PHARMACOLOGY 2

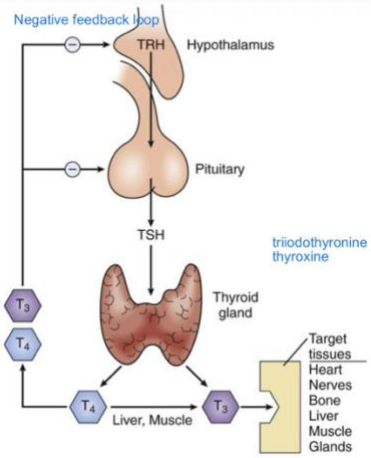
MIDTERM | PHM | YKS

SEMESTER 1st
SY. 2026-2027

III. Thyroid Drugs

A. THYROID HORMONES

- normal growth and development
- affect every organ system and have a crucial role in metabolic processes
- augment sympathetic nervous system function



B. BIOSYNTHESIS OF THYROID HORMONES

1. Uptake
   - active transport via Na^+/I^- symporter
   - actively transported to the thyroid follicle cell (via Na^+/I^- symporter)
2. Oxidation
   - Iodine to iodide
3. Organification
   - iodination of tyrosine residues of TG thyroglobulin
   - I_2 + TG → MIT & DIT
     Monoiodotyrosine, diiodotyrosine
4. Coupling
   - MIT + DIT → T_3
   - DIT + DIT → T_4

   Steps 2 to 4: peroxidase-catalyzed reactions
5. Proteolytic Release
   - thyroglobulin recenters the follicular cell by endocytosis
6. Peripheral conversion of T_4 to T_3
   80% of T3 is derived from T4

IV. Drugs Affecting Fertility and Reproduction

A. OVERVIEW

1. The hypothalamus produces GnRH
2. The anterior pituitary gland produces FSH & LH
3. Target organs:
   - Male: Testis
   - Female: Ovaries

Hypothyroidism: Hormone replacement therapy (Levothyroxine)
Hyperthyroidism: Thioamides (Methimazole, Propylthiouracil PTU - for pregnant)

III. Thyroid Drugs

HYPERTHYROIDISM

Primary hyperthyroidism (most common)	Overactive thyroid gland
Secondary hyperthyroidism	Overproduction of TSH
Tertiary hyperthyroidism	Overproduction of TRH
Most common hyperthyroidism	Grave's Disease
Toxic multinodular goiter	Plummer's Disease
Rare but life-threatening complications of untreated hyperthyroidism	Thyroid Storm
Elevated levels of thyroid hormone in the body, regardless of cause	Thyrotoxicosis

B. HORMONAL ACTIONS OF GONADAL STEROIDS

1. **Estrogens**
   - Growth and development
   - Secondary sex characteristics
   - Affect mood and emotions
   - Influence the distribution of body fat
   - Enhance blood coagulation
   - Prevent osteoporosis
   - Increase HDL and decrease LDL
2. **Progesterone**
   - Emotional state
   - Increase LDL and decrease HDL
   - Increase basal body temperature
   - Has mineralocorticoid properties

   Aldosterone - inc. Na and H2O reabsorption -> erymatus condition (pamamanas)
3. **Testosterone**
   - Primary and secondary sex characteristics in males during puberty
   - Increase lean body mass and skeletal growth
   - Increase the production of erythropoietin in the kidneys

C. ESTROGENS

- MOA: (+) estrogen receptors (ER) → interaction with co-activators and co-repressors of gene transcription

1. **Estrogens**
   a. Estradiol (most predominant) ->premenopausal stage
   b. Estrone ->postmenopausal
   c. Estriol ->produce in the body during pregnancy (unique)
2. **Semisynthetic**
   a. Ethinylestradiol (prodrug: Mestranol)
3. **Premarin** ->from pregnant mares (horse)
   a. Conjugated equine estrogen

- Upon hydrolysis: Equilin + Estrone
- Indications: [Estrogens]
  - HRT (menopause)
  - Tx of osteoporosis and dysmenorrhea
  - Tx of heavy menstrual bleeding
  - Oral contraception (birth control pills)
  - Tx of primary hypogonadism
- Problem: If given alone, risk of endometrial Hyperplasia->thick uterine lining
- Mx: combine with progestins
- AEs: N&V, HA, Edema, HTN, Thromboembolism

D. PROGESTINS

- Uses:
  - Tx of endometriosis ->long term condition where uterine lining is misplaced in the ovaries
  - Tx of uterine bleeding and dysmenorrhea

