 ADRENERGIC BLOCKERS

**USED FOR** BPH and passage of distal ureteral stones

**WATCH** Orthostatic hypotension; rise slowly, especially after the first dose.



#### FINASTERIDE

*Proscar*

##### 5 ALPHA REDUCTASE INHIBITORS

**USED FOR** BPH with an enlarged prostate

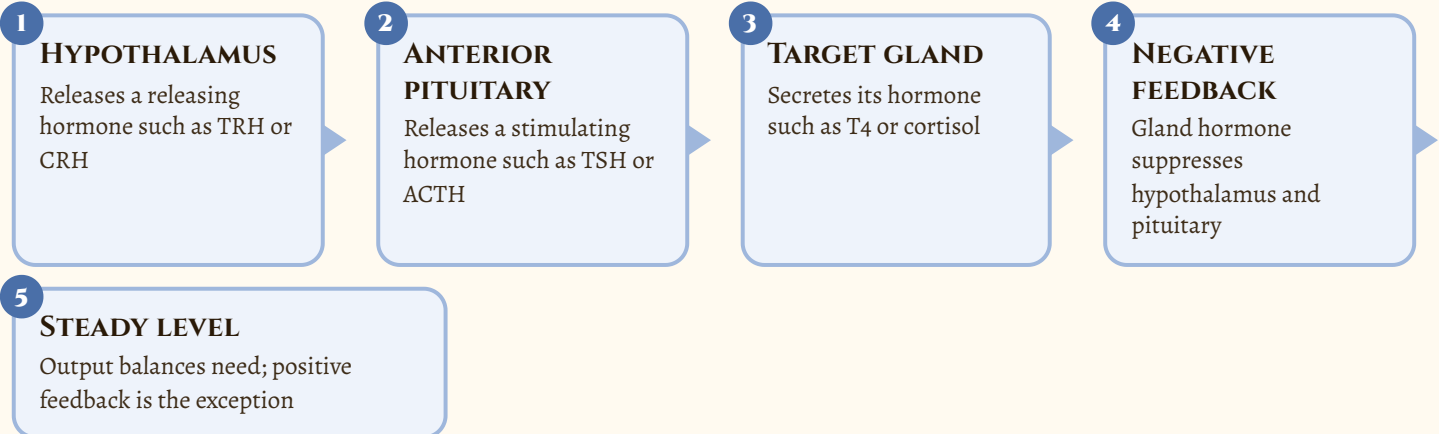
**WATCH** Takes months to work and lowers PSA; pregnant people should not handle crushed tablets.

# GLAND OASIS: HORMONES AND REPRODUCTION

Dr. Akash Garg · Dr. Garg Learning

## 1 FEEDBACK LOOPS AND LEVELS OF DYSFUNCTION

### ◆ NEGATIVE FEEDBACK AXIS



### ◆ PRIMARY VERSUS SECONDARY DISEASE

| FEATURE             | PRIMARY (GLAND)                       | SECONDARY (PITUITARY)          |
|---------------------|---------------------------------------|--------------------------------|
| WHERE IT FAILS      | Target gland                          | Pituitary                      |
| HORMONE DIRECTION   | Gland and pituitary hormones opposite | Both move the same way         |
| HYPOTHYROID EXAMPLE | High TSH, low free T4                 | Low TSH, low free T4           |
| ADRENAL EXAMPLE     | Addison: high ACTH, low cortisol      | Low ACTH, low cortisol         |
| THYROID MONITORING  | Follow TSH                            | Follow free T4; TSH unreliable |



*Opposite directions point to the gland; same direction points upstream to the pituitary.*

### WRITTEN NOTES: FEEDBACK LOOPS AND LEVELS OF DYSFUNCTION

- Most endocrine axes run hypothalamus to pituitary to gland, with negative feedback from the gland hormone.
- Primary disease: problem in the gland; gland hormone and pituitary hormone move in opposite directions.
- Secondary disease: problem in the pituitary; both hormones move in the same direction.
- Positive feedback amplifies a signal, as with oxytocin during labor and the LH surge before ovulation.

- Posterior pituitary releases ADH and oxytocin; anterior pituitary releases TSH, ACTH, GH, prolactin, FSH, and LH.

## 2 DIABETES MELLITUS

### ◆ TYPE 1 VERSUS TYPE 2 DIABETES

| FEATURE       | TYPE 1                                           | TYPE 2                                     |
|---------------|--------------------------------------------------|--------------------------------------------|
| MECHANISM     | Autoimmune beta cell destruction                 | Insulin resistance, then beta cell failure |
| MARKERS       | Islet antibodies, low C peptide                  | Obesity, acanthosis nigricans              |
| INSULIN       | Always required                                  | Oral agents first, insulin if needed       |
| ACUTE RISK    | DKA                                              | HHS                                        |
| COMPLICATIONS | Retinopathy, nephropathy, neuropathy, MI, stroke | Same micro and macrovascular set           |

### ◆ DIAGNOSING DIABETES

#### HEMOGLOBIN A1C

Normal Below 5.7 percent

**6.5 percent or more**

Diabetes; 5.7 to 6.4 is prediabetes

#### FASTING PLASMA GLUCOSE

Normal 70 to 99 mg/dL

**126 mg/dL or more**

Diabetes; 100 to 125 is prediabetes

#### 2 HOUR OGTT

Normal Below 140 mg/dL

**200 mg/dL or more**

Diabetes

#### RANDOM GLUCOSE

Normal Below 140 mg/dL

**200 mg/dL or more with symptoms**

Diabetes

#### URINE GLUCOSE

Normal Negative

**Positive above about 180 mg/dL serum**

Osmotic diuresis: polyuria, polydipsia



*Type 1 lacks insulin and makes ketones; type 2 resists insulin until beta cells tire.*

### WRITTEN NOTES: DIABETES MELLITUS

- Type 1: autoimmune beta cell destruction, islet antibodies, low C peptide, insulin required, prone to DKA.
- Type 2: insulin resistance with progressive beta cell failure, linked to obesity; acanthosis nigricans is a skin marker.
- Diagnosis: A1C of 6.5 percent or more, fasting glucose of 126 mg/dL or more, 2 hour OGTT of 200 mg/dL or more, or random glucose of 200 mg/dL or more with symptoms.

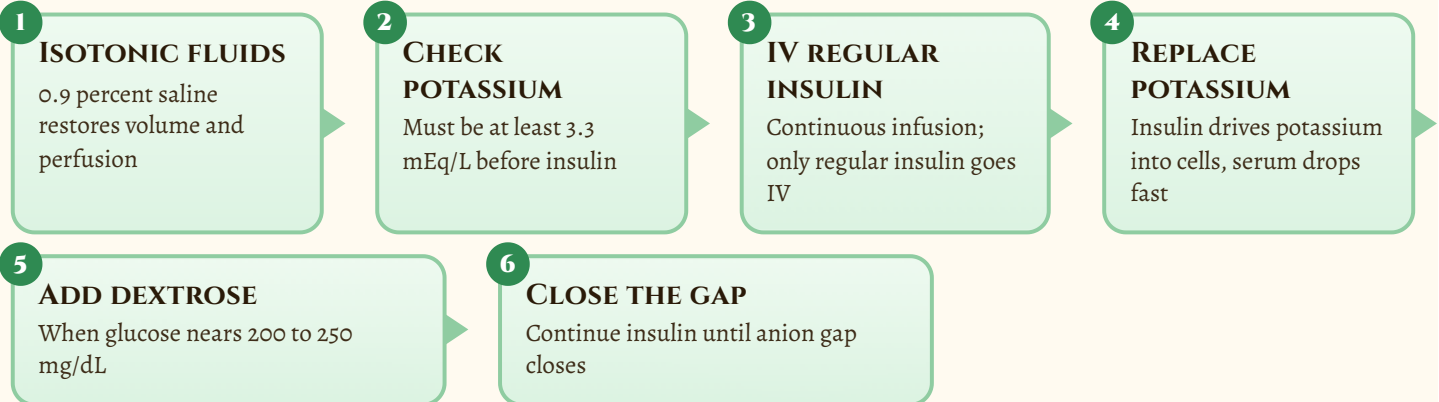
- Polyuria results from osmotic diuresis when glucose exceeds the renal threshold of about 180 mg/dL.
- Microvascular complications: retinopathy, nephropathy, neuropathy. Macrovascular: MI, stroke, peripheral artery disease.
- Gestational diabetes: placental hormones cause insulin resistance; risks include macrosomia and neonatal hypoglycemia.

### 3 ACUTE GLUCOSE EMERGENCIES

#### ◆ DKA VERSUS HHS

| FEATURE        | DKA                               | HHS                             |
|----------------|-----------------------------------|---------------------------------|
| TYPICAL CLIENT | Type 1, younger                   | Older adult with type 2         |
| GLUCOSE        | Usually above 250 mg/dL           | Often above 600 mg/dL           |
| KETONES AND PH | High ketones, anion gap acidosis  | Minimal ketones, near normal pH |
| OSMOLALITY     | Variable                          | Above 320 mOsm/kg               |
| HALLMARKS      | Kussmaul breathing, fruity breath | Profound dehydration, confusion |

#### ◆ DKA TREATMENT SEQUENCE



*In DKA serum potassium lies: confirm at least 3.3 mEq/L before insulin, then replace as it falls.*

#### WRITTEN NOTES: ACUTE GLUCOSE EMERGENCIES

- DKA: insulin deficiency, ketoacids, anion gap acidosis, Kussmaul breathing, fruity breath, dehydration.
- DKA treatment: isotonic fluids, IV regular insulin once potassium is at least 3.3 mEq/L, potassium replacement, dextrose added when glucose nears 200 to 250 mg/dL, continue insulin until the gap closes.
- HHS: older adults with type 2 diabetes, glucose often above 600 mg/dL, osmolality above 320, profound dehydration and confusion, minimal ketones.

- Hypoglycemia: treat with 15 to 20 g fast carbohydrate and recheck in 15 minutes; glucagon or IV dextrose if unable to swallow.
- Beta blockers mask adrenergic warning signs of hypoglycemia.
- Dawn phenomenon: normal 3 AM glucose, high fasting glucose. Somogyi effect: low 3 AM glucose with rebound.

## 4 THYROID AND PARATHYROID

### ◆ HYPOTHYROIDISM VERSUS GRAVES DISEASE

| FEATURE      | HYPOTHYROIDISM                              | GRAVES DISEASE                                           |
|--------------|---------------------------------------------|----------------------------------------------------------|
| COMMON CAUSE | Hashimoto, anti TPO antibodies              | Thyroid stimulating immunoglobulins                      |
| LABS         | High TSH, low free T4                       | Low TSH, high free T4                                    |
| FINDINGS     | Fatigue, cold, weight gain, bradycardia     | Heat intolerance, weight loss, tachycardia, exophthalmos |
| CRISIS       | Myxedema coma: hypothermia, hypoventilation | Thyroid storm: fever, tachycardia, delirium              |
| CRISIS CARE  | Airway, IV thyroid hormone, steroids        | Beta blocker, thionamide, then iodine, cooling           |

### ◆ HYPERCALCEMIA OF HYPERPARATHYROIDISM

**S**

#### STONES

Kidney stones from high urine calcium

**B**

#### BONES

Bone pain and loss from PTH resorption

**G**

#### GROANS

Abdominal pain, constipation, nausea

**M**

#### MOANS

Fatigue, depression, confusion



*Hypothyroid slows everything and Graves speeds it up; after thyroidectomy guard airway, voice, and calcium.*

### WRITTEN NOTES: THYROID AND PARATHYROID

- Hypothyroidism: slow everything; Hashimoto (anti TPO antibodies) is the most common cause; high TSH and low free T4.
- Myxedema coma: hypothermia, hypoventilation, hyponatremia, hypotension; treat with airway support, IV thyroid hormone, and steroids.
- Graves disease: thyroid stimulating immunoglobulins, goiter, exophthalmos, low TSH and high T4.
- Thyroid storm: fever, severe tachycardia, delirium; treat with beta blocker, thionamide, then iodine, steroids, cooling.
- After thyroidectomy: airway, bleeding, voice, and calcium; keep a tracheostomy tray at the bedside.
- Hyperparathyroidism causes hypercalcemia (stones, bones, groans, moans); hypoparathyroidism causes hypocalcemia with Chvostek and Trousseau signs.

## 5 ADRENAL DISORDERS

### ◆ CUSHING SYNDROME VERSUS ADDISON DISEASE

| FEATURE              | CUSHING SYNDROME                           | ADDISON DISEASE                         |
|----------------------|--------------------------------------------|-----------------------------------------|
| CORTISOL             | Excess                                     | Deficient, plus low aldosterone         |
| COMMON CAUSE         | Glucocorticoid therapy                     | Autoimmune adrenal destruction          |
| APPEARANCE           | Moon face, buffalo hump, striae, thin skin | Bronze skin from high ACTH, weight loss |
| PRESSURE AND GLUCOSE | Hypertension, hyperglycemia                | Hypotension, hypoglycemia               |
| ELECTROLYTES         | Possible hypokalemia                       | Hyponatremia, hyperkalemia              |
| KEY RISK             | Infection, fractures                       | Adrenal crisis with stress              |

### ◆ ADRENAL DRUGS



#### HYDROCORTISONE

*Solu-Cortef, Cortef*

##### GLUCOCORTICOID

**USED FOR** Adrenal insufficiency and crisis

**WATCH** Stress dosing in illness; never stop abruptly



#### FLUDROCORTISONE

*Generic now (formerly Florinef)*

##### MINERALOCORTICOID

**USED FOR** Aldosterone replacement in Addison disease

**WATCH** Edema, hypertension, hypokalemia



#### SPIRONOLACTONE

*Aldactone*

##### ALDOSTERONE ANTAGONIST

**USED FOR** Primary hyperaldosteronism

**WATCH** Hyperkalemia, gynecomastia



#### PHENOXYBENZAMINE

*Dibenzylamine*

##### ALPHA BLOCKER

**USED FOR** Pheochromocytoma before surgery

**WATCH** Alpha blockade before any beta blocker



*Never stop long term steroids abruptly; adrenal crisis needs IV hydrocortisone and saline with dextrose.*

WRITTEN NOTES: ADRENAL DISORDERS

- Cushing syndrome is cortisol excess from any cause, most often glucocorticoid therapy; Cushing disease is a pituitary ACTH adenoma.
- Cushing findings: moon face, buffalo hump, central obesity, striae, thin skin, hyperglycemia, hypertension, infection risk.
- Addison disease (primary): low cortisol and aldosterone, hyponatremia, hyperkalemia, hypotension, hypoglycemia, bronze skin from high ACTH.
- Abrupt steroid withdrawal causes secondary insufficiency with low ACTH and less hyperkalemia.
- Adrenal crisis: IV hydrocortisone, saline with dextrose; teach stress dosing and medical ID.
- Primary hyperaldosteronism: hypertension, hypokalemia, metabolic alkalosis, low renin.
- Pheochromocytoma: paroxysmal hypertension, headache, palpitations, sweating; alpha blockade before beta blockade.

