Communication and Control in the Human Endocrine System

Lexington Computer and Technology Group

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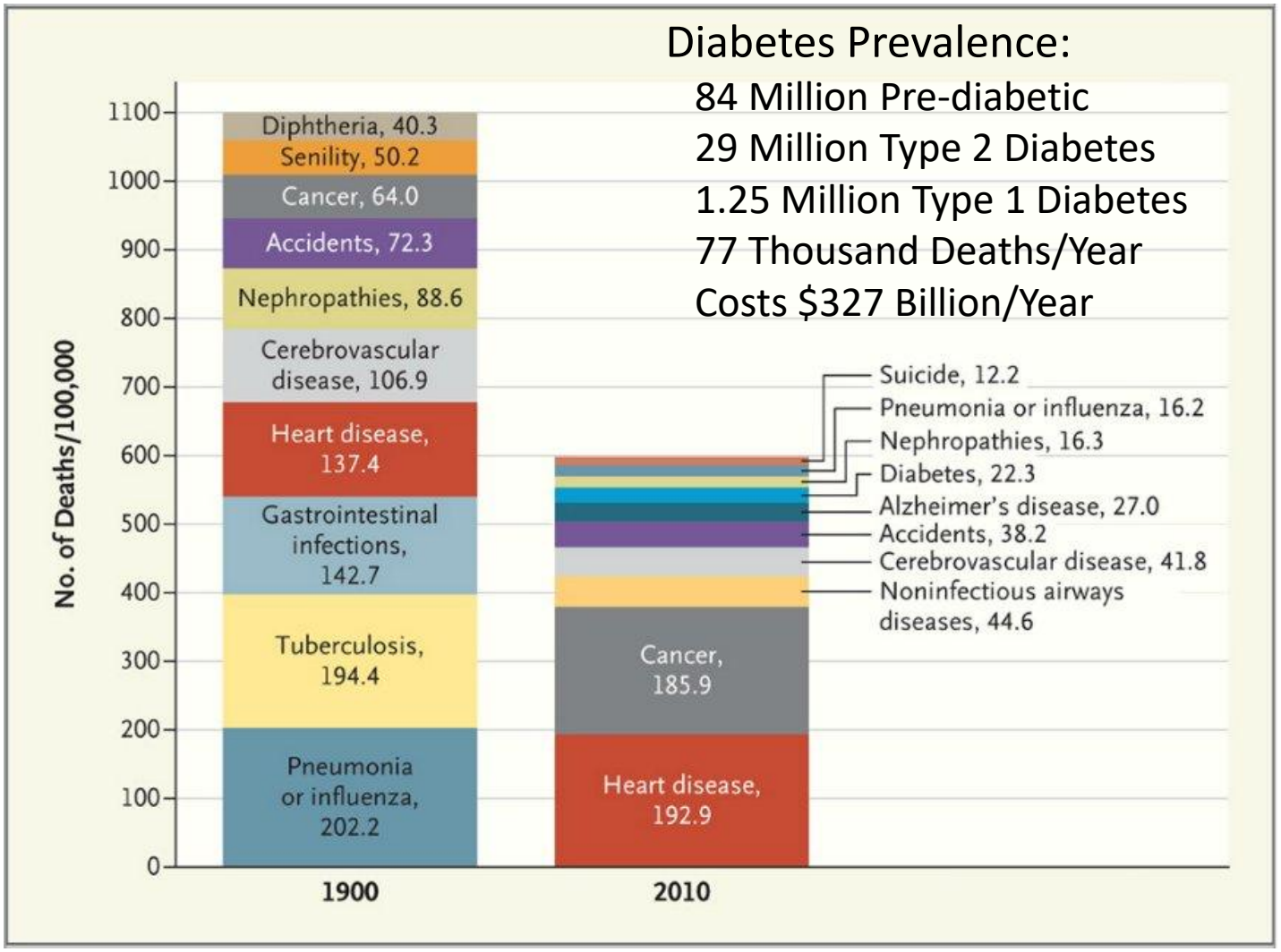
Disclaimer

- I am a retired engineer and former volunteer tour guide at Jackson Laboratory in Bar Harbor, ME
- I first got interested in medical diseases and discoveries to treat them 20 years ago
- I am not a Doctor and cannot dispense medical advice – but I can refer you to literature
- I am not a medical researcher – but have arranged for them to answer questions that I cannot answer

Quick Survey

- Do You Have Friends or Relatives With:
  - An Endocrine System Disorder
  - Difficulty Getting Pregnant
  - Stress Related Conditions
  - Hot Flashes
  - Overweight, Obese, Difficulty Losing Weight

Changes in Death Rates by Disease



Notable Quotes

- 1905: From Ernest Starling lecture:

"These chemical messengers, however, or "hormones" (Greek for "I arouse") as we may call them, have to be carried from the organ where they are produced to the organ which they affect"

- 2018: From Aroused by Randi Hutter Epstein:

"Hormones are substances secreted by a gland that target a distant site; they travel via the blood; they are crucial for the maintenance of the body; they are crucial for survival"

"They control just about everything" – mineral levels, growth, reproduction, survival from threats

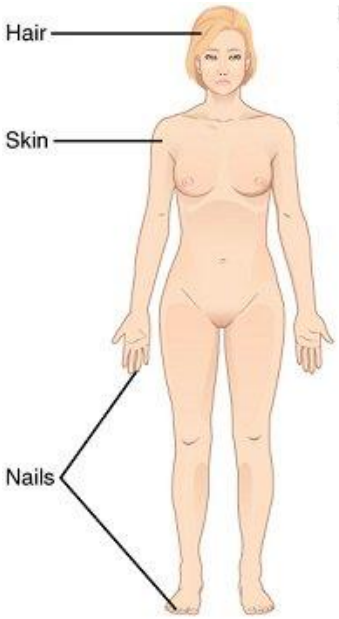
"The Endocrine System is the Master Regulator of Your Body"

Dr Kamyar Hedayat, President of the Endobiogeny Society

Key Concepts

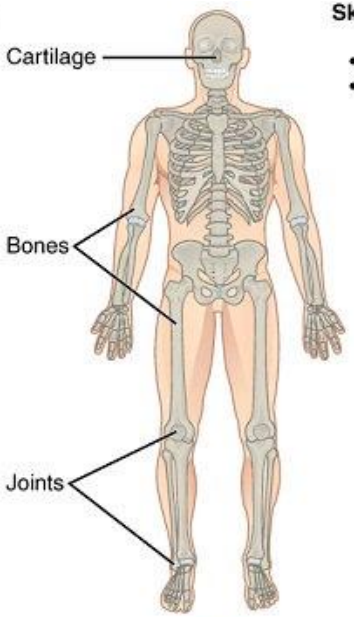
- There is a general common pattern of how all glands produce hormones in response to their environment or other hormones which regulate the body by feedback control loops
- Endocrine vs Nervous System Communication
  - Chemical Messages vs Electrical Impulses
  - Broadcast to all cells simultaneously via hormones in blood vs directed to specific cells in only one direction along a chain of nerve cells via neurotransmitters
  - Slow (minutes) vs fast (milliseconds) response time
  - Reaction lasts a long time vs a short time

Systems of the Human Body



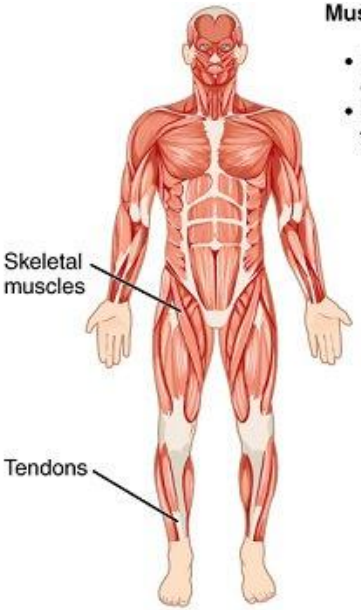
Integumentary System

- Encloses internal body structures
- Site of many sensory receptors



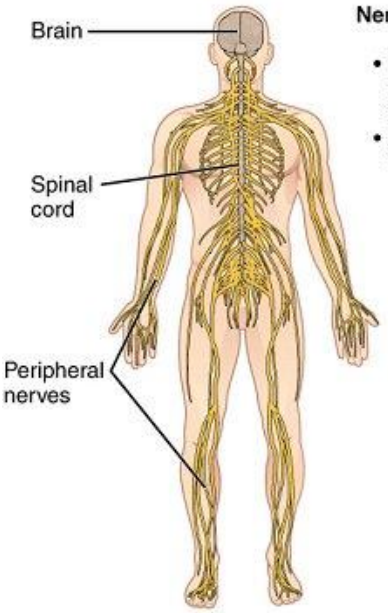
Skeletal System

- Supports the body
- Enables movement (with muscular system)



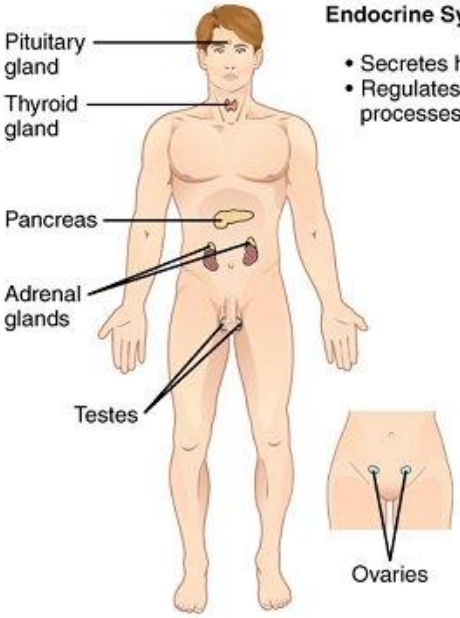
Muscular System

- Enables movement (with skeletal system)
- Helps maintain body temperature



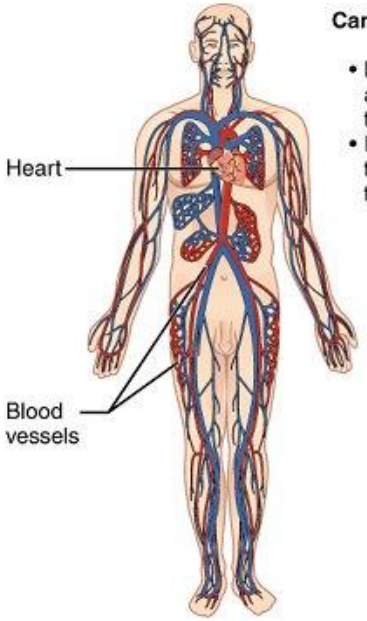
Nervous System

- Detects and processes sensory information
- Activates bodily responses



Endocrine System

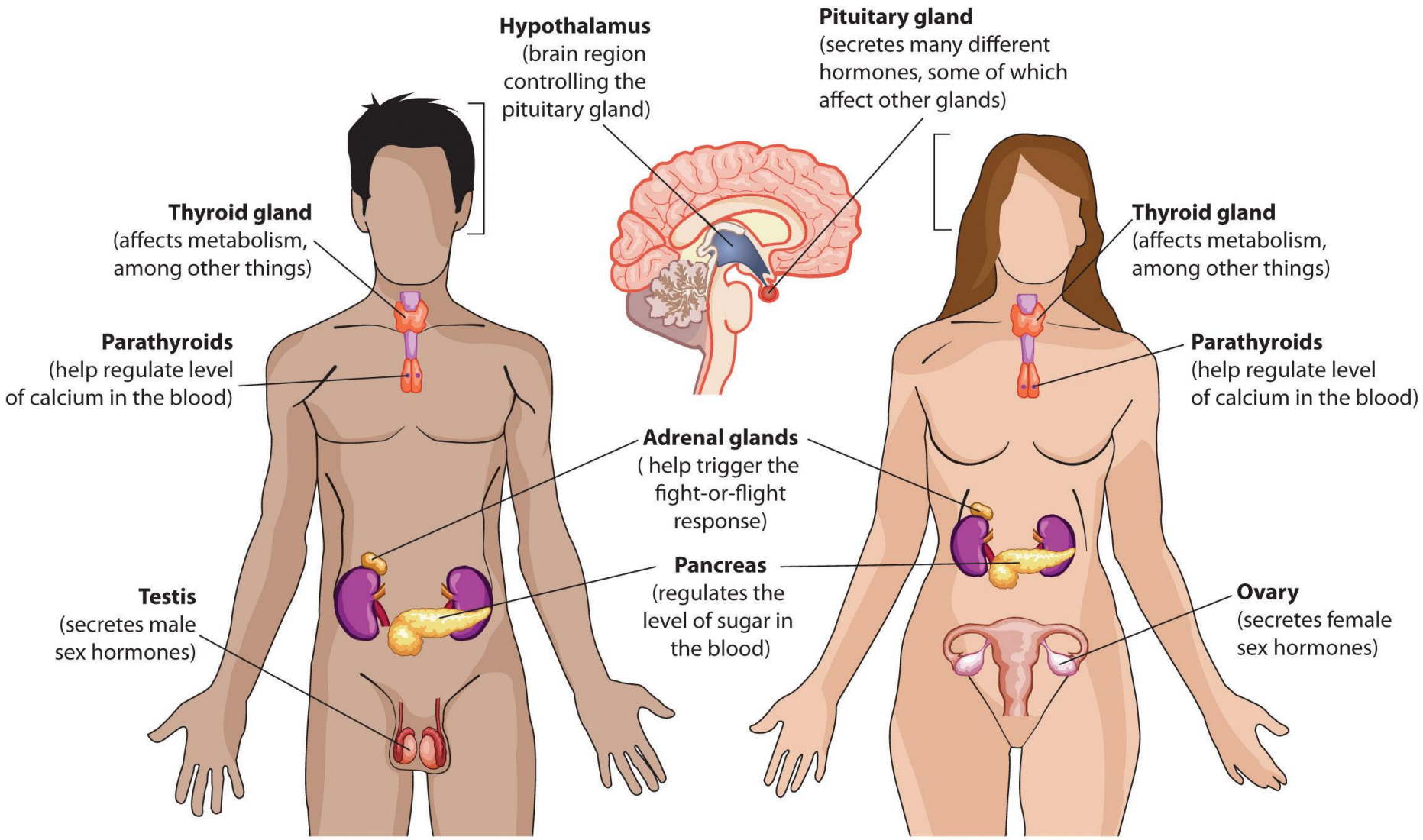
- Secretes hormones
- Regulates bodily processes



Cardiovascular System

- Delivers oxygen and nutrients to tissues
- Equalizes temperature in the body

Endocrine System Overview

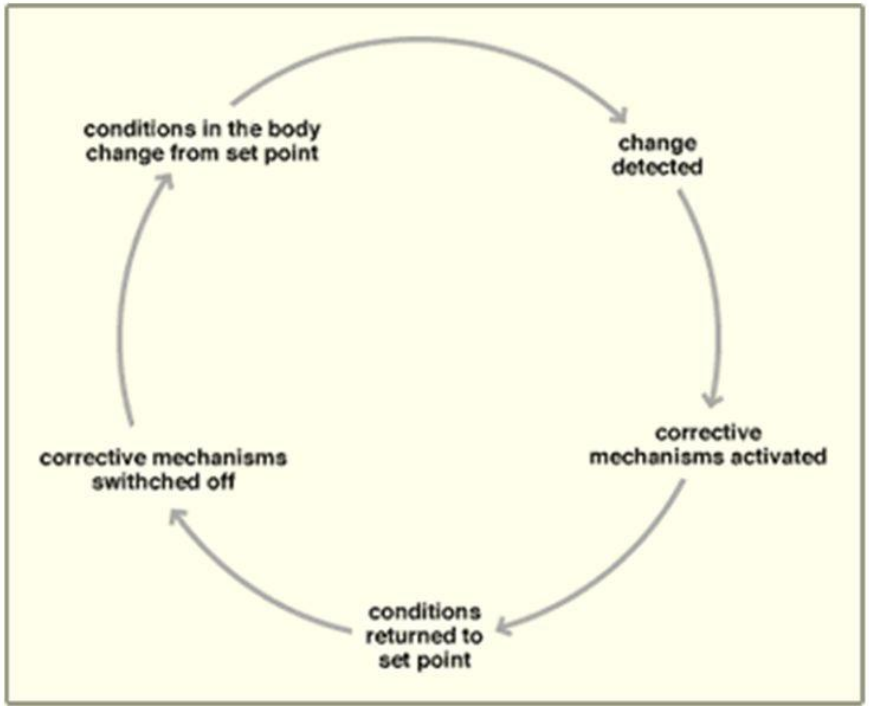


The Endocrine System in Action

- The endocrine system is a dynamic system that responds to the body's internal and external environment
- Video
  - https://www.youtube.com/watch?v=e4cuIfgMsNs#action=share

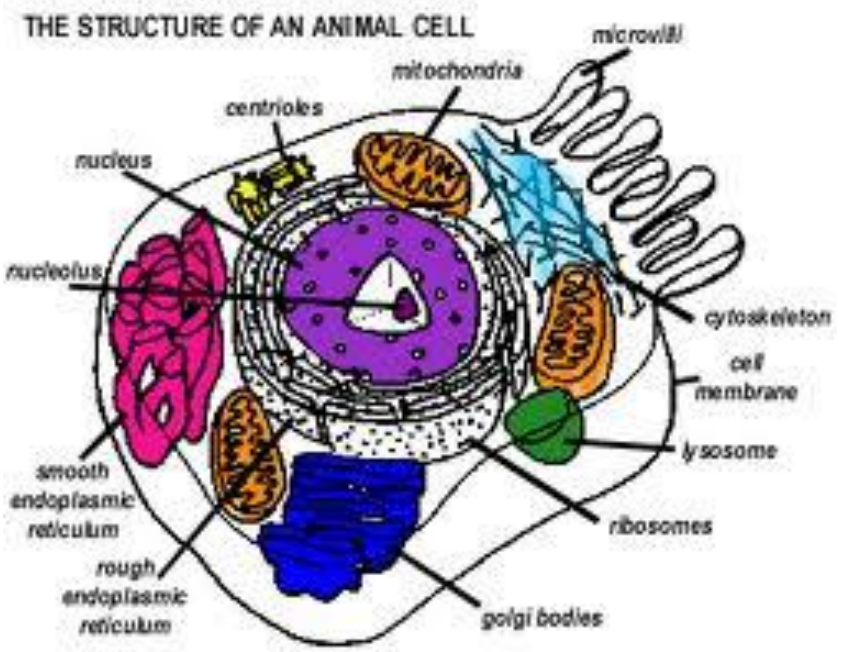
Hormones Control Most of Your Body Systems

Negative Feedback Loop (In General)



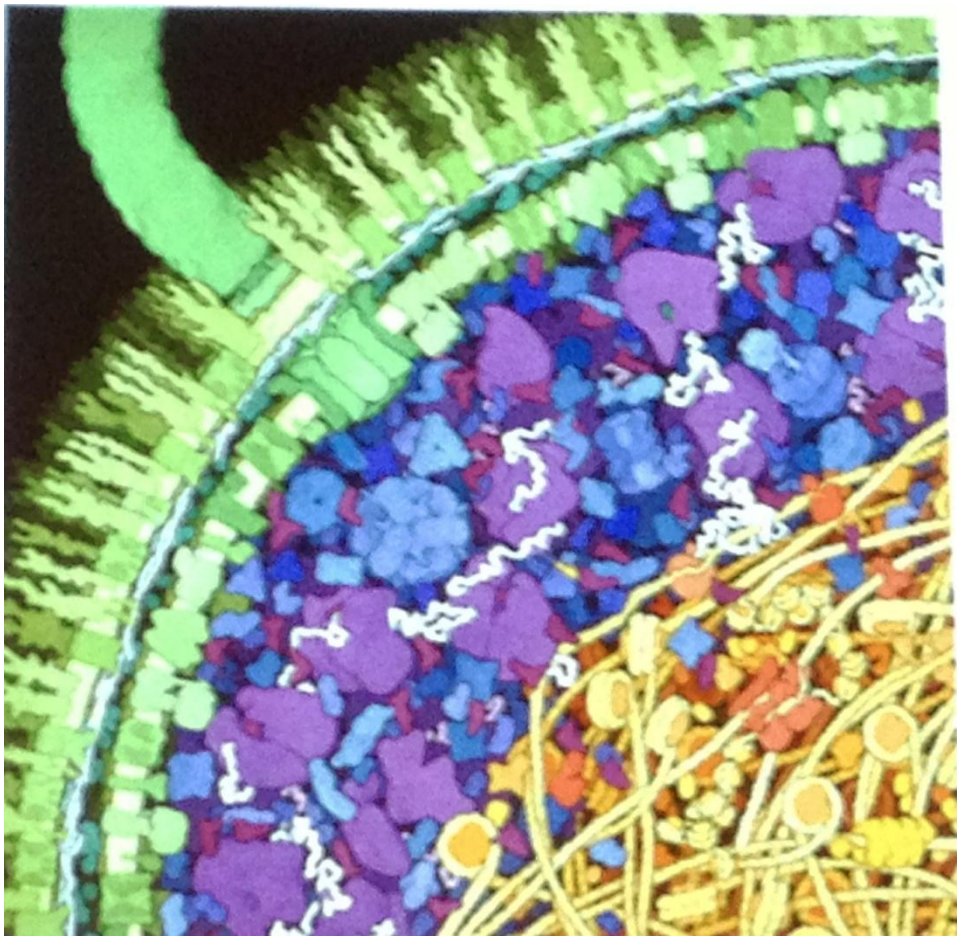
- Homeostasis
  - Provides a constant environment to each cell (equilibrium) – temperature, pressure, water, pH nutrients, sugar, Calcium
  - It's hard to grow a human cell in a laboratory

Cell Basics



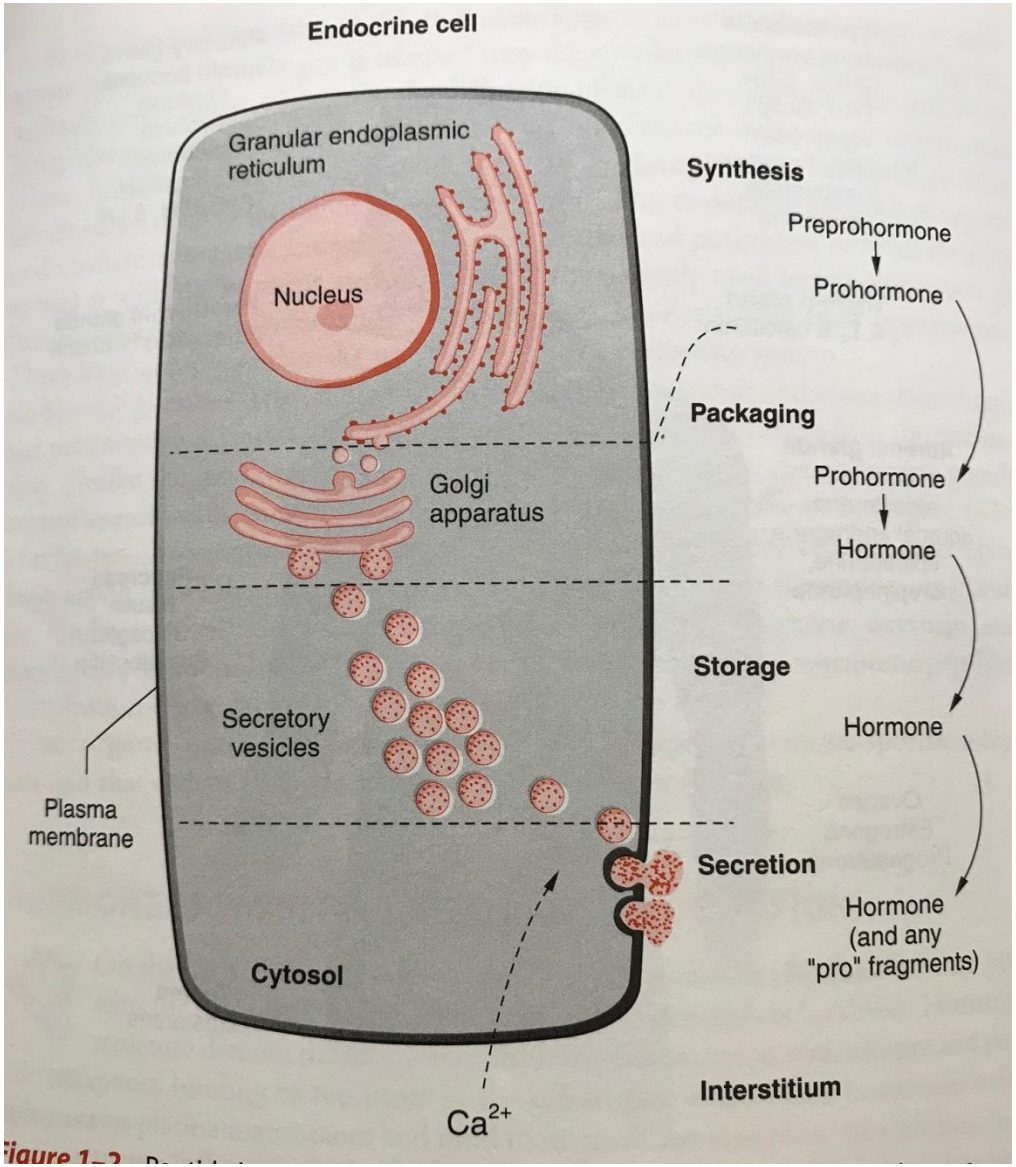
- Our bodies contain 10 trillion cells of 200 types
- Eukaryotic cells have a nucleus, Prokaryotics (bacteria) do not
- Our DNA resides in the nucleus on 46 chromosomes
- Proteins = “workhorses”
  - Structural elements
  - Muscles
  - Enzymes – speed reactions
  - Signals – turn on/off DNA

Cells are Made of Proteins and Lipids



- Complex and Chaotic
  - Everything is vibrating
- Membranes with Pores
- Surface Receptors
  - Like a fuzzy tennis ball
- Interior Structures
- Organelles
- Metabolize to Live
- Chemical Factories
- Divide to Reproduce
- Primitive “Immunity”
- Took Billions of Years

A Typical Endocrine Cell



- Vesicles are tiny bubbles with a membrane and filled with a fluid (hormone)
- Slowly build up then quickly released when needed
- Acts as transmitters of the signal

Receptors in Action

- Receptors are protein structures on the surface of cells that molecules attach to to create a response in that target cell
- Acts as receivers of the signal
- Video of an insulin receptor
  - https://www.youtube.com/watch?v=VbwRYFMPZS4

Protein/Peptide vs Steroidal Hormones

Table 1-1. Peptide vs. Steroid Hormones

PEPTIDE HORMONES		STEROID-TYPE HORMONES
Attach to receptors on cell surface	Luteinizing hormone (LH)	Enter cell cytoplasm and nucleus
Subsequent activation of second messengers	Growth hormone	Interact with receptors in cytoplasm and nucleus
Changes in cell phosphorylation state, calcium, etc.	Thyroid-stimulating hormone (TSH)	Hormone-receptor complex interacts with DNA
Changes in cell secretion and protein synthesis	Prolactin (somatomammotropin)	Changes in protein synthesis
Water soluble	**Posterior Pituitary Hormones**	Fat soluble
Catabolized in GI tract; poorly absorbed from skin	Antidiuretic hormone (ADH)	Absorbed from GI tract and skin
Short half-life	Oxytocin	Longer half-life if protein bound or stored in fat
Hypothalamic Hormones	**Pancreatic Islet Hormones**	**Adrenal and Gonadal Hormones**
Corticotropin-releasing hormone (CRH)	Glucagon	Aldosterone
Growth hormone–releasing hormone (GHRH)	Insulin	Cortisol
Gonadotropic hormone–releasing hormone (GnRH)	Somatostatin	Dehydroepiandrosterone
Thyrotropin-releasing hormone (TRH)	**Calcium-Regulating Hormones**	Dihydrotestosterone
Somatostatin	Calcitonin	Estradiol
Anterior Pituitary Hormones	Parathyroid hormone (PTH)	Progesterone
Adrenocorticotropic hormone (ACTH)	Parathyroid hormone–related protein (PTHrP)	Testosterone
Follicle-stimulating hormone (FSH)	**Additional Peptide Hormones**	**Steroid-Type Hormones**
	Epinephrine	Triiodothyronine (T_3)
	Human chorionic gonadotropin (HCG)	Thyroxine (T_4)
	Human chorionic somatomammotropin (HCS) (human placental lactogen[HPL])	1,25-Dihydroxyvitamin D ($1,25[OH]_2$ D)
	Inhibin	
	Insulin-like growth factor-1 (IGF-1)	

Protein/Peptide Hormone Synthesis/Reception

Synthesis

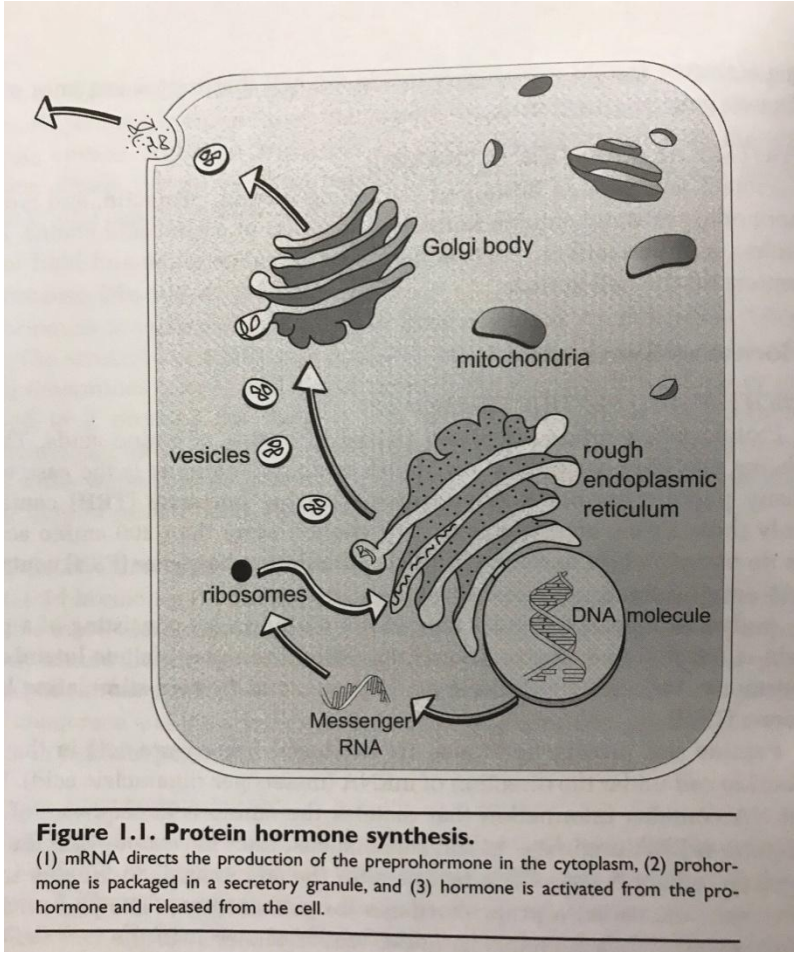


Figure 1.1. Protein hormone synthesis.
(1) mRNA directs the production of the preprohormone in the cytoplasm, (2) prohormone is packaged in a secretory granule, and (3) hormone is activated from the prohormone and released from the cell.

Reception / Action

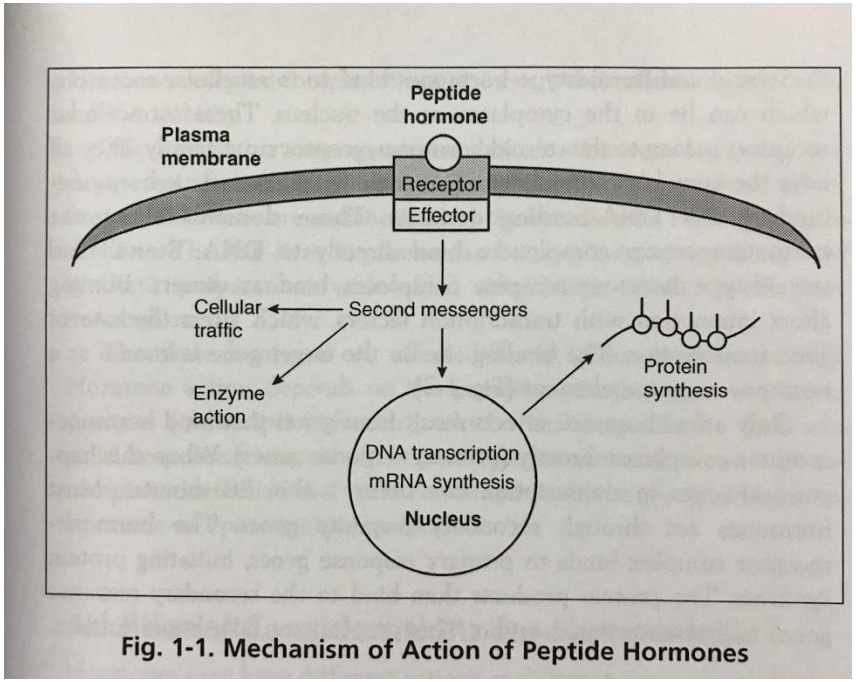


Fig. 1-1. Mechanism of Action of Peptide Hormones

Steroidal Hormone Synthesis/Reception

Synthesis

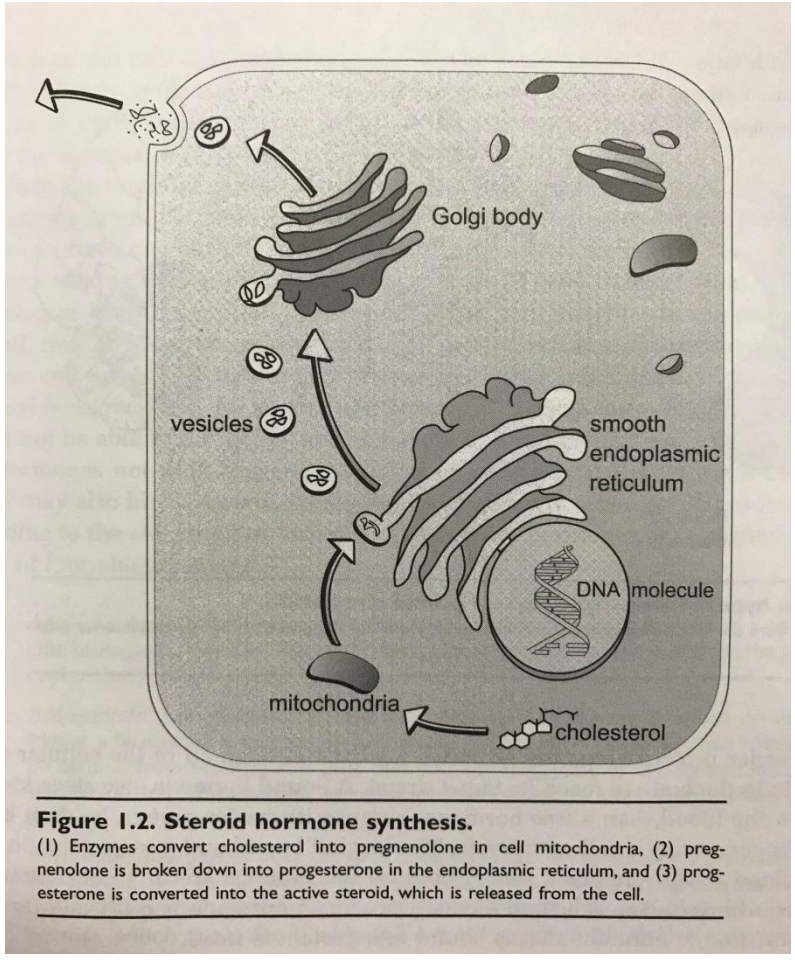


Figure 1.2. Steroid hormone synthesis.
(1) Enzymes convert cholesterol into pregnenolone in cell mitochondria, (2) pregnenolone is broken down into progesterone in the endoplasmic reticulum, and (3) progesterone is converted into the active steroid, which is released from the cell.

Reception and Actions

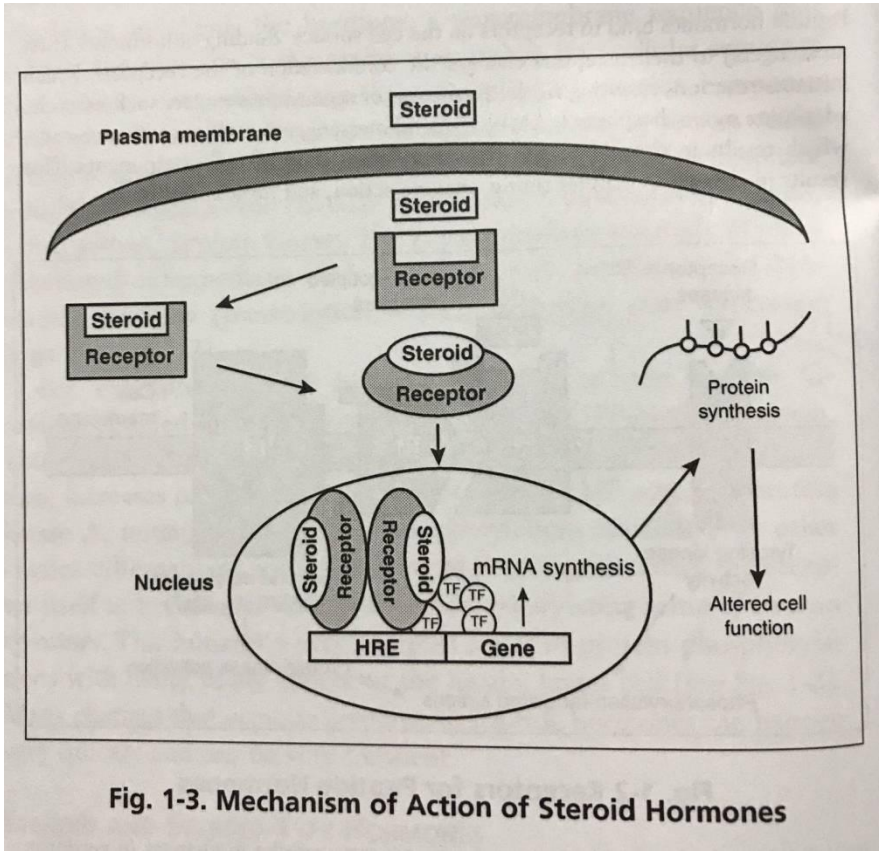
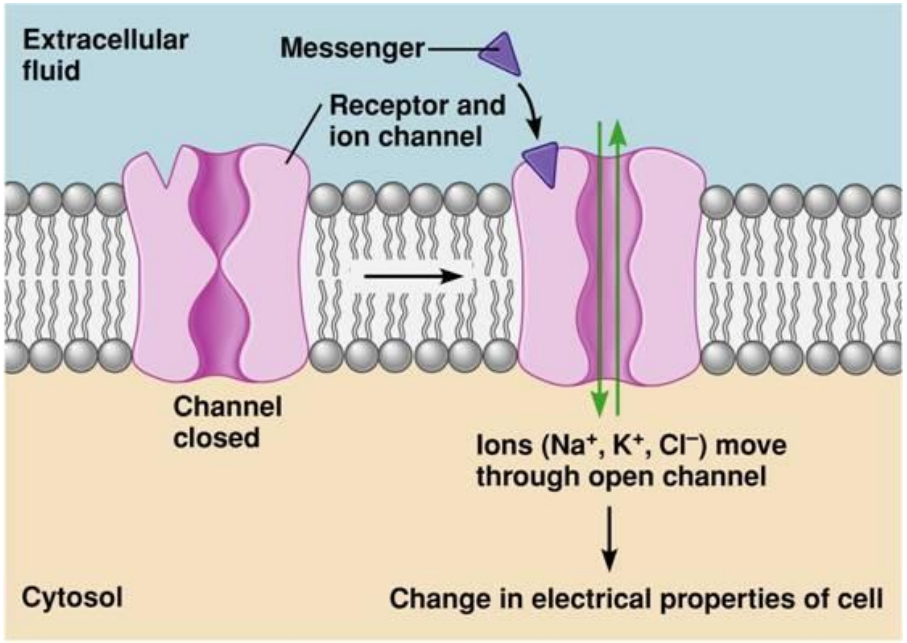


Fig. 1-3. Mechanism of Action of Steroid Hormones

Receptor Controlled Ion Channels



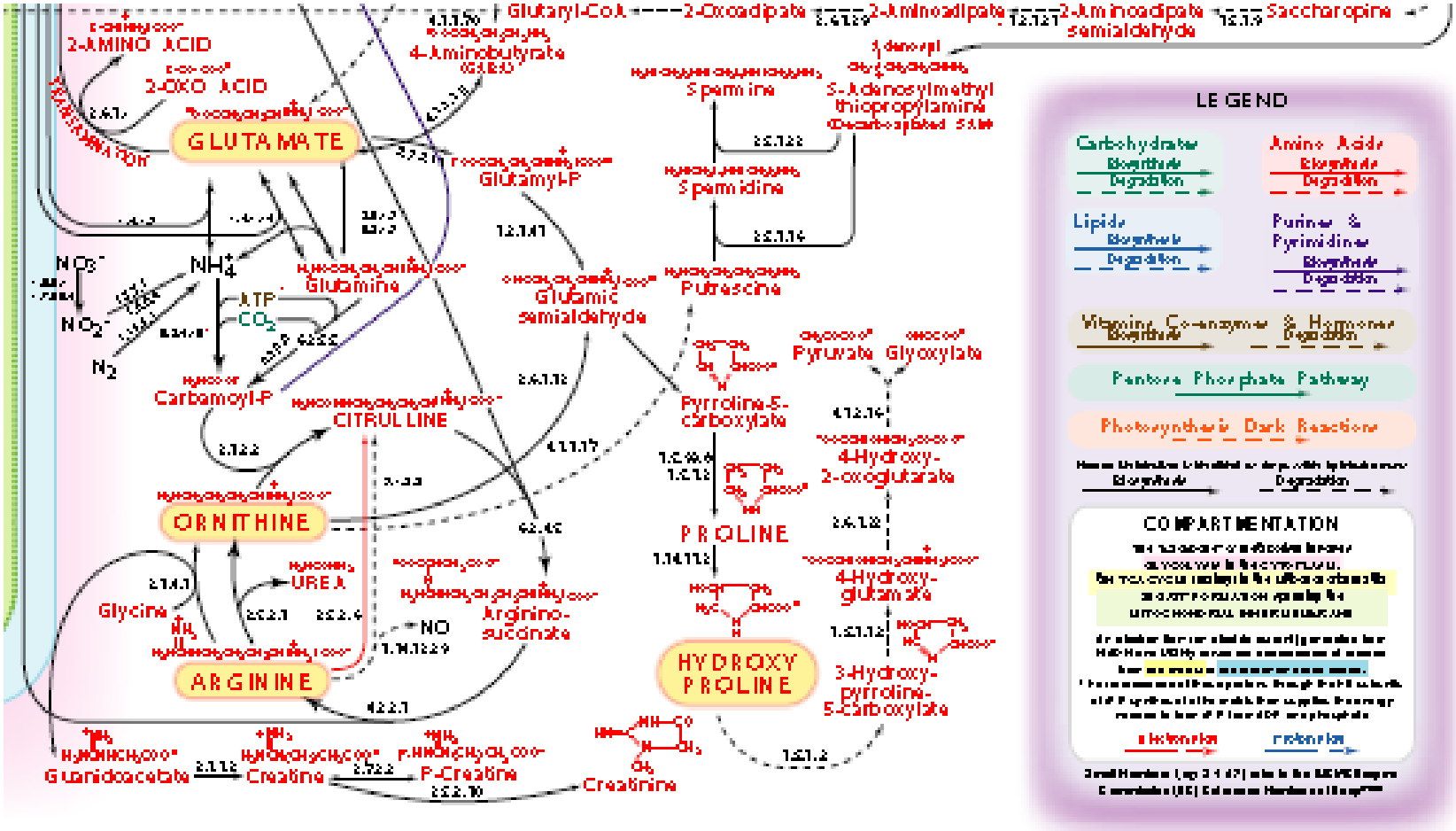
- Channels open when hormone messenger attaches to the receptor
- Allows Sodium, Potassium, Calcium, Glucose to pass through cell membrane to enter cell

How insulin receptor works: https://www.youtube.com/watch?v=DY7avIl3GNg

Metabolic Pathways

- Description of the underlying biological mechanisms at the cellular level in health and disease
- Interrelationships and interactions appear as a circuit diagram showing up regulation and down regulation of biologically significant compounds

Excerpt - Metabolic Pathways



Discovery of Hormones

- Observational studies provide a clue
  - Serendipity – Random mutations, Freaks
  - Autopsies – Sick patients had diseased adrenal glands (Addison, 1849)
- Experiments that removed and transplanted glands – Castrated roosters restored with a new testes or testes fluids (Berthold 1849)
- Experiments with dogs to show pancreatic secretions stimulated by a chemical compound and not a nerve. First to isolate a hormone, Secretin (Bayliss & Starling 1902)

Key Hormones and Their Actions

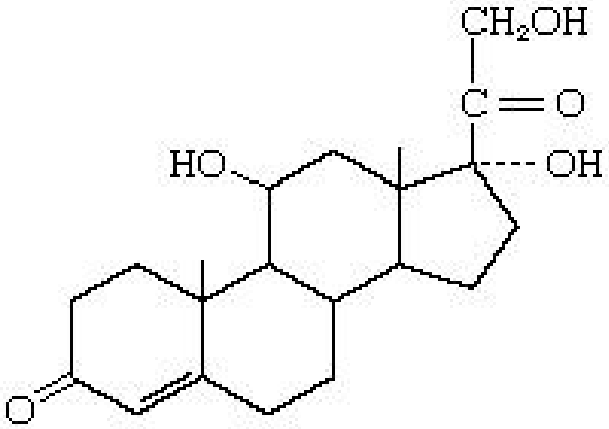
KEY HORMONES AND THEIR MAIN ACTIONS

HORMONE	WHERE IT IS MADE	WHAT IT DOES
Growth Hormone	pituitary	Stimulates body growth.
ACTH (adrenocorticotropic hormone)	pituitary	Controls adrenal glands' release of hormones, especially cortisol.
TSH (thyroid-stimulating hormone)	pituitary	Stimulates the thyroid gland to release T3 and T4.
FSH (follicle-stimulating hormone)	pituitary	Controls hormone production by ovaries and testes; supports egg and sperm production.
LH (luteinizing hormone)	pituitary	Controls hormone production by ovaries and testes; supports egg and sperm production.
Prolactin	pituitary	Stimulates milk production in women; helps create healthy sperm in men.
ADH (antidiuretic hormone)	pituitary	Causes kidneys to conserve water that would be lost in urine.
Oxytocin	pituitary	In women, causes milk to flow from breasts while a baby is nursing; tenses muscles of the uterus (womb) during birth to push out the baby.
Melatonin	pineal	Helps cause a sense of sleepiness at nighttime.
T3 and T4	thyroid	Helps all cells stay active by using food particles for energy.
Calcitonin	thyroid	Lowers the amount of calcium in blood.
PTH (parathyroid hormone)	parathyroids	Increases the amount of calcium in blood
Insulin	pancreas	Lowers the amount of sugar and other food particles in blood after a meal by helping cells store the particles.
Glucagon	pancreas	Increases the amount of sugar in blood between meals by helping cells release stored food particles.
Aldosterone	adrenals	Causes kidney cells to save sodium from being lost in urine.
Cortisol	adrenals	Helps cells release stored food particles.
Estrogen	ovaries	Creates female appearance and maintains a healthy uterus during pregnancy.
Progesterone	ovaries	Maintains a healthy womb during pregnancy.
Testosterone	testes	Creates male appearance and helps make the fluid (semen) that carries sperm.

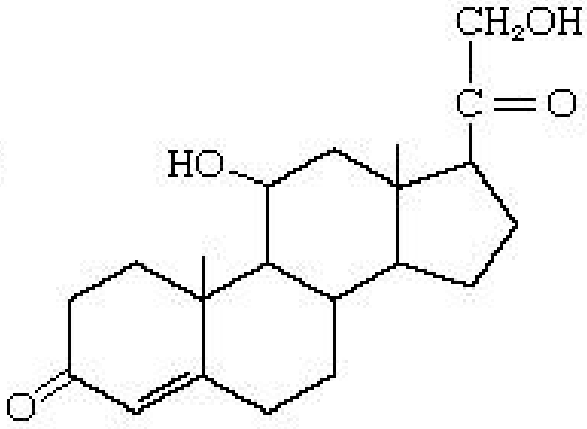
For a list of all 50 human hormones: https://en.wikipedia.org/wiki/List_of_human_hormones

Notice hormone / "anti-hormone" pairings: insulin/glucagon, calcitonin/PTH, leptin/ghrehlin

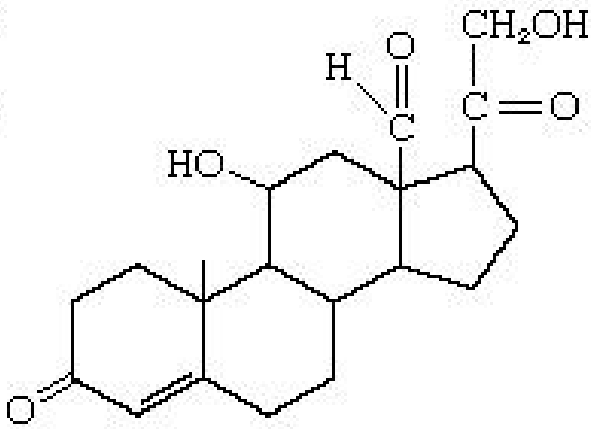
Hormone Molecular Structure



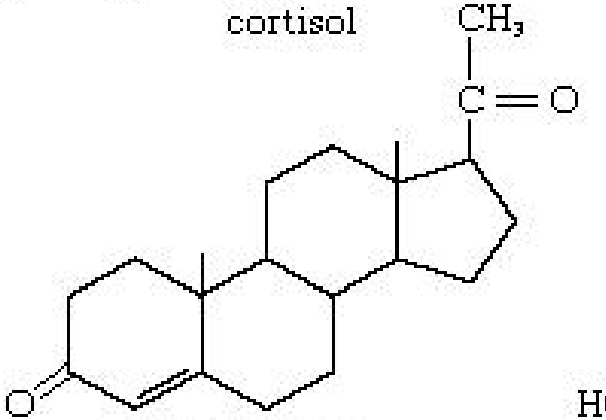
cortisol



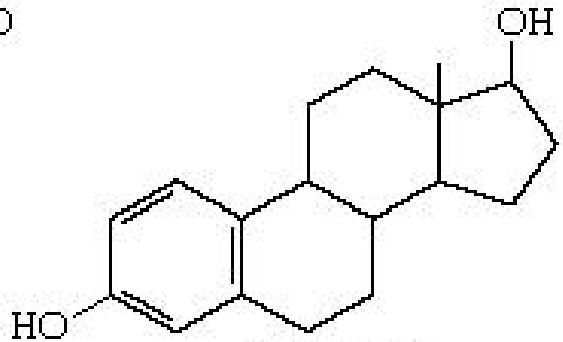
corticosterone



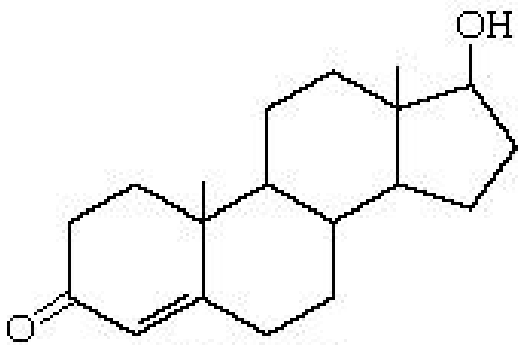
aldosterone



progesterone

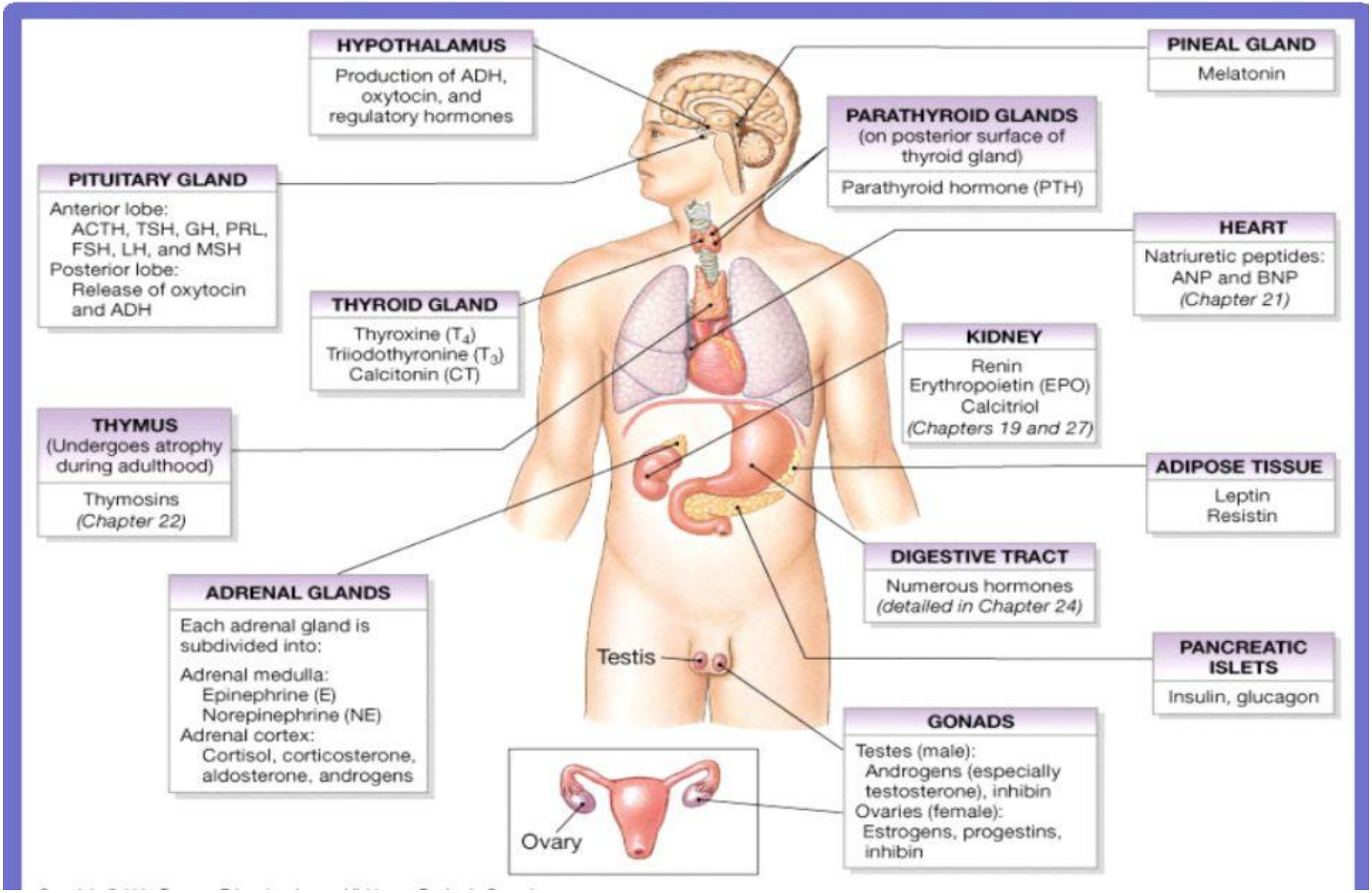


β-estradiol

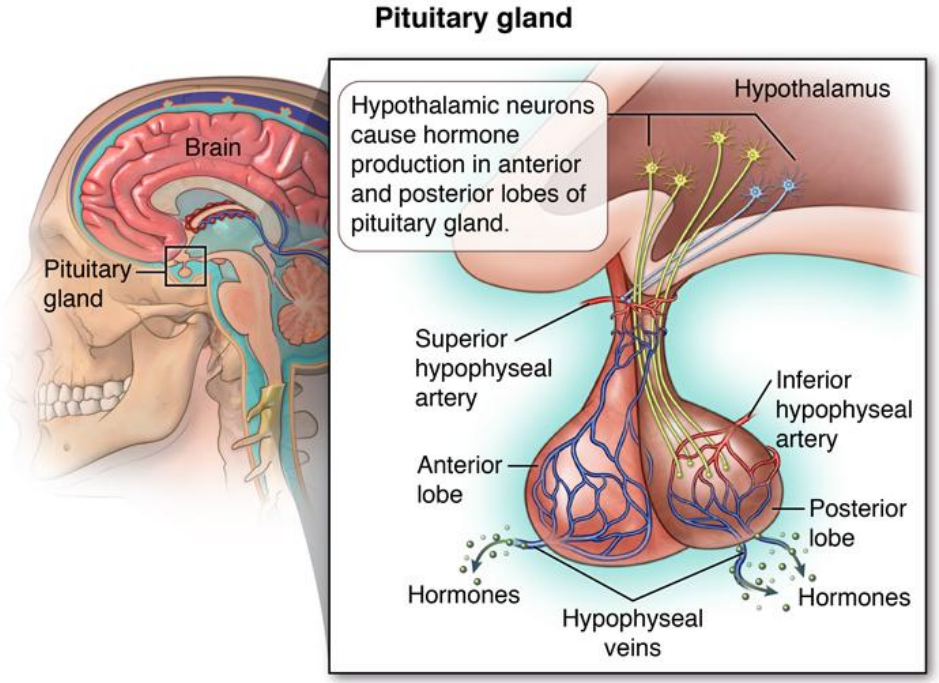


testosterone

THE ENDOCRINE SYSTEM

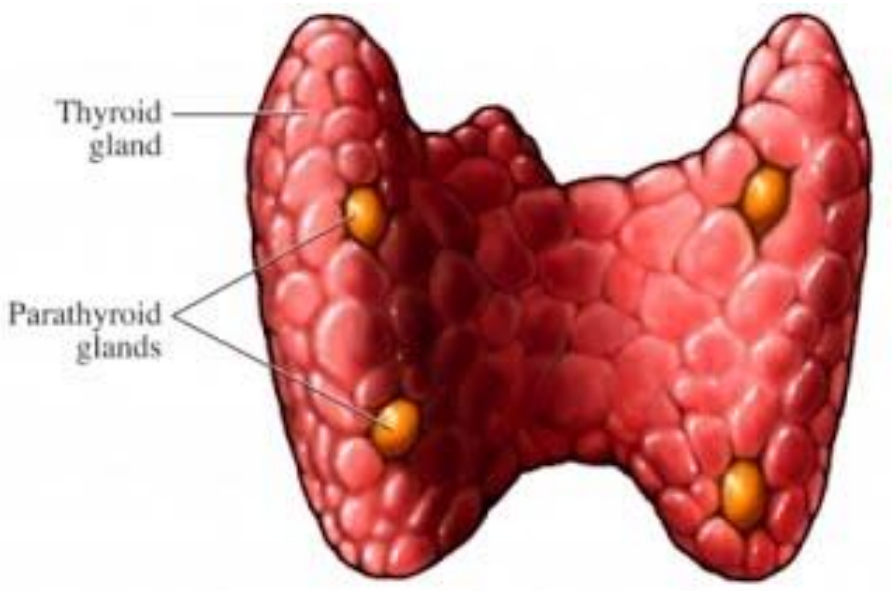


The Pituitary Gland



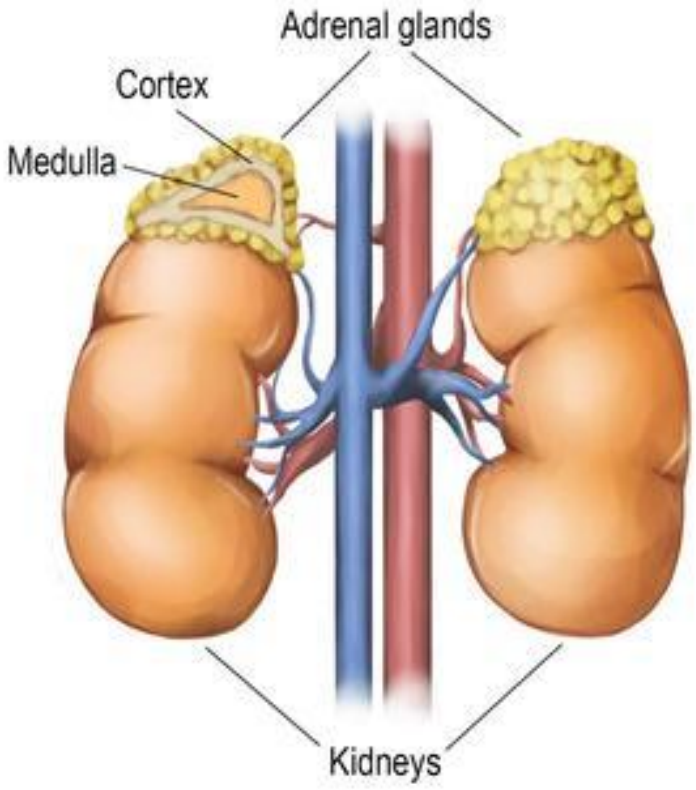
- Anterior Lobe – Front
  - TSH – Thyroid Stimulating Hormone
  - GH – Growth Hormone
  - FSH – Follicle Stimulating Hormone
  - LH - Luteinizing Hormone (to Gonads)
  - ACTH – Adrenocorticotropic Hormone
  - PRL - Prolactin
- Posterior Lobe – Back
  - ADH – Antidiuretic Hormone
  - Oxytocin

The Thyroid and Parathyroid



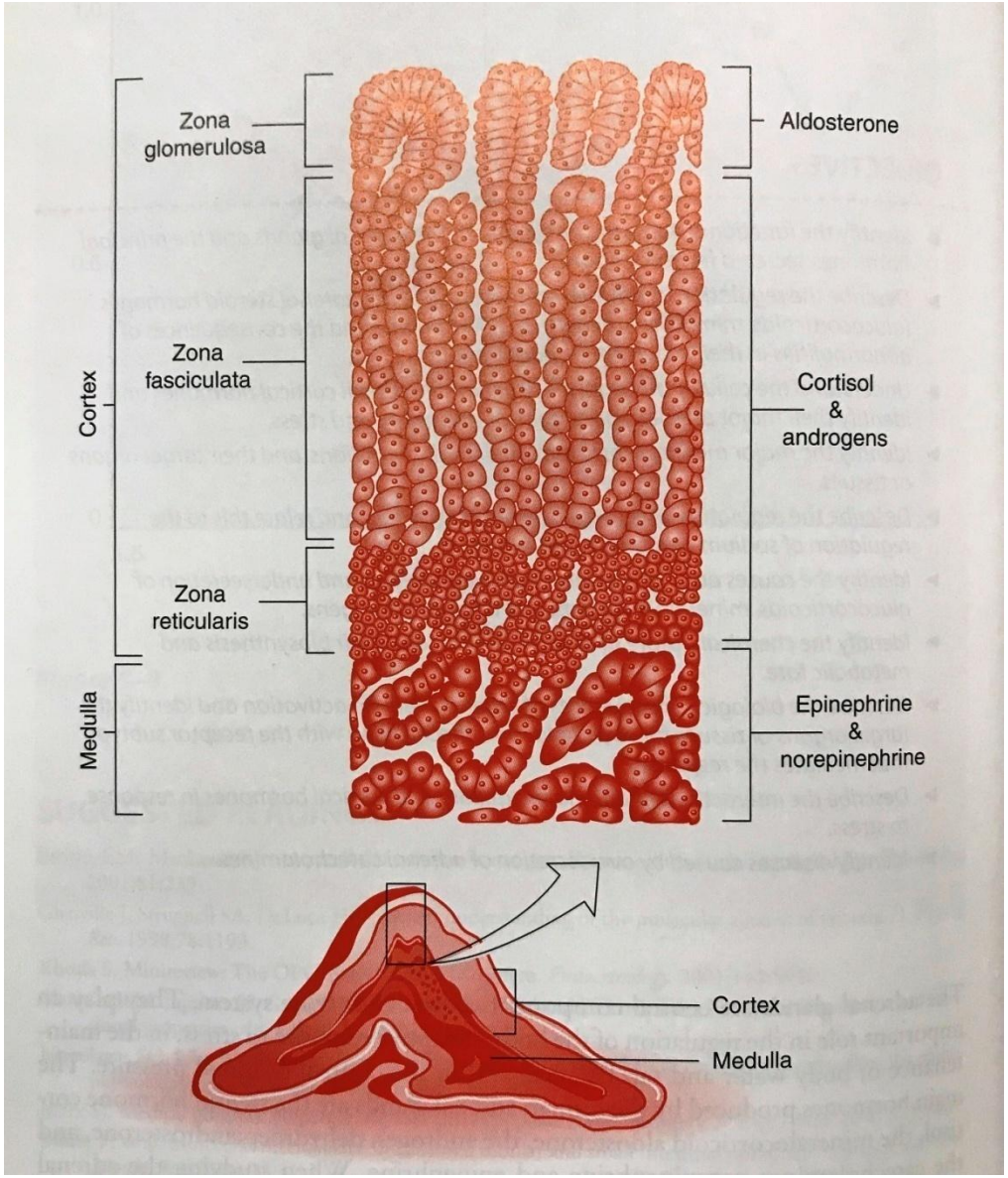
- Thyroid
  - T4 – Thyroxine
  - T3 – Thiiodothyronine
  - Calcitonin
- Parathyroid
  - PTH – Parathyroid Hormone
  - Vitamin D

The Adrenal Glands

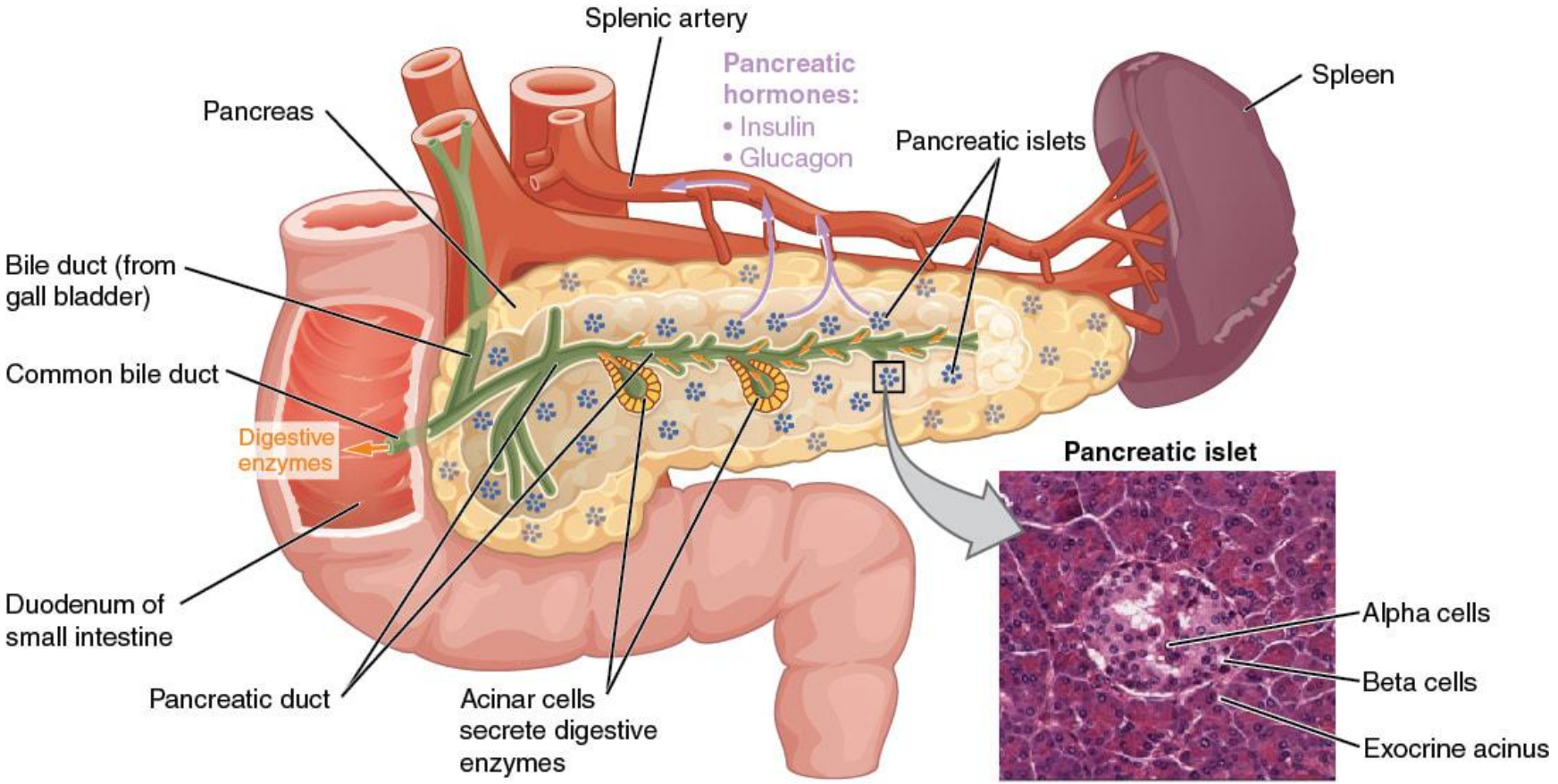


Adrenals secrete:

Epinephrine (Adrenaline)
Norepinephrine
Cortisol & Androgens
Aldosterone

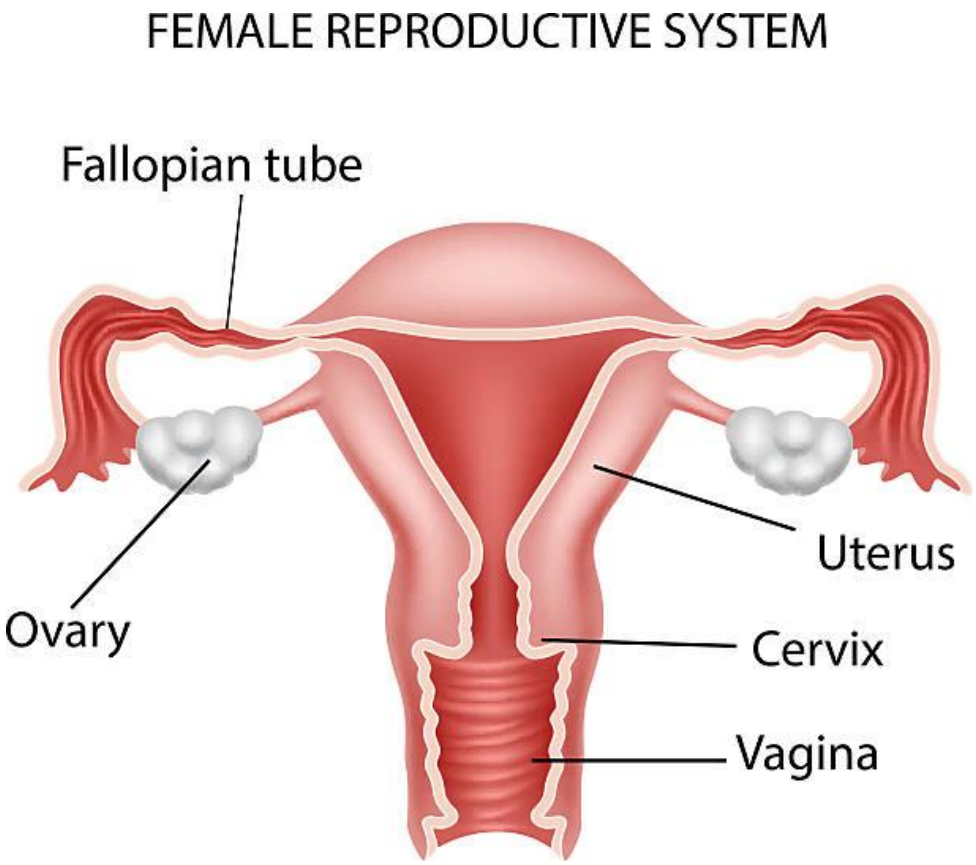


The Pancreas

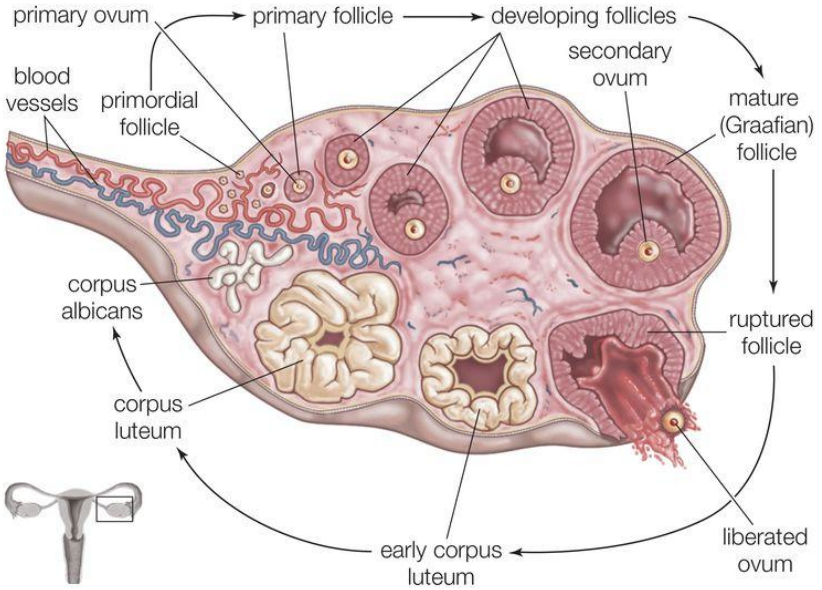


Insulin is secreted by Beta Cells

Ovaries

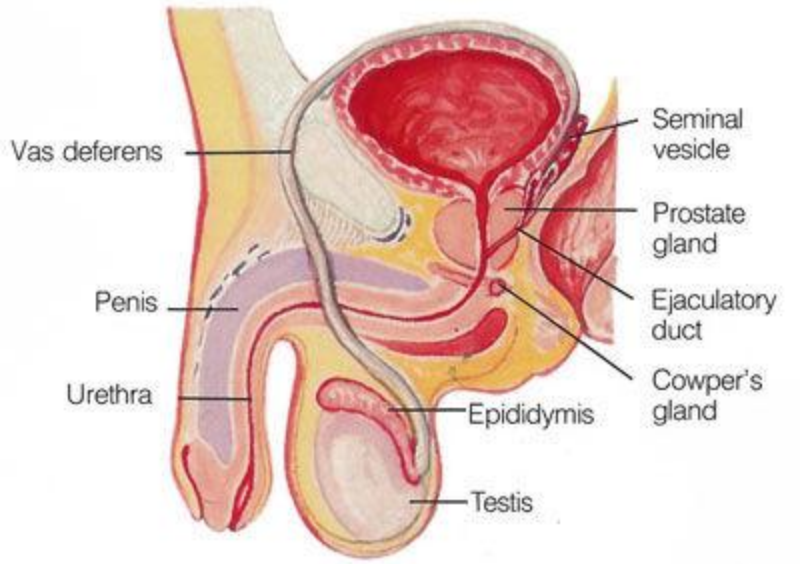


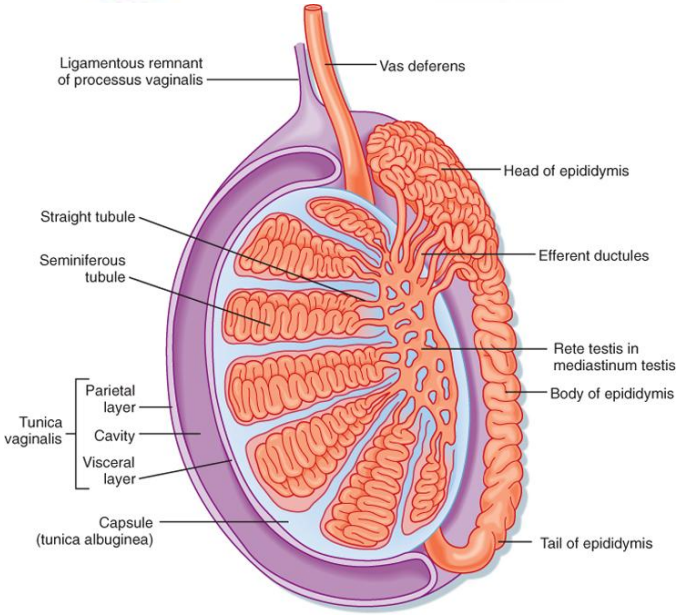
- Ovary



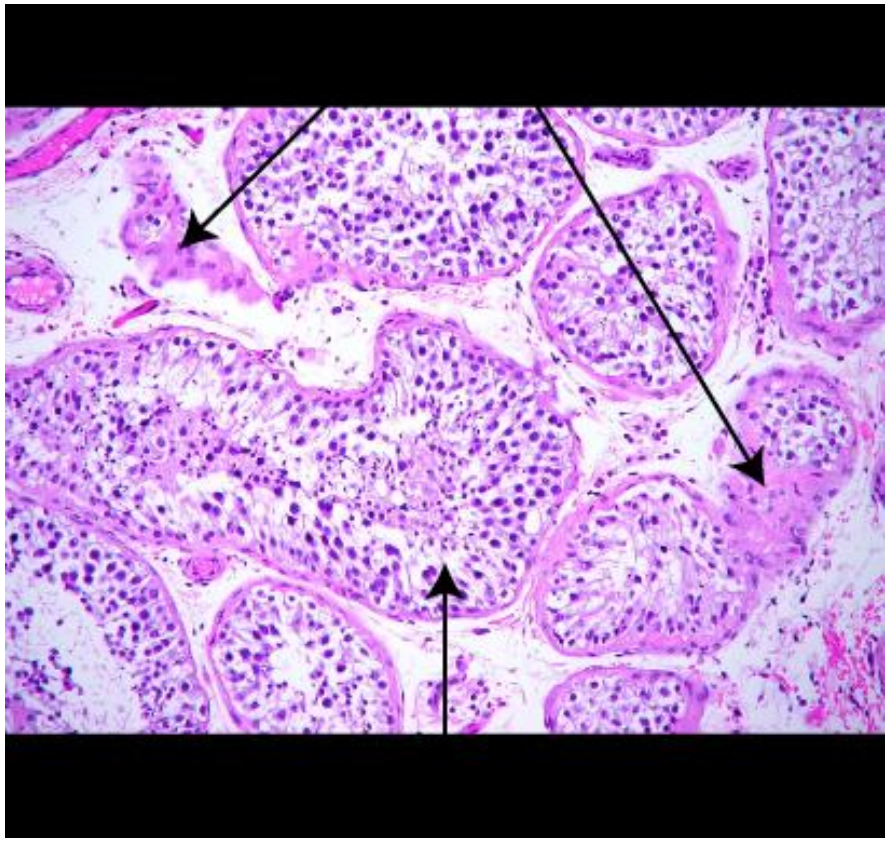
Estrogen and Progesterone are secreted by the corpus luteum

Testes





Testosterone Made Here in Leydig Cells

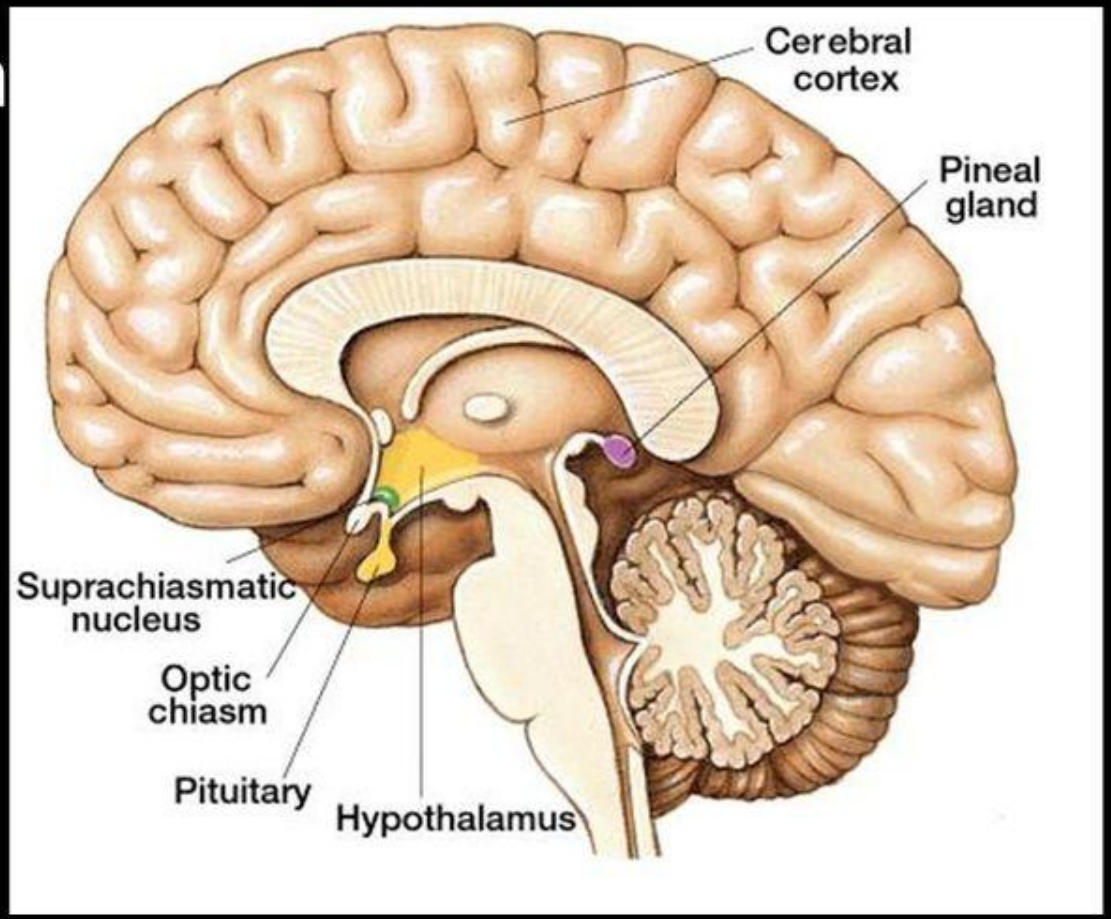


Sperm Made Here

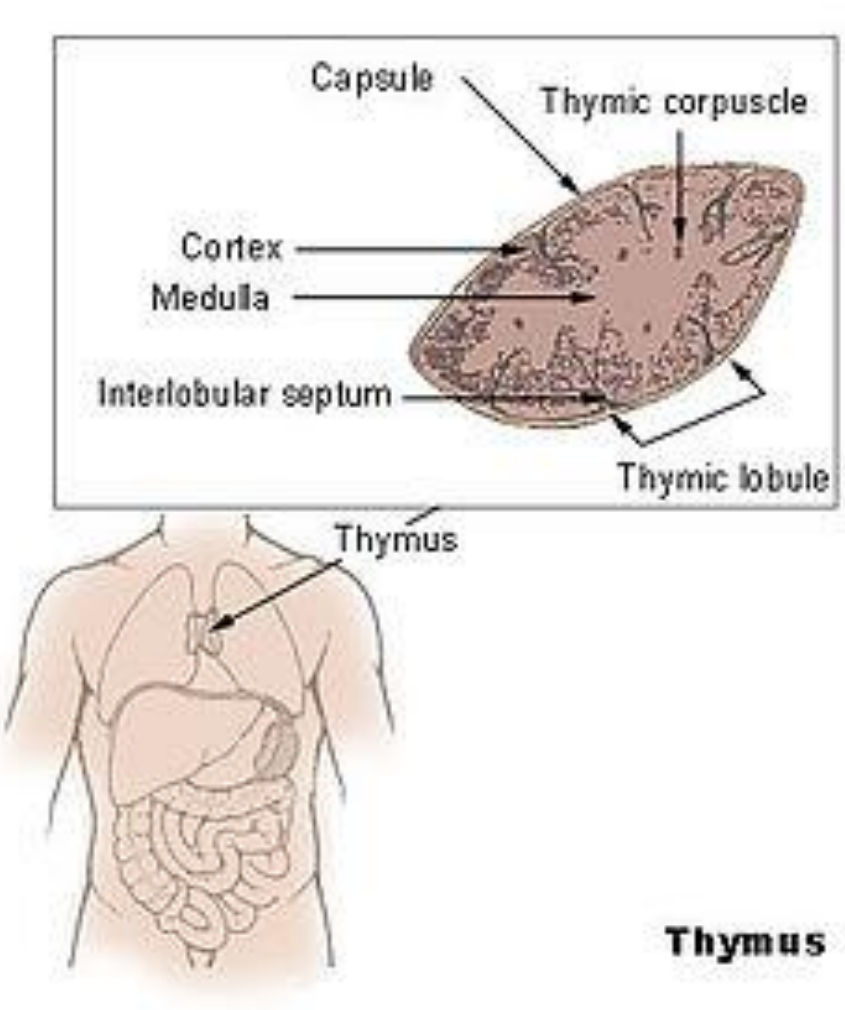
Pineal

The Pineal Glan

- Functions: the pineal gland releases hormones that control circadian rhythm and regulate certain reproductive hormones.
- Hormones:
  - Melatonin
  - Serotonin

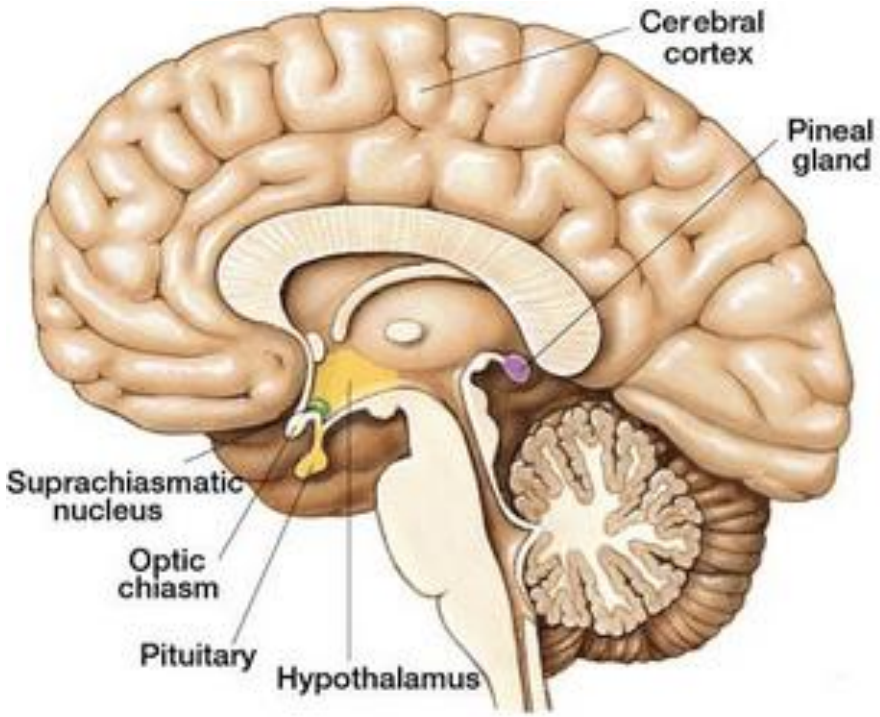


Thymus



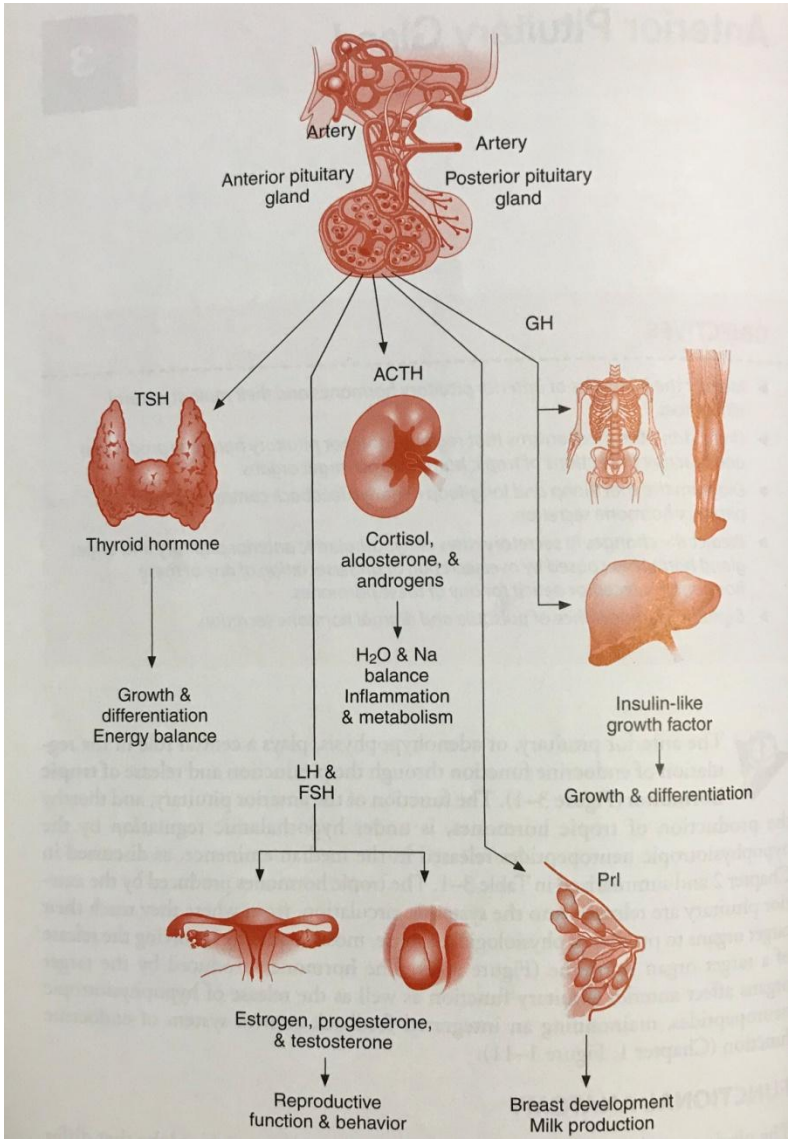
- Links the Endocrine and Immune Systems
- Endocrine System Role
  - Secretes Thymosin, Thymic Humoral Factor (THF), Thymic Factor (TF) and thypoietin which control the production of T cells and the activation of B cells
- Immune System Role
  - Creates T lymphocites, Helper T cells, Killer T cells
  - Retains memory of invaders in Memory T cells

The Hypothalamus



- The Real Master Controller of the Endocrine System Directing the Secretion of Pituitary Hormones
- Connected to the Pituitary Posterior Lobe by Nerves not Hormones
- Links the Endocrine System to the Nervous System

Glandular Signaling Cascades/Axes



- Hypothalamic Pituitary Adrenal (HPA) Axis
  - TRH-TSH-T3/T4
  - GnRH-LH/FSH-sex hormones
  - CRH-ACTH-cortisol
  - Renin-angiotensin-aldosterone
  - leptin vs insulin
- Hypothalamic Pituitary Thyroid (HPT) Axis
  - TRH-TSH-T3/T4
- Hypothalamic Pituitary Gonadal (HGA) Axis

Pituitary Hormone Regulation

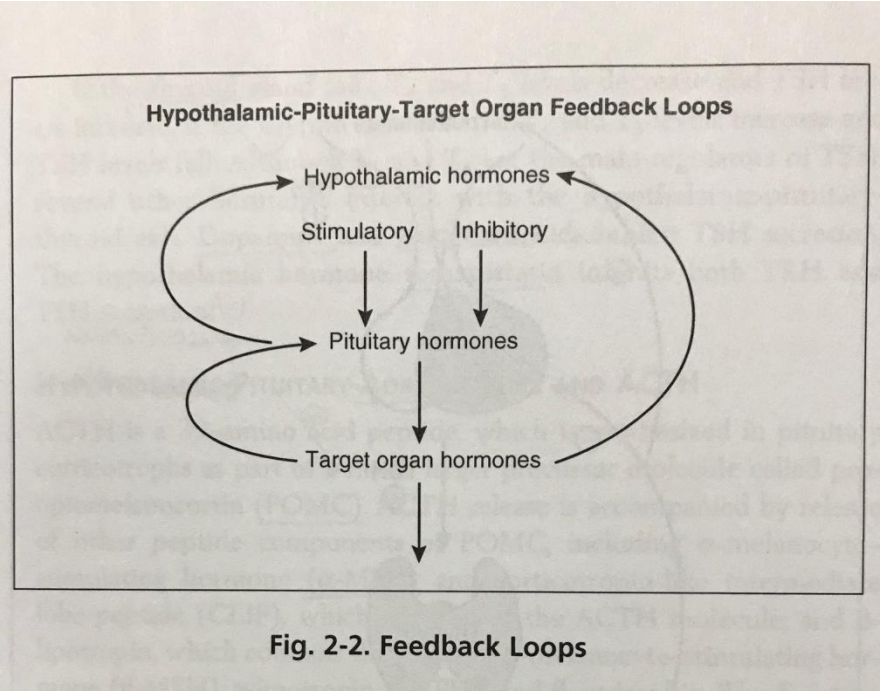


Fig. 2-2. Feedback Loops

Stimulating/Inhibiting Pairings Control:

Calcium – PTH/Calcitonin
Glucose – Glucagon/Insulin
Appetite - Ghrehlin/Leptin

- Hypothalamus senses the internal/external environment and signals Pituitary to make controlling hormones
- Pituitary in turn makes hormones to control other body organs and cells
- These send signals back to the Hypothalamus to keep the body systems in balance (Homeostasis)

Positive and Negative Feedback Loops

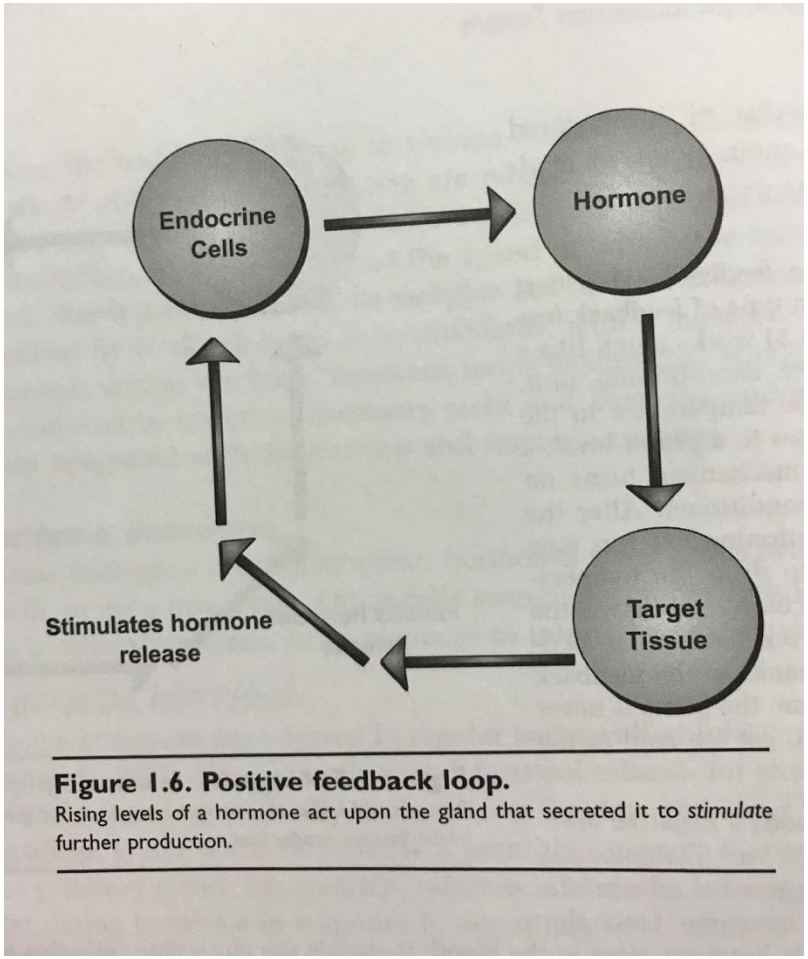


Figure 1.6. Positive feedback loop.
Rising levels of a hormone act upon the gland that secreted it to *stimulate* further production.

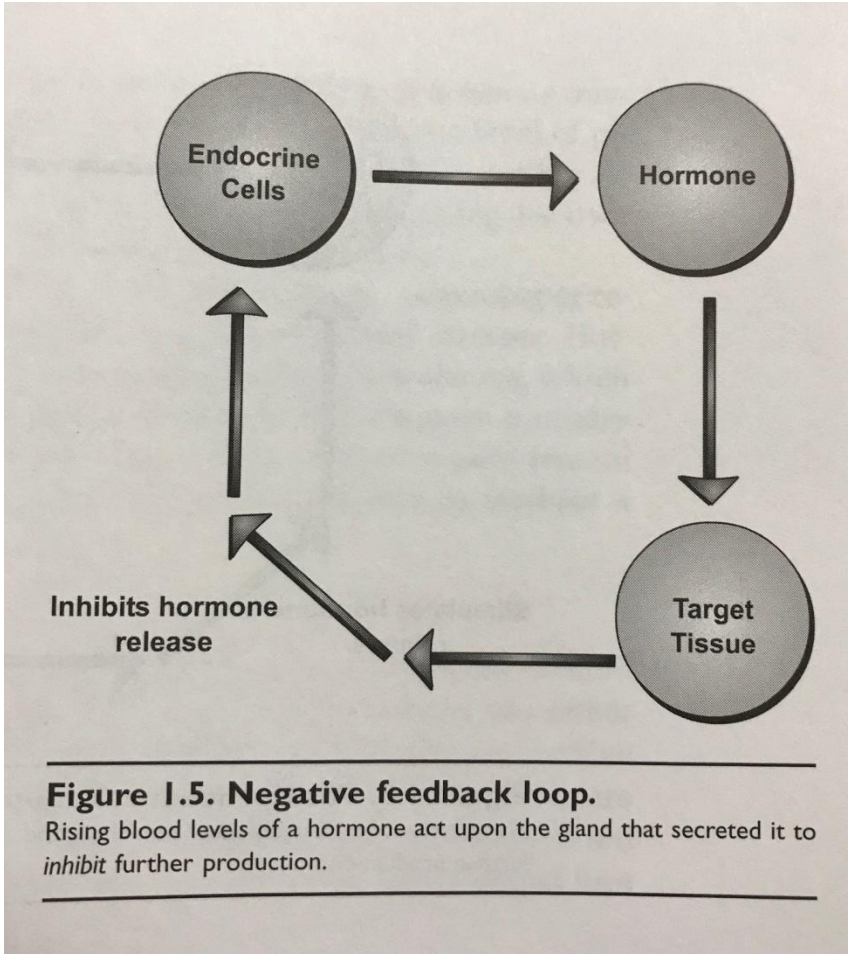


Figure 1.5. Negative feedback loop.
Rising blood levels of a hormone act upon the gland that secreted it to *inhibit* further production.

Restores levels of controlled substance to that required at the time = set point
Hormones that are generated and no longer needed get eliminated by enzymes
Residence time in the blood is measured in half lives from minutes to hours

Blood Pressure Regulation

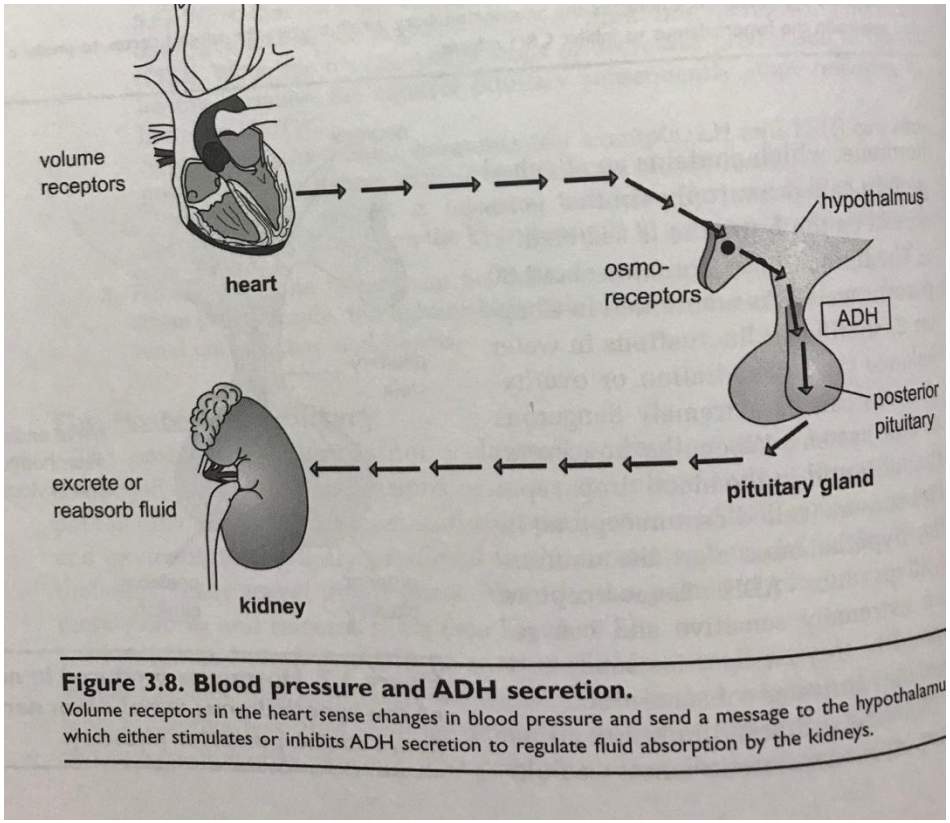
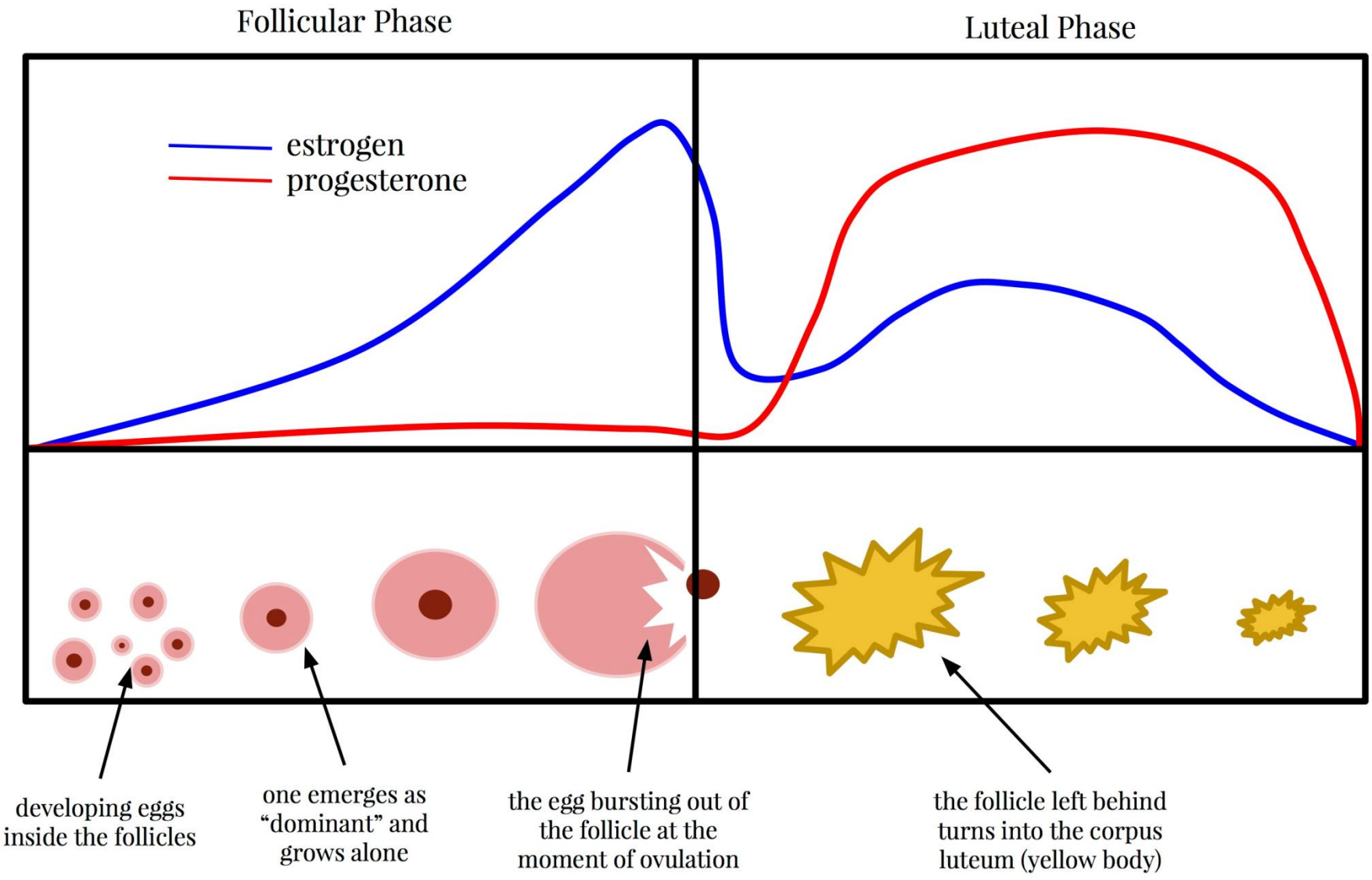


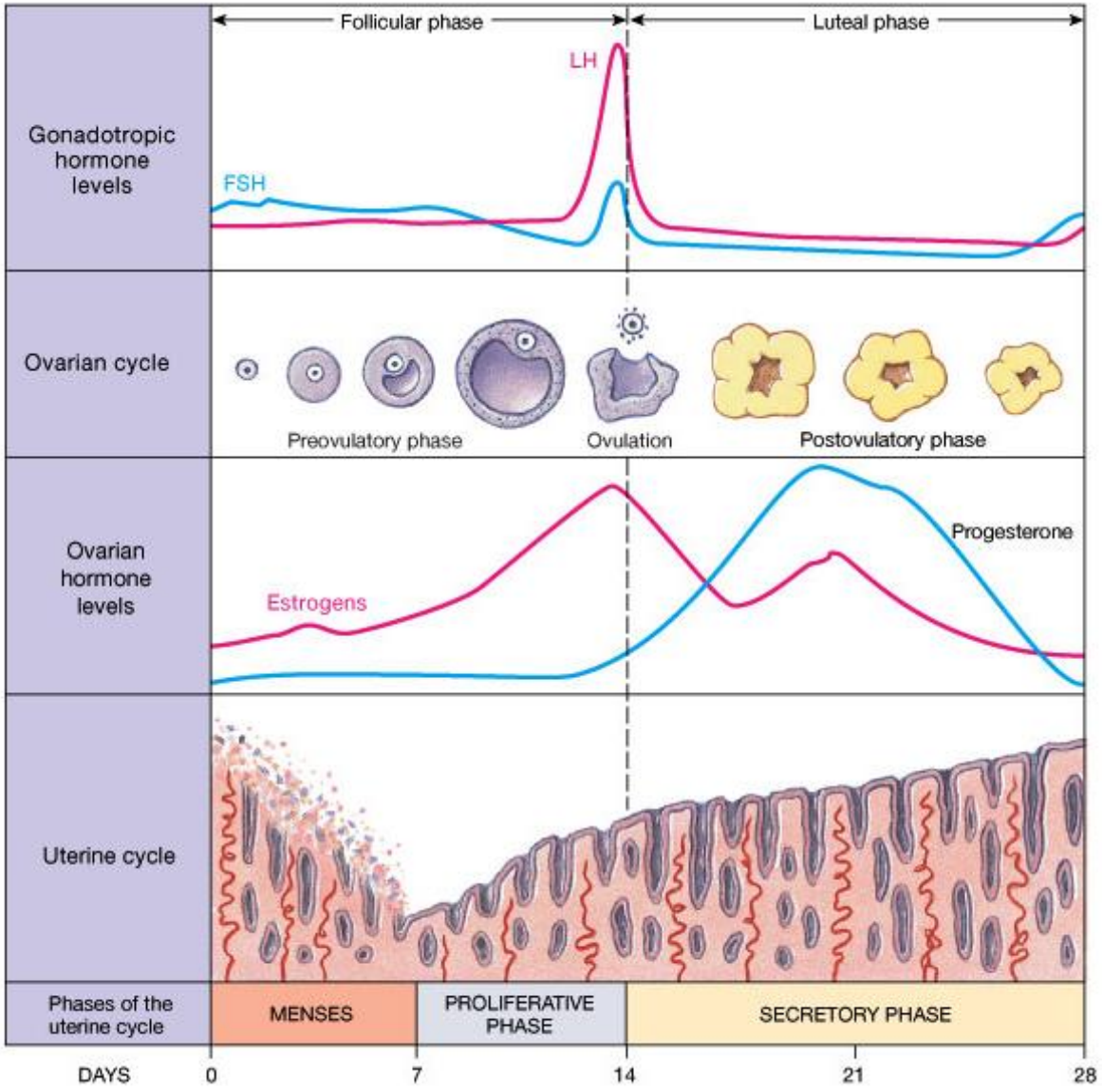
Figure 3.8. Blood pressure and ADH secretion.
Volume receptors in the heart sense changes in blood pressure and send a message to the hypothalamu which either stimulates or inhibits ADH secretion to regulate fluid absorption by the kidneys.

- Blood pressure sensors in the heart send electrical signals to the hypothalamus
- If BP too low hypothalamus signals the posterior pituitary to produce additional antidiuretic hormone (ADH) to kidneys to conserve water
- If BP too high hypothalamus signals the pituitary to produce less ADH and the kidney excretes excess water into urine

The Female Fertility Cycle



Female Fertility Cycle



Manipulation of Sex Hormones

- Ovarian Hyperstimulation
  - Active Compound
    - Gonadotropin Releasing Hormone (GnRH)
  - Method of Action
    - Stimulates the release of gonadotropins (LH and FSH)
    - Oocyte retrieval (4-20) for use in IVF otherwise a high risk of multiple pregnancy
  - Side Effects
    - OHSS – Shift of fluid from blood to other body cavities
- Birth Control Pill
  - Active Compounds
    - Estrogen and Progestin
  - Method of Action
    - Prevents ovulation
    - Thickens cervical mucus and lining of uterus impede sperm
  - Effective 99.7% if used as directed, 91% actual
  - Side Effects
    - Blood clots
    - Heart attack, Stroke
    - Progestin to reduce cancer

Hormone Replacement Therapy

- For Men
  - To retain strength and vigor in the elderly
  - Testosterone and growth hormone supplements
- For Women
  - To relieve post menopausal symptoms
  - Estrogen and Progesterone supplements

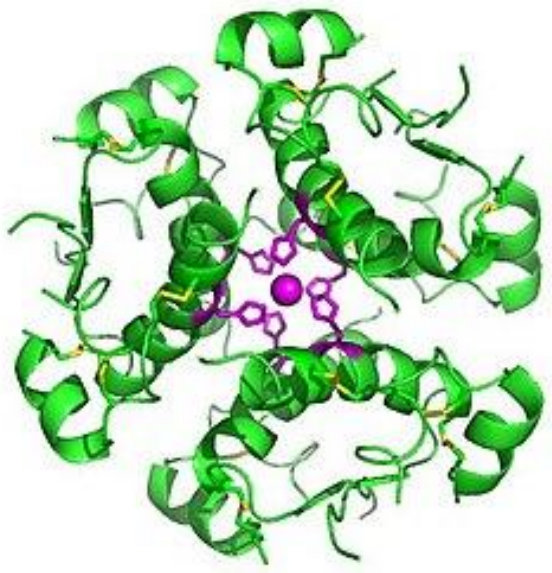
An early endocrinologist in 1900 attempted hormone replacement therapy on himself:

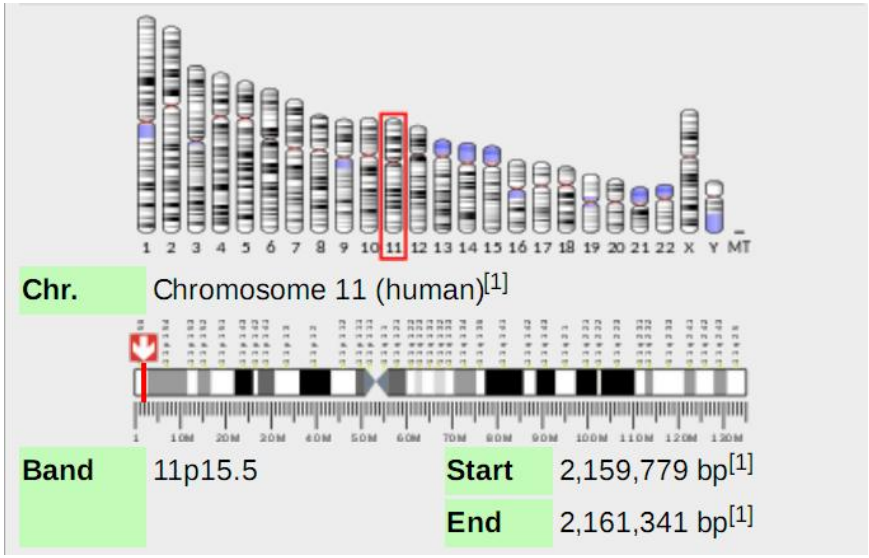
> Endocrinologist Charles-Édouard Brown-Séquard injected himself with extracts from dog and guinea-pig testes in a pioneering attempt at a kind of hormone replacement therapy. In the journal The Lancet, the 72-year-old scientist reported that the treatment rejuvenated him, restoring his strength, digestive functions and "intellectual labor."

Endocrine System Pathologies

- Hormone Insufficiency
- Hormone Excess
- Receptor Malfunction – Damaged, Too Few, Too Many
- Causes
  - Genetic
  - Tumors
  - Autoimmune Disorders, Antibodies kill endocrine cells
  - Infection
  - Environmental Toxins, Radiation

Insulin Biosynthesis and Structure



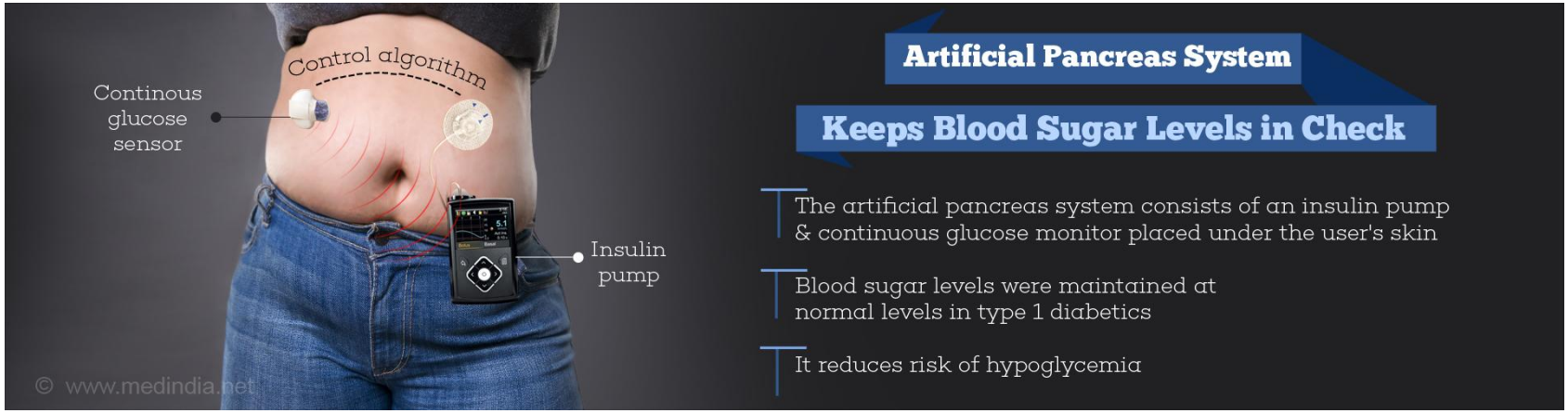


- The human insulin protein is composed of 51 amino acids, and has a molecular mass of 5808 Da. It is a dimer of an A-chain and a B-chain, which are linked together by disulfide bonds.
- Insulin's structure varies slightly between species of animals. Insulin from animal sources differs somewhat in effectiveness (in carbohydrate metabolism effects) from human insulin because of these variations
- Porcine insulin is especially close to the human version, and was widely used to treat type 1 diabetics before human insulin could be produced in large quantities by recombinant DNA technologies
- Humulin developed by Genentech in 1987 and licensed to Eli Lily

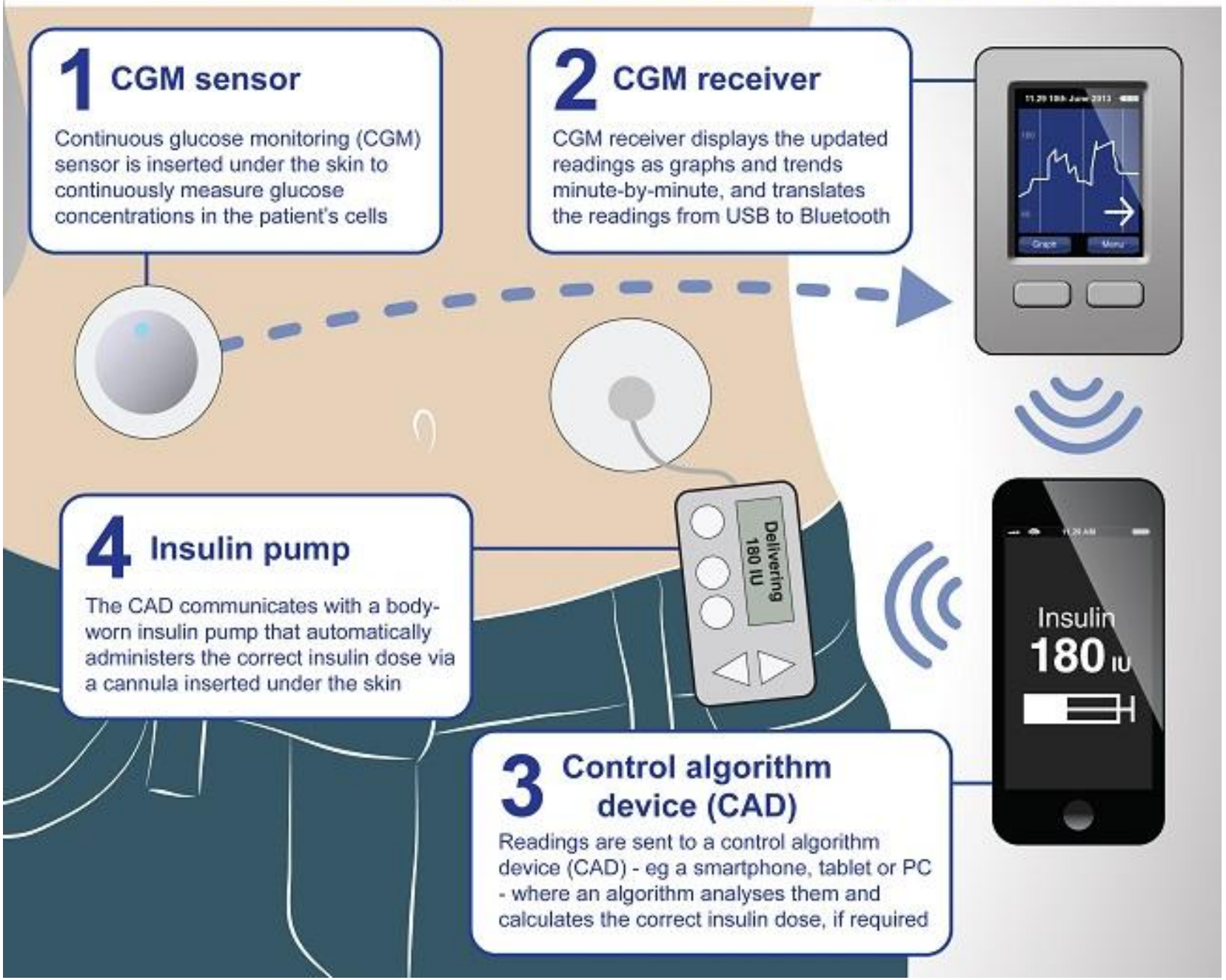
Type 1 Diabetes

- Caused by an insufficiency of insulin due to an autoimmune antibody attack that destroys beta cells in the pancreatic islets of Langerhans
- Untreated hyperglycemia will lead to death due to body's protein digestion
- Treated with insulin injections (HRT)

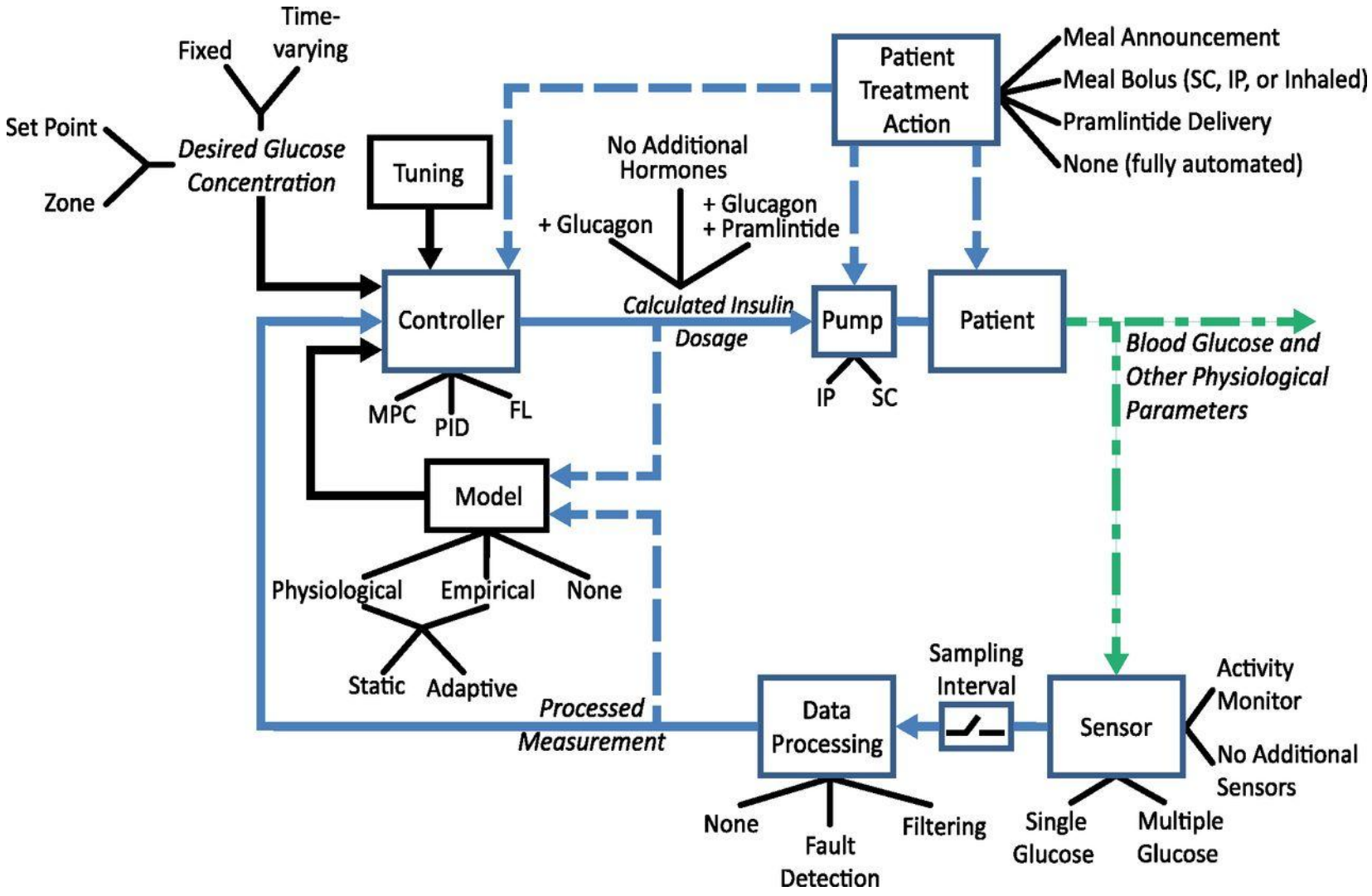
- Even when treated Diabetes can cause loss of limbs, toes, kidney failure and blindness due to poor blood circulation to extremities



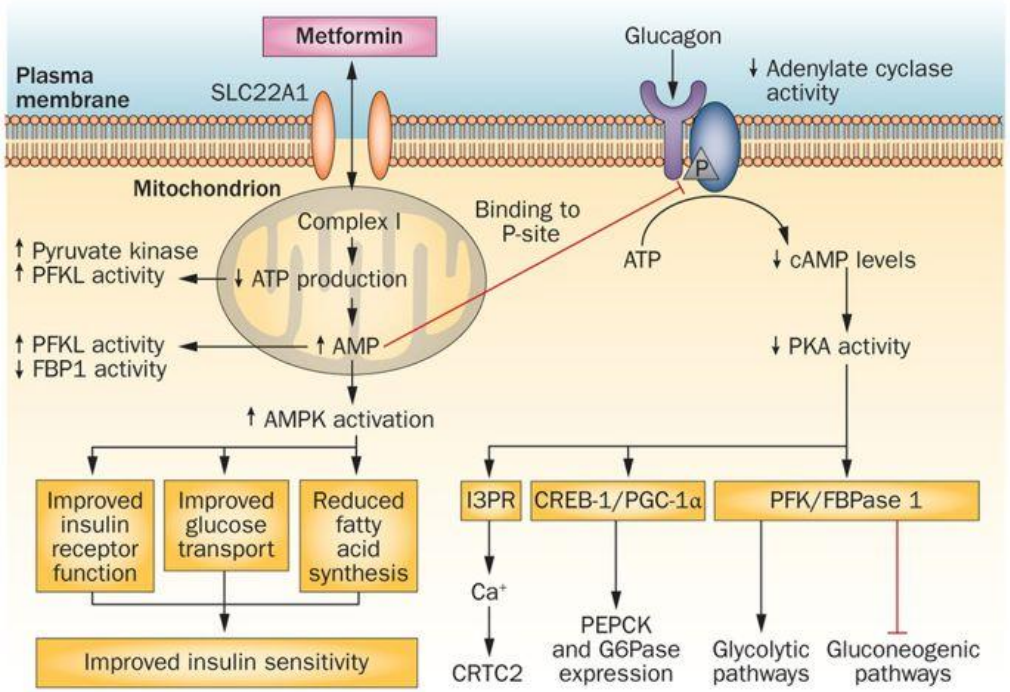
Artificial pancreas *at a glance*



Artificial Pancreas System Diagram



Type 2 Diabetes



- Caused by a malfunctioning insulin receptor or reduced number of receptors due to obesity and excess sugar in diet
- Prevention and recovery by exercise and diet
- Treated with metformin

"The glucose-lowering, insulin-sensitizing agent metformin works mainly by reducing gluconeogenesis and opposing glucagon-mediated signalling in the liver and, to a lesser extent, by increasing glucose uptake in skeletal muscle"

Measuring Hormones to Research Their Function Diagnose Diseases and Understand Their Chemistry

Table I.2 Discovery of hormones.

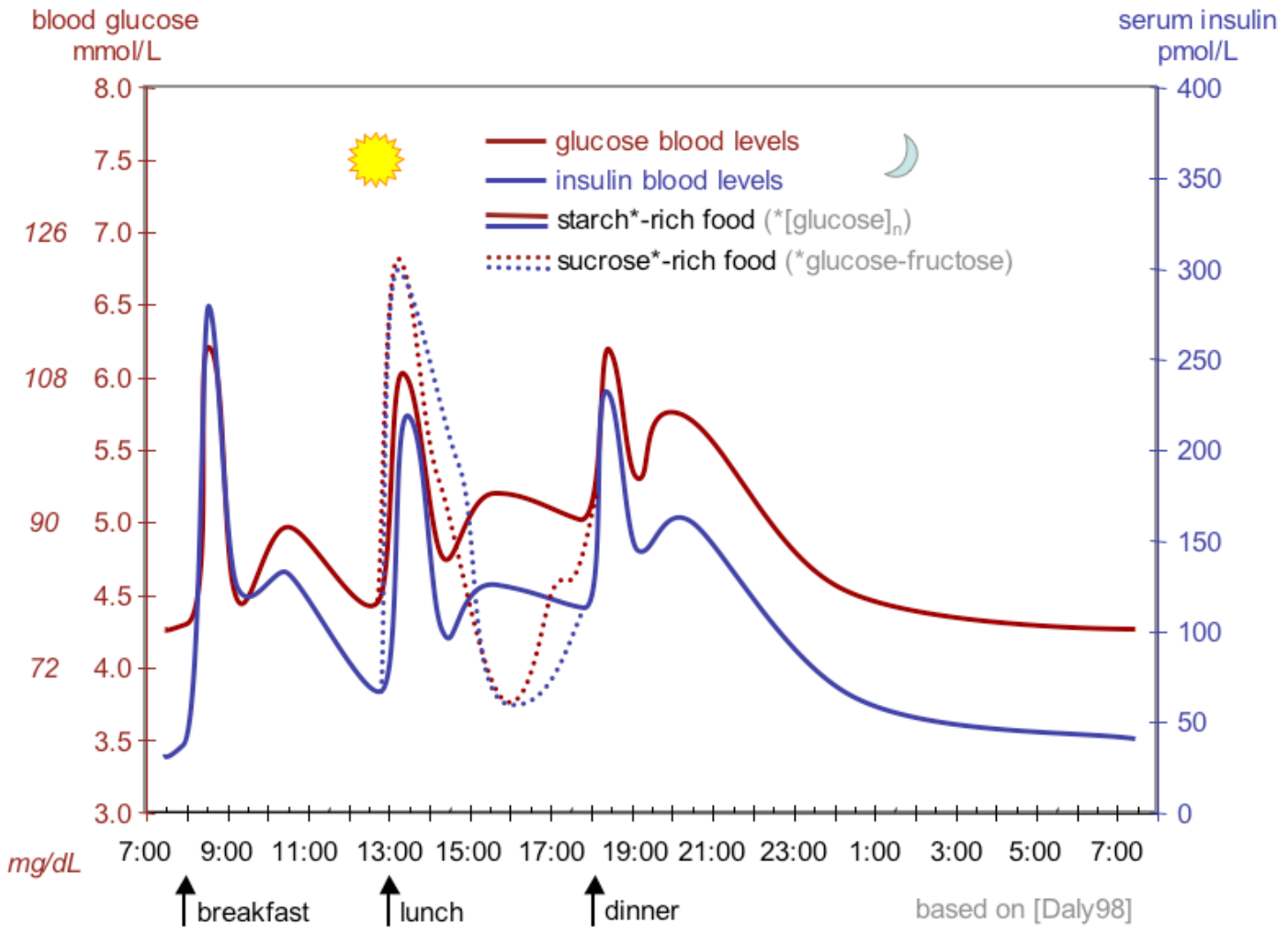
	Hormonal function	Structure
TRH	1962	1969
GnRH	1960	1971
GH	1921	1969
ACTH	1922	1956
FSH and LH	1926	1974
PRL	1928	1969
Somatostatin	1968	1973
GRF	1964	1982
CRF	1955	1981
Inhibin	1932	1985
ANF	1981	1981
VIP	1970	1983
Oxytocin	1901	1954
Insulin	1889	1953
Gastrin and secretin	1902	1964
Calcitonin	1961	1968
Aldosterone	1934	1954
Cortisol	1935	1940
Testosterone	1889	1935
DHEA-S	1960	1935
Estradiol	1925	1931
T_4	1895	1926
T_3	1951	1953
Norepinephrine	1895	1901

- Measure Quantity
  - Radioimmunoassay
  - ELISA
  - For Blood/Urine Testing
- Determine Structure
  - X-ray Diffraction
  - Electron Diffraction
  - Needed to Synthesize Chemically or by Genetic Engineering (Recombinant DNA)

Endocrine System Modeling

- Motivation
  - Models and Simulations Capture Biological Processes
  - Use to Design a Control System for Manipulating Hormones
- Example for Glucose Regulation – Normal/Diabetic
  - Flows and Equations
  - On-line Model – AIDA
    - http://www.2aida.org/
  - Thought Experiments
    - Normal Glucose Metabolism
    - Diabetes
      - 1x (Daily insulin injection) vs
      - 2x (Daily finger prick and test using glucose monitor, then inject)
      - Continuous monitoring and glucose/glucogon pump

Normal Glucose and Insulin Levels



Blood Plasma Glucose Regulation

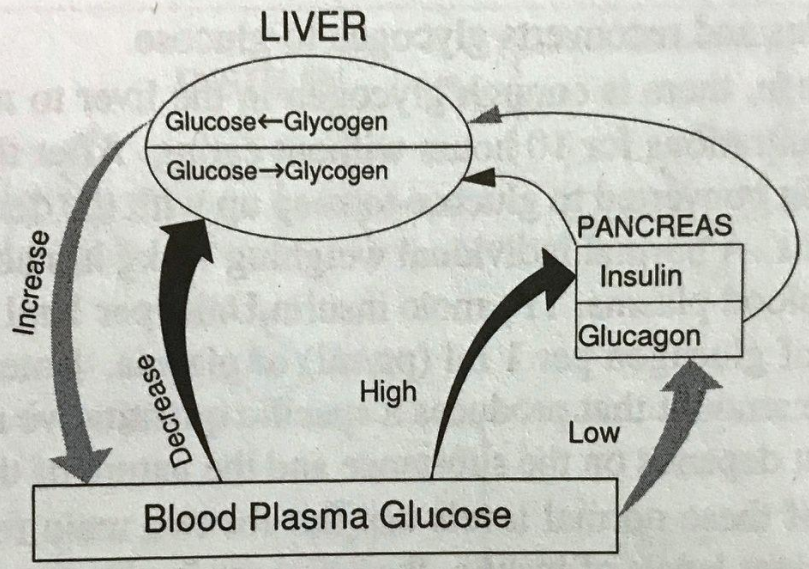


Figure 12.1: Blood plasma glucose is regulated by insulin and glucagon. When glucose concentration in the bloodstream is high, insulin production is stimulated, which results in the storage of glucose as glycogen in the liver. When blood glucose is low, glucagon converts liver glycogen to glucose, which is then added to the bloodstream.

Model Variables

Table 12.1: Variables used in the glucose-insulin model. Functional relationships are diagrammed in 12.2. U = international units.

STATE VARIABLES

c	glucagon in plasma and interstitial fluids (nU)
g	glucose in plasma and extracellular fluid (mg)
i	interstitial fluid insulin (μU)
l	liver insulin (μU)
p	plasma insulin (μU)
r	releasable pancreatic insulin (μU)
s	stored pancreatic insulin (μU)

AUXILIARY VARIABLES

NHGB	Net Hepatic (liver) Glucose Balance ($F_1 - F_2$)
F_1	Liver glucose production rate
F_2	Liver glucose uptake rate
F_3	Renal (kidney) glucose excretion rate
F_4	Peripheral system (muscles) glucose use rate
F_5	Non-peripheral system (central nervous system and red blood cells) glucose uptake rate
F_6	Insulin secretion rate
F_7	Glucagon secretion rate
I_g, I_p	Glucose, insulin ingestion rate
W	Insulin synthesis rate

Systems Dynamics Flow Model

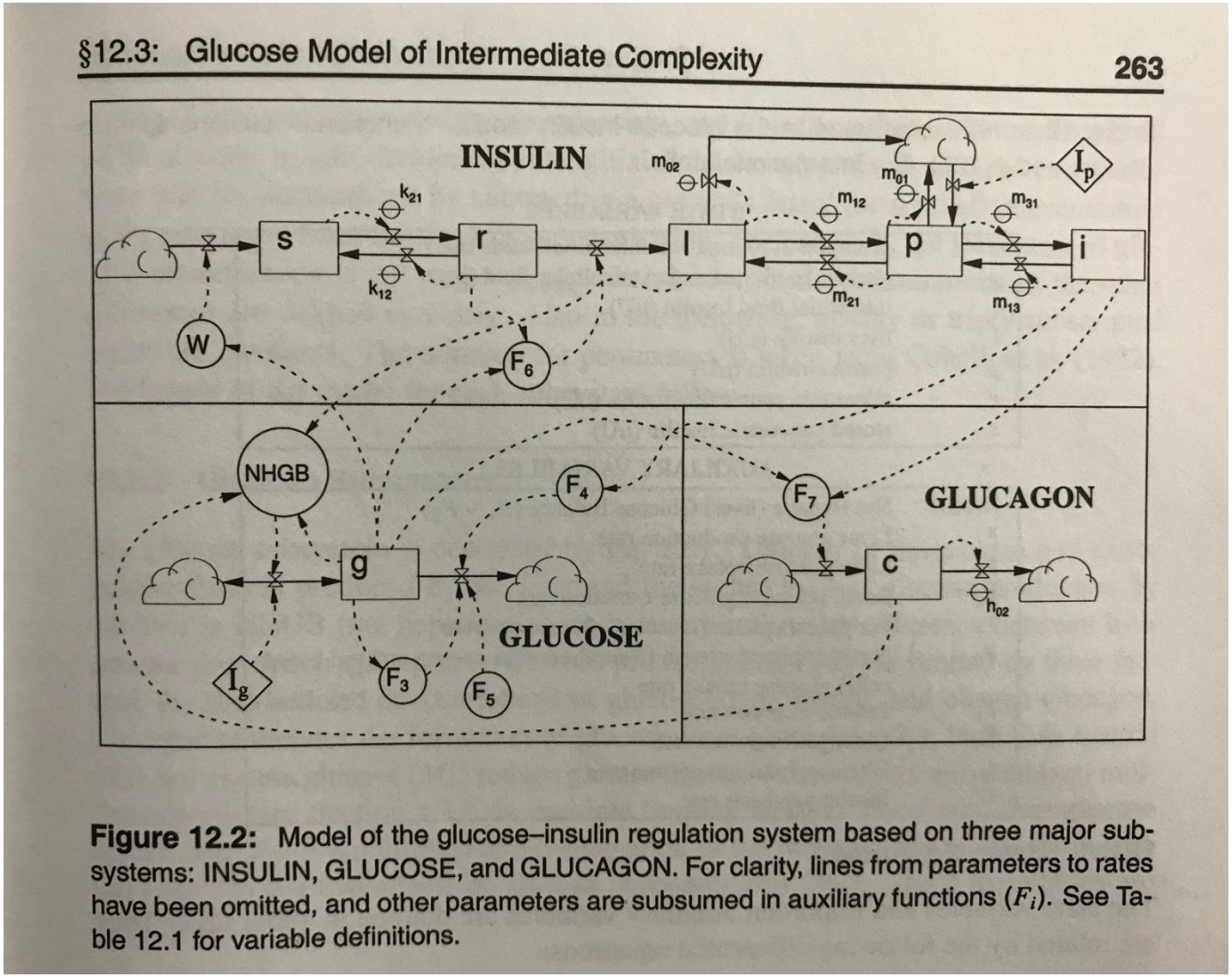


Figure 12.2: Model of the glucose–insulin regulation system based on three major subsystems: INSULIN, GLUCOSE, and GLUCAGON. For clarity, lines from parameters to rates have been omitted, and other parameters are subsumed in auxiliary functions (F_i). See Table 12.1 for variable definitions.

Model Differential Equations

12.3.1 Basic Equations

The state variables and important auxiliary variables are defined in Table 12.1. They are related by the following differential equations:

$$\frac{dg}{dt} = \text{NHGB} - F_3 - F_4 - F_5 + I_g(t) \tag{12.1}$$

$$\frac{dc}{dt} = -h_{02}c + F_7 \tag{12.2}$$

$$\frac{di}{dt} = -m_{13}i + m_{31}p \tag{12.3}$$

$$\frac{dl}{dt} = -(m_{02} + m_{12})l + m_{21}p + F_6 \tag{12.4}$$

$$\frac{dp}{dt} = -(m_{01} + m_{21} + m_{31})p + m_{12}l + m_{13}i + I_p(t) \tag{12.5}$$

$$\frac{dr}{dt} = k_{21}s - k_{12}r - F_6 \tag{12.6}$$

$$\frac{ds}{dt} = -k_{21}s + k_{12}r + W. \tag{12.7}$$

Normal IVGTT Response

