

## 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; principle type of hormones (structure-activity relationships, location and type of receptors). 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 are commonly linked to 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: 1.5 hr</b>		
<b>Drug Classes and Drugs to consider</b>		
<b>Growth hormone</b>	<b>Prolactin</b>	<b>Gonadotropins</b>
Bromocriptine OCTREOTIDE pegvisomant SERMORELIN Somatrem SOMATOMEDINS (IGF-1) SOMATROPIN	BROMOCRIPTINE Cabergoline Pergolide PROLACTIN	abarelix follitropin GANIRELIX GnRH (Gonadorelin) Goserelin HUMAN CHORIONIC GONADOTROPIN (hCG) LEUPROLIDE Menotropins Nafarelin UROFOLLITROPIN
<b>Learning Objectives</b>		
<p><b>Physiology and pathophysiology</b></p> <p>Understand the regulation of growth hormone (GH) biosynthesis and secretion including the roles of growth hormone releasing hormone (GH-RH) and GH-releasing peptides, glucose levels, somatotatin, and dopamine – age; body composition.</p> <p>Know the physiological conditions that elicit growth hormone secretion; outline how specific diagnostic maneuvers can elicit GH secretion.</p> <p>Understand the regulation of prolactin biosynthesis secretion and release by suckling; effect of dopaminergic and serotonergic agonists and antagonists</p> <p>List pharmacological actions that can induce hyperprolactinemia.</p> <p>Understand the medical problems related to hypersecretion of prolactin in the female (galactorrhea, amenorrhea, infertility) and in the male (hypogonadism, infertility).</p> <p>Describe the kinetics of secretion for GnRH and the relationship to the therapeutic uses of synthetic analogs, the mode of administration and therapeutic considerations.</p>		
<p><b>Mechanism of action</b></p> <p>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 IGFs (somatomedins).

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.

Understand the structure-activity relationships of gonadotropin releasing hormone (GnRH) and synthetic 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.

**Notes**

<b>Hypothalamus, Anterior and Posterior Pituitary 2</b>		
<b>Recommended Curriculum Equivalent: 1.5 hr</b>		
<b>Drug Classes and Drugs to consider</b>		
<b>ACTH</b>	<b>Vasopressin</b>	<b>Oxytocin</b>
Corticotropin COSYNTROPIN	Chlorpropamide Demeclocycline DESMOPRESSIN VASOPRESSIN	OXYTOCIN
<b>Learning Objectives</b>		
<p><b>Physiology and pathophysiology</b>            Discuss the effects of vasopressin on receptor subtypes and signal transduction systems in vascular smooth muscle and the kidney.            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 structure, pharmacokinetics and actions of oxytocin and roles in parturition and lactation.</p>		
<p><b>Mechanism of action</b>            Explain the molecular mechanism of action of each drug in each drug class.</p>		
<p><b>Actions on organ systems</b>            Describe the structure, pharmacokinetics and actions of vasopressin and analogs, such as desmopressin.</p>		
<p><b>Pharmacokinetics</b>            Understand by what route (s) must cosyntropin be administered.</p>		
<p><b>Adverse effects, drug interactions and contraindications</b>            List the possible (rare) side effects of cosyntropin administration.            Understand the toxicity and contraindications for oxytocin.</p>		
<p><b>Therapeutic uses</b>            Describe the utility of the rapid ACTH stimulation test in diagnosing pituitary-adrenal disorders and what endpoint is measured.            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.</p>		
<b>Notes</b>		

<b>ADRENAL CORTEX</b>	
<b>Recommended Curriculum Equivalent: 1.5 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
Glucocorticoid-related	Mineralocorticoid-related
Aminogluthethimide BECLOMETHASONE CORTISOL (hydrocortisone) DEXAMETHASONE fluticasone KETOCONAZOLE METYRAPONE Mifepristone Mitotane PREDNISONE triamcinolone	ALDOSTERONE FLUDROCORTISONE SPIRONOLACTONE
<b>Learning Objectives</b>	
<b>Physiology and pathophysiology</b> Know the major steps in the biosynthesis of steroids. 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 each drug in each drug class.	
<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 mechanism of action of corticosteroids. Know the structure-activity relationship of synthetic glucocorticoids, especially those modifications that enhance pharmacodynamics 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.	

**Therapeutic uses**

Explain the rationale for corticosteroid use in replacement therapy, as antiinflammatory and immunosuppressive agents, and as diagnostic agents in hypothalmo-pituitary adrenocortical disease/dysfunction.

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.

**Notes**

<b>THYROID</b>
<b>Recommended Curriculum Equivalent: 1.0</b>
<b>Drug Classes and Drugs to consider</b>
Iodide salts Iodate LEVOTHYROXINE Lithium METHIMAZOLE POTASSIUM IODIDE PROPRANOLOL RADIOIODINE (131I) PROPYLTHIOURACIL 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 drug in each drug class.</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 antithyroid 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 antithyroid medications and identify those that are potentially life threatening.</p>

**Therapeutic uses**

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.

**Notes**

<b>PARATHYROID</b>
<b>Recommended Curriculum Equivalent: 0.5 hr</b>
<b>Drug Classes and Drugs to consider</b>
ALENDRONATE CALCITONIN CALCITRIOL CALCIUM GLUCONATE cinacalcet ETIDRONATE Furosemide PARATHYROID HORMONE Plicamycin Prednisone sodium fluoride
<b>Learning Objectives</b>
<p><b>Physiology and pathophysiology</b>            Understand the regulation of calcium homeostasis and the physiological actions of parathyroid hormone (PTH), calcitonin (CT) and 1,25-dihydroxyvitamin D<sub>3</sub> [1,25-(OH)<sub>2</sub>D<sub>3</sub>]; understand the role(s) of kidney, liver and GI tract in vitamin D homeostasis.            Describe the mechanisms regulating synthesis, secretion of PTH and actions and CT their mechanism(s) of action on bone, kidney and intestine.</p>
<p><b>Mechanism of action</b>            Explain the molecular mechanism of action of each drug in each drug class.</p>
<p><b>Adverse effects, drug interactions and contraindications</b>            Review the possible adverse effects of CT, 1,25-(OH)<sub>2</sub>D<sub>3</sub> and calcium supplements. Describe the chronic toxicity associated with long-term use of sodium fluoride.</p>
<p><b>Therapeutic uses</b>            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.            Know the available preparations of CT and 1,25-(OH)<sub>2</sub>D<sub>3</sub> and calcium supplements. Understand the clinical value of bisphosphonates and CT in the treatment of: hypercalcemia, Paget's disease, osteoporosis (postmenopausal and glucocorticoid-induced).</p>
<p><b>Notes</b></p>

<b>THE ENDOCRINE PANCREAS</b>
<b>Recommended Curriculum Equivalent: 1.5 Hr</b>
<b>Drug Classes and Drugs to consider</b>
ACARBOSE Chlorpropamide Diazoxide exenatide Glucagon GLIPIZIDE Glyburide INSULINS (aspart, glulisine, lispro, regular, NPH, detemir, glargine) METFORMIN Nateglinide PIOGLITAZONE REPAGLINIDE Rosiglitazone sitagliptin tolbutamide
<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 protein on glucagon secretion. Describe the pathophysiology of the primary types of diabetes mellitus (bihormonal disease – insulin and glucagon), and their sequelae: diabetic ketoacidosis and nonketotic 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.

**Therapeutic uses**

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.

**Notes**

<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 conjugated/esterified estrogens diethylstilbestrol drospirinone estradiol 17β estrone ETHINYL ESTRADIOL EXEMESTANE Levonogestrel Mestranol Mifepristone MEDROXYPROGESTERONE NORETHINDRONE Phytoestrogens PROGESTERONE RALOXIFENE TAMOXIFEN	bicalutamide cyproterone danazol FINASTERIDE FLUTAMIDE leuprolide OXANDROLONE TESTOSTERONE
<b>Learning Objectives</b>	
<b>Physiology and pathophysiology</b> Describe the gametogenic and steroidogenic functions of the ovary and their regulation by gonadotropins. Know the sources of androgens (ovary, testes, adrenal) and understand their regulation of secretion; define the roles of LH and FSH on gonadal function. Define the importance of androgens for sexual differentiation and puberty. Understand medical problems associated with hypo- (hypogonadism) and hyperfunction (precocious puberty, hyperandrogenism) and rationale for therapy. Describe the rationale for the clinical uses of androgens in: replacement therapy, anemia, and catabolic states.	
<b>Mechanism of action</b> Explain the molecular mechanism of action of each drug in each drug class.	

**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).

Delineate the importance of dihydrotestosterone formation and binding to androgen receptors in the prostate gland and other organs.

**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 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**

<b>FEMALE UROGENITAL SYSTEM</b>	
<b>Recommended Curriculum Equivalent: 1 hr</b>	
<b>Drug Classes and Drugs to consider</b>	
Oxytocics	Tocolytics
DINOPROST Dinoprostone ERGONOVINE MIFEPRISTONE Misoprostol OXYTOCIN	INDOMETHACIN magnesium sulfate RITODRINE 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 agents to the mother and baby.	
<b>Notes</b>	

<b>MALE UROGENITAL SYSTEM 1 hr</b>
<b>Recommended Curriculum Equivalent:</b>
<b>Drug Classes and Drugs to consider</b>
Alprostadil Doxazosin saw palmetto SILDENAFIL TAMSULOSIN TERAZOSIN
<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> List 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>