## 6 PITUITARY AND ADH

### ◆ DIABETES INSIPIDUS VERSUS SIADH

| FEATURE      | DIABETES INSIPIDUS                         | SIADH                                             |
|--------------|--------------------------------------------|---------------------------------------------------|
| ADH EFFECT   | Absent or kidneys resist it                | Excess ADH                                        |
| URINE        | Large volume, dilute, low specific gravity | Low volume, concentrated                          |
| SERUM SODIUM | High                                       | Low                                               |
| RISK         | Dehydration, hypovolemia                   | Seizures, cerebral edema                          |
| TREATMENT    | Desmopressin for central type              | Fluid restriction; hypertonic saline for seizures |
| CAUTION      | Nephrogenic: lithium, hypercalcemia        | Correct sodium slowly: osmotic demyelination      |

## ◆ PITUITARY AND WATER HORMONE DRUGS



### DESMOPRESSIN

DDAVP

#### SYNTHETIC ADH ANALOG

**USED FOR** Central diabetes insipidus

**WATCH** Hyponatremia, fluid retention



### CABERGOLINE

Generic now (formerly Dostinex)

#### DOPAMINE AGONIST

**USED FOR** Prolactinoma

**WATCH** Orthostatic hypotension, nausea



### BROMOCRIPTINE

Parlodel

#### DOPAMINE AGONIST

**USED FOR** Prolactinoma, acromegaly

**WATCH** Orthostatic hypotension, nausea



### TOLVAPTAN

Samsca

#### VASOPRESSIN RECEPTOR ANTAGONIST

**USED FOR** Hyponatremia from SIADH

**WATCH** Too rapid sodium rise, liver injury



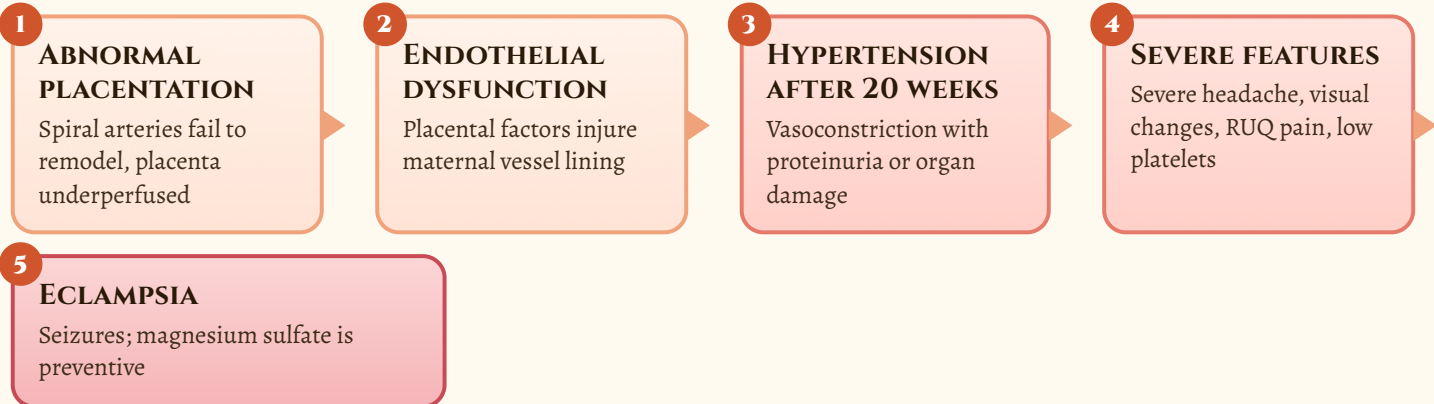
SIADH soaks with low sodium and concentrated urine; DI dries with high sodium and dilute urine.

## WRITTEN NOTES: PITUITARY AND ADH

- Acromegaly: GH excess after growth plate closure; gigantism before closure.
- GH deficiency in children: proportional short stature and delayed puberty.
- Large pituitary tumors compress the optic chiasm, causing bitemporal hemianopia.
- Prolactinoma: amenorrhea, galactorrhea, infertility; treated with dopamine agonists.
- Central DI: no ADH, responds to desmopressin. Nephrogenic DI: kidney resistance, often from lithium or hypercalcemia.
- SIADH: water retention, hyponatremia, concentrated urine; fluid restriction, hypertonic saline for seizures, and slow correction to prevent osmotic demyelination.

## 7 REPRODUCTIVE DISORDERS

### ◆ HOW PREECLAMPSIA DEVELOPS



### ◆ PREECLAMPSIA AND MAGNESIUM MONITORING

#### SERUM MAGNESIUM

Normal 1.7 to 2.2 mg/dL

**Therapeutic 4.8 to 8.4 mg/dL (4 to 7 mEq/L)**

Higher levels: lost reflexes, respiratory depression

#### PLATELETS

Normal 150,000 to 400,000/mm<sup>3</sup>

**Below 100,000/mm<sup>3</sup>**

Severe feature

#### 24 HOUR URINE PROTEIN

Normal Below 300 mg/day

**300 mg/day or more**

Proteinuria of preeclampsia

#### AST AND ALT

Normal About 10 to 40 units/L

**Twice normal or more**

Liver involvement, severe feature

#### SERUM CREATININE

Normal 0.6 to 1.2 mg/dL

**Above 1.1 mg/dL**

Renal involvement, severe feature



*Magnesium sulfate prevents eclamptic seizures; lost reflexes or slow breathing calls for calcium gluconate.*

### WRITTEN NOTES: REPRODUCTIVE DISORDERS

- PCOS: insulin resistance and high LH drive ovarian androgens; irregular cycles, hirsutism, acne; risks include type 2 diabetes and endometrial hyperplasia.
- Endometriosis: ectopic endometrial tissue causing cyclic pain, dyspareunia, and infertility.
- Preeclampsia: abnormal placentation and endothelial dysfunction; hypertension after 20 weeks with proteinuria or organ damage.
- Severe features: severe headache, visual changes, right upper quadrant pain, low platelets; magnesium sulfate prevents seizures.
- Magnesium toxicity: loss of reflexes, respiratory depression; antidote is calcium gluconate.

- Testicular torsion is a surgical emergency with roughly a 6 hour window.

## 8 STIS AND REPRODUCTIVE CANCERS

### ◆ STI AND CANCER CLUES

#### SILENT STIS

- Chlamydia and gonorrhea often silent
- Cause PID and tubal infertility
- Raise ectopic pregnancy risk

#### GENITAL LESIONS

- Syphilis: painless chancre
- Herpes: painful clustered vesicles

#### BREAST CANCER WARNINGS

- Hard, fixed, painless mass
- Skin dimpling, peau d'orange
- Nipple retraction
- Risk: BRCA, long estrogen exposure

#### CERVIX AND PROSTATE

- HPV 16 and 18 cause cervical cancer
- Prostate cancer: peripheral zone, bone spread
- BPH: transition zone, early obstruction



*Silent chlamydia and gonorrhea scar tubes; HPV 16 and 18 drive cervical cancer, preventable by vaccine.*

### WRITTEN NOTES: STIS AND REPRODUCTIVE CANCERS

- Chlamydia and gonorrhea are often silent and are the main causes of PID, ectopic pregnancy, and tubal infertility.
- Primary syphilis: painless chancre. Genital herpes: painful clustered vesicles.
- High risk HPV types 16 and 18 cause most cervical cancers; vaccination and screening prevent them.
- Breast cancer warning signs: hard, fixed, painless mass, skin dimpling, peau d'orange, nipple retraction.
- Breast cancer risk rises with BRCA mutations and longer lifetime estrogen exposure.
- Prostate cancer arises in the peripheral zone and often spreads to bone; BPH arises in the transition zone and obstructs early.

### + CLINICAL PEARLS

- Find the level: if the gland hormone and the pituitary hormone move in opposite directions, the gland is the problem (primary). If they move together, look upstream.
- DKA versus HHS: ketones and Kussmaul mean DKA. Higher glucose, extreme dehydration, and confusion with little ketosis mean HHS.
- In DKA, serum potassium lies. Total body potassium is low, and insulin will drop the serum level fast.
- SIADH soaks (water retained, low sodium, concentrated urine). DI dries (water lost, high sodium, dilute urine).
- Cushing is too much cortisol: moon face, high glucose, thin skin. Addison is too little: low pressure, low sodium, high potassium, bronze skin. Never stop long term steroids abruptly.

◆ **MEDICATIONS FOR HORMONES AND REPRODUCTION**



**INSULIN LISPRO**

*Humalog, Admelog, Lyumjev*

**INSULINS**

**USED FOR** Type 1 diabetes, DKA, and type 2 diabetes when needed

**WATCH** Hypoglycemia; only regular insulin is given IV, and potassium must be monitored during infusion.



**METFORMIN**

*Glucophage*

**BIGUANIDES**

**USED FOR** Type 2 diabetes and insulin resistance in PCOS

**WATCH** Hold for reduced kidney function or around iodinated contrast per protocol because of lactic acidosis risk; GI upset is common.



**LEVOTHYROXINE**

*Synthroid, Levoxyl, Unithroid*

**THYROID HORMONE REPLACEMENT**

**USED FOR** Hypothyroidism and myxedema coma

**WATCH** Take on an empty stomach in the morning; start low in older adults and cardiac clients; watch for tachycardia and chest pain.



**METHIMAZOLE**

*Tapazole*

**THIONAMIDE ANTITHYROID DRUGS**

**USED FOR** Graves disease and thyroid storm

**WATCH** Report sore throat or fever because of agranulocytosis risk; propylthiouracil can injure the liver.



**HYDROCORTISONE**

*Solu-Cortef, Cortef*

**GLUCOCORTICOIDS**

**USED FOR** Adrenal insufficiency and adrenal crisis

**WATCH** Never stop long term therapy abruptly; increase dose during illness as instructed; monitor glucose.

**1 STROKE****◆ ISCHEMIC VERSUS HEMORRHAGIC STROKE**

| FEATURE       | ISCHEMIC                                    | HEMORRHAGIC                               |
|---------------|---------------------------------------------|-------------------------------------------|
| SHARE         | About 85 percent                            | About 15 percent                          |
| CAUSES        | Thrombosis, emboli from atrial fibrillation | Hypertension, aneurysm, anticoagulation   |
| CT            | May be normal early                         | Shows blood                               |
| KEY TREATMENT | Thrombolytic within 4.5 hours               | Control pressure, reverse anticoagulation |
| WARNING       | TIA: transient, no infarction               | SAH: thunderclap headache, vasospasm      |

**◆ DEFICITS BY HEMISPHERE****LEFT HEMISPHERE**

- Right sided weakness
- Aphasia
- Slow, cautious behavior

**RIGHT HEMISPHERE**

- Left sided weakness
- Left neglect
- Impulsivity, poor judgment

**ANY STROKE**

- Swallow screen before anything by mouth
- BP below 185/110 before thrombolytic



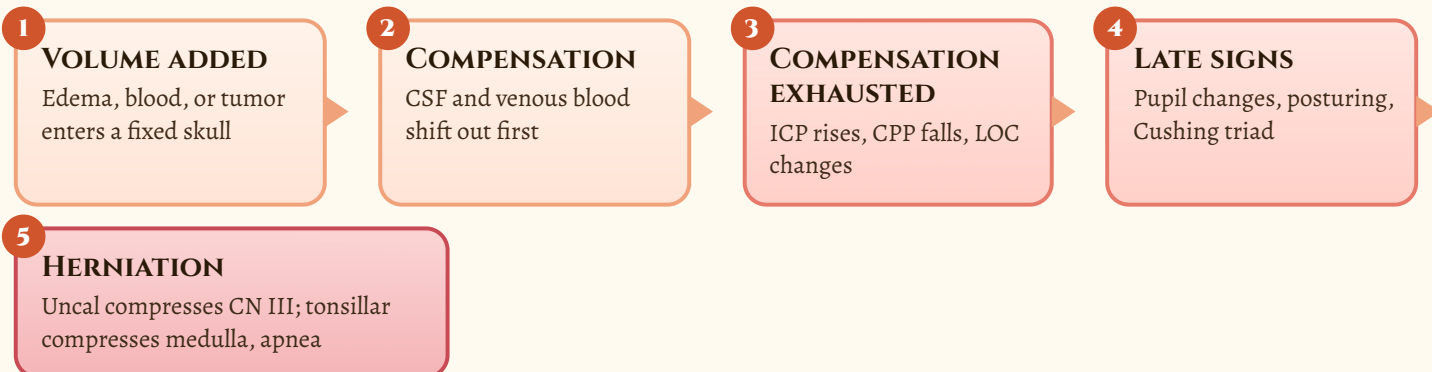
*Time is brain: CT first to exclude bleeding, then thrombolytics within 4.5 hours of last known well.*

**WRITTEN NOTES: STROKE**

- Ischemic strokes (about 85 percent) come from thrombosis or emboli, often from atrial fibrillation. Hemorrhagic strokes come from hypertension, aneurysm, or anticoagulation.
- TIA is transient ischemia without infarction and warns of stroke within days.
- Thrombolytics within 4.5 hours of last known well after CT excludes hemorrhage; BP below 185/110 before treatment.
- Left hemisphere: right weakness and aphasia. Right hemisphere: left weakness, left neglect, impulsivity.
- Swallow screen before anything by mouth.
- Subarachnoid hemorrhage: thunderclap headache from a ruptured berry aneurysm; watch for vasospasm and hydrocephalus.

## 2 INCREASED ICP AND HERNIATION

### ◆ RISING ICP TO HERNIATION



### ◆ PRESSURE TARGETS IN BRAIN INJURY

#### ICP

Normal 5 to 15 mm Hg

Above 20 mm Hg sustained

Intracranial hypertension, needs treatment

#### CPP (MAP MINUS ICP)

Normal Target about 60 to 70 mm Hg

Below 60 mm Hg

Brain ischemia risk

#### PACO<sub>2</sub>

Normal 35 to 45 mm Hg

Above 45 mm Hg

Vasodilation raises ICP; keep normal

#### SERUM SODIUM

Normal 135 to 145 mEq/L

Falling during osmotic therapy

Worsens cerebral edema; recheck often



*Earliest sign of rising ICP is a change in consciousness; Cushing triad and a blown pupil are late.*

### WRITTEN NOTES: INCREASED ICP AND HERNIATION

- Monro Kellie: brain, blood, and CSF share a fixed space; CSF and venous blood shift first.
- Normal ICP is about 5 to 15 mm Hg. CPP equals MAP minus ICP, with a target of about 60 to 70.
- Early sign: change in level of consciousness. Late signs: pupil changes, posturing, Cushing triad (wide pulse pressure, bradycardia, irregular respirations).
- Uncal herniation compresses cranial nerve III (ipsilateral dilated pupil). Tonsillar herniation compresses the medulla (respiratory arrest).
- Nursing: head of bed 30 degrees, neck midline, avoid hip flexion and clustered care, normal carbon dioxide, osmotic therapy as ordered.
- Infants with hydrocephalus show enlarging head circumference and bulging fontanelle.

