

## **Endocrine Pharmacology**

### **Subcommittee**

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<b>Introduction to Endocrine Pharmacology</b>
<b>Recommended Curriculum Equivalent: 0.5 hr</b>
<b>Learning Objectives</b>
<b>Physiology and pathophysiology</b> General functions of hormones and their target organs; principal type of hormones (structure-activity relationships, location and type of receptors). Types of feedback regulation involved in maintaining necessary blood level of hormone. Etiology of endocrine syndromes including those due to: hormone deficiency/excess, receptor defect, hormone resistance, abnormal hormone dynamics, binding proteins
<b>Mechanism of action</b> Mechanisms of hormone action including: receptors and signal transduction pathways for hormones (the location of receptors, molecular events activated by hormones that interact with intracellular receptors and second messenger systems that are commonly linked to membrane-associated extracellular receptors)
<b>Pharmacokinetics</b> Regulation of hormone synthesis/release/disposition: the role of day-night rhythms, patterns of release, binding proteins, modulating factors (neurotransmitters, releasing hormones, nutrients), and measurement in biological fluids

<b>Hypothalamus, Anterior Pituitary 1</b>				
<b>Recommended Curriculum Equivalent: 2.0 hr</b>				
<b>Drug Classes and Drugs to consider</b>				
Growth Hormone	Prolactin	Gonadotropins	ACTH	TSH
OCTREOTIDE PEGVISOMAN T SERMORELIN SOMATROPIN bromocriptine lanreotide mecasermin	BROMOCRIPTIN E CABERGOLINE	CHORIONIC -hCG GANIRELIX GONADOTROPIN HUMAN LEUPROLIDE UROFOLLITROPIN abarelix cetorelix follitropin goserelin histrelin lutropin alpha menotropins nafarelin triptorelin	cosyntropin	thyrotropin
<b>Learning Objectives</b>				
<p><b>Physiology and pathophysiology</b>            Know releasing factors (GHRH, GnRH, DA) and trophic hormones (ACTH, TSH, GH, LH, FSH, prolactin) of the anterior pituitary.            Understand the regulation of growth hormone (GH) biosynthesis and secretion including the roles of growth hormone releasing hormone (GHRH) and GH-releasing peptides, glucose levels, somatostatin, and dopamine – age; body composition.            Know role of insulin-like growth factor 1 in secondary effects of GH and in feedback regulation of GH secretion            Know the physiological conditions that elicit growth hormone secretion; outline how specific diagnostic maneuvers can elicit GH secretion.            Understand the regulation of prolactin biosynthesis secretion and release by suckling; effect of dopaminergic and serotonergic agonists and antagonists            List pharmacological actions that can induce hyperprolactinemia.            Understand the medical problems related to hypersecretion of prolactin in the female (galactorrhea, amenorrhea, infertility) and in the male (hypogonadism, infertility).            Know the hypothalamic-anterior pituitary-gonadal axis, target tissue products (inhibin and sex steroids), and feedback pathways. Describe the kinetics of secretion for GnRH and the relationship to the therapeutic uses of synthetic analogs, the mode of administration and therapeutic considerations.            Understand the physiological importance of ACTH suppression by pharmacological glucocorticoids</p>				
<p><b>Mechanism of action</b>            Explain the molecular mechanism of action of each drug in each drug class.</p>				

**Actions on organ systems**

Describe the biological actions of growth hormone on peripheral tissues (e.g., protein synthesis, intermediary metabolism).

Outline the role(s) of IGF-1.

Describe the biological actions of prolactin on breast development and lactation; learn the interrelationship of the hormones that are involved in breast development and lactation: growth hormone, estrogen, progesterone, glucocorticoids, TRH, prolactin, oxytocin, and insulin.

Know clinical uses of GnRH and its agonist and antagonist analogs.

**Adverse effects, drug interactions and contraindications**

List the adverse effects of GH therapy in children and adults.

Describe the adverse effects of GnRH and analogs as therapeutic agents when used to treat infertility, prostatic carcinoma, endometriosis, central precocious puberty.

**Therapeutic uses**

Understand the medical problems related to hypo- or hyper- secretion of GH and the role of releasing/replacement therapy and release inhibiting drugs in the management of these states, respectively.