1. **Progesterone**
   - primary natural progestin in mammals
2. **Progesterone esters** RCOOR in orgchem
   - to enhance oral bioavailability
   i. Megestrol acetate – oral
   ii. Medroxyprogesterone acetate (MPA) - oral/IM

2. Synthetic progestins

a. Norgestrel
b. Norgestimate
c. Drospirenone (spironolactone derivative)

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E. ORAL CONTRACEPTIVE PILLS

- Birth control pills that contain female sex hormones
- Estrogen:
  - Ovary – increase ovulation
  - Cervix – thinner
  - Uterine lining -thicker

- Progesterone:
  - Releases fluid - to maintain pregnancy
  - Cervix – thicker

1. Combination pill

- Ethinyl estradiol + progestin
- 21 or 28 tablets
- Reminder pills (seven inert pills)/placebo

Placebo -> I shall please (wala nmn talaga syang effect sa katawan)
Nocebo-> I shall harm (may feel have effect pero wla talaga)

2. Progestin-only pills

- Norethindrone products (sometimes called mini pills)

3. Emergency contraceptives

- Levonorgestrel (non-Rx sa ibang bansa)
- Prevent pregnancy after unprotected sex
- Taken within 72 hours after intercourse

F. ANTI-ESTROGENS

1. Selective Estrogen Receptor Modulators (SERMs)

- acting at ERs exhibit either agonist or antagonist action

- **Clomiphene**
  - Weak estrogen agonist; moderate estrogen antagonist
  - Use: tx of anovulatory infertility
  - MOA: blocks ERs in the hypothalamus and pituitary
  - Result: increases FSH and LH secretion (include follicle development and ovulation)
  - AE: multiple births magkakaron ng kambal

- Tamoxifen (DOC)
  - Tamoxifen → 4-hydroxytamoxifen
  - Breast: ER antagonist (tx of breast cancer)
  - Endometrium: ER agonist (AE: endometrial hyperplasia
- Raloxifene
  - prevention of osteoporosis
  - reduce the risk of breast cancer in postmenopausal women

2. Aromatase Inhibitors

- decrease the secretion of estrogen
- first-line tx for locally advanced or metastatic breast cancer in postmenopausal women

a. Anastrozole
b. Letrozole
c. Exemestane

- tx of anovulatory infertility
- increased success rates compared to clomiphene

G. ANTI- PROGESTENS

1. Mifepristone

- Progesterone receptor antagonist when progesterone is present
  Use: medical abortion

2. Ulipristal

- Use: emergency contraceptive after unprotected sex

H. ANDROGENS

1. Testosterone and Methyltestosterone

- Tx of hypogonadism (low motility yung sperm or not produce well or mabilis mamatay)
- In older men: prevent osteoporosis
- Seldom used because long-term use can cause hepatotoxicity

2. Anabolic Steroids

- Increase body mass, strength, and physical performance

a. **Oxandrolone**

- Approved to increase weight (in HIV/advanced HIV)

b. **Fluoxymesterone**

- Tx of delayed puberty

3. Danazol

- Weak androgenic activity
- Anti-estrogenic action
- So si danazol kahit na androgen sya pineprescribe sya sa females

Tx of:

- Endometriosis
- Heavy uterine bleeding
- Fibrocystic breast disease

I. ANTI-ANDROGENS

1) Gonadotropin-releasing Hormone Analogs (GnRH Analogs)

- administered in a non-pulsatile rather than a pulsatile fashion to alter sex hormone production
  Leuprolide- advanced prostate cancer
  Goserelin- prostate cancer, endometriosis, breast cancer

2) Androgen Receptor Antagonists

- Flutamide, Bicalutamid
- Use: tx of prostate cancer
- AE: impotence

3) 5α-reductase Inhibitors

-5a reductase
- enzyme that catalyzes the conversion of testosterone (active) to dihydrotestosterone (inactive)

- Finasteride, Dutasteride
- Uses: tx of
  - BPH benign prostatic hyperplasia
  - Androgenic alopecia male pattern baldness
- AE: Erectile dysfunction, decreased libido

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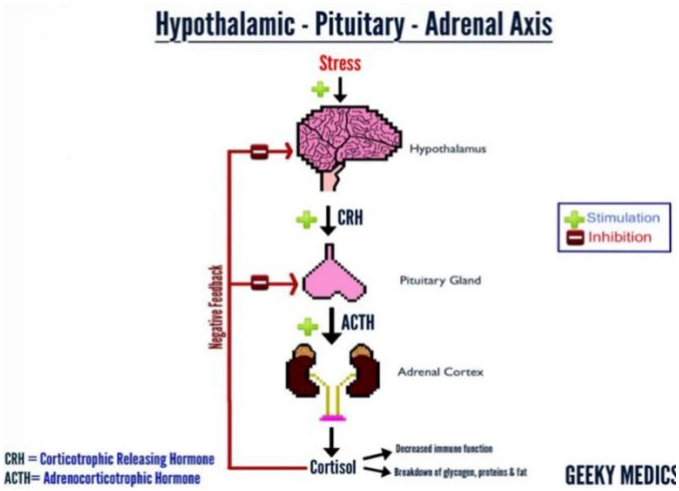
V. ADRENAL STEROIDS AND RELATED DRUGS