## ◆ EPIDURAL VERSUS SUBDURAL HEMATOMA

| FEATURE       | EPIDURAL                           | SUBDURAL                                 |
|---------------|------------------------------------|------------------------------------------|
| VESSEL        | Artery, often middle meningeal     | Bridging veins                           |
| TYPICAL CAUSE | Temporal bone fracture             | Falls, older adults on anticoagulants    |
| COURSE        | Lucid interval, then rapid decline | Acute, or chronic with gradual confusion |
| CT SHAPE      | Lens shaped, biconvex              | Crescent shaped                          |

## ◆ HEAD INJURY PRIORITIES

## AIRWAY

- GCS 8 or less: intubate

## BASILAR SKULL FRACTURE

- Battle sign
- Raccoon eyes
- CSF leak from nose or ear
- No nasal tubes or suction

## PREVENT SECONDARY INJURY

- Avoid hypoxia
- Avoid hypotension
- Avoid hyperthermia
- Avoid glucose extremes

CONCUSSION RETURN  
PRECAUTIONS

- Worsening headache
- Repeated vomiting
- Confusion



*Epidural is arterial with a lucid interval; chronic subdural is venous and creeps up on anticoagulated elders.*

## WRITTEN NOTES: TRAUMATIC BRAIN INJURY AND HEMATOMAS

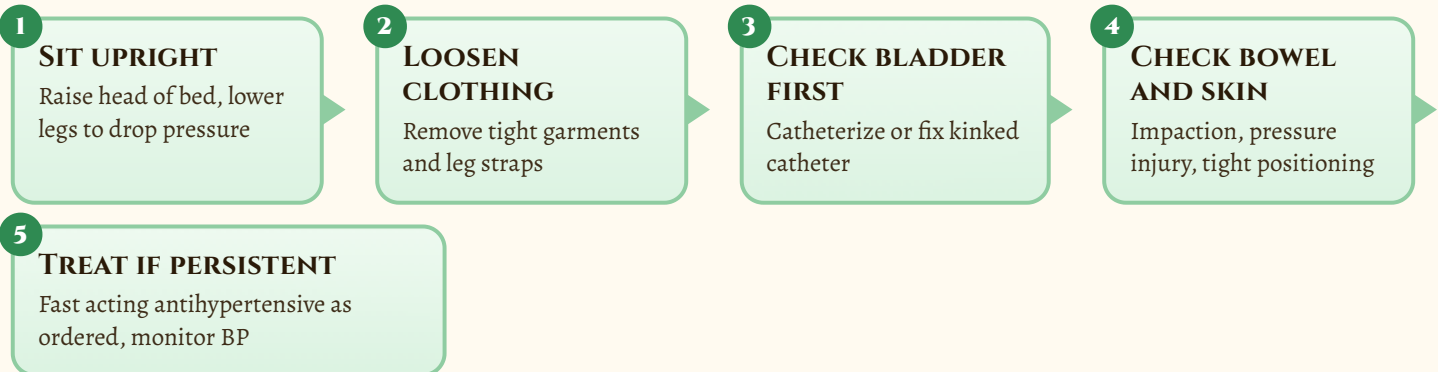
- Epidural: arterial, often middle meningeal artery with temporal fracture; lucid interval then rapid decline; lens shaped on CT.
- Subdural: venous bridging veins; chronic subdurals in older adults on anticoagulants cause gradual confusion.
- GCS of 8 or less: protect the airway.
- Basilar skull fracture: Battle sign, raccoon eyes, CSF leak; no nasal tubes or suction.
- Prevent secondary injury: avoid hypoxia, hypotension, hyperthermia, and glucose extremes.
- Concussion discharge: return for worsening headache, repeated vomiting, or confusion.

## 4 SPINAL CORD INJURY

### ◆ NEUROGENIC SHOCK VERSUS AUTONOMIC DYSREFLEXIA

| FEATURE        | NEUROGENIC SHOCK                          | AUTONOMIC DYSREFLEXIA                    |
|----------------|-------------------------------------------|------------------------------------------|
| TIMING         | Acute, after injury                       | After spinal shock resolves              |
| LEVEL          | Usually T6 or above                       | T6 or above                              |
| BLOOD PRESSURE | Hypotension                               | Severe hypertension                      |
| HEART RATE     | Bradycardia                               | Bradycardia                              |
| OTHER          | Warm, dry skin from lost sympathetic tone | Pounding headache, flushing above lesion |
| ACTION         | Fluids, vasopressors, atropine            | Sit up, find and remove trigger          |

### ◆ AUTONOMIC DYSREFLEXIA RESPONSE



*Above C5 the diaphragm is at risk; T6 or above invites neurogenic shock and autonomic dysreflexia.*

### WRITTEN NOTES: SPINAL CORD INJURY

- Mechanisms: flexion, hyperextension, rotation, and axial loading (diving).
- C3 to C5 innervate the diaphragm through the phrenic nerve.
- Spinal shock: temporary loss of reflexes, motor, and sensory function below the lesion.
- Neurogenic shock: hypotension and bradycardia from lost sympathetic tone, usually T6 or above.
- Autonomic dysreflexia: severe hypertension, headache, bradycardia, flushing above the lesion; sit up and remove the trigger, often a full bladder.

## ◆ SEIZURE, HEADACHE, AND MENINGITIS DRUGS

**LORAZEPAM***Ativan***BENZODIAZEPINE****USED FOR** First line for status epilepticus**WATCH** Respiratory depression, keep airway ready**LEVETIRACETAM***Keppra***ANTISEIZURE DRUG****USED FOR** Ongoing seizure control**WATCH** Mood changes, drowsiness**PHENYTOIN***Dilantin***ANTISEIZURE DRUG****USED FOR** Seizure control, status after benzodiazepine**WATCH** Narrow range, gingival hyperplasia, IV hypotension**SUMATRIPTAN***Imitrex***TRIPTAN****USED FOR** Acute migraine and cluster headache**WATCH** Avoid in coronary disease**CEFTRIAXONE***Rocephin***THIRD GENERATION  
CEPHALOSPORIN****USED FOR** Bacterial meningitis, given without delay**WATCH** Allergy; draw cultures but do not delay

## ◆ CSF IN BACTERIAL MENINGITIS

**CSF APPEARANCE**

Normal Clear

**Cloudy**

White cells and bacteria present

**CSF PROTEIN**

Normal 15 to 45 mg/dL

**High**

Inflammation, leaky blood brain barrier

**CSF GLUCOSE**

Normal 40 to 70 mg/dL

**Low**

Bacteria consume glucose

**CSF WHITE CELLS**Normal 0 to 5 cells/mm<sup>3</sup>**High, mostly neutrophils**

Bacterial infection

*Seizure over 5 minutes is status epilepticus: IV lorazepam first, protect the airway, nothing in the mouth.***WRITTEN NOTES: SEIZURES, HEADACHE, AND INFECTION**

- Seizures reflect excess excitation (glutamate) relative to inhibition (GABA).
- Status epilepticus: more than 5 minutes or repeated seizures without recovery; IV lorazepam first.

- Seizure care: side lying, time it, nothing in the mouth, no restraint.
- Migraine: unilateral throbbing with nausea and photophobia. Cluster: stabbing periorbital pain with tearing, restless.
- Bacterial meningitis: fever, headache, stiff neck; CSF cloudy with high protein, low glucose, and neutrophils; antibiotics without delay.
- Meningococcal disease: petechial rash, droplet precautions, prophylaxis for close contacts.

## 6 NEURODEGENERATIVE AND DEMYELINATING DISEASE

### ◆ TRAP: PARKINSON DISEASE SIGNS

**T** **TREMOR**  
Resting, pill rolling,  
eases with movement

**R** **RIGIDITY**  
Cogwheel or lead  
pipe stiffness

**A** **AKINESIA**  
Bradykinesia, slow to  
start moving

**P** **POSTURAL  
INSTABILITY**  
Shuffling gait, fall  
risk

### ◆ DEGENERATIVE AND DEMYELINATING DISEASE

| FEATURE   | ALZHEIMER DISEASE            | MULTIPLE SCLEROSIS                              | ALS                               |
|-----------|------------------------------|-------------------------------------------------|-----------------------------------|
| LESION    | Amyloid plaques, tau tangles | Autoimmune CNS demyelination                    | Upper and lower motor neuron loss |
| HALLMARK  | Memory loss first            | Optic neuritis, heat sensitivity                | Weakness with intact sensation    |
| COURSE    | Gradual decline              | Relapses and remissions                         | Progressive                       |
| KEY CLUE  | Acetylcholine loss           | MRI lesions, oligoclonal bands                  | Death from respiratory failure    |
| TREATMENT | Cholinesterase inhibitors    | Disease modifying therapy, steroids for relapse | Supportive, ventilation planning  |



*Parkinson loses dopamine, Alzheimer loses acetylcholine, MS loses myelin, ALS loses motor neurons but spares sensation.*

### WRITTEN NOTES: NEURODEGENERATIVE AND DEMYELINATING DISEASE

- Parkinson disease: loss of substantia nigra dopamine neurons; bradykinesia, resting tremor, rigidity; carbidopa levodopa.
- Alzheimer disease: amyloid plaques and tau tangles, acetylcholine loss; memory loss first; cholinesterase inhibitors.
- Huntington disease: autosomal dominant CAG repeat; chorea, psychiatric change, dementia.
- Multiple sclerosis: autoimmune CNS demyelination; optic neuritis, heat sensitivity, relapses and remissions; MRI lesions and oligoclonal bands.
- ALS: upper and lower motor neuron loss with intact sensation; respiratory failure is the usual cause of death.

- Delirium is acute and fluctuating with an underlying cause; dementia is gradual.

## 7 NEUROMUSCULAR JUNCTION AND PERIPHERAL NERVE

### ◆ PATTERNS OF WEAKNESS

| FEATURE   | GUILLAIN BARRE                           | BOTULISM                           | MYASTHENIA GRAVIS                     |
|-----------|------------------------------------------|------------------------------------|---------------------------------------|
| MECHANISM | Post infectious peripheral demyelination | Toxin blocks acetylcholine release | Antibodies to acetylcholine receptors |
| DIRECTION | Ascending                                | Descending                         | Fatigable, ptosis first               |
| REFLEXES  | Absent or reduced early                  | Normal early, may fade later       | Normal                                |
| PRIORITY  | Monitor vital capacity                   | Airway, antitoxin                  | Pyridostigmine before meals           |

### ◆ MYASTHENIC VERSUS CHOLINERGIC CRISIS

#### MYASTHENIC CRISIS

- Undertreated
- Severe weakness, ptosis
- Respiratory failure risk

#### CHOLINERGIC CRISIS

- Overtreated
- Heavy secretions
- Miosis, cramping, bradycardia

#### OTHER TOXINS AND NERVES

- Tetanus: trismus, rigidity, spasms
- Bell palsy: CN VII, forehead involved



*Guillain Barre climbs, botulism descends, myasthenia tires with use; watch vital capacity in all of them.*

### WRITTEN NOTES: NEUROMUSCULAR JUNCTION AND PERIPHERAL NERVE

- Myasthenia gravis: antibodies to acetylcholine receptors; fatigable weakness, ptosis first; pyridostigmine before meals; thymus involvement.
- Myasthenic crisis (undertreated) versus cholinergic crisis (overtreated, with secretions and miosis); both threaten breathing.
- Guillain Barre syndrome: post infectious peripheral demyelination; ascending weakness, absent reflexes; monitor vital capacity.
- Botulism: toxin blocks acetylcholine release; descending flaccid paralysis.
- Tetanus: toxin blocks inhibitory transmitters; trismus, rigidity, spasms.
- Bell palsy: peripheral CN VII palsy including the forehead.

## ◆ PSYCHIATRIC MEDICATIONS

**SERTRALINE***Zoloft***SSRI****USED FOR** Depression, anxiety**WATCH** 2 to 6 weeks to work; suicide risk early**LITHIUM***Lithobid***MOOD STABILIZER****USED FOR** Bipolar disorder**WATCH** Keep 0.6 to 1.2 mEq/L; dehydration raises levels**ALPRAZOLAM***Xanax***BENZODIAZEPINE****USED FOR** Acute anxiety**WATCH** Sedation, dependence, do not stop abruptly**HALOPERIDOL***Haldol***FIRST GENERATION  
ANTIPSYCHOTIC****USED FOR** Schizophrenia, acute psychosis**WATCH** Extrapyramidal effects, NMS**RISPERIDONE***Risperdal***SECOND GENERATION  
ANTIPSYCHOTIC****USED FOR** Schizophrenia, bipolar mania**WATCH** Weight gain, glucose, NMS

## ◆ SEROTONIN SYNDROME VERSUS NMS

| FEATURE     | SEROTONIN SYNDROME          | NEUROLEPTIC MALIGNANT SYNDROME |
|-------------|-----------------------------|--------------------------------|
| TRIGGER     | Combined serotonergic drugs | Dopamine blockers              |
| ONSET       | Rapid, within hours         | Slower, over days              |
| MUSCLES     | Clonus, hyperreflexia       | Lead pipe rigidity             |
| TEMPERATURE | Elevated                    | High fever                     |
| LAB CLUE    | Clinical diagnosis          | High CK                        |



*SSRIs take weeks and need suicide monitoring; lithium has a narrow range that dehydration pushes higher.*

## WRITTEN NOTES: MENTAL HEALTH NEUROBIOLOGY

- Depression: monoamine dysregulation; SSRIs take 2 to 6 weeks; monitor suicide risk.
- Bipolar disorder: lithium has a narrow range; dehydration and low sodium raise levels.
- Anxiety: GABA is the main inhibitory transmitter; benzodiazepines enhance it but cause sedation and dependence.
- Schizophrenia: excess mesolimbic dopamine drives positive symptoms; antipsychotics block D2 receptors.
- Serotonin syndrome: rapid onset, clonus, hyperreflexia after combining serotonergic drugs.

- Neuroleptic malignant syndrome: high fever, lead pipe rigidity, high CK after dopamine blockers.

## + CLINICAL PEARLS

- Brain lesions show on the opposite side of the body. Left brain strokes steal words; right brain strokes steal awareness of the left side.
- Earliest ICP sign is a change in mental status; Cushing triad and a blown pupil are late. CPP equals MAP minus ICP; aim for about 60 to 70.
- Paralysis direction: Guillain Barre ascends after an infection, botulism descends after a toxin, myasthenia gravis tires with use.
- Autonomic dysreflexia at T6 or above: sit up, then check the bladder first.
- Dopamine is the pivot: too little in the substantia nigra is Parkinson disease, too much in the mesolimbic pathway drives schizophrenia's positive symptoms.

## RX KEY MEDICATIONS

### ♦ MEDICATIONS FOR BRAIN, NERVES AND MIND



#### ALTEPLASE

*Activase*

##### THROMBOLYTICS

**USED FOR** Acute ischemic stroke within 4.5 hours of last known well

**WATCH** Rule out hemorrhage on CT first; keep blood pressure below 185/110 before and 180/105 after; watch for bleeding and neuro changes.