Understand the mode of administration and therapeutic considerations: intermittent (infertility) versus continuous administration (endometriosis, uterine fibroids, prostate cancer), precocious puberty.

Describe the utility of the rapid ACTH stimulation test in diagnosing pituitary-adrenal disorders and what endpoint is measured.

**Notes****Clinical Pharmacology**

Low bioavailability of bromocriptine makes it very susceptible to drug interactions, because it is metabolized by CYP3A4, a P450 isoform that is readily induced or inhibited by concurrently administered medications. It has recently been approved for management of type 2 diabetes, but it is only marginally effective for this indication.

**Relevance**

<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Endocrine system-Normal Processes- hypothalamus and anterior pituitary gland</li> <li>2) Endocrine system-Abnormal Processes-neoplastic disorder, metabolic and regulatory processes, systemic disorders, congenital and genetic disorders affecting the endocrine system</li> <li>3) Reproductive System-Normal processes, hypothalamic-pituitary-gonadal axis</li> <li>4) Reproductive System-Abnormal processes-congenital and genetic disorders-disorders relating to pregnancy</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the endocrine system</p> <p>Hormones and hormone analogs</p> <p>Stimulators of hormone production</p> <p>Inhibitors of hormone production</p> <p>Hormone antagonists</p> <p>Potentiators of hormone action</p> <p>Gonadotropin-releasing hormone and gonadotropin replacement, incudin all gonadotropin-releasing antagonists</p> <p>Stimulators and inhibitors of lactation</p>
<p><b>AAMC Medical School Objectives</b>  <b>Project Report X Patient Safety – Table</b>  1</p>	<p><b>Topic C:</b> Drug treatment of common conditions</p>

<b>Hypothalamus and Posterior Pituitary</b>	
<b>Recommended Curriculum Equivalent: 1.0 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
Vasopressin	Oxytocin
DESMOPRESSIN VASOPRESSIN chlorpropamide conivaptan demeclocycline tolvaptan	OXYTOCIN
<b>Learning Objectives</b>	
<b>Physiology and pathophysiology</b> Discuss the effects of vasopressin on receptor subtypes and signal transduction systems in vascular smooth muscle and the kidney. Describe the mechanisms by which vasopressin increases renal water conservation. Consider drugs that affect vasopressin release/action and their relationship to the therapy of diabetes insipidus (DI) and SIADH List drugs that can cause diabetes insipidus (nephrogenic and neurogenic) and SIADH. Describe the pharmacokinetics and actions of oxytocin and roles in parturition and lactation.	
<b>Mechanism of action</b> Explain the molecular mechanism of action of each drug in each drug class.	
<b>Actions on organ systems</b> Describe the pharmacokinetics and actions of vasopressin and analogs.	
<b>Adverse effects, drug interactions and contraindications</b> Understand the toxicity and contraindications for oxytocin.	
<b>Therapeutic uses</b> Preparations and routes administration of vasopressin analogs available for treating neurogenic and partial diabetes insipidus, bleeding of esophageal varices and deficient blood clotting factors in hemophilia. Understand the diagnostic and therapeutic uses of oxytocin.	
<b>Notes</b>	
<b>Clinical Pharmacology</b>	
<b>Relevance</b>	

<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Endocrine system-Normal Processes- hypothalamus and posterior pituitary pituitary gland</li> <li>2) Endocrine system-Abnormal Processes-neoplastic disorder, metabolic and regulatory processes, systemic disorders</li> <li>3) Renal/Urinary System-Abnormal Processes-metabolic and regulatory disorders, systemic diseases affecting the renal system</li> <li>4) Reproductive system-Normal processes-pregnancy, labor and delivery</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the endocrine system</p> <p>Hormones and hormone analogs</p> <p>Inhibitors of hormone production</p> <p>Hormone antagonists</p> <p>Drugs used to treat volume, electrolyte and acid-base disorders</p> <p>Female reproductive tract-Stimulants and inhibitors of labor</p>
<p><b>AAMC Medical School Objectives</b>  <b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions</p>