A. CORTICOSTEROIDS



1. Mineralcorticoids

b. Aldosterone

- major mineralocorticoid in humans
- 3000x more potent than cortisol

c. Fludrocortisone

- as HRT in Addison's disease

2. **Glucocorticoids**

Low potency, short-acting (8 to 12 hours)	Medium potency, intermediate-acting (12 to 36 hours)	High potency, long-acting
1. Cortisol ◦ major glucocorticoid in humans ◦ aka Hydrocortisone ◦ Use: preferred HRT for adrenal insufficiency 2. Cortisone	1. Prednisone 2. Prednisolone 3. Methylprednisolone 4. Triamcinolone	1. Betamethasone 2. Dexamethasone

B. CLINICAL USE OF GLUCOCORTICOIDS

1.**Inflammation, Allergy, and Autoimmune Disorders**

Autoimmune diseases	Allergic reactions
1. Mutliple sclerosis (MS) 2. Systemic lupus erythematosus (SLE) 3. Irritable Bowel Syndrome (IBD)/Ulcerative colitis	1. Asthma 2. Allergic rhinitis DOC: Inhaled corticosteroids (ICs)

1. Cancer
Ondansetron - prevent N&V in chemotherapy (not a glucocorticoid)

- Tx of lymphocytic leukemias and lymphomas
- prevent N&V during cancer chemotherapy (Dexamethasone)

2. Respiratory Distress Syndrome

- Betamethasone, Dexamethasone

- Hustle (pinapabilis) fetal lung maturation
  DOC for sarcoidosis
  -> when organs have inflammed lumps called granulomas (mga bukol kung saan saan sa katawan natin that causes inflammation most often target lungs and chest)

3. **Immunosuppressants**
   - prevents tissue rejection after organ transplant
4. **Adrenal Insufficiency**

Primary adrenal insufficiency	Secondary adrenal insufficiency
• aka Addison's disease	• Addisonian crisis

5. **Congenital Adrenal Hyperplasia**
   - caused by specific enzyme deficiencies that impair the synthesis of cortisol and aldosterone
6. **Cushing Syndrome** -> too much cortisol

Endogenous Cushing syndrome	Exogenous Cushing syndrome
• due to adrenal adenoma • result: increased ACTH and cortisol • tx: surgery *During surgery: give large dose of hydrocortisone to prevent Addisonian crisis	• due to glucocorticoid therapy • result: decreased ACTH, increased cortisol • tx: dose tapering -> slowly decrease the dose No abrupt withdrawal

C. ADRENAL ANDROGENS

1.DHEA Dehydroepiandrosterone
- major androgen secreted by the adrenal cortex
- dietary supplement (USA)
- potential uses:
  - improve sexual function
  - anti-aging

D. CORTICOSTEROID SYNTHESIS INHIBITORS

1.Metyrapone
- blocks IIB-hydroxylase enzyme
- use: tx of Cushing syndrome(in patients not candidates for surgery

2. Ketoconazole and Fluconazole
- antifungal drugs that inhibit several cytochrome P450 enzymes (including IIB-hydroxylase)
- use: Cushing syndrome
- disadvantage: gynecomastia in male patients

E. CORTICOSTEROID RECEPTOR ANTAGONISTS

1.**Spironolactone**
- competes with aldosterone for the mineralocorticoid (aldosterone) receptor in the renal tubules
- DOC for Conn's disease (hyperaldosteronism)
- tx for Bartter syndrome ->rare condition where Na is not properly reabsorbed ->heavy loss of potassium-> (+) Spiro K-sparing = inc. K levels
- AE: gynecomastia
  - alternative: Eplerenone

2. **Mifepristone**
- antagonist at both progesterone and glucocorticoid receptors
- use: recently approved for the tx of hyperglycemia in patients with Cushing syndrome

VI. DRUGS FOR DIABETES MELLITUS

- Hormones are produced in clusters of cells called Islets of Langerhans
- Alpha cells -Glucagon
- Beta cells - Insulin
- Delta cells –Somatostatin

A. PANCREATIC HORMONES

Insulin	Glucagon
• aka "storage hormone" • promotes: ◦ Glucose uptake ◦ Glucose utilization -> glycolysis ◦ Storage of glucose -> glycogenesis Result: Hypoglycemia	• increases hepatic glucose output Result: Hyperglycemia

B. DIABETES MELLITUS

Type 1 DM	Type 2 DM "insulin resistance"
• absolute deficiency of insulin due to destruction of pancreas • aka IDDM insulin-dependent DM Ketoacidosis: prone DM	• inadequate secretion of insulin from beta cells or less insulin action • aka NIDDM non-insulin-dependent DM first-line: Metformin

C. SECRETAGOGUES

-promotes secretion

1. **Insulin** (SQ), Receptor tyrosine kinase (type 3 receptor)
   - MOA: (+) RTK → cascade of signaling events

Only ultra-rapid: Afrezza® (inhalational insulin)

Rapid-acting a. Glulisin biLIS b. Aspart fASTPART c. Lispro	**Short-acting** a. Semilente b. Regular (IM or IV)
Intermediate-acting a. NPH/Isophane Neutral Protamine Hagedorn b. Lente	**Long-acting (aka peakless insulin)** a. Glargine b. Ultralente c. Detemir

2. Sulfonylureas

- MOA: (-) potassium channels (ATP-sensitive channels) → B-cell depolarization (Calcium influx) → Insulin release
- AEs: weight gain, hypoglycemia

First generation	Second generation
• low potency • greater incidence of SEs a. Tolbutamide b. Acetohexamide c. Chlorpropramide	• 100x more potent than 1st gen • DOA: 24 hours (once daily) a. Glibenclamide - alternative for gestational DM b. Glipizide c. Gliclazide

3. **Meglitinides**

Postprandial ->after eating

- control postprandial glycemia (taken before meals)
- MOA: inhibits ATP-sensitive potassium channels
  a. Repaglinide
  b. Nateglinide

D. INSULIN SENSITIZERS

1. **Metformin**
   - only biguanide type of oral antidiabetic medication currently available
   - used in PMOS for sugar mx and weight loss
   - MOA
     - Liver: (-) hepatic gluconeogenesis -> formation of glucose units from non-carbohydrate precursors
     - Adipose tissue increases uptake of glucose
     - Muscle: increases uptake of glucose
       - advantage: no hypoglycemia
       - AEs: weight loss, diarrhea, lactic acidosis (rarely)

2. Thiazolidinediones ->kinikiliti ang insulin rec.

Suffix: -glitazone

i. Pioglitazone
ii. Rosiglitazone

- MOA: (+) PPAR-y → increased transcription of insulin-responsive genes
  - Adipose tissue: increases uptake of glucose
  - Muscle: increases uptake of glucose
  - Liver: (-) gluconeogenesis
- AEs: Edema (CI: CHF), weight gain
- Not first-line, adjunct only ginagamit lng para makatulong

E. DRUGS AFFECTING GLUCOSE ABSORPTION AND REABSORPTION

1. **alpha-glucosidase Inhibitors**
   - a-glucosidases: a-amylase, maltase, sucrase
   - MOA: decrease absorption of glucose
     i. Acarbose
     ii. Miglitol
     iii. Voglibose
   - AEs: GIT upset (diarrhea, flatulence, abdominal bloating)
2. **Glucose Reabsorption Inhibitors**
   - MOA: SGLT2 inhibitors Sodium glucose cotransporter-2
   - Suffix: -gliflozin
     i. Dapagliflozin
     ii. Canagliflozin
   - AEs: UTI, Dehydration

F. OTHER ANTI-DM DRUGS

1. **Amylin mimetics** (decrease glucagon secretion)
   a. Pramlintide acetate
      - a synthetic analog of human amylin
      - slows the rate at which food is delivered from the stomach to the intestines (GET)
      - AE: anorexia and weight loss, nausea, headache

2. Incretin (GLP-1) mimetics

glucagon-like peptide-1, Go Lose Pounds (GL P-1)

- MOA: increased production of cAMP (inc. Ca^{2+}) → closure of ATP-dependent K^+ channels → inc. insulin secretion

i. Exenatide
ii. Liraglutide
iii. Semaglutide (mx of obesity) ->Ozempic, Wegovy

- AEs: nausea, weight loss, inc. risk of pancreatitis (px with high VLDL)

3. DPP4 blockers Dipeptidyl peptidase-4 - enzyme that catalyzes the breakdown of incretin hormones
   - aka gliptins
     i. Sitagliptin
     ii. Alogliptin
   - advantages:
     - less weight loss (weight neutral)
     - no GIT side effects, no hypoglycemia → suited for older/frail px