

# Association for Medical School Pharmacology



## Knowledge Objectives in Medical Pharmacology -2005

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### ENDOCRINE PHARMACOLOGY (9.0 hr)

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**Drug List**



**First Edition**

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#### 1. Introduction (0.5)

a. Prerequisites

#### a. Prerequisites

##### Review:

1) General functions of hormones and their target organs; principle type of hormones (structure-activity relationships, location and type of receptors)

2) 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

3) 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)

4) Etiology of endocrine syndromes including those due to: hormone deficiency/excess, receptor defect, hormone resistance, abnormal hormone dynamics, binding proteins

#### b. Objective

##### Learn:

1) Rational basis of endocrine therapy including: indications for hormones/drugs in specific disorders (replacement therapy, diagnosis, medical therapy), route/frequency of administration, site(s)/mechanism(s) of action, adverse effects/contraindications

## **2. Hypothalamus, Anterior and Posterior Pituitary (1.5)**

#### a. General objectives

## Review:

- 1) Hypothalamic neurotransmitters/hormones that regulate hormone secretion from the anterior pituitary; structures and dynamics (feed forward/feed back) of hormones secreted by the anterior pituitary
- 2) Dynamics of various axes with respect to target gland function, i.e. hypothalamo-pituitary-adrenal axis; hypothalamo-pituitary-thyroid axis; hypothalamo-pituitary-gonadal axis; dynamics of portal system neurosecretion and its significance in the control of the anterior pituitary hormone secretion
- 3) Know the structures of hormones, i.e., glycoproteins, proteins, polypeptides, amino acid-derived; be cognizant of structural homology among the various families
- 4) Effects of pharmacologic agents on hypothalamic-pituitary function (e.g. selective serotonin reuptake inhibitors, effects of dopamine agonists and antagonists)

## b. Anterior Pituitary

- 1) Growth hormone/related drugs
  - a) Understand the regulation of growth hormone (GH) biosynthesis and secretion including the roles of growth hormone releasing hormone (GH-RH), glucose levels, somatostatin, and dopamine – age; body composition; know the physiological conditions that elicit growth hormone secretion; outline how specific diagnostic maneuvers can elicit GH secretion
  - b) Describe the biological actions of growth hormone on peripheral

of growth hormone on peripheral tissues (e.g., protein synthesis, intermediary metabolism). Outline the role(s) of IGFs (somatomedins)

c) 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

d) Describe the mechanism of action and the therapeutic indications of the following hormones and GH modulating drugs: sermorelin, bromocriptine, octreotide

e) Compare the therapeutic doses of GH for children versus adults; consider the rationale and justification for the use in elderly (retard aging) and athletes (enhance muscle strength)

f) List the adverse effects of GH therapy in children and adults

**Drugs to Consider:**

Bromocriptine  
OCTREOTIDE  
SERMORELIN  
Somatrem  
SOMATOMEDINS  
(IGF-1)  
SOMATROPIN

2) Prolactin/related drugs

a) Understand the regulation of prolactin biosynthesis secretion and release by suckling: effect of dopaminergic and serotonergic

dopaminergic and serotonergic agonists and antagonists; describe the biological actions of prolactin on breast development and lactation; learn the interrelationship of the hormones, which are involved in breast development and lactation: growth hormone, estrogen, progesterone, glucocorticoids, TRH, prolactin, oxytocin, and insulin

b) List pharmacological actions that can induce hyperprolactinemia

c) Understand the medical problems related to hypersecretion of prolactin in the female (galactorrhea, amenorrhea, infertility); in the male (hypogonadism, infertility)

d) Describe the mechanism of action of dopaminergic agonists used to treat hyperprolactinemia and the concerns about using these drugs to prevent postpartum lactation

**Drugs to Consider:**

BROMOCRIPTINE

Cabergoline

Pergolide

PROLACTIN

3) Gonadotropins/related drugs

a) Structure-activity relationships of gonadotropin releasing hormone (GnRH) and synthetic analogs

b) Describe the kinetics of secretion for GnRH and the

secretion for GnRH and the relationship to the therapeutic uses of synthetic analogs

c) Mode of administration and therapeutic considerations: intermittent (infertility) versus continuous administration (endometriosis, uterine fibroids, prostate cancer), precocious puberty

d) Adverse effects of GnRH and analogs as therapeutic agents when used to treat infertility, prostatic carcinoma, endometriosis, central precocious puberty

e) Steroidogenic actions/uses (diagnostic/therapeutic) and adverse effects of follicle stimulating hormone (FSH), luteinizing hormone (LH) and human chorionic gonadotropin (hCG).