<b>ADRENAL CORTEX</b>	
<b>Recommended Curriculum Equivalent: 1.5 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
Glucocorticoid-related	Mineralocorticoid-related
CORTISOL (hydrocortisone) DEXAMETHASONE KETOCONAZOLE METYRAPONE PREDNISON aminoglutethimide beclomethasone betamethasone etomidate fluticasone mifepristone mitotane prednisolone triamcinolone	ALDOSTERONE FLUDROCORTISONE SPIRONOLACTONE eplerenone
<b>Learning Objectives</b>	
<b>Physiology and pathophysiology</b> Describe the regulation of corticosteroid synthesis by ACTH and angiotensin. Review the regulation of aldosterone secretion by angiotensin (I, II, and III).	
<b>Mechanism of action</b> Explain the molecular mechanism of action of agonists and antagonists in each drug class. Be aware of receptor-independent effects via 11-beta-steroid hydroxylase on corticosteroid specificity.	
<b>Actions on organ systems</b> Describe the actions of corticosteroids on intermediary metabolism, growth and development, electrolyte homeostasis, immune and inflammatory responses. Understand the cellular/molecular mechanisms of action of corticosteroids. Know the importance of synthetic glucocorticoids, especially those modifications that enhance pharmacodynamic activity and/or determine activity based on route of administration.	
<b>Pharmacokinetics</b> Describe the significance of corticosteroid disposition (protein binding, biotransformation, enzyme induction) that may necessitate changes in dosage regimens.	
<b>Adverse effects, drug interactions and contraindications</b> List the adverse effects/contraindications related to corticosteroid use. List the adverse effects of excessive mineralocorticoid activity.	

<p><b>Therapeutic uses</b>          Explain the rationale for corticosteroid use in replacement therapy, as anti-inflammatory and immunosuppressive agents, and as diagnostic agents in hypothalamo-pituitary adrenocortical disease/dysfunction.          Explain the use of fludrocortisone in replacement therapy.          Explain the rationale for alternate day therapy and the necessity for slow withdrawal following chronic therapy with glucocorticoids.          Explain the rationale for spironolactone in treating primary hyperaldosteronism.</p>	
<p><b>Notes</b></p>	
<p><b>Clinical Pharmacology</b>          Prednisone is a prodrug and may be poorly activated in patients with severe liver disease.          Ketoconazole is a potent inhibitor of both CYP3A4 and P-glycoprotein. It is to be used with caution in patients receiving other drug therapies that are modulated by this transporter (P-gp) and drug metabolizing enzyme (3A4).</p>	
<p><b>Relevance</b></p>	
<p><b>USMLE topic</b>          1) Normal Processes – adrenal cortex, adrenal medulla          2) Normal process – cell tissue structure function, hormone synthesis secretion action and metabolism          3) Abnormal process – adrenal disorders, neoplastic disorders          4) Abnormal processes – drug-induced adverse effects on the endocrine system          5) Abnormal processes – systemic disorder affecting the endocrine system</p>	<p><b>Principles of therapeutics</b>          Mechanisms of action and use of drugs for treatment of disorders of the endocrine system          Hormones and hormone analogs          Inhibitors of hormone production          Hormone antagonists          Drugs used to treat volume, electrolyte and acid-base disorders</p>
<p><b>AAMC Medical School Objectives</b>  <b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions  <b>Topic D:</b> Management of less common but severe medical conditions and emergencies</p>



<b>THYROID</b>
<b>Recommended Curriculum Equivalent: 1.0</b>
<b>Drug Classes and Drugs to consider</b>
LEVOTHYROXINE METHIMAZOLE POTASSIUM IODIDE PROPRANOLOL PROPYLTHIOURACIL RADIOIODINE ( <sup>131</sup> I) carbimazole iodide salts ipodate triiodothyronine (liothyronine)
<b>Learning Objectives</b>
<p><b>Physiology and pathophysiology</b>            Outline the regulation and the key steps in thyroid hormone synthesis and peripheral conversion.            Explain the mechanisms by which thyroid hormones regulate cellular function.            Describe the signs/symptoms of hypothyroidism (myxedema) and the consequences of the disease that can alter drug therapy for other concurrent diseases.</p>
<p><b>Mechanism of action</b>            Explain the molecular mechanism of action of each of the drugs listed above.</p>
<p><b>Actions on organ systems</b>            Delineate the relationship between thyroid hormones and the actions of catecholamines and provide the rationale for the use of propranolol in the treatment of hyperthyroidism.</p>
<p><b>Pharmacokinetics</b>            Provide the pharmacokinetic rationale for selecting the most appropriate form of thyroid hormone as replacement therapy.            Identify the best index of adequate replacement therapy with thyroid hormone.            Provide the pharmacokinetic rationale for selecting the most appropriate anti-thyroid drug for treating hyperthyroidism (diffuse toxic goiter) in a non-pregnant versus a pregnant female.</p>
<p><b>Adverse effects, drug interactions and contraindications</b>            Describe the adverse effects of anti-thyroid medications and identify those that are potentially life threatening.</p>
<p><b>Therapeutic uses</b>            Describe the caution necessary when replacing thyroid hormone in a patient with a history of coronary artery disease.            Describe the rationale and order of administration of drugs given to treat thyroid storm.            Provide the rationale for the uses of drugs/radioiodine in treating hyperthyroidism; explain their mechanism(s) of action; consequences of radioiodine use.</p>
<p><b>Notes</b></p>

<p><b>Clinical Pharmacology</b></p> <p>Only thyroxine is indicated for the treatment of hypothyroidism. Use of tri-iodothyronine is dangerous because of its increased potency and rapid and potential adverse effects on cardiac function.</p> <p>Propylthiouracil is the antithyroid drug of choice in pregnancy because of its shorter half-life and its lesser tendency to cross the placenta.</p> <p>Although propranolol is active in decreasing conversion of T4 to T3, this has no place in the therapeutic approach to management of hyperthyroidism to reduce T3 production. Propranolol is only indicated in thyroid storm to decrease the enhancement of catecholamine stimulation of cardiac contractility in the hyperthyroid state.</p>	
<p><b>Relevance</b></p>	
<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Normal Processes – thyroid gland</li> <li>2) Normal processes – thyroid hormone synthesis, secretion action and metabolism</li> <li>3) Abnormal process – thyroid disorders, neoplastic disorders</li> <li>4) Abnormal processes, metabolic and regulatory processes</li> <li>5) Abnormal processes – infectious, inflammatory and immunological disorders</li> <li>6) abnormal processes – drug-induced adverse effects on the endocrine system</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the endocrine system</p> <p>Hormones and hormone analogs</p> <p>Inhibitors of hormone production</p> <p>Hormone antagonists</p>
<p><b>AAMC Medical School Objectives</b></p> <p><b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions</p> <p><b>Topic D:</b> Management of less common but severe medical conditions and emergencies</p>

<b>PARATHYROID and Ca<sup>++</sup> and PO<sub>4</sub><sup>-</sup> Homeostasis</b>
<b>Recommended Curriculum Equivalent: 0.5 hr</b>
<b>Drug Classes and Drugs to consider</b>
ALENDRONATE CALCITRIOL CALCIUM GLUCONATE PARATHYROID HORMONE calcitonin cinacalcet denosumab furosemide ibandronate pamidronate paracalcitol plicamycin prednisone sevelamer sodium fluoride teriparatide vitamin D (cholecalciferol/ergocalciferol) zoledronate
<b>Learning Objectives</b>
<p><b>Physiology and pathophysiology</b></p> <p>Understand the regulation of calcium homeostasis and the physiological actions of parathyroid hormone (PTH), calcitonin (CT) and 1,25-dihydroxyvitaminD<sub>3</sub> [1,25-(OH)<sub>2</sub>D<sub>3</sub>]; understand the role(s) of 1alpha-hydroxylation of 25-OH vitamin D, and of kidney, liver and GI tract in vitamin D homeostasis.</p> <p>Describe the mechanisms regulating synthesis, secretion of PTH and actions and CT their mechanism(s) of action on bone, kidney and intestine.</p> <p>Be aware of the extra-renal 1alpha-hydroxylation of 25-OH vitamin D and potential importance in the innate immune system and in cancer prevention and therapy</p>
<p><b>Mechanism of action</b></p> <p>Explain the molecular mechanism of action of each drug in each drug class.</p>
<p><b>Adverse effects, drug interactions and contraindications</b></p> <p>Review the possible adverse effects of CT, 1,25-(OH)<sub>2</sub>D<sub>3</sub> and calcium supplements.</p> <p>Describe the chronic toxicity associated with long-term use of sodium fluoride.</p>

<p><b>Therapeutic uses</b></p> <p>Know the available preparations of CT, 1,25-(OH)<sub>2</sub>D<sub>3</sub>, and calcium supplements and their clinical uses; compare and contrast the treatment of hypo- and hyper-parathyroidism.</p> <p>Understand the clinical value of bisphosphonates and CT in the treatment of: hypercalcemia, Paget's disease, osteoporosis (postmenopausal and glucocorticoid-induced).</p> <p>Know current guideline for vitamin D supplementation and goals for blood level of vitamin D.</p> <p>Know current recommendations for treating osteoporosis, especially with respect to use of bisphosphonates, estrogens (esp. raloxifene), teriparatide, and denosumab.</p>	
<p><b>Notes</b></p>	
<p><b>Clinical Pharmacology</b></p> <p>Calcium carbonate preparations remain the most cost effective form for patients requiring calcium supplementation. Calcium supplements should always be taken with vitamin D to enhance their bioavailability.</p> <p>Chronic use of bisphosphonates is being questioned, since there is lack of evidence for efficacy for fracture prevention beyond 3-5 years of ingestion.</p>	
<p><b>Relevance</b></p>	
<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Normal Processes – parathyroid gland</li> <li>2) Normal processes – vitamin D synthesis, secretion, action and metabolism</li> <li>3) Abnormal process – parathyroid disorders, neoplastic disorders</li> <li>4) Abnormal processes, metabolic and regulatory processes</li> <li>5) Abnormal processes – idiopathic disorders</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the endocrine system</p> <p>Hormones and hormone analogs</p> <p>Inhibitors of hormone production</p> <p>Hormone antagonists</p>
<p><b>AAMC Medical School Objectives</b></p> <p><b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions</p>

<b>THE ENDOCRINE PANCREAS</b>
<b>Recommended Curriculum Equivalent: 1.5 Hr</b>
<b>Drug Classes and Drugs to consider</b>
ACARBOSE INSULINS (aspart, glulisine, lispro, regular, NPH, detemir, glargine) METFORMIN GLIPIZIDE PIOGLITAZONE REPAGLINIDE chlorpropamide exenatide liraglutide glucagon glimepiride glyburide nateglinide pramlintide rosiglitazone saxagliptin sitagliptin
<b>Learning Objectives</b>
<p><b>Physiology and pathophysiology</b></p> Describe the normal daily patterns insulin secretion and changes that occur in different types of diabetes mellitus. Describe the effects of insulin and glucagon on intermediary metabolism and ion transport. Describe the effects of incretin hormones, esp. GLP-1, on insulin and glucagon secretion. Describe the effects of amylin on glucagon secretion. Describe the pathophysiology of the primary types of diabetes mellitus (bihormonal disease – insulin and glucagon), and their sequelae: diabetic ketoacidosis and non-ketotic hyperosmolar coma.
<p><b>Mechanism of action</b></p> Explain the molecular mechanism of action of each drug in each drug class.
<p><b>Pharmacokinetics</b></p> Describe the pharmacokinetic (onset and duration of action) rationale for the use of insulin preparations in 'split-mixed' or continuous s.c. infusion. List commonly used drugs with which sulfonylurea compounds are known to interact and the postulated mechanisms for these interactions (first vs. second generation).
<p><b>Adverse effects, drug interactions and contraindications</b></p> Describe the clinical manifestations and management of overdose with insulin and oral hypoglycemic agents, respectively.

<p><b>Therapeutic uses</b></p> <p>Explain the mechanisms by which oral anti-diabetic agents act and the influence these mechanisms have on selection for therapy in individual patients (e.g., obese). Describe the relative roles of insulin and oral hypoglycemics in the treatment of type I and type II diabetes mellitus. Discuss the use of recombinant DNA insulin preparations and the insulin pumps that are employed in certain patients. Know the utility of assessing HbA1c.</p>	
<p><b>Notes</b></p>	
<p><b>Clinical Pharmacology</b></p> <p>Metformin has become the defacto first line agent for drug therapy of type 2 diabetes. The next step is usually to add a sulfonylurea. Combination drug products are being heavily marketed and are consistently more expensive than ingestion of the generic durgs separately. If a DPP-4 inhibitor is considered as add-on therapy, linagliptin may be preferable in patients with renal impairment, since there is no need to adjust drug dose for this pathology. However safety of DDP-4 inhibitor with long-term use remains to be established. Use of glitaxones as add-on therapy is associated with weight gain and the potential increased risk of heart failure.</p>	
<p><b>Relevance</b></p>	
<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Normal Processes – pancreatic islets</li> <li>2) Normal processes – insulin synthesis, secretion action and metabolism</li> <li>3) Abnormal process – neoplastic disorders, pancreatic islets</li> <li>4) Abnormal processes, metabolic and regulatory processes, diabetes mellitus</li> <li>5) Abnormal processes – infectious, inflammatory and immunologic disorders</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the endocrine system Hormones and hormone analogs Inhibitors of hormone production Hormone antagonists Potentiators of hormone action Other treatment for diabetes</p>
<p><b>AAMC Medical School Objectives</b> <b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions</p>

<b>GONADAL HORMONES</b>	
<b>Recommended Curriculum Equivalent: 1.5 HR</b>	
<b>Drug Classes and Drugs to consider</b>	
<b>Estrogen/progestins</b>	<b>Androgens</b>
ANASTROZOLE CLOMIPHENE ETHINYL ESTRADIOL EXEMESTANE MEDROXYPROGESTERONE NORETHINDRONE PROGESTERONE RALOXIFENE TAMOXIFEN conjugated/esterified estrogens diethylstilbestrol drospirinone estradiol 17 $\beta$ estrone levonogestrel mestranol mifepristone norgestrel phytoestrogens ulipristal	FINASTERIDE FLUTAMIDE OXANDROLONE TESTOSTERONE cicalutamide cyproterone danazol leuprolide
<b>Learning Objectives</b>	
<p><b>Physiology and pathophysiology</b></p> <p>Describe the gametogenic and steroidogenic functions of the ovary and their regulation by gonadotropins.</p> <p>Know the sources of androgens (ovary, testes, adrenal) and understand their regulation of secretion; define the roles of LH and FSH on gonadal function.</p> <p>Define the importance of androgens for sexual differentiation and puberty.</p> <p>Understand medical problems associated with hypo- (hypogonadism) and hyperfunction (precocious puberty, hyperandrogenism) and rationale for therapy.</p> <p>Describe the rationale for the clinical uses of androgens in: replacement therapy, anemia, and catabolic states.</p>	
<p><b>Mechanism of action</b></p> <p>Describe, in general terms, the cellular/molecular mechanism of action of sex steroids. Distinguish between direct effects of testosterone and those mediated by dihydrotestosterone and estradiol. Know the mechanisms of action of all agents listed above.</p>	

**Actions on organ systems**

Elucidate the effects of estrogen on: cardiovascular function, intermediary metabolism, electrolyte and water balance, cognition, reproductive function, skin, plasma proteins and blood lipids hepatic function

Describe the effects of estrogens on laboratory tests, including liver function, clotting factors, thyroid hormone disposition and adrenocortical function.

Describe the effects of androgens on growth and development (anabolic actions vs. androgenic actions).

**Pharmacokinetics**

Describe differences in absorption, distribution, and elimination between synthetic and natural estrogens, including those in the environment (e.g., phytoestrogens).

Compare the routes of administration, absorption and relative duration of action of synthetic androgens and testosterone.

**Adverse effects, drug interactions and contraindications**

List major adverse effects/contraindications for estrogens and progestins alone and in combination.

List the most common drug and nutraceutical interactions with estrogens and progestins.

Describe the adverse effects of androgens/anabolic steroids when used in male and female.

Correlate the hepatotoxicity of certain androgens/anabolic steroids with their chemical structure.

**Therapeutic uses**

Describe the use of drugs such as clomiphene and gonadotropic drugs for the treatment of infertility.

State the rationale for the various dosage schedule (e.g., biphasics, triphasics), for oral contraception when combination (estrogen-progestin) therapy is used.

List agents used for postcoital contraception.

List types of hormonal contraceptive agents, other than combination agents, and their routes of administration.

Describe some of the therapeutic and diagnostic uses of estrogens and progestins other than their utility as oral contraceptives.

Describe the rationale for use of long-acting progestins for long-term suppression of ovulation.

Describe the rationale for the replacement use of estrogens and estrogen/progestin in postmenopausal osteoporosis, cognitive disorders, and cardiovascular disease.

Describe the use of estrogen receptor antagonists and aromatase inhibitors in breast cancer.

Define the term "selective estrogen receptor modifier" (SERM); provide examples and outline their therapeutic utility.

Explain the mechanism of action mifepristone (RU 486) and other abortifacients.

**Notes**



<p><b>Clinical Pharmacology</b>          If androgens are used concurrently in patients receiving anticoagulant therapy, increased monitoring of INR (clotting time) is indicated.          Use of SSRI's concurrently with tamoxifen must be limited to those antidepressants that are not potent CYP2D6 substrates, since tamoxifen is pharmacologically activated by metabolism via CYP2D6.</p>	
<p><b>Relevance</b></p>	
<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Normal Processes – female structure and function, including breast</li> <li>2) Normal processes – male structure and function</li> <li>3) Abnormal process – infectious, inflammatory and immunologic disorders</li> <li>4) Abnormal processes – traumatic and mechanical disorders</li> <li>5) Abnormal processes, neoplastic disorders</li> <li>6) Abnormal processes – metabolic and regulatory processes</li> <li>7) Abnormal processes – systemic disorders affecting reproductive function</li> <li>8) Abnormal processes – drug-induced abnormal effects on the reproductive system</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the reproductive system</p> <p>Female reproductive tract</p> <ul style="list-style-type: none"> <li>- Fertility drugs</li> <li>- Contraceptives</li> <li>- Estrogen, progesterone replacement, treatment of menopause</li> <li>- Estrogen and progesterone antagonists</li> </ul> <p>Male reproductive tract</p> <ul style="list-style-type: none"> <li>- Fertility drugs</li> <li>- Androgen replacement and antagonists</li> </ul>
<p><b>AAMC Medical School Objectives</b>  <b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions</p>

<b>FEMALE UROGENITAL SYSTEM</b>	
<b>Recommended Curriculum Equivalent: 1 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
Oxytocics	Tocolytics
DINOPROST OXYTOCIN MIFEPRISTONE ERGONOVINE dinoprostone misoprostol	INDOMETHACIN atosiban magnesium sulfate nifedipine terbutaline
<b>Learning Objectives</b>	
<b>Mechanism of action</b> Explain the molecular mechanism of action of each drug in each drug class.	
<b>Actions on organ systems</b> Describe the receptors targeted by the oxytocics and the sensitivity of the uterus to the various oxytocics during the three trimesters of pregnancy.	
<b>Pharmacokinetics</b> State the usual route(s) of administration, onset and duration of action of the various oxytocic agents. State the usual route(s) of administration as well as onset and duration of action of the various tocolytic agents.	
<b>Adverse effects, drug interactions and contraindications</b> Describe the potential adverse effects of the oxytocic agents in the mother (uterine, extrauterine) and in the infant.	
<b>Therapeutic uses</b> Describe the clinical use of the individual oxytocics. Discuss the utilization of RU486 (mifepristone) versus prostaglandins and oxtocics in therapeutic abortion. Identify the potential benefits and risks of administering tocolytic (anti-contraction) agents to the mother and baby.	
<b>Notes</b>	
<b>Clinical Pharmacology</b> There is some concern that there are good data to support efficacy of any of the tocolytic agents (anti-contraction medications or labor repressants) in humans.	
<b>Relevance</b>	

<p><b>USMLE topic</b></p> <ol style="list-style-type: none"> <li>1) Normal Processes – female structure and function</li> <li>2) Normal processes – pregnancy, labor and delivery, gestational uterus, placenta</li> <li>3) Abnormal process – infectious, inflammatory and immunologic disorders</li> <li>4) Abnormal processes – disorders of pregnancy</li> </ol>	<p><b>Principles of therapeutics</b></p> <p>Mechanisms of action and use of drugs for treatment of disorders of the reproductive system</p> <p>Female reproductive tract</p> <ul style="list-style-type: none"> <li>- Stimulants and inhibitors of labor</li> <li>- abortifacients</li> </ul>
<p><b>AAMC Medical School Objectives</b>  <b>Project Report X Patient Safety – Table 1</b></p>	<p><b>Topic C:</b> Drug treatment of common conditions</p>

<b>MALE UROGENITAL SYSTEM</b>	
<b>Recommended Curriculum Equivalent: 1 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
SILDENAFIL TAMSULOSIN TERAZOSIN alprostadil doxazosin tadalafil vardenafil	
<b>Learning Objectives</b>	
<b>Physiology and pathophysiology</b>	
Describe the neuroendocrine factors that regulate functions of the male urogenital tract.	
<b>Mechanism of action</b>	
Explain the molecular mechanism of action of each drug in each drug class.	
<b>Adverse effects, drug interactions and contraindications</b>	
List the adverse effects and contraindications of the prototype agents in the drug list.	
<b>Therapeutic uses</b>	
Know the drugs that can be used to treat benign prostatic hyperplasia and impotence. State the usual routes of administration of alprostadil and sildenafil. Describe the proposed mechanism of action of the drug listed above and relate the resulting pharmacological effects to their clinical use.	
<b>Notes</b>	
<b>Clinical Pharmacology</b>	
Alpha-1 adrenergic receptor blockers remain the standard of care for symptomatic management of BPH.	
<b>Relevance</b>	
<b>USMLE topic</b> 1) Normal Processes – Male structure and function 2) Abnormal processes – neoplastic disorders 3) Abnormal process – infectious, inflammatory and immunologic disorders 4) Abnormal processes – metabolic and regulatory processes 5) Abnormal processes – drug-induced effects on the reproductive system 6) Abnormal Processes – traumatic and mechanical disorders	<b>Principles of therapeutics</b> Mechanisms of action and use of drugs for treatment of disorders of the reproductive system Male reproductive tract <ul style="list-style-type: none"> <li>- fertility drugs</li> <li>- gonadotropin replacement</li> <li>- antineoplastics</li> <li>- restoration of potency</li> </ul>

<b>AAMC Medical School Objectives</b> <b>Project Report X Patient Safety – Table</b> <b>1</b>	<b>Topic C: Drug treatment of common</b> <b>conditions</b>
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<b>OBESITY</b>	
<b>Recommended Curriculum Equivalent: 1 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
orlistat lorcaserin phentermine/topiramate extended-release	
<b>Learning Objectives</b>	
<b>Physiology and pathophysiology</b>	
Describe the neuroendocrine factors that regulate feeding and satiation	
<b>Mechanism of action</b>	
Explain the molecular mechanism of action of each drug in each drug class.	
<b>Adverse effects, drug interactions and contraindications</b>	
List the adverse effects and contraindications of the agents in the drug list.	
<b>Therapeutic uses</b>	
Know the drugs that can be used to treat obesity. State the usual routes of administration of the drugs. Describe the proposed mechanism of action of the drug listed above and relate the resulting pharmacological effects to their clinical use.	
<b>Notes</b>	
<b>Clinical Pharmacology</b>	
Diet and exercise remain the most effective interventions to treat obesity. Drug therapy for this health condition has been disappointing for the most part. Rebound weight gain on discontinuation of drug therapy occurs universally. Surgical management of severely obese patients, although risky, is likely to be the only intervention with the potential for lasting benefit.	
<b>Relevance</b>	
<b>USMLE topic</b> 1) Normal Processes – Adipose tissue 2) Abnormal processes – systemic disorders affecting the endocrine system 3) Abnormal processes – metabolic and regulatory processes	<b>Principles of therapeutics</b> Mechanisms of action and use of drugs for treatment of disorders of the endocrine system Antiobesity agents
<b>AAMC Medical School Objectives</b> <b>Project Report X Patient Safety – Table</b> <b>1</b>	<b>Topic C: Drug treatment of common</b> <b>conditions</b>