Textbooks and Course Syllabi

Limit your use of textbooks and course syllabi for Step 1 review. Many textbooks are too detailed for high-yield review and include material that is generally not tested on the USMLE Step 1 (e.g., drug dosages, complex chemical structures). Syllabi, although familiar, are inconsistent across medical schools and frequently reflect the emphasis of individual faculty, which often does not correspond to that of the USMLE Step 1. Syllabi also tend to be less organized than top-rated books and generally contain fewer diagrams and study questions.

Integration of AI in Medical Education: Transforming USMLE Preparation

The integration of AI into education signals a paradigm shift in the acquisition and application of medical knowledge. AI’s increasing ability to process extensive data sets and adapt to various learning styles makes it an attractive tool in medical training and practice. Studies have demonstrated that AI language models are capable of achieving high accuracy rates when answering USMLE-style questions, underscoring its potential in supporting medical education.

Although undeniably powerful, effectively utilizing AI as a study tool requires both practice and individual trial and error. We suggest the following approaches and prompts that might help learners more effectively harness AI for exam preparation:

Tailored Mnemonic Creation: Devise unique mnemonics to aid in memorizing complex medical terms efficiently. AI models can be highly creative in generating new ones, although feedback and iteration will likely be needed to produce mnemonics that are both accurate and memorable.

Example prompt: Create a food-related mnemonic for remembering adverse effects 1, 2, and 3 of Drug A.

Custom Summarization of Medical Texts: Efficiently condense extensive medical literature into concise summaries, facilitating efficient and rapid topic reviews.

Example prompt: Summarize this medical school lecture into bullet points. Decrease length by 80%.

AI-Generated Custom Quizzes: Create focused practice questions.

Example Prompt: Create three vignette-style multiple choice questions testing presentations of lysosomal storage disorders.

Clinical Case Simulations: Utilize AI-powered simulations of realistic clinical scenarios to practice decision-making skills and application of medical knowledge.

Example prompt: Create an exercise to practice analyzing acid-base disorders requiring Winter’s formula with step-by-step explanations.
Personalized Learning Schedules: Create customized study schedules, adjusting time allocation based on challenging subjects. Modify schedules daily based on progress.

Example prompt: Prepare a schedule to review this book over 4 weeks.

Though both exciting and promising, pitfalls of using AI models for studying include the potential for outdated information or reliance on data that are not validated, resulting in a potential source of misinformation. AI can become unintentionally trained with human biases, and thus produce results that further reinforce or perpetuate potentially harmful biases. When using AI for personal studying, always validate information and maintain a critical eye when creating prompts.

AI is clearly a rapidly evolving study tool, however, how it can be best integrated with proven study methods remains to be seen. For the most recent updates on effectively leveraging AI in medical education, we encourage you to explore our blog at firstaidteam.com and scan a variety of student-centered discussion forums.

**TEST-TAKING STRATEGIES**

Your test performance will be influenced by both your knowledge and your test-taking skills. You can strengthen your performance by considering each of these factors. Test-taking skills and strategies should be developed and perfected well in advance of the test date so that you can concentrate on the test itself. We suggest that you try the following strategies to see if they might work for you.

**Pacing**

You have seven hours to complete up to 280 questions. Note that each one-hour block contains up to 40 questions. This works out to approximately 90 seconds per question. We recommend following the “1 minute rule” to pace yourself. Spend no more than 1 minute on each question. If you are still unsure about the answer after this time, mark the question, make an educated guess, and move on. Following this rule, you should have approximately 20 minutes left after all questions are answered, which you can use to revisit all of your marked questions. Remember that some questions may be experimental and do not count for points (and reassure yourself that these experimental questions are the ones that are stumpying you). In the past, pacing errors have been detrimental to the performance of even highly prepared examinees. The bottom line is to keep one eye on the clock at all times!
**Bacillus cereus**

Gram − rod. Causes food poisoning. Spores survive cooking rice (reheated rice syndrome). Keeping rice warm results in germination of spores and enterotoxin formation. Emetic type causes nausea and vomiting within 1–5 hours. Caused by cereulide, a preformed toxin. Diarrheal type causes watery, nonbloody diarrhea and GI pain within 8–18 hours. Management: supportive care (antibiotics are ineffective against toxins).

**Clostridioides difficile**

Produces toxins A and B, which damage enterocytes. Both toxins lead to watery diarrhea → pseudomembranous colitis 📌. Often 2° to antibiotic use, especially clindamycin, ampicillin, cephalosporins, fluoroquinolones; associated with PPIs. Fulminant infection: toxic megacolon, ileus, shock.

Difficile causes diarrhea. Diagnosed by PCR or antigen detection of one or both toxins in stool. Treatment: oral vancomycin or fidaxomicin. For recurrent cases, consider repeating prior regimen or fecal microbiota transplant.

**Clostridia**

Gram −, spore-forming, obligate anaerobic rods. Tetanus toxin and botulinum toxin are proteases that cleave SNARE proteins involved in neurotransmission.

**Clostridium tetani**

Pathogen is noninvasive and remains localized to wound site. Produces tetanospasmin, an exotoxin causing tetanus. Tetanospasmin spreads by retrograde axonal transport to CNS and blocks release of GABA and glycine from Renshaw cells in spinal cord. Causes spastic paralysis, trismus (lockjaw), risus sardonicus (raised eyebrows and open grin), opisthotonos (spasms of spinal extensors).

Tetanus is tetanic paralysis. Prevent with tetanus vaccine. Treat with antitoxin +/− vaccine booster, antibiotics, diazepam (for muscle spasms), and wound debridement.

**Clostridium botulinum**

Produces a heat-labile toxin that damages SNARE proteins, thus preventing ACh release at the neuromuscular junction, causing botulism. In babies, ingestion of spores (eg, in honey) leads to disease (floppy baby syndrome). In adults, disease is caused by ingestion of preformed toxin (eg, in canned food). Symptoms of botulism (the 5 D’s): diplopia, dysarthria, dysphagia, dyspnea, descending flaccid paralysis. Does not present with sensory deficits.

Botulinum is from bad bottles of food, juice, and honey. Treatment: human botulinum immunoglobulin. Local botulinum toxin A (Botox) injections used to treat focal dystonia, hyperhidrosis, muscle spasms, and cosmetic reduction of facial wrinkles.

**Clostridium perfringens**

Produces α-toxin (lecithinase, a phospholipase) that can cause myonecrosis (gas gangrene 📌: presents as soft tissue crepitus) and hemolysis. If heavily spore-contaminated food is cooked but left standing too long at < 60°C, spore germinate → vegetative bacteria ingested → enterotoxin → late-onset (10–12 hours) food poisoning symptoms, resolution in 24 hours.

Perfringens perforates a gangrenous leg. Spontaneous gas gangrene (via hematogenous seeding; associated with colonic malignancy) is most commonly caused by Clostridium septicum.
**Protease inhibitors**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MECHANISM</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir</td>
<td>Prevents maturation of new virions. Maturation depends on HIV-1 protease (pol gene), which cleaves the polypeptide products of HIV mRNA into their functional parts. All protease inhibitors require boosting with either ritonavir or cobicistat.</td>
<td>Hyperglycemia, GI intolerance (nausea, diarrhea). Ritonavir (cytochrome P-450 inhibitor) is only used as a boosting agent.</td>
</tr>
<tr>
<td>Darunavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Entry inhibitors**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MECHANISM</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enfuvirtide</td>
<td>Binds gp41, inhibiting viral entry. Enfuvirtide inhibits fusion.</td>
<td>Skin reaction at injection sites.</td>
</tr>
<tr>
<td>Maraviroc</td>
<td>Binds CCR-5 on surface of T cells/monocytes, inhibiting interaction with gp120. Maraviroc inhibits docking.</td>
<td></td>
</tr>
</tbody>
</table>

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All protease inhibitors require boosting with either ritonavir (protease inhibitor only used as a boosting agent) or cobicistat (cytochrome P450 inhibitor).
Gender- and sexuality-inclusive history taking

Avoid making assumptions about sexual orientation, gender identity, gender expression, and behavior (e.g., a patient who identifies as heterosexual may engage in same-sex sexual activity). Use gender-neutral terms when referring to the patient or the patient’s family (e.g., “partner” rather than “husband” or “wife”) upon first meeting the patient until the patient instructs otherwise or uses specific pronouns. A patient’s assigned sex at birth and gender identity may differ. Do not bring up gender or sexuality if it is not relevant to the visit (e.g., a gender-nonconforming patient seeking care for a hand laceration).

Consider stating what pronouns you use when you introduce yourself (e.g., “I’m Dr. Smith, and I use she/her pronouns”) and asking patients how they would like to be addressed. Also consider ways of being inclusive (e.g., ensuring correct name and pronouns are in the EMR).

Reassure them about the confidentiality of their visits and be sensitive to the fact that patients may not be open about their sexual orientation or gender identity to others in their life.

Remember: trust is built over time, and listening to and learning from patients about how they would like to approach the topics discussed above is key.

Cultural formulation interview

Identify the problem through the patient’s perspective. Ask the patient to describe the problem in their own words, or how the patient would describe the problem to their family and friends.

Identify cultural perceptions of factors leading to a problem. Ask the patient to explain why they think they are experiencing their problem.

Identify how the patient’s background influences their problem. Ask the patient about what makes their problem better or worse. Investigate roles of family, community, and spirituality.

Identify how culture may impact current and future interventions. Ask the patient if they have any concerns or suggestions about the current plan of treatment. If they do not want to follow medical advice, investigate if there is a way to combine their plans with the standard medical regimen.

Identify possible barriers to care based on culture. Ask the patient if there is anything that would prevent them from seeking care in a standard medical institution. Probe for explanations and what may increase the chance of maintaining a good patient-physician relationship.

Motivational interviewing

Counseling technique to facilitate behavior modification by helping patients resolve ambivalence about change. Useful for many conditions (e.g., nicotine dependence, obesity). Helpful when patient has some desire to change, but it does not require that the patient be committed to making the change. May involve asking patients to examine how their behavior interferes with their life or why they might want to change it. Assess barriers (e.g., food access, untreated trauma) that may make behavior change difficult.

Assessing a patient’s readiness for change is also important for guiding physician-suggested goals. These goals should be Specific, Measurable, Achievable, Relevant, and Time bound (SMART).

Trauma-informed care

Patients with history of psychological trauma should receive thorough behavioral health screenings. Regularly assess mood, substance use, social supports, and suicide risk.

Focus assessments on trauma-related symptoms that interfere with social and occupational function. Always be empathetic. Do not ask invasive questions requiring the patient to describe trauma in detail. Ask permission prior to discussion.

Before the physical exam, reassure patients that they may signal to end it immediately if they experience too much physical or emotional discomfort. Offer the presence of additional staff for support. Psychological counseling may be indicated. Follow-up counseling is offered (or advised) as appropriate. Remember: Realize, Recognize, Respond, Resist retraumatization.
## Coronary artery disease

### Angina
- **Stable**—usually 2° to atherosclerosis (≥ 70% occlusion); exertional chest pain in classic distribution resolving with rest or nitroglycerin.
- **Unstable**—thrombosis with incomplete coronary artery occlusion; † in frequency or intensity of chest pain or any chest pain at rest. No cardiac biomarker elevation (vs non-ST-segment elevation MI [NSTEMI]).
- **Vasospastic** (formerly Prinzmetal or variant)—occurs at rest 2° to coronary artery spasm; transient ischemic ST changes on ECG. Tobacco smoking is a major risk factor. Triggers include cocaine, amphetamines, alcohol, triptans. Treat with Ca²⁺ channel blockers, nitrates, and smoking cessation (if applicable).

### Myocardial infarction
Most often due to rupture of coronary artery atherosclerotic plaque → acute thrombosis. † cardiac biomarkers (CK-MB, troponins) are diagnostic.

<table>
<thead>
<tr>
<th></th>
<th>Stable angina</th>
<th>Unstable angina</th>
<th>NSTEMI</th>
<th>STEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAIN</strong></td>
<td>On exertion</td>
<td>Mild exertion or at rest</td>
<td>At rest</td>
<td>At rest</td>
</tr>
<tr>
<td><strong>TROPONIN LEVEL</strong></td>
<td>No elevation</td>
<td>No elevation</td>
<td>Elevated</td>
<td>Elevated</td>
</tr>
<tr>
<td><strong>INFARCTION</strong></td>
<td>None</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ECG CHANGES</strong></td>
<td>Possible ST depression and/or T-wave inversion</td>
<td>Possible ST depression and/or T-wave inversion</td>
<td>ST depression and/or T-wave inversion</td>
<td>ST elevation, pathologic Q waves</td>
</tr>
</tbody>
</table>

## Ischemic heart disease manifestations

### Coronary steal syndrome
Distal to coronary stenosis, vessels are maximally dilated at baseline. Administration of vasodilators (eg, dipyridamole, regadenoson) dilates normal vessels → blood is shunted toward well-perfused areas → ischemia in myocardium perfused by stenosed vessels. Vasodilator stress tests rely on differential flow to detect potential ischemia. Rarely, they can cause coronary steal and true ischemia.

### Sudden cardiac death
Unexpected death due to cardiac causes within 1 hour of symptom onset, most commonly due to lethal arrhythmia (eg, ventricular fibrillation). Associated with CAD (up to 70% of cases), cardiomyopathy (hypertrophic, dilated), and hereditary channelopathies (eg, long QT syndrome, Brugada syndrome). Prevent with implantable cardioverter-defibrillator.

### Chronic ischemic heart disease
Progressive onset of HF over many years due to chronic ischemic myocardial damage. **Myocardial hibernation**—potentially reversible LV systolic dysfunction in the setting of chronic ischemia. Contrast with **myocardial stunning**, a transient LV systolic dysfunction after a brief episode of acute ischemia.
Gastrin ↑ acid secretion primarily through its effects on enterochromaffin-like (ECL) cells (leading to histamine release) rather than through its direct effect on parietal cells.

**Pancreatic secretions**

<table>
<thead>
<tr>
<th>ENZYME</th>
<th>ROLE</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-amylase</td>
<td>Starch digestion</td>
<td>Secreted in active form</td>
</tr>
<tr>
<td>Lipases</td>
<td>Lipid digestion</td>
<td></td>
</tr>
<tr>
<td>Proteases</td>
<td>Protein digestion</td>
<td>Includes trypsin, chymotrypsin, elastase, carboxypeptidases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Secreted as proenzymes also called zymogens</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dipeptides and tripeptides degraded within intestinal mucosa via intracellular process</td>
</tr>
<tr>
<td>Trypsinogen</td>
<td>Converted to active enzyme trypsin</td>
<td>Converted to trypsin by enterokinase/enteropeptidase, a brush-border enzyme on duodenal and jejunal mucosa</td>
</tr>
</tbody>
</table>

Isotonic fluid; low flow → high Cl⁻, high flow → high HCO₃⁻.
### Cells of the nervous system

**Neurons**—permanent, signal-transmitting cells of the nervous system composed of dendrites (receive input), cell bodies, and axons (send output). Dendrites and cell bodies can be seen on Nissl staining (stains RER; not present in axons). Markers: neurofilament protein, synaptophysin.

**CNS glial cells** — neuroectoderm (except microglia, which derive from mesoderm). PNS glial cells—neural crest ectoderm. Myelin is a multilayer wrapping of electrical insulation formed around axons → † conduction velocity of transmitted signals via saltatory conduction of action potentials at nodes of Ranvier († † Na⁺ channel density).

<table>
<thead>
<tr>
<th>CNS glial cells</th>
<th>Astrocytes</th>
<th>Largest and most abundant glial cell in CNS. Reactive gliosis in response to neural injury.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Physical support, repair, removal of excess neurotransmitters, component of</td>
<td></td>
</tr>
<tr>
<td></td>
<td>blood-brain barrier, glycogen fuel reserve buffer.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GFAP ⊕</td>
<td></td>
</tr>
<tr>
<td><strong>Oligodendrocytes</strong></td>
<td>Myelinate axons in CNS (including CN II). “Fried egg” appearance histologically</td>
<td>Each myelinates many axons (~ 30). Predominant type of glial cell in white matter. Injured in multiple sclerosis, leukodystrophies, progressive multifocal leukoencephalopathy.</td>
</tr>
<tr>
<td></td>
<td>(“oligodendrocytes”).</td>
<td></td>
</tr>
<tr>
<td><strong>Ependymal cells</strong></td>
<td>Ciliated simple columnar glial cells lining ventricles and central canal of</td>
<td>Specialized ependymal cells (choroid plexus) produce CSF.</td>
</tr>
<tr>
<td></td>
<td>spinal cord. Apical surfaces are covered with cilia (which circulate CSF) and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>microvilli (which help with CSF absorption).</td>
<td></td>
</tr>
<tr>
<td><strong>Microglia</strong></td>
<td>Activation in response to tissue damage → release of inflammatory mediators</td>
<td>Phagocytic scavenger cells of CNS. HIV-infected microglia fuse to form multinucleated giant cells in CNS in HIV-associated dementia.</td>
</tr>
<tr>
<td></td>
<td>(eg, nitric oxide, glutamate). Not readily discernible by Nissl stain.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PNS glial cells</th>
<th>Satellite cells</th>
<th>Myelinate axons in ganglia. Similar supportive role to astrocytes.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Schwann cells</td>
<td>Each myelinates a single axon (“Schwone”). Injured in Guillain-Barré syndrome.</td>
</tr>
<tr>
<td></td>
<td>S100 ⊕</td>
<td></td>
</tr>
</tbody>
</table>
Meninges

Three membranes that surround and protect the brain and spinal cord. Derived from both neural crest and mesoderm:
- Dura mater—thick outer layer closest to skull.
- Arachnoid mater—middle layer, contains weblike connections.
- Pia mater—thin, fibrous inner layer that firmly adheres to brain and spinal cord.

CSF flows in the subarachnoid space, located between arachnoid and pia mater.
Epidural space—potential space between dura mater and skull/vertebral column containing fat and blood vessels. Site of blood collection associated with middle meningeal artery injury.

Blood-brain barrier

Prevents circulating blood substances (eg, bacteria, drugs) from reaching the CSF/CNS. Formed by 4 structures:
- Tight junctions between nonfenestrated capillary endothelial cells
- Basement membrane
- Pericytes
- Astrocyte foot processes


Circumventricular organs with fenestrated capillaries and no blood-brain barrier allow molecules in blood to affects brain function (eg, area postrema—vomiting after chemotherapy; OVLT [organum vasculosum lamina terminalis]—osmoreceptors) or neurosecretory products to enter circulation (eg, neurohypophysis—ADH release).

BBB disruption (eg, stroke) → vasogenic edema. Hyperosmolar agents (eg, mannitol) can disrupt the BBB → ↑ permeability of medications.

Vomiting center

Coordinated by NTS in the medulla, which receives information from the chemoreceptor trigger zone (CTZ, located within area postrema (pronounce “puke“-stremah) in 4th ventricle), GI tract (via vagus nerve), vestibular system, and CNS.

CTZ and adjacent vomiting center nuclei receive input through 5 major receptors: histamine (H₁), muscarinic (M₁), neurokinin (NK-1), dopamine (D₂), and serotonin (5-HT₃).
- 5-HT₃, D₂, and NK-1 antagonists treat chemotherapy-induced vomiting.
- H₁ and M₁ antagonists treat motion sickness; H₁ antagonists treat hyperemesis gravidarum.
Sleep occurs in 4-6 cycles per night, each lasting ~90 mins and consisting of 2 main stages:

- Non-rapid eye movement (non-REM) sleep
- Rapid-eye movement (REM) sleep; duration of REM sleep ↑ through the night

Sleep-wake cycle is regulated by circadian rhythm, which is driven by suprachiasmatic nucleus (SCN) of hypothalamus. Low light conditions → ↓ SCN activity → ↑ norepinephrine from superior cervical ganglion → ↑ melatonin from pineal gland.

<table>
<thead>
<tr>
<th>SLEEP STAGE (% OF TOTAL SLEEP)</th>
<th>DESCRIPTION</th>
<th>EEG WAVEFORM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake</td>
<td>Alert, active mental concentration. Eyes open—beta waves (highest frequency, lowest amplitude). Eyes closed—alpha waves.</td>
<td><img src="beta.png" alt="" /> ![alpha.png]</td>
</tr>
<tr>
<td>Non-REM sleep</td>
<td>Light sleep; theta waves.</td>
<td>![Theta.png]</td>
</tr>
<tr>
<td>Stage N1 (5%)</td>
<td>Deeper sleep; sleep spindles and K complexes. When bruxism occurs (&quot;twoth&quot; grinding in N2).</td>
<td>![Sleep spindle.png] ![K-complex.png]</td>
</tr>
<tr>
<td>Stage N2 (45%)</td>
<td>Deepest non-REM sleep (slow-wave sleep); delta waves (lowest frequency, highest amplitude). When bedwetting, sleepwalking, and night terrors occur (wee and flee in N3).</td>
<td>![Delta.png]</td>
</tr>
<tr>
<td>Stage N3 (25%)</td>
<td>Loss of motor tone, ↑ brain O₂ use, variable pulse/BP. Extraocular movements due to activity of PPRF (paramedian pontine reticular formation/conjugate gaze center). May serve memory processing function. When dreaming, nightmares, and penile/clitoral tumescence occur (remember dreams in REM).</td>
<td>![Beta.png]</td>
</tr>
<tr>
<td>REM sleep (25%)</td>
<td>Alcohol, benzodiazepines, barbiturates: ↓ N3 and REM sleep (benzodiazepines are useful for sleepwalking and night terrors). Aging: ↓ N3 and REM sleep, ↑ sleep-onset latency, early morning awakening. Depression: ↓ N3 sleep, ↑ REM sleep, ↓ REM latency, repeated nighttime awakenings, early morning awakening (terminal insomnia). Narcolepsy: ↓ REM latency.</td>
<td><img src="beta.png" alt="" /></td>
</tr>
</tbody>
</table>

Factors affecting sleep architecture

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Hormones acting on kidney

**Angiotensin II**
Synthesized in response to ↓ BP. Causes efferent arteriole constriction → ↑ GFR and ↑ Na+ reabsorption in proximal and distal nephron. Net effect: ↓ BP. Causes efferent arteriole ↓ constriction ↑ GFR and ↑ FF but with compensatory Na+ preservation of renal function (↑ FF) in low-volume state with simultaneous Na+ reabsorption (both proximal and distal) to maintain circulating volume.

**Angiotensin II**
Synthesized in response to ↓ BP. Causes efferent arteriole constriction → ↑ GFR and ↑ Na+ reabsorption in proximal and distal nephron. Net effect: preservation of renal function (↑ FF) in low-volume state with simultaneous Na+ reabsorption (both proximal and distal) to maintain circulating volume.

**Atrial natriuretic peptide**

**Parathyroid hormone**
Secreted in response to ↓ plasma [Ca2+], ↑ plasma [PO4^3–], or ↓ plasma 1,25-(OH)2 D3. Causes ↑ Ca2+ reabsorption (DCT), ↓ PO4^3– reabsorption (PCT), and ↑ 1,25-(OH)2 D3 production (↑ Ca2+ and PO4^3– absorption from gut via vitamin D).

**Aldosterone**
Secreted in response to ↓ blood volume (via AT II) and ↑ plasma [K+]; causes ↑ Na+ reabsorption, ↑ K+ secretion, ↑ H+ secretion.

**ADH (vasopressin)**
Secreted in response to ↑ plasma osmolality and ↓ blood volume. Binds to receptors on principal cells, causing ↑ number of aquaporins and ↑ H2O reabsorption. ↑ reabsorption of urea in medullary collecting ducts to maximize corticopapillary osmotic gradient.

**Potassium shifts**

### Shifts K+ into cell
- **Serum hypoosmolarity**: Osmotic movement of H2O into cell. K+ follows (solute drag)
- **Alkalemia**: Net loss of H+ in urine and cell.
- **β-agonists**: Cause cellular uptake of K+
- **Insulin**: Causes extrusion of K+ out of cell and entry of H+ into cell

### Shifts K+ out of cell
- **Digoxin**: Causes hypokalemia
- **β-blocker**: Causes hypokalemia
- **Acidemia**: Causes extrusion of K+ out of cell and entry of H+ into cell
- **Succinylcholine**: Causes extrusion of K+ out of cell and entry of Na+ into cell
- **Cell lysis**: Causes extrusion of K+ out of cell and entry of H2O into cell
### Diuretics: site of action

- **Glomerulus:**
  - **Afferent:**
  - **Efferent:**

- **Proximal convoluted tubule:**
  - Sugars
  - Amino acids
  - Na^+ (permeable to water)

- **Loop of Henle (permeable to salts):**
  - Na^+ + Cl^–
  - Ca^2+ + Mg^2+
  - HCO_3^- is reabsorbed

- **Distal convoluted tubule:**
  - Na^+ + K^+
  - H^+ (rather than K^+) is exchanged for Na^+ in cortical collecting tubule
  - Na^+ entering all cells (via H^+/K^+ exchanger)

- **Collecting duct:**
  - Na^+ + Ca^2+ (permeable to salts)

### Diuretics: effects on electrolyte excretion

<table>
<thead>
<tr>
<th>Diuretic Type</th>
<th>Na^+</th>
<th>HCO_3^-</th>
<th>K^+</th>
<th>Cl^-</th>
<th>Ca^{2+}</th>
<th>Mg^{2+}</th>
<th>H^+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonic anhydrase inhibitors</td>
<td>↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>–/↑</td>
<td>–</td>
<td>–</td>
<td>↓</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>↑↑</td>
<td>↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>↑</td>
<td>↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↓</td>
<td>–/↑</td>
<td>↑</td>
</tr>
<tr>
<td>K^+-sparing diuretics</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓/–</td>
<td>↓/–</td>
<td>↑</td>
</tr>
</tbody>
</table>

**Blood pH:***

- **Acidemia:**
  - carbonic anhydrase inhibitors: ↑ HCO_3^- reabsorption
  - K^+ sparing: aldosterone blockade prevents K^+ secretion and H^+ secretion
  - Hyperkalemia leads to K^+ entering all cells (via H^+/K^+ exchanger)

- **Alkalemia:**
  - Loop diuretics and thiazides cause alkalemia through several mechanisms:
    - Volume contraction → ↑ AT II → ↑ Na^+ / H^+ exchange in PCT → ↑ HCO_3^- reabsorption ("contraction alkalosis")
    - K^+ loss leads to K^+ exiting all cells (via H^+/K^+ exchanger)
    - In low K^+ state, H^+ (rather than K^+) is exchanged for Na^+ in cortical collecting tubule → alkalosis and "paradoxical aciduria"
Early embryonic development

- **Week 1**: hCG secretion begins around the time of blastocyst implantation. Blastocyst “sticks” on day six.

- **Week 2**: Formation of bilaminar embryonic disc; two layers = epiblast, hypoblast.

- **Week 3**: Formation of trilaminar embryonic disc via gastrulation (epiblast cell invagination through primitive streak); three layers = endoderm, mesoderm, ectoderm. Notochord arises from midline mesoderm and induces overlying ectoderm (via SHH) to become neural plate, which gives rise to neural tube via neurulation.

- **Week 4**: Heart begins to beat (four chambers). Cardiac activity visible by transvaginal ultrasound. Upper and lower limb buds begin to form (four limbs).

- **Week 8**: Genitalia have male/female characteristics (pronounce “geneightalia”).
Descent of testes and ovaries

<table>
<thead>
<tr>
<th>DESCRIPTION</th>
<th>MALE REMNANT</th>
<th>FEMALE REMNANT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gubernaculum</strong></td>
<td>Band of fibrous tissue</td>
<td>Anchors testes within scrotum</td>
</tr>
<tr>
<td><strong>Processus vaginalis</strong></td>
<td>Evagination of peritoneum</td>
<td>Forms tunica vaginalis</td>
</tr>
</tbody>
</table>

### REPRODUCTIVE—ANATOMY

**Drainage of reproductive organs**

**Venous drainage**
- Right ovary/testis → right gonadal vein → IVC.
- Left ovary/testis → left gonadal vein → left renal vein → IVC (takes the longer way).
- Left testicular vein enters left renal vein at 90° angle → flow is less laminar on the left than on the right → left venous pressure > right venous pressure → varicocele is more common on the left.

**Lymphatic drainage**

- **PARA-AORTIC**
  - Female: Ovaries, fallopian tubes, uterine fundus, Testes
  - Male: Ovaries, fallopian tubes, uterine fundus, Testes

- **EXTERNAL ILIAC**
  - Superior part of bladder, Body of uterus, cervix

- **INTERNAL ILIAC**
  - Inferior part of bladder, Cervix, proximal vagina, Prostate, corpus cavernosum

- **SUPERFICIAL INGUINAL**
  - Distal anal canal, Distal vagina, vulva, Scrotum

- **DEEP INGUINAL**
  - Female: Glans clitoris
  - Male: Glans clitoris, Glans penis

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### Progestins

<table>
<thead>
<tr>
<th>MECHANISM</th>
<th>CLINICAL USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bind progesterone receptors, ↓ growth and ↑ vascularization of endometrium, thicken cervical mucus.</td>
<td>Contraception (forms include pill, intrauterine device, implant, depot injection), endometrial cancer, abnormal uterine bleeding. Progestin challenge: presence of bleeding upon withdrawal of progestins excludes anatomic defects (eg, Asherman syndrome) and chronic anovulation without estrogen.</td>
</tr>
</tbody>
</table>

### Antiprogestins

<table>
<thead>
<tr>
<th>MECHANISM</th>
<th>CLINICAL USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competitive inhibitors of progestins at progesterone receptors.</td>
<td>Termination of pregnancy (mifepristone with misoprostol); emergency contraception (ulipristal).</td>
</tr>
</tbody>
</table>

### Contraception

<table>
<thead>
<tr>
<th>METHOD</th>
<th>MECHANISM</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal</td>
<td>Estrogen combined with progestins Progestin-only</td>
<td>Prevent ovulation by ↓ GnRH → ↓ LH/FSH → no estrogen surge → no LH surge Progestins also thicken cervical mucus (↓ sperm entry) and thin endometrium (less suitable for implantation)</td>
</tr>
<tr>
<td>Intrauterine device</td>
<td>Copper IUD (hormone free)</td>
<td>Copper IUD causes local inflammation that is toxic to sperm and ova preventing fertilization and implantation</td>
</tr>
<tr>
<td>Surgical</td>
<td>Males—vasectomy Females—tubal ligation</td>
<td>No sperm in ejaculate Sperm cannot reach ova</td>
</tr>
</tbody>
</table>

### Tocolytics

Medications that relax the uterus; include terbutaline (β₂-agonist action), nifedipine (Ca²⁺ channel blocker), indomethacin (NSAID). Used to ↓ contraction frequency in preterm labor and allow time for administration of glucocorticoids (to promote fetal lung maturity) or transfer to appropriate medical center with obstetrical care.