**Drugs to Consider:**

follitropin alfa/beta

GANIRELIX

Gonadorelin

Goserelin

HUMAN

CHORIONIC

GONADOTROPIN

(hCG)

LEUPROLIDE

Menotropins

Nafrelin

UROFOLLITROPIN

4) Adrenocorticotrophic Hormone (ACTH)/related drugs

a) Describe the utility of the rapid ACTH stimulation test in

ACTH stimulation test in diagnosing pituitary-adrenal disorders; what endpoint is measured?

b) By what route (s) must cosyntropin be administered

c) List the possible (rare) side effects of cosyntropin administration

**Drugs to Consider:**

Corticotropin

COSYNTROPIN

c. Posterior Pituitary

Factors that regulate the release of hormones from the posterior pituitary

Structure and dynamics of hormones secreted by the posterior pituitary

1) Vasopressin/related drugs

a) Structure, pharmacokinetics and actions of vasopressin and analogs, such as desmopressin

b) Discuss the effects of vasopressin on receptor subtypes and signal transduction systems in vascular smooth muscle and the kidney.

c) 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.

d) Preparations and routes administration of vasopressin

administration of vasopressin analogs available for treating neurogenic and partial diabetes insipidus, bleeding of esophageal varices and deficient blood clotting factors in hemophilia.

**Drugs to Consider:**

Chlorpropamide  
Demeclocycline  
DESMOPRESSIN  
VASOPRESSIN

2) Oxytocin/related drugs

a) Structure, pharmacokinetics and actions of oxytocin; roles in parturition and lactation

b) Diagnostic and therapeutic uses of oxytocin

c) Toxicity and contraindications for oxytocin

**Drug to Consider:**

OXYTOCIN

**3. Adrenal Cortex (1.5)**

a. Glucocorticoids/related drugs

1) Know the major steps in the biosynthesis of steroids

2) Describe the regulation of corticosteroid synthesis by ACTH and angiotensin

3) 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

4) Know the structure-activity relationship of synthetic glucocorticoids, especially those

synthetic glucocorticoids, especially those modifications that enhance pharmacodynamics activity and/or determine activity based on route of administration

5) Describe the significance of corticosteroid disposition (protein binding, biotransformation, enzyme induction) that may necessitate changes in dosage regimens

6) Explain the rationale for corticosteroid use in replacement therapy, as anti-inflammatory and immunosuppressive agents, and as diagnostic agents in hypothalmo-pituitary adrenocortical disease/dysfunction

7) List the adverse effects/contraindications related to corticosteroid use

8) Explain the rationale for alternate day therapy and the necessity for slow withdrawal following chronic therapy with glucocorticoids

**Drugs to Consider:**

Aminogluthethimide  
BECLOMETHASONE  
CORTISOL (hydrocortisone)  
DEXAMETHASONE  
KETOCONAZOLE  
METYRAPONE  
Mifepristone  
Mitotane  
PREDNISONONE  
triamcinolone

b. Mineralocorticoids/related drugs

1) Review the regulation of aldosterone secretion by angiotensin (I, II, and III)

2) List the analogs used in mineralocorticoid replacement therapy

3) List the adverse effects of excessive mineralocorticoid activity

mineralocorticoid activity

4) Explain the rationale for spironolactone in treating primary hyperaldosteronism

**Drugs to Consider:**

ALDOSTERONE

FLUDROCORTISONE

SPIRONOLACTONE

**4. Gonads (1.5)**

a. Estrogens/Progestins/related drugs

1) Describe the gametogenic and steroidogenic functions of the ovary and their regulation by gonadotropins

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

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

4) 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

5) 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

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

of administration

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

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

9) List major adverse effects/contraindications for estrogens and progestins alone and in combination; list the most common drug interactions with estrogens and progestins

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

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

12) Define the term “selective estrogen receptor modifier” (SERM); provide examples and outline their therapeutic utility

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

14) List the drugs used to treat hirsutism

15) By what mechanisms do drugs produce gynecomastia; list at least one drug for each mechanism you identify

**Drugs to Consider:**

ANASTROZOLE

CLOMIPHENE

conjugated/esterified estrogens

danazol

diethylstilbestrol

ETHINYL ESTRADIOL

EXEMESTANE

Levonorgestrel

Levonogestrel  
Mestranol  
Mifepristone  
MEDROXYPROGESTERONE  
NORETHINDRONE  
Phytoestrogens  
PROGESTERONE  
RALOXIFENE  
TAMOXIFEN

b. Androgens/related drugs

1) 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

2) 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

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

4) 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, catabolic states

5) 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

6) Relate the mechanism of action of antiandrogens to their potential therapeutic uses: e.g. flutamide, finasteride

uses: e.g., flutamide, finasteride, spironolactone, leuprolide

**Drugs to Consider:**

Cyproterone

Danazol

FINASTERIDE

FLUTAMIDE

Leuprolide

OXANDROLONE

Spironolactone

TESTOSTERONE

**5. Thyroid (1.0)**

a. Outline the regulation and the key steps in thyroid hormone synthesis and peripheral conversion; explain the mechanisms by which thyroid hormones regulate cellular function

b. Delineate the relationship between thyroid hormones and the actions of catecholamines; provide the rationale for the use of propranolol in the treatment of hyperthyroidism

c. Describe the signs/symptoms of hypothyroidism (myxedema) and the consequences of the disease that can alter drug therapy for other concurrent diseases

d. 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

e. Describe the caution necessary when replacing thyroid hormone in a patient with a history of coronary artery disease

f. Describe the rationale and order of administration of drugs administered to treat thyroid storm

g. Provide the rationale for the uses of drugs/radioiodine in treating hyperthyroidism:

drugs/radioiodine in treating hyperthyroidism;  
explain their mechanism(s) of action;  
consequences of radioiodine use

h. 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

i. Describe the adverse effects of antithyroid medications and identify those that are potentially life threatening

**Drugs to Consider:**

Iodate

LEVOTHYROXINE

Liothyronine

Lithium

METHIMAZOLE

POTASSIUM IODIDE

PROPRANOLOL

RADIOIODINE (131I)

PROPYLTHIOURACIL

**6. Parathyroid/related Drugs (0.5)**

a. 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

b. Describe the mechanisms regulating synthesis, secretion of PTH and actions and CT their mechanism(s) of action on bone, kidney and intestine

c. 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

d. Know the available preparations of CT and 1,25-(OH)<sub>2</sub>D<sub>3</sub> and review the possible adverse effects of CT, 1,25-(OH)<sub>2</sub>D<sub>3</sub> and calcium supplement

e. Understand the clinical value of bisphosphonates and CT in the treatment of: hypercalcemia, Paget's disease, osteoporosis (postmenopausal and glucocorticoid-induced)

f. Describe the chronic toxicity associated with long-term use of sodium fluoride

**Drugs to Consider:**

ALENDRONATE

CALCITONIN

CALCITRIOL

CALCIUM GLUCONATE

ETIDRONATE

Furosemide

PARATHYROID HORMONE

Plicamycin

Prednisone

sodium fluoride

**7. Pancreas/related Drugs (1.5)**

a. Describe the normal daily patterns insulin secretion and changes that occur in different types of diabetes mellitus

b. Describe the effects of insulin and glucagon on intermediary metabolism and ion transport

c. Describe the pathophysiology of the primary types of diabetes mellitus (bihormonal disease – insulin and glucagon), and their sequelae: diabetic ketoacidosis and nonketotic hyperosmolar coma

d. Describe the pharmacokinetic (onset and duration of action) rationale for the use of insulin preparations in 'split-mixed' or continuous s.c. infusion

e. 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)

f. Describe the relative roles of insulin and oral hypoglycemics in the treatment of type I and type II diabetes mellitus

g. List commonly used drugs with which sulfonylurea compounds are known to interact and the postulated

compounds are known to interact and the postulated mechanisms for these interactions (first vs. second generation)

h. State the nature of the adverse effects of oral hypoglycemics and identify those that may require cessation of therapy or preclude their use

i. Describe the clinical manifestations and management of overdose with insulin and oral hypoglycemic agents, respectively

j. Discuss the use of recombinant DNA insulin preparations and the insulin pumps that are employed in certain patients

**Drugs to Consider:**

ACARBOSE

Chlorpropamide

Diazoxide

Glucagons

GLIPIZIDE

Glyburide

INSULINS (lispro, regular, lente, NPH, ultralente, glargine)

METFORMIN

Nateglinide

PIOGLITAZONE

REPAGLINIDE

Rosiglitazone

tolbutamide

8. Urogenital System (1.0)

a. Female Urogenital Tract

1) Oxytocics (Uterine stimulants)/related drugs

b. Describe the receptors targeted by the oxytocics and the sensitivity of the uterus to the various oxytocics during the three trimesters of pregnancy.

c. State the usual route(s) of administration, onset and duration of action of the various oxytocic agents

- d. Describe the clinical use of the individual oxytocics
- e. Discuss the utilization of RU486 (mifepristone) versus prostaglandins and oxytocics in therapeutic abortion
- f. Describe the potential adverse effects of the oxytocic agents in the mother (uterine, extrauterine) and in the infant

**Drugs to Consider:**

DINOPROST  
Dinoprostone  
ERGONOVINE  
MIFEPRISTONE  
Misoprostol  
OXYTOCIN

- g. Tocolytics (Uterine relaxants)/related drugs

- 1) Describe the mechanism of action of the various tocolytic agents
- 2) Identify the potential benefits and risks of administering tocolytic agents to the mother and baby
- c) State the usual route(s) of administration as well as onset and duration of action of the various tocolytic agents

**Drugs to Consider:**

INDOMETHACIN  
magnesium sulfate  
RITODRINE  
terbutaline

- h. Male Urogenital Tract

- 1) Describe the neuroendocrine factors that regulate functions of the male urogenital tract
- 2) 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

and relate the resulting pharmacological effects to their clinical use

3) List the adverse effects and contraindications of the prototype agents in the drug list

**Drugs to Consider:**

Alprostadil

Doxazosin

saw palmetto

SILDENAFIL

TAMSULOSIN

TERAZOSIN