#### MANNITOL

*Osmitol*

##### OSMOTIC DIURETICS

**USED FOR** Cerebral edema and increased ICP

**WATCH** Monitor urine output, serum sodium, and osmolality; avoid in heart failure with fluid overload.



#### LORAZEPAM

*Ativan*

##### BENZODIAZEPINES

**USED FOR** Status epilepticus and acute anxiety

**WATCH** Respiratory depression, especially with opioids or alcohol; keep airway equipment ready.



#### CARBIDOPA LEVODOPA

*Sinemet, Rytary*

##### DOPAMINE PRECURSOR WITH DECARBOXYLASE INHIBITOR

**USED FOR** Parkinson disease

**WATCH** Orthostatic hypotension and dyskinesias; high protein meals can reduce absorption.



#### PYRIDOSTIGMINE

*Mestinon*

##### CHOLINESTERASE INHIBITORS

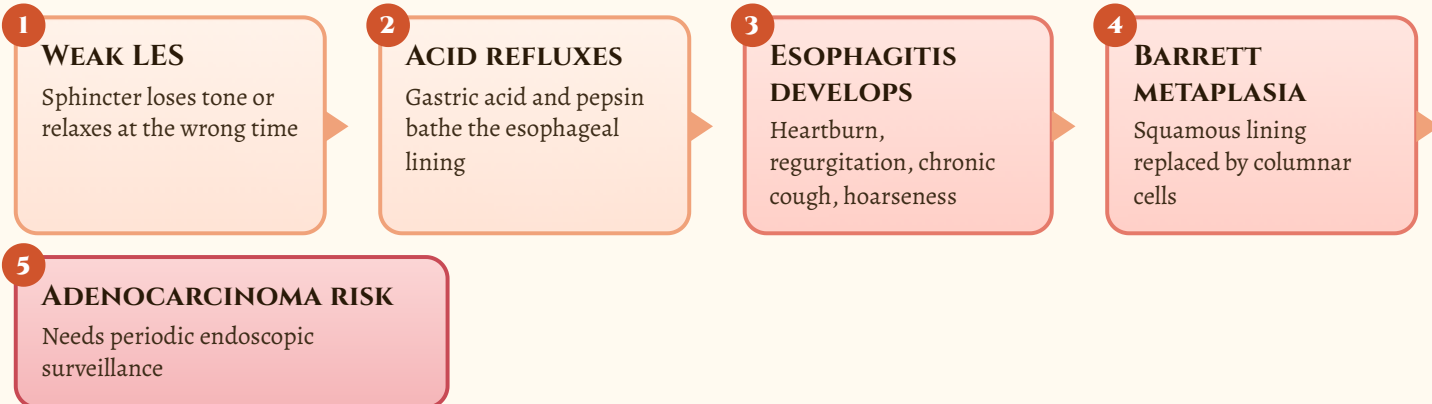
**USED FOR** Myasthenia gravis and Alzheimer disease

**WATCH** Excess dosing causes cholinergic crisis: secretions, cramping, bradycardia, and weakness.

# DIGESTIA CAVERNS: GUT, LIVER AND PANCREAS

## 1 ESOPHAGUS AND STOMACH

### ◆ FROM REFLUX TO BARRETT ESOPHAGUS



### ◆ DUODENAL VERSUS GASTRIC ULCER

| FEATURE         | DUODENAL ULCER                           | GASTRIC ULCER                           |
|-----------------|------------------------------------------|-----------------------------------------|
| EFFECT OF FOOD  | Pain eases with food                     | Pain worsens with food                  |
| PAIN TIMING     | 2 to 3 hours after meals, often at night | Soon after eating                       |
| WEIGHT          | Often stable or gained                   | Loss is common                          |
| MAIN CAUSES     | H. pylori most often                     | NSAIDs and H. pylori                    |
| H. PYLORI TESTS | Urea breath test, stool antigen, biopsy  | Urea breath test, stool antigen, biopsy |
| EMERGENCY       | Perforation: sudden pain, rigid abdomen  | Perforation: sudden pain, rigid abdomen |



*Duodenal ulcer pain eases with food, gastric ulcer pain worsens. Sudden board like abdomen means perforation.*

### WRITTEN NOTES: ESOPHAGUS AND STOMACH

- GERD comes from a weak or inappropriately relaxing lower esophageal sphincter; acid irritates the esophageal lining.
- Chronic GERD can cause Barrett esophagus, a squamous to columnar metaplasia that raises adenocarcinoma risk.

- Peptic ulcers form when acid and pepsin overcome mucosal defenses; H. pylori and NSAIDs are the two main causes.
- Duodenal ulcer pain often improves with food; gastric ulcer pain often worsens with food.
- H. pylori is diagnosed with the urea breath test, stool antigen, or biopsy and is treated with a PPI plus antibiotics, often with bismuth.
- Perforation presents with sudden severe pain and a rigid abdomen and is a surgical emergency.

## 2 GI BLEEDING

### ◆ WHERE IS THE BLEED?

#### UPPER GI BLEED

- Hematemesis
- Coffee ground emesis
- Melena: black, tarry stool
- BUN rises from digested blood

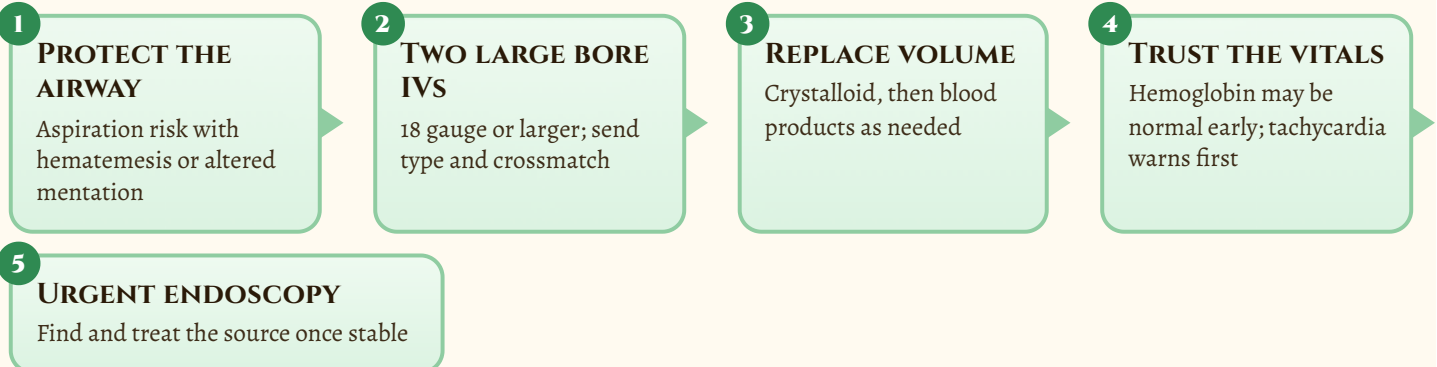
#### LOWER GI BLEED

- Hematochezia: bright red or maroon
- BUN usually normal

#### COMMON CAUSES

- Peptic ulcer
- Esophageal varices
- Diverticular bleeding
- Colorectal cancer

### ◆ ACUTE GI BLEED PRIORITIES



*Coffee grounds, tar, and a high BUN point upward. Vital signs, not the first hemoglobin, show early blood loss.*

### WRITTEN NOTES: GI BLEEDING

- Upper GI bleeding causes hematemesis, coffee ground emesis, and melena; lower GI bleeding usually causes hematochezia.
- An upper GI bleed raises the BUN because digested blood is a protein load.
- Hemoglobin may be normal early in acute hemorrhage; vital signs and clinical signs guide early care.
- Priorities are airway protection, two large bore IVs, fluid and blood replacement, then endoscopy.
- Common causes include peptic ulcers, varices, diverticular bleeding, and colorectal cancer.

### 3 INFLAMMATORY AND FUNCTIONAL BOWEL DISEASE

#### ◆ CROHN DISEASE VERSUS ULCERATIVE COLITIS

| FEATURE       | CROHN DISEASE                                | ULCERATIVE COLITIS                 |
|---------------|----------------------------------------------|------------------------------------|
| LOCATION      | Mouth to anus, often terminal ileum          | Rectum and colon only              |
| PATTERN       | Skip lesions                                 | Continuous from the rectum         |
| DEPTH         | Transmural                                   | Mucosal                            |
| STOOL         | Diarrhea, less often bloody                  | Bloody diarrhea with tenesmus      |
| COMPLICATIONS | Fistulas, strictures, B12 and bile acid loss | Toxic megacolon, colorectal cancer |
| SURGERY       | Not curative, disease recurs                 | Colectomy is curative              |

#### ◆ INFLAMMATORY BOWEL DISEASE DRUGS



##### MESALAMINE

*Lialda, Asacol HD*

AMINOSALICYLATE

**USED FOR** Mild to moderate ulcerative colitis

**WATCH** Monitor kidney function



##### SULFASALAZINE

*Azulfidine*

AMINOSALICYLATE

**USED FOR** Ulcerative colitis, rheumatoid arthritis

**WATCH** Sulfa allergy, folate deficiency, orange urine



##### BUDESONIDE

*Entocort EC, Uceris*

CORTICOSTEROID

**USED FOR** Flares of Crohn disease or colitis

**WATCH** Hyperglycemia, infection; taper, do not stop abruptly



##### INFLIXIMAB

*Remicade*

TNF ALPHA INHIBITOR

**USED FOR** Moderate to severe Crohn disease and colitis

**WATCH** Screen for TB and hepatitis B first



*Crohn skips through the whole wall anywhere; colitis climbs continuously from the rectum. Never give opioids in toxic megacolon.*

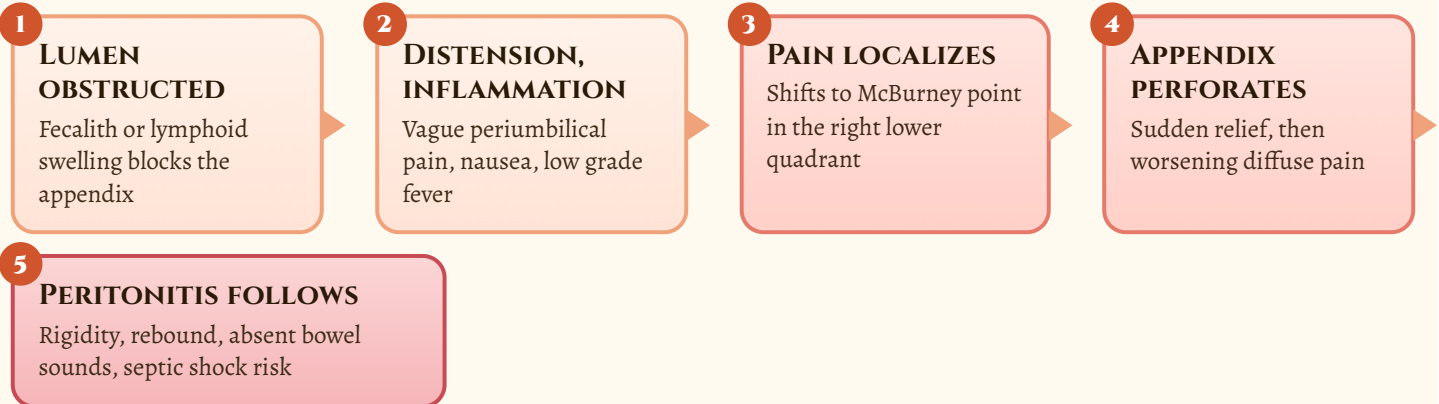
#### WRITTEN NOTES: INFLAMMATORY AND FUNCTIONAL BOWEL DISEASE

- Crohn disease: anywhere from mouth to anus, skip lesions, transmural, fistulas and strictures, often the terminal ileum.
- Ulcerative colitis: rectum and colon only, continuous, mucosal, bloody diarrhea with tenesmus.
- Toxic megacolon is a dangerous complication of severe colitis; avoid antidiarrheals and opioids.

- Terminal ileum disease or resection causes B12 deficiency and bile acid malabsorption.
- Ulcerative colitis can be cured by colectomy and raises colorectal cancer risk over time.
- IBS is a disorder of gut and brain interaction with no structural damage; weight loss, bleeding, and nocturnal symptoms are red flags.
- Celiac disease is an immune response to gluten that flattens villi, causing malabsorption, iron deficiency, and secondary lactose intolerance.

## 4 ACUTE ABDOMEN

### ◆ APPENDICITIS PROGRESSION



### ◆ BOWEL OBSTRUCTION AND ILEUS

| FEATURE      | SMALL BOWEL        | LARGE BOWEL                     | PARALYTIC ILEUS               |
|--------------|--------------------|---------------------------------|-------------------------------|
| COMMON CAUSE | Adhesions, hernias | Cancer, volvulus                | Surgery, opioids, hypokalemia |
| PAIN         | Colicky, crampy    | Crampy, lower abdomen           | Diffuse discomfort            |
| VOMITING     | Early and frequent | Late                            | Nausea, may vomit             |
| DISTENSION   | Mild to moderate   | Marked                          | Diffuse                       |
| BOWEL SOUNDS | High pitched       | High pitched early, later quiet | Absent                        |



*Sudden relief of appendicitis pain is not good news: think perforation. Keep NPO, no heat, no enemas.*

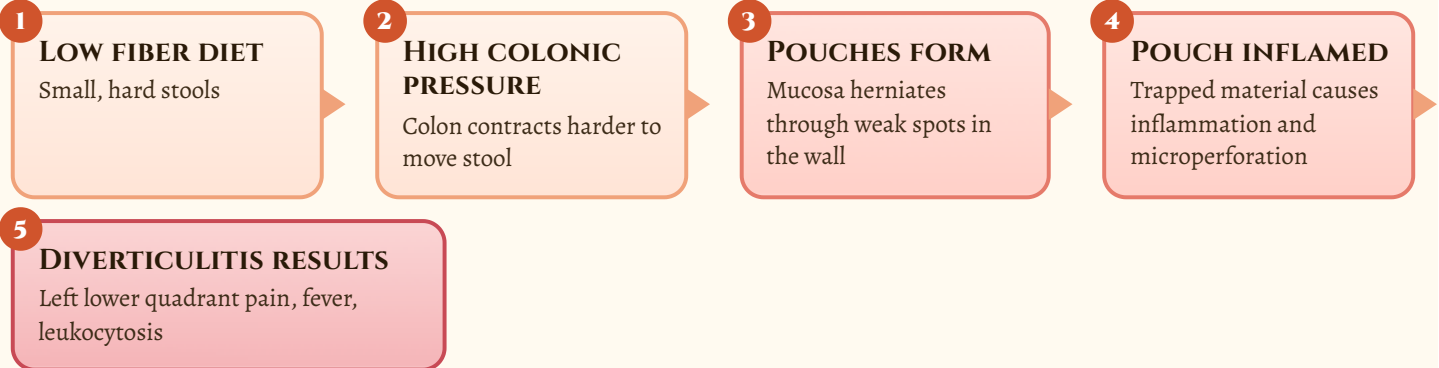
### WRITTEN NOTES: ACUTE ABDOMEN

- Appendicitis starts with luminal obstruction; pain moves from the umbilicus to McBurney point.
- Sudden pain relief in appendicitis followed by worsening suggests perforation.
- Avoid heat and enemas in suspected appendicitis; keep the client NPO.
- Small bowel obstruction: colicky pain, early vomiting, high pitched sounds; often from adhesions or hernias.
- Large bowel obstruction: marked distension, late vomiting; often from cancer or volvulus.

- Paralytic ileus has absent bowel sounds and follows surgery, opioids, or hypokalemia.
- Peritonitis presents with rigidity, rebound tenderness, absent bowel sounds, and risk of septic shock.

## 5 DIVERTICULAR DISEASE

### ◆ HOW DIVERTICULAR DISEASE DEVELOPS



### ◆ DIVERTICULAR DISEASE AT A GLANCE

#### DIVERTICULOSIS

- Often no symptoms
- Painless, brisk rectal bleeding

#### DIVERTICULITIS

- Left lower quadrant pain
- Fever
- Leukocytosis

#### COMPLICATIONS

- Abscess
- Perforation
- Fistula
- Peritonitis

#### PREVENTION

- High fiber diet
- Adequate fluid intake



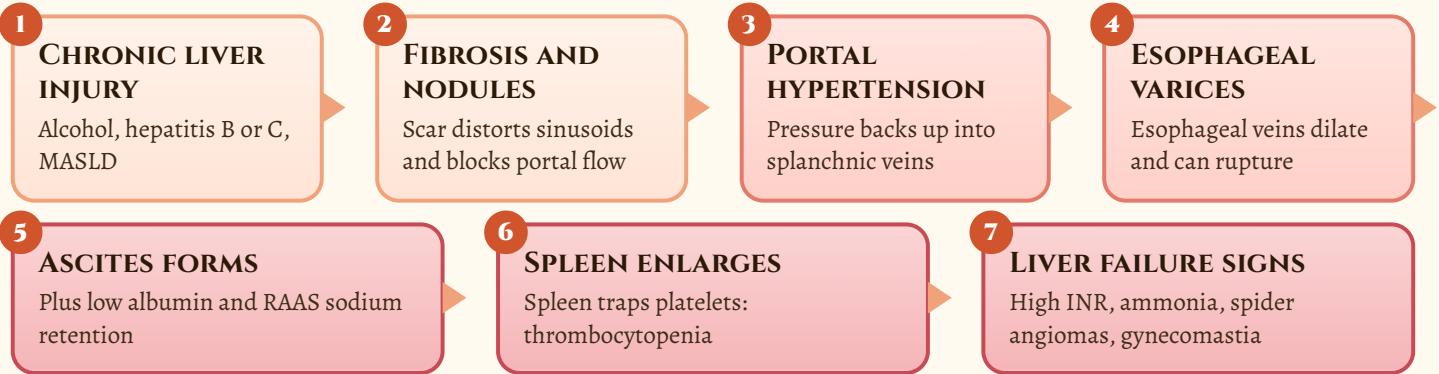
*Diverticulosis is silent pouches; diverticulitis is inflamed pouches with LLQ pain and fever. Fiber and fluid prevent both.*

### WRITTEN NOTES: DIVERTICULAR DISEASE

- Diverticulosis is the presence of colon wall pouches without inflammation and is often silent.
- Diverticulitis presents with left lower quadrant pain, fever, and leukocytosis.
- Complications include abscess, perforation, fistula, and peritonitis.
- A high fiber diet with adequate fluid lowers colonic pressure and helps prevent disease.
- Diverticular bleeding is painless and can be brisk.

## 6 CIRRHOSIS AND PORTAL HYPERTENSION

### ◆ CIRRHOSIS AND PORTAL HYPERTENSION



### ◆ TREATING DECOMPENSATED CIRRHOSIS



#### LACTULOSE

*Enulose, Kristalose*

##### OSMOTIC LAXATIVE

**USED FOR** Hepatic encephalopathy

**WATCH** Aim for 2 to 3 soft stools; dehydration, low potassium



#### RIFAXIMIN

*Xifaxan*

##### NONABSORBED ANTIBIOTIC

**USED FOR** Prevent recurrent encephalopathy

**WATCH** Usually given with lactulose



#### SPIRONOLACTONE

*Aldactone*

##### ALDOSTERONE ANTAGONIST

**USED FOR** Ascites

**WATCH** Hyperkalemia; avoid salt substitutes



#### FUROSEMIDE

*Lasix*

##### LOOP DIURETIC

**USED FOR** Ascites, paired with spironolactone

**WATCH** Low potassium; overdiuresis can trigger encephalopathy



#### OCTREOTIDE

*Sandostatin*

##### SOMATOSTATIN ANALOG

**USED FOR** Acute variceal bleeding

**WATCH** Glucose swings, bradycardia



#### PROPRANOLOL

*Inderal LA*

##### NONSELECTIVE BETA BLOCKER

**USED FOR** Prevent variceal bleeding

**WATCH** Hold for low heart rate or blood pressure



*Portal pressure has three exits: esophagus for varices, belly for ascites, spleen for low platelets.*

### WRITTEN NOTES: CIRRHOSIS AND PORTAL HYPERTENSION

- Cirrhosis is fibrosis with regenerative nodules caused by chronic injury from alcohol, hepatitis B or C, or MASLD.
- Portal hypertension causes varices, ascites, splenomegaly with low platelets, and caput medusae.
- Ascites arises from portal hypertension, low albumin, and RAAS driven sodium and water retention.
- Hepatic encephalopathy results from ammonia; lactulose and rifaximin lower it.
- Loss of synthetic function causes a prolonged INR, low albumin, and hypoglycemia.
- Reduced estrogen clearance causes spider angiomas, palmar erythema, and gynecomastia.

- Spontaneous bacterial peritonitis and hepatorenal syndrome are serious complications of decompensated disease.

## 7 VIRAL HEPATITIS

### ◆ VIRAL HEPATITIS TYPES

| FEATURE   | HEPATITIS A AND E        | HEPATITIS B AND D                | HEPATITIS C                     |
|-----------|--------------------------|----------------------------------|---------------------------------|
| SPREAD    | Fecal oral               | Blood, sex, birth                | Blood, shared needles           |
| COURSE    | Usually acute            | Acute or chronic                 | Often chronic                   |
| VACCINE   | Yes for A                | Yes for B, also prevents D       | None                            |
| TREATMENT | Supportive               | Antivirals suppress, rarely cure | Direct acting antivirals cure   |
| KEY POINT | E dangerous in pregnancy | D needs B to replicate           | Cirrhosis and liver cancer risk |

### ◆ HEPATITIS LABS

#### ALT

Normal 7 to 56 units/L

**Elevated**

Hepatocyte injury, most liver specific

#### AST

Normal 10 to 40 units/L

**Elevated**

Hepatocyte injury

#### TOTAL BILIRUBIN

Normal 0.3 to 1.2 mg/dL

**Elevated**

Icteric phase: jaundice, dark urine

#### HBSAG

Normal Negative

**Positive**

Current hepatitis B infection

#### ANTI HBS

Normal Negative unless immune

**Positive alone**

Immunity from vaccination

#### ANTI HBC

Normal Negative

**Positive**

Past or current natural infection



*Vowels go to the bowels: A and E are fecal oral. Vaccine gives anti HBs only, never anti HBC.*

### WRITTEN NOTES: VIRAL HEPATITIS

- Hepatitis A and E spread by the fecal oral route and are usually acute.
- Hepatitis B spreads through blood, sex, and birth; vaccination produces anti HBs only.
- Hepatitis C is bloodborne, often chronic, and curable with direct acting antivirals; there is no vaccine.
- Hepatitis D requires hepatitis B to replicate.
- Hepatitis E is especially dangerous in pregnancy.
- ALT and AST rise with hepatocyte injury; bilirubin rises in the icteric phase.

## 8 GALLBLADDER AND PANCREAS

### ◆ BILIARY AND PANCREATIC EMERGENCIES

| FEATURE  | CHOLECYSTITIS         | CHOLANGITIS                              | ACUTE PANCREATITIS                     |
|----------|-----------------------|------------------------------------------|----------------------------------------|
| PAIN     | RUQ after fatty meals | RUQ pain                                 | Epigastric, radiates to back           |
| KEY SIGN | Positive Murphy sign  | Charcot triad: fever, RUQ pain, jaundice | Cullen and Grey Turner signs if severe |
| CAUSE    | Stone in cystic duct  | Infected, blocked common bile duct       | Gallstones, alcohol                    |
| KEY LAB  | Leukocytosis          | High bilirubin and ALP                   | Lipase 3 times normal or more          |
| DANGER   | Gangrene, perforation | Sepsis; needs urgent drainage            | Hypocalcemia, ARDS, shock              |

### ◆ GALLBLADDER AND PANCREAS LABS

#### LIPASE

Normal 0 to 160 units/L

**3 times upper limit or more**

Supports acute pancreatitis

#### CALCIUM

Normal 9.0 to 10.5 mg/dL

**Low**

Fat saponification: severe pancreatitis

#### GLUCOSE

Normal 70 to 99 mg/dL fasting

**High**

Islet damage; chronic disease causes diabetes

#### DIRECT BILIRUBIN

Normal 0.1 to 0.3 mg/dL

**High**

Duct obstruction: dark urine, pale stools

#### ALKALINE PHOSPHATASE

Normal 40 to 120 units/L

**High**

Cholestasis from a duct stone

#### WBC

Normal 4,500 to 11,000/mm<sup>3</sup>

**High**

Inflammation or cholangitis



*Pancreatitis is the gland digesting itself: gallstones and alcohol cause it, lipase confirms it, low calcium signals severity.*

### WRITTEN NOTES: GALLBLADDER AND PANCREAS

- Gallstones form when bile is supersaturated with cholesterol and the gallbladder empties poorly.
- Cholecystitis causes right upper quadrant pain after fatty meals and a positive Murphy sign.
- A common bile duct stone causes obstructive jaundice with dark urine and pale stools.
- Charcot triad of fever, right upper quadrant pain, and jaundice signals cholangitis.
- Acute pancreatitis is autodigestion; diagnosis uses pain, lipase at least three times normal, and imaging.
- Hypocalcemia, Cullen and Grey Turner signs, and ARDS indicate severe pancreatitis.
- Chronic pancreatitis causes steatorrhea and diabetes.



## CLINICAL PEARLS

- Crohn crawls, colitis climbs: Crohn skips anywhere from mouth to anus and goes through the whole wall, while ulcerative colitis starts at the rectum and climbs continuously in the mucosa.
- Portal pressure has three exits: up into the esophagus (varices), out into the belly (ascites), and over to the spleen (low platelets).
- In pancreatitis, the gland eats itself. Gallstones and alcohol are the top two causes; lipase confirms; low calcium warns of severe disease.
- Hepatitis vowels go to the bowels: A and E are fecal oral and acute. B, C, and D travel by blood and body fluids and can become chronic.
- Coffee grounds and tar mean the bleed is high; bright red usually means low, unless the bleeding is massive.



## KEY MEDICATIONS

### ◆ MEDICATIONS FOR GUT, LIVER AND PANCREAS



#### OMEPRAZOLE

*Prilosec*

##### PROTON PUMP INHIBITOR

**USED FOR** GERD, peptic ulcer disease, H. pylori regimens, upper GI bleeding

**WATCH** Give 30 to 60 minutes before breakfast; long term use raises risk of C. difficile infection, low magnesium, B12 deficiency, and fractures.



#### LACTULOSE

*Enulose, Kristalose*

##### OSMOTIC LAXATIVE (AMMONIA LOWERING)

**USED FOR** Hepatic encephalopathy

**WATCH** Titrate to 2 to 3 soft stools daily and watch for dehydration and low potassium from excess diarrhea.



#### OCTREOTIDE

*Sandostatin*

##### SOMATOSTATIN ANALOG

**USED FOR** Acute esophageal variceal bleeding

**WATCH** Monitor glucose, since it suppresses insulin and glucagon, and watch for bradycardia.



#### MESALAMINE

*Lialda, Asacol HD, Pentasa*

##### AMINOSALICYLATE

**USED FOR** Mild to moderate ulcerative colitis

**WATCH** Sulfasalazine can cause folate deficiency and orange urine; avoid in sulfa allergy and monitor CBC and kidney function.



#### SPIRONOLACTONE

*Aldactone*

##### POTASSIUM SPARING DIURETIC (ALDOSTERONE ANTAGONIST)

**USED FOR** Ascites in cirrhosis

**WATCH** Watch for hyperkalemia and rising creatinine; avoid potassium supplements and salt substitutes.

# STONEHIDE RIDGE: BONES, JOINTS, MUSCLE AND SKIN

## 1 BONE HEALTH

### ◆ BONE HEALTH NUMBERS

#### DEXA T SCORE

Normal Minus 1.0 or higher

Below minus 1.0, above minus 2.5

Osteopenia

#### DEXA T SCORE

Normal Minus 1.0 or higher

Minus 2.5 or lower

Osteoporosis: high fracture risk

#### 25 OH VITAMIN D

Normal 30 to 100 ng/mL

Below 20 ng/mL

Deficiency: osteomalacia, rickets in children

#### CALCIUM

Normal 9.0 to 10.5 mg/dL

Usually normal

Osteoporosis has normal mineralization

#### ALKALINE PHOSPHATASE

Normal 40 to 120 units/L

High

Increased bone turnover, as in osteomalacia

### ◆ OSTEOPOROSIS DRUGS



#### ALENDRONATE

*Fosamax*

**BISPHOSPHONATE**

**USED FOR** Osteoporosis

**WATCH** Empty stomach, full glass of water, upright 30 minutes



#### RISEDRONATE

*Actonel*

**BISPHOSPHONATE**

**USED FOR** Osteoporosis

**WATCH** Same upright rule; report jaw pain



#### ZOLEDRONIC ACID

*Reclast*

**IV BISPHOSPHONATE**

**USED FOR** Osteoporosis, once yearly

**WATCH** Check calcium and kidney function first



#### DENOSUMAB

*Prolia*

**RANKL INHIBITOR**

**USED FOR** High fracture risk osteoporosis

**WATCH** Hypocalcemia; do not stop without follow up therapy



#### TERIPARATIDE

*Forteo*

**PTH ANALOG, BONE BUILDER**

**USED FOR** Severe osteoporosis

**WATCH** Orthostatic hypotension, high calcium



*Osteoporosis is too little bone; osteomalacia is soft, poorly mineralized bone. T score minus 2.5 or lower defines osteoporosis.*

## WRITTEN NOTES: BONE HEALTH

- Osteoporosis: resorption exceeds formation, causing low bone mass with normal mineralization.
- Estrogen loss, aging, smoking, alcohol, inactivity, steroids, and low calcium or vitamin D increase risk.
- T score of minus 2.5 or lower on DEXA defines osteoporosis; minus 1 to minus 2.5 is osteopenia.
- Typical fractures: vertebral compression, hip, and distal radius; kyphosis and height loss follow vertebral fractures.
- Bisphosphonates inhibit osteoclasts; take with water on an empty stomach and stay upright 30 minutes.
- Osteomalacia is poor mineralization from vitamin D deficiency, with bone pain and weakness; rickets in children.

## 2 ARTHRITIS

### ◆ OSTEOARTHRITIS, RHEUMATOID ARTHRITIS, GOUT

| FEATURE            | OSTEOARTHRITIS                           | RHEUMATOID ARTHRITIS                  | GOUT                                          |
|--------------------|------------------------------------------|---------------------------------------|-----------------------------------------------|
| CAUSE              | Cartilage degeneration                   | Autoimmune synovitis with pannus      | Urate crystals in joints                      |
| JOINTS             | Weight bearing joints, DIP and PIP       | Symmetric small joints                | Great toe, often one joint                    |
| STIFFNESS AND PAIN | Under 30 minutes, worse with use         | Over 30 minutes, eases with movement  | Sudden hot, red, swollen joint                |
| FINDINGS           | Heberden and Bouchard nodes, osteophytes | Nodules, fatigue, anemia, heart risk  | Tophi, uric acid stones                       |
| LABS               | Usually normal                           | Anti CCP most specific; high ESR, CRP | High uric acid; crystals in fluid             |
| TREATMENT          | Weight loss, exercise, NSAIDs            | Methotrexate and other DMARDs         | Colchicine for flares, allopurinol to prevent |

## ● ARTHRITIS AND GOUT DRUGS



### METHOTREXATE

*Trexall, Otrexup*

**DMARD, FOLATE ANTAGONIST**

**USED FOR** Rheumatoid arthritis, psoriasis

**WATCH** Once weekly with folic acid; CBC, LFTs, no alcohol, no pregnancy



### HYDROXYCHLOROQUINE

*Plaquenil*

**DMARD**

**USED FOR** Rheumatoid arthritis, lupus

**WATCH** Regular eye exams for retinal toxicity



### ADALIMUMAB

*Humira*

**TNF ALPHA INHIBITOR**

**USED FOR** Rheumatoid arthritis

**WATCH** Screen for TB; avoid live vaccines



### COLCHICINE

*Colcrys, Mitigare*

**ANTIGOUT ANTI INFLAMMATORY**

**USED FOR** Acute gout flare

**WATCH** Diarrhea signals toxicity; avoid grapefruit



### ALLOPURINOL

*Zyloprim*

**XANTHINE OXIDASE INHIBITOR**

**USED FOR** Prevent gout, tophi

**WATCH** Stop and report any rash; push fluids



### INDOMETHACIN

*Indocin*

**NSAID**

**USED FOR** Acute gout flare

**WATCH** GI bleeding, kidney injury



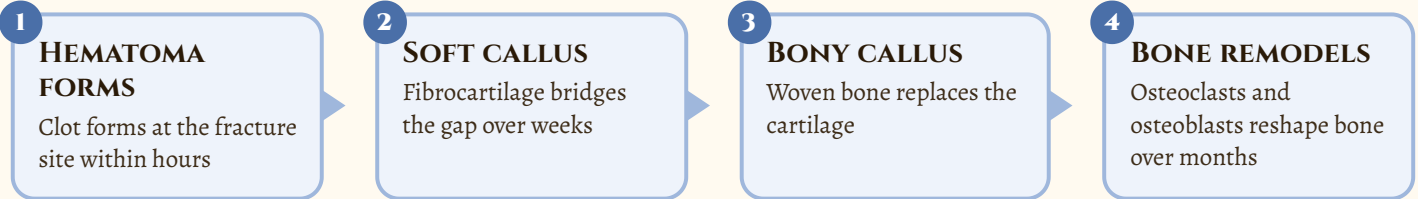
*Osteo wears, rheumatoid flares: OA worsens with use; RA brings long morning stiffness that eases with movement.*

## WRITTEN NOTES: ARTHRITIS

- Osteoarthritis: cartilage degeneration, osteophytes, Heberden and Bouchard nodes, pain worse with use.
- Rheumatoid arthritis: autoimmune, symmetric small joint synovitis, pannus, morning stiffness over 30 minutes.
- Anti CCP is the most specific test for rheumatoid arthritis; ESR and CRP track activity.
- Rheumatoid arthritis is systemic: fatigue, anemia of chronic disease, nodules, and higher cardiovascular risk.
- Methotrexate is the anchor DMARD; monitor CBC and liver tests and avoid alcohol and pregnancy.
- Gout: urate crystals in joints, often the great toe; triggered by alcohol, purines, diuretics, and dehydration.
- Treat gout flares with colchicine, NSAIDs, or steroids; prevent with xanthine oxidase inhibitors.

### 3 FRACTURES AND INJURY

#### ◆ HOW BONE HEALS



#### ◆ FRACTURE RED FLAGS

##### HIP FRACTURE

- Shortened, externally rotated leg
- Bleeding
- Delirium
- DVT and PE risk

##### FAT EMBOLISM, 24 TO 72 HOURS

- Respiratory distress
- Confusion
- Petechiae
- After long bone fracture

##### OPEN FRACTURE

- High infection risk
- Antibiotics and surgical cleaning

##### CONCERN FOR ABUSE

- Spiral fracture in a nonambulatory infant



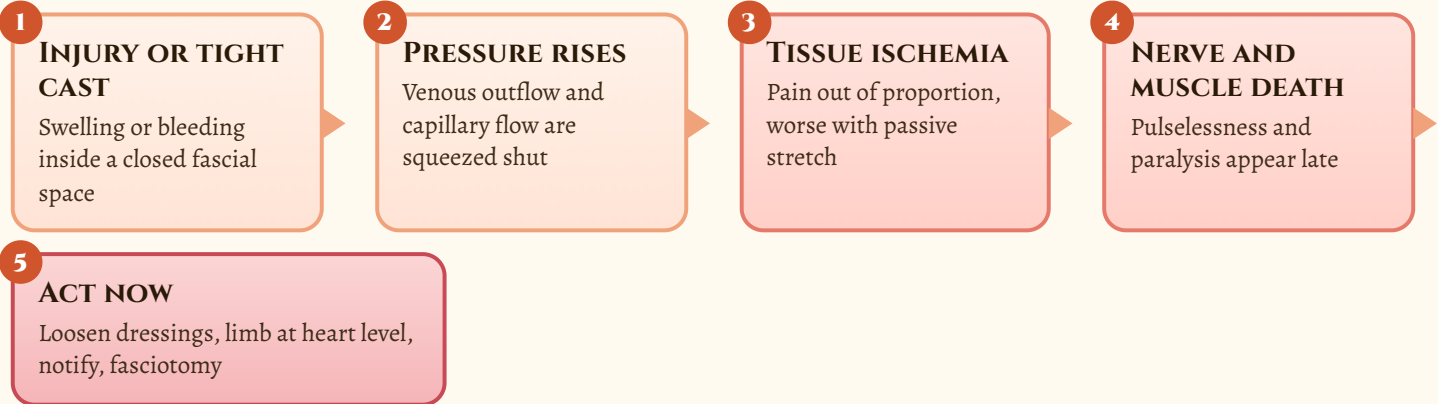
*Sprain means ligament, strain means muscle or tendon. A shortened, externally rotated leg means hip fracture.*

#### WRITTEN NOTES: FRACTURES AND INJURY

- Sprain is a ligament injury; strain is a muscle or tendon injury.
- Open fractures need antibiotics and surgical cleaning because of infection risk.
- Spiral fractures in nonambulatory infants raise concern for abuse.
- Bone heals through hematoma, soft callus, bony callus, and remodeling.
- Hip fracture: shortened, externally rotated leg; watch for bleeding, delirium, and clots.
- Fat embolism syndrome: respiratory distress, confusion, and petechiae 24 to 72 hours after a long bone fracture.

## 4 COMPARTMENT SYNDROME AND NEUROVASCULAR CHECKS

### COMPARTMENT SYNDROME



### NEUROVASCULAR CHECK: THE 5 Ps

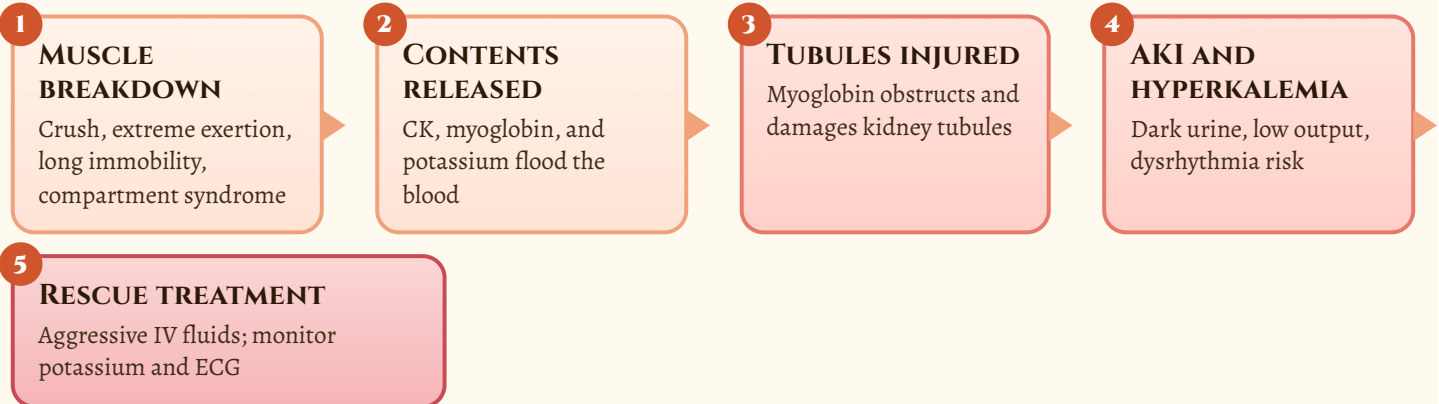


*Pain with passive stretch is the earliest alarm. Pulselessness is late. Keep the limb at heart level and call.*

### WRITTEN NOTES: COMPARTMENT SYNDROME AND NEUROVASCULAR CHECKS

- Compartment syndrome is rising pressure in a closed fascial space that causes ischemia.
- Earliest sign: pain out of proportion that increases with passive stretch.
- Pulselessness and paralysis are late signs.
- Loosen dressings, keep the limb at heart level, and notify the provider; fasciotomy may be needed.
- Neurovascular checks: pain, pulse, pallor, paresthesia, and paralysis.

### ◆ RHABDOMYOLYSIS TO KIDNEY INJURY



### ◆ MUSCLE AND BONE BREAKDOWN LABS

#### CK

Normal Men 55 to 170, women 30 to 135 units/L

**Over 5 times upper limit**

Rhabdomyolysis

#### POTASSIUM

Normal 3.5 to 5.0 mEq/L

**Above 5.0**

Released from muscle; watch the ECG

#### CREATININE

Normal 0.6 to 1.2 mg/dL

**Rising**

AKI from myoglobin

#### URINALYSIS

Normal No blood

**Dipstick blood, few or no RBCs**

Myoglobinuria

#### ESR

Normal Men 0 to 15, women 0 to 20 mm/hr

**Elevated**

Supports osteomyelitis; tracks response

#### CRP

Normal Under 1.0 mg/dL

**Elevated**

Active inflammation or infection



*Osteomyelitis pain does not ease with rest and early X rays lie. Dark urine after crush injury means rhabdomyolysis.*

### WRITTEN NOTES: BONE AND MUSCLE INFECTION AND BREAKDOWN

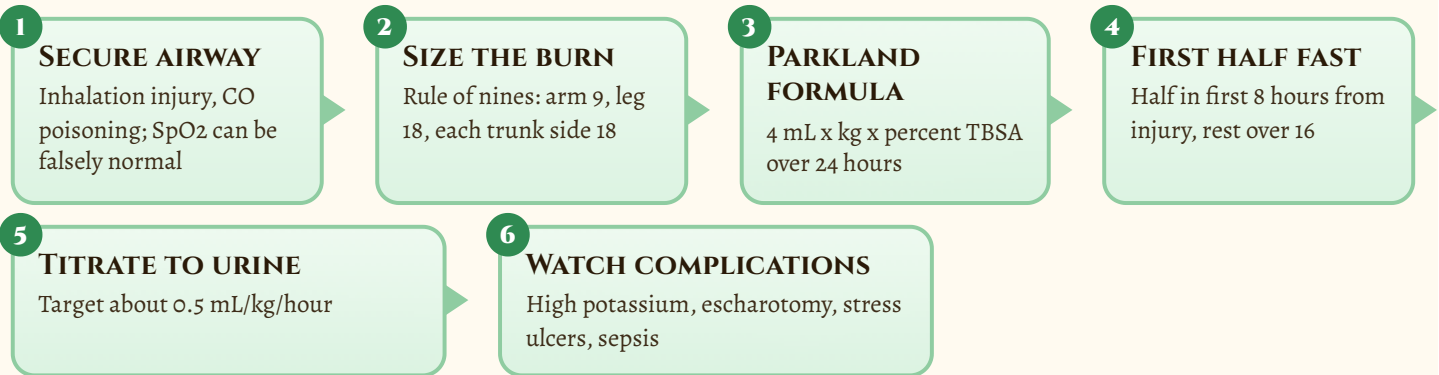
- Osteomyelitis is most often caused by *Staphylococcus aureus*.
- Pain is constant and not relieved by rest; early X rays may be normal, so MRI is more sensitive.
- Chronic osteomyelitis forms dead bone (sequestrum) that often requires surgery.
- Rhabdomyolysis releases CK, myoglobin, and potassium; it causes dark urine and AKI.
- Treat rhabdomyolysis with aggressive IV fluids and monitor potassium and the ECG.

## 6 BURNS

### BURN DEPTH

| FEATURE | SUPERFICIAL         | PARTIAL THICKNESS                 | FULL THICKNESS                    |
|---------|---------------------|-----------------------------------|-----------------------------------|
| LAYERS  | Epidermis only      | Epidermis and part of dermis      | Entire dermis and beyond          |
| LOOK    | Red, dry, blanches  | Moist, red, blisters              | Leathery, white, brown, or black  |
| PAIN    | Painful             | Very painful                      | Painless, nerve endings destroyed |
| HEALING | Within about a week | Weeks; deep burns may need grafts | Needs grafting                    |

### BURN RESUSCITATION



*Parkland is 4 x kg x percent burned: half in 8 hours from injury, then titrate to urine.*

### WRITTEN NOTES: BURNS

- Depth: superficial (epidermis), partial thickness (blisters, painful), full thickness (leathery, painless, needs grafting).
- Rule of nines: head 9, each arm 9, each leg 18, anterior trunk 18, posterior trunk 18, perineum 1.
- Parkland: 4 mL x kg x percent TBSA, half in the first 8 hours from injury; target urine output about 0.5 mL/kg/hour.
- Early labs show hyperkalemia and hemoconcentration from cell destruction and plasma loss.
- Inhalation injury and carbon monoxide poisoning threaten the airway and oxygen delivery; pulse oximetry can be falsely normal.
- Circumferential eschar may need escharotomy.
- Burns cause hypermetabolism, stress ulcers, and high sepsis risk.

## 7 PRESSURE INJURIES AND LEG ULCERS

### ◆ PRESSURE INJURY STAGES

#### STAGES 1 AND 2

- Stage 1: intact skin, nonblanchable redness
- Stage 2: partial thickness, exposed dermis

#### STAGES 3 AND 4

- Stage 3: full thickness into fat
- Stage 4: exposed bone, tendon, or muscle

#### CANNOT STAGE

- Unstageable: slough or eschar hides base
- Deep tissue injury: purple or maroon skin

#### PREVENTION

- Braden scale risk assessment
- Reposition regularly
- Limit shear and friction
- Manage moisture and nutrition

### ◆ VENOUS VERSUS ARTERIAL ULCERS

| FEATURE          | VENOUS ULCER                      | ARTERIAL ULCER                      |
|------------------|-----------------------------------|-------------------------------------|
| LOCATION         | Medial ankle                      | Toes, feet, pressure points         |
| APPEARANCE       | Shallow, irregular, moist         | Punched out, pale base              |
| SURROUNDING SKIN | Brown hemosiderin staining, edema | Shiny, hairless, cool               |
| PAIN             | Aching, eased by elevation        | Severe, worse with elevation        |
| PULSES           | Present                           | Weak or absent                      |
| CARE             | Elevate legs, compression         | Keep legs dependent, no compression |



*Venous ulcers like legs up, arterial ulcers hurt when legs go up. Braden score guides pressure prevention.*

### WRITTEN NOTES: PRESSURE INJURIES AND LEG ULCERS

- Stage 1: nonblanchable redness of intact skin. Stage 2: partial thickness with exposed dermis.
- Stage 3: full thickness into fat. Stage 4: exposed bone, tendon, or muscle.
- Unstageable: base obscured by slough or eschar. Deep tissue injury: purple or maroon intact skin.
- Use the Braden scale to assess risk; reposition regularly and limit shear.
- Venous ulcers: medial ankle, brown hemosiderin staining, improve with elevation; arterial ulcers: pale, painful, worse with elevation.

## ◆ MELANOMA ABCDE

**A** **ASYMMETRY**  
Halves do not match

**B** **BORDER**  
Irregular, notched, or blurred edges

**C** **COLOR**  
Several shades or uneven color

**D** **DIAMETER**  
Over 6 mm

**E** **EVOLVING**  
Changing size, shape, color, or symptoms

## ◆ THREE SKIN CANCERS

| FEATURE              | BASAL CELL                  | SQUAMOUS CELL                | MELANOMA                               |
|----------------------|-----------------------------|------------------------------|----------------------------------------|
| CELL OF ORIGIN       | Basal keratinocytes         | Squamous keratinocytes       | Melanocytes                            |
| FREQUENCY            | Most common                 | Second most common           | Less common, most deadly               |
| LOOK                 | Pearly papule, rolled edges | Scaly, crusted, may ulcerate | Changing pigmented lesion              |
| PRECURSOR            | None typical                | Actinic keratosis            | Can arise from a mole                  |
| SPREAD               | Rarely metastasizes         | Can metastasize              | Metastasizes; depth predicts prognosis |
| CAUSE AND PREVENTION | UV B damage; sunscreen      | UV B damage; sunscreen       | UV damage; skin checks                 |



*Basal cell is most common and rarely spreads; melanoma is the killer, and depth decides prognosis.*

## WRITTEN NOTES: SKIN CANCER

- Basal cell carcinoma is the most common skin cancer; it rarely metastasizes.
- Squamous cell carcinoma can arise from actinic keratoses and can metastasize.
- Melanoma arises from melanocytes; use ABCDE and remember that depth predicts prognosis.
- UV B creates pyrimidine dimers that can cause mutations in p53 and other genes.
- Prevention includes sunscreen, protective clothing, and regular skin checks.

## ◆ PSORIASIS VERSUS ATOPIC DERMATITIS

| FEATURE   | PSORIASIS                                 | ATOPIC DERMATITIS                       |
|-----------|-------------------------------------------|-----------------------------------------|
| MECHANISM | T cells drive rapid keratinocyte turnover | Skin barrier defect, itch scratch cycle |
| LOCATION  | Extensor surfaces, scalp                  | Flexor surfaces                         |
| LESION    | Plaques with silvery scale                | Dry, itchy, thickened patches           |
| CARE      | Topical steroids, methotrexate, biologics | Daily emollients, topical steroids      |

## ◆ SKIN INFECTIONS AND REACTIONS

**BACTERIAL**

- Cellulitis: deep dermal, warm, spreading
- Impetigo: superficial, honey colored crusts

**NECROTIZING FASCIITIS**

- Pain out of proportion
- Crepitus
- Shock
- Needs emergency surgery

**VIRAL**

- Zoster: painful dermatomal vesicles
- Measles: Koplik spots, head to toe rash
- Measles: airborne precautions

**HYPERSENSITIVITY**

- Contact dermatitis: type IV, delayed
- Urticaria: type I, IgE, wheals



*Psoriasis plates the extensors; eczema creases the flexors. Pain out of proportion with crepitus means necrotizing fasciitis.*

**WRITTEN NOTES: INFLAMMATORY AND INFECTIOUS SKIN CONDITIONS**

- Psoriasis: T cell driven rapid keratinocyte turnover with silvery plaques on extensor surfaces.
- Atopic dermatitis: barrier defect, flexor surfaces, itch scratch cycle; use emollients daily.
- Allergic contact dermatitis is a type IV delayed reaction; urticaria is a type I IgE reaction.
- Cellulitis is a deep dermal infection; impetigo is superficial with honey colored crusts.
- Necrotizing fasciitis: pain out of proportion, crepitus, and shock; needs surgery.
- Herpes zoster is a dermatomal reactivation of varicella zoster virus.
- Measles: Koplik spots and a head to toe rash; airborne precautions.

**CLINICAL PEARLS**

- Osteo wears, rheumatoid flares: osteoarthritis worsens with use and has brief stiffness; rheumatoid arthritis has long morning stiffness that eases with movement.

- Pain with passive stretch is the earliest alarm in compartment syndrome. Pulselessness is late. Keep the limb at heart level and call.
- Parkland is 4 x kg x percent burned. Half in the first 8 hours from the time of the burn, then titrate to urine output.
- Gout loves the big toe, beer, organ meats, and diuretics. Colchicine calms the flare; allopurinol prevents the next one.
- Melanoma ABCDE: asymmetry, border, color, diameter over 6 mm, evolving. Depth decides prognosis.

## RX KEY MEDICATIONS

### ◆ MEDICATIONS FOR BONES, JOINTS, MUSCLE AND SKIN



#### ALENDRONATE

*Fosamax*

##### BISPHOSPHONATE

**USED FOR** Osteoporosis

**WATCH** Take oral forms with a full glass of water on an empty stomach and stay upright 30 minutes; report jaw pain or difficulty swallowing.



#### METHOTREXATE

*Trexall, Otrexup, Rasuvo*

##### CONVENTIONAL DISEASE MODIFYING ANTIRHEUMATIC DRUG (FOLATE ANTAGONIST)

**USED FOR** Rheumatoid arthritis, psoriasis

**WATCH** Usually dosed once weekly with folic acid; monitor CBC and liver tests, avoid alcohol, and avoid pregnancy.



#### ALLOPURINOL

*Zyloprim*

##### XANTHINE OXIDASE INHIBITOR

**USED FOR** Chronic gout, tophi, uric acid stones

**WATCH** Encourage plenty of fluids; stop and report any rash, which can signal a severe hypersensitivity reaction.



#### COLCHICINE

*Colcrys, Mitigare*

##### ANTIGOUT ANTI INFLAMMATORY

**USED FOR** Acute gout flare and flare prophylaxis

**WATCH** Diarrhea is an early sign of toxicity; avoid grapefruit and use caution with renal impairment and interacting drugs.



#### SILVER SULFADIAZINE

*Silvadene*

##### TOPICAL ANTIMICROBIAL FOR BURNS

**USED FOR** Partial and full thickness burns

**WATCH** Silver sulfadiazine can cause transient leukopenia and is avoided in sulfa allergy; mafenide can cause metabolic acidosis.

# THE ROYAL KEEP: SEPSIS, SHOCK AND THE WHOLE BODY

## 1 SIRS AND SEPSIS

### ◆ SCREENING FOR SEPSIS

#### SIRS: 2 OR MORE

- Temp over 38 C or under 36 C
- Heart rate over 90
- Respiratory rate over 20
- WBC over 12,000 or under 4,000

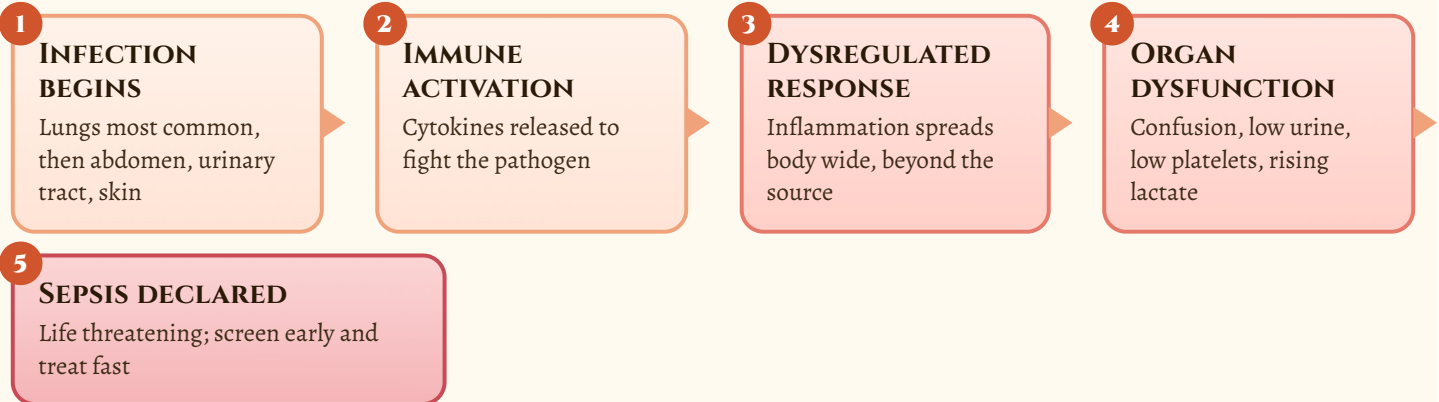
#### qSOFA: 2 OR MORE

- Respiratory rate 22 or more
- Altered mentation
- Systolic BP 100 or less

#### ATYPICAL: OLDER OR NEUTROPENIC

- Confusion alone
- Fever alone
- Hypothermia

### ◆ INFECTION TO SEPSIS



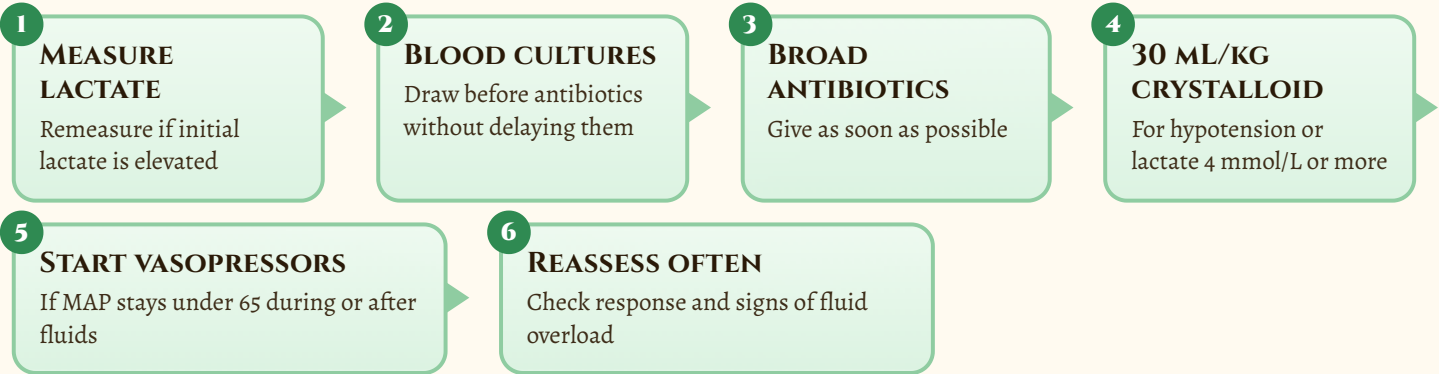
*Sepsis is the host response gone too far. Older adults may show only confusion, or even hypothermia.*

### WRITTEN NOTES: SIRS AND SEPSIS

- SIRS: two or more of temperature over 38 C or under 36 C, heart rate over 90, respiratory rate over 20, WBC over 12,000 or under 4,000.
- Sepsis is life threatening organ dysfunction from a dysregulated host response to infection.
- qSOFA: respiratory rate 22 or more, altered mentation, systolic blood pressure 100 or less.
- Lungs are the most common source, followed by abdomen, urinary tract, and skin.
- Older adults and neutropenic clients may present with confusion or fever alone, or even hypothermia.

## 2 THE HOUR ONE BUNDLE

### ◆ THE HOUR ONE BUNDLE



### ◆ BUNDLE NUMBERS

#### LACTATE

Normal 0.5 to 2.0 mmol/L

**Above 2**

Hypoperfusion; remeasure

#### LACTATE

Normal 0.5 to 2.0 mmol/L

**4 or more**

Give 30 mL/kg crystalloid

#### MAP

Normal 70 to 100 mm Hg

**Under 65**

Start vasopressors if fluids fail

#### BLOOD CULTURES

Normal No growth

**Positive**

Names the organism; narrow antibiotics

#### WBC

Normal 4,500 to 11,000/mm<sup>3</sup>

**Over 12,000 or under 4,000**

Meets a SIRS criterion



*Cultures first, but never let them delay antibiotics. Lactate of 4 or more earns 30 mL/kg.*

### WRITTEN NOTES: THE HOUR ONE BUNDLE

- Measure lactate and remeasure if elevated.
- Draw blood cultures before antibiotics without delaying them.
- Give broad spectrum antibiotics as soon as possible.
- Give 30 mL/kg crystalloid for hypotension or lactate of 4 mmol/L or more.
- Start vasopressors if MAP stays under 65 during or after fluids.
- Reassess frequently for response and fluid overload.

### 3 SEPTIC SHOCK

#### ◆ WARM VERSUS COLD SEPTIC SHOCK

| FEATURE          | WARM PHASE, EARLY                           | COLD PHASE, LATE                           |
|------------------|---------------------------------------------|--------------------------------------------|
| CARDIAC OUTPUT   | High                                        | Low, failing                               |
| SKIN             | Warm, flushed                               | Cool, mottled                              |
| PULSES           | Bounding                                    | Weak, thready                              |
| CAPILLARY REFILL | Brisk                                       | Delayed                                    |
| MECHANISM        | Cytokines, nitric oxide, vasodilation, leak | Myocardial depression, cell oxygen failure |

#### ◆ SEPTIC SHOCK DRUGS



##### NOREPINEPHRINE

*Levophed*

**VASOPRESSOR, ALPHA AGONIST**

**USED FOR** First line in septic shock

**WATCH** Central line preferred; watch for extravasation



##### VASOPRESSIN

*Vasotrist*

**VASOPRESSOR**

**USED FOR** Added to norepinephrine

**WATCH** Ischemia of fingers and gut



##### HYDROCORTISONE

*Solu-Cortef*

**CORTICOSTEROID**

**USED FOR** Shock needing ongoing vasopressors

**WATCH** Hyperglycemia, infection, hyponatremia



##### PIPERACILLIN TAZOBACTAM

*Zosyn*

**PENICILLIN WITH BETA LACTAMASE INHIBITOR**

**USED FOR** Broad empiric sepsis coverage

**WATCH** Give after cultures; monitor kidney function



##### VANCOMYCIN

*Generic IV (Vancocin is oral)*

**GLYCOPEPTIDE ANTIBIOTIC**

**USED FOR** MRSA coverage

**WATCH** Drug levels; nephrotoxicity



##### MEROPENEM

*Merrem*

**CARBAPENEM**

**USED FOR** Resistant gram negative infection

**WATCH** Seizure risk; check allergy history



*Septic shock is warm and leaky first, then cold and failing. MAP equals SBP plus 2 DBP, over 3.*

#### WRITTEN NOTES: SEPTIC SHOCK

- Defined by the need for vasopressors to keep MAP at least 65 and lactate above 2 despite fluids.
- Mechanism: cytokines and nitric oxide cause vasodilation and capillary leak, a distributive shock.
- Early warm phase with high output; late cold phase with failing output.

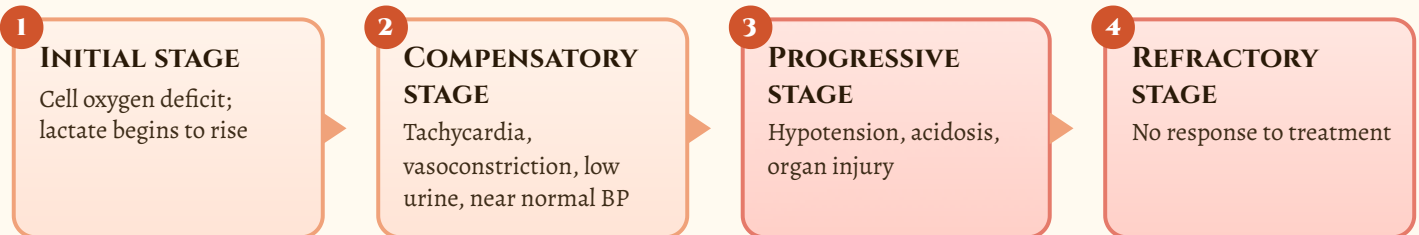
- Norepinephrine is first line; vasopressin and hydrocortisone may be added.
- MAP equals systolic plus 2 times diastolic, divided by 3.
- Rising lactate with normal SpO<sub>2</sub> suggests microcirculatory and mitochondrial dysfunction.

## 4 SHOCK STAGES AND TYPES

### ◆ TYPES OF SHOCK

| FEATURE        | HYPOVOLEMIC                    | CARDIOGENIC       | DISTRIBUTIVE                    |
|----------------|--------------------------------|-------------------|---------------------------------|
| PROBLEM        | Low volume                     | Pump failure      | Vessels dilate and leak         |
| PRELOAD        | Low                            | High              | Low                             |
| CARDIAC OUTPUT | Low                            | Low               | Often high early                |
| SVR            | High                           | High              | Low                             |
| EXAMPLES       | Hemorrhage, burns, dehydration | MI, heart failure | Sepsis, anaphylaxis, neurogenic |

### ◆ STAGES OF SHOCK



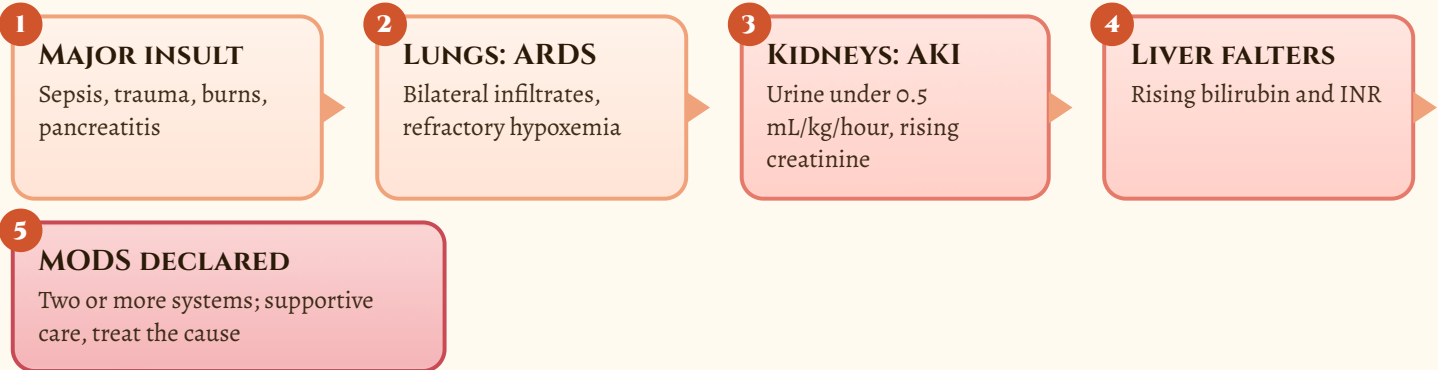
*Compensation buys time but raises oxygen demand. A normal blood pressure does not rule out shock.*

### WRITTEN NOTES: SHOCK STAGES AND TYPES

- Initial and compensatory stages: tachycardia, vasoconstriction, low urine output, normal or near normal blood pressure.
- Progressive stage: hypotension, acidosis, organ injury.
- Refractory stage: no response to treatment.
- Distributive shock has low SVR; cardiogenic shock has high SVR and low output; hypovolemic shock has low preload.
- Compensation buys time but raises oxygen demand and can injure organs if prolonged.

## 5 MODS AND ARDS

### ◆ THE ORGAN FAILURE DOMINO



### ◆ TRACKING ORGAN DYSFUNCTION

|                                                                                                    |                                                                                        |                                                                                           |
|----------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| <b>PAO2 TO FIO2 RATIO</b><br>Normal About 400 to 500<br>300 or less, bilateral infiltrates<br>ARDS | <b>URINE OUTPUT</b><br>Normal 0.5 mL/kg/hour or more<br>Under 0.5 for 6 hours<br>AKI   | <b>CREATININE</b><br>Normal 0.6 to 1.2 mg/dL<br>Rising<br>AKI                             |
| <b>TOTAL BILIRUBIN</b><br>Normal 0.3 to 1.2 mg/dL<br>Rising<br>Liver dysfunction                   | <b>INR</b><br>Normal 0.8 to 1.1<br>Rising<br>Liver failure or consumptive coagulopathy | <b>PLATELETS</b><br>Normal 150,000 to 400,000/mm <sup>3</sup><br>Falling<br>Sepsis or DIC |



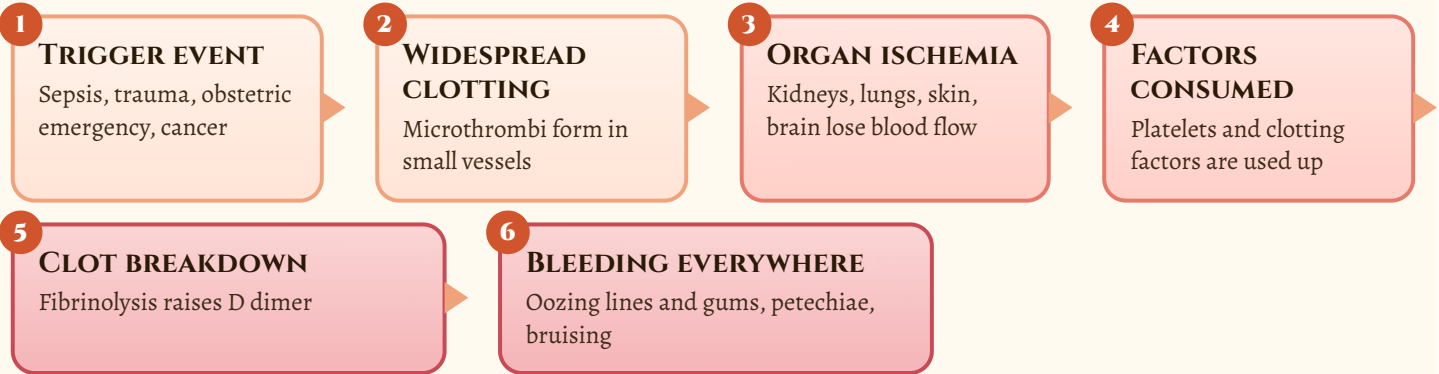
*In MODS the lungs often fail first. Each additional failing organ raises mortality.*

### WRITTEN NOTES: MODS AND ARDS

- MODS is progressive dysfunction of two or more organ systems after a major insult.
- The lungs often fail first; ARDS shows bilateral infiltrates and refractory hypoxemia.
- AKI shows urine output under 0.5 mL/kg/hour and rising creatinine.
- Liver dysfunction shows rising bilirubin and INR.
- Mortality rises with each failing organ; care is supportive while the cause is treated.

## 6 DIC

### ◆ DIC: CLOTTING THAT CAUSES BLEEDING



### ◆ THE DIC PANEL

#### PLATELETS

Normal 150,000 to 400,000/mm<sup>3</sup>

**Low**

Consumed in clots

#### FIBRINOGEN

Normal 200 to 400 mg/dL

**Low**

Consumed; may need cryoprecipitate

#### PT

Normal 11 to 12.5 seconds

**Prolonged**

Clotting factors depleted

#### APTT

Normal 30 to 40 seconds

**Prolonged**

Clotting factors depleted

#### D DIMER

Normal Under 0.5 mcg/mL FEU

**High**

Active clot breakdown



*DIC clots and bleeds at once: everything low except the clotting times and D dimer. Treat the cause.*

### WRITTEN NOTES: DIC

- Widespread clotting consumes platelets and clotting factors, leading to bleeding.
- Triggers: sepsis, trauma, obstetric emergencies, and cancer.
- Labs: low platelets, low fibrinogen, prolonged PT and aPTT, high D dimer.
- Signs: oozing from lines and gums, petechiae, bruising, and organ ischemia.
- Treat the cause; replace platelets, plasma, or cryoprecipitate for bleeding; use bleeding precautions.

## 7 HIGH YIELD REVIEW: CELLS, FLUIDS, AND IMMUNITY

### ◆ HIGH YIELD EMERGENCY DRUGS



#### EPINEPHRINE

*EpiPen, Auvi-Q*

**ADRENERGIC AGONIST**

**USED FOR** Anaphylaxis, IM first

**WATCH** Lateral thigh; repeat in 5 to 15 minutes if needed



#### REGULAR INSULIN

*Humulin R, Novolin R*

**SHORT ACTING INSULIN**

**USED FOR** Shift potassium into cells

**WATCH** Give with dextrose; check glucose often



#### ALBUTEROL

*ProAir HFA, Ventolin HFA*

**BETA 2 AGONIST**

**USED FOR** Shift potassium into cells

**WATCH** Tachycardia, tremor



#### SODIUM ZIRCONIUM CYCLOSILICATE

*Lokelma*

**POTASSIUM BINDER**

**USED FOR** Remove potassium through the gut

**WATCH** Edema from sodium content



#### PATIROMER

*Veltassa*

**POTASSIUM BINDER**

**USED FOR** Remove potassium, slower onset

**WATCH** Low magnesium; separate other drugs by 3 hours

### ◆ MUDDPILES: ANION GAP METABOLIC ACIDOSIS

**M**

#### METHANOL

Toxic alcohol

**U**

#### UREMIA

Kidney failure retains acids

**D**

#### DIABETIC KETOACIDOSIS

Ketoacids

**P**

#### PROPYLENE GLYCOL

Solvent in some IV drugs

**I**

#### IRON, ISONIAZID

Overdose

**L**

#### LACTIC ACIDOSIS

Shock, sepsis, hypoxia

**E**

#### ETHYLENE GLYCOL

Antifreeze

**S**

#### SALICYLATES

Aspirin overdose



*Hyperkalemia with ECG changes: calcium first to protect the heart, then shift and remove potassium.*

### WRITTEN NOTES: HIGH YIELD REVIEW: CELLS, FLUIDS, AND IMMUNITY

- Hypoxic cell injury begins with ATP loss, pump failure, and cell swelling.
- Histamine causes early vasodilation and leaky vessels; chronic inflammation brings macrophages, lymphocytes, and fibrosis.
- Fever results from PGE<sub>2</sub> resetting the hypothalamic set point.
- Hyperkalemia with ECG changes: give calcium first, then shift and remove potassium.
- Anion gap metabolic acidosis includes lactic acidosis and ketoacidosis.

- Anaphylaxis: IM epinephrine first; AIDS is defined by CD4 under 200.

## 8 HIGH YIELD REVIEW: ORGAN SYSTEMS

### ◆ DKA VERSUS HHS

| FEATURE        | DKA                                            | HHS                                   |
|----------------|------------------------------------------------|---------------------------------------|
| TYPICAL CLIENT | Type 1 diabetes, younger                       | Type 2 diabetes, older                |
| GLUCOSE        | Usually over 250 mg/dL                         | Often over 600 mg/dL                  |
| KETONES        | Significant                                    | Minimal or absent                     |
| PH             | Under 7.30                                     | Over 7.30                             |
| KEY CARE       | Fluids, potassium before insulin, insulin drip | Aggressive fluids, potassium, insulin |

### ◆ CROSS SYSTEM RED FLAGS

#### HEART AND VESSELS

- Left HF: pulmonary congestion, crackles
- Right HF: JVD, edema, hepatomegaly
- Atrial fibrillation: stroke from atrial clots
- Virchow triad: stasis, injury, hypercoagulability

#### LUNGS

- COPD target SpO<sub>2</sub> 88 to 92 percent
- Silent chest in asthma is ominous

#### KIDNEYS

- Prerenal AKI: BUN to creatinine over 20
- CKD anemia: low erythropoietin

#### BRAIN

- Cushing triad signals rising ICP
- CT excludes bleed before thrombolytics



*In DKA and HHS, check potassium before insulin. Exclude hemorrhage on CT before any thrombolytic.*

### WRITTEN NOTES: HIGH YIELD REVIEW: ORGAN SYSTEMS

- Left heart failure causes pulmonary congestion; right heart failure causes systemic venous congestion.
- Atrial fibrillation raises stroke risk through atrial clots; Virchow triad drives DVT.
- COPD target SpO<sub>2</sub> is often 88 to 92 percent; a silent chest in asthma is ominous.
- Prerenal AKI has a BUN to creatinine ratio over 20 to 1; CKD causes anemia through low erythropoietin.

- DKA has ketoacidosis; HHS has extreme hyperglycemia without significant ketosis; replace potassium before insulin.
- Cushing triad signals rising ICP; CT must exclude hemorrhage before thrombolytics.

## + CLINICAL PEARLS

- Sepsis is the host's response gone too far, not just the germ. Look for organ dysfunction: confusion, low urine, low platelets, rising bilirubin, rising lactate.
- Hour one bundle: lactate, cultures, antibiotics, 30 mL/kg fluid for hypotension or lactate of 4 or more, vasopressors for MAP under 65.
- Septic shock is warm and leaky first, then cold and failing. Norepinephrine is the first vasopressor.
- DIC clots and bleeds at once: low platelets, low fibrinogen, long PT and aPTT, high D dimer. Treat the cause.
- Compensation is the body's best idea in the moment. In chronic illness and critical illness, the most harmful process is often a helpful response that never shut off.

## RX KEY MEDICATIONS

### ◆ MEDICATIONS FOR SEPSIS, SHOCK AND THE WHOLE BODY



#### PIPERACILLIN TAZOBACTAM

*Zosyn*

**BROAD SPECTRUM  
ANTIBIOTICS**

**USED FOR** Sepsis and septic shock

**WATCH** Give within the first hour after cultures are drawn; monitor kidney function and drug levels, especially with vancomycin.



#### NOREPINEPHRINE

*Levophed*

**VASOPRESSOR (ALPHA  
ADRENERGIC AGONIST)**

**USED FOR** Septic shock after adequate fluids

**WATCH** Prefer central line administration, monitor the IV site for extravasation, and titrate to MAP of at least 65.



#### LACTATED RINGER SOLUTION

*Generic only*

**ISOTONIC CRYSTALLOID**

**USED FOR** Sepsis induced hypoperfusion

**WATCH** Reassess after each bolus for crackles, dyspnea, and edema; large volumes of normal saline can cause hyperchloremic acidosis.



#### HYDROCORTISONE

*Solu-Cortef*

**CORTICOSTEROID**

**USED FOR** Septic shock that needs ongoing vasopressors

**WATCH** Monitor for hyperglycemia, new infections, and hypnatremia.



#### PLATELETS

*Generic only (blood bank product)*

**BLOOD COMPONENT  
REPLACEMENT**

**USED FOR** DIC with active bleeding or before procedures

**WATCH** Verify the product and client with two identifiers and monitor for transfusion reactions and fluid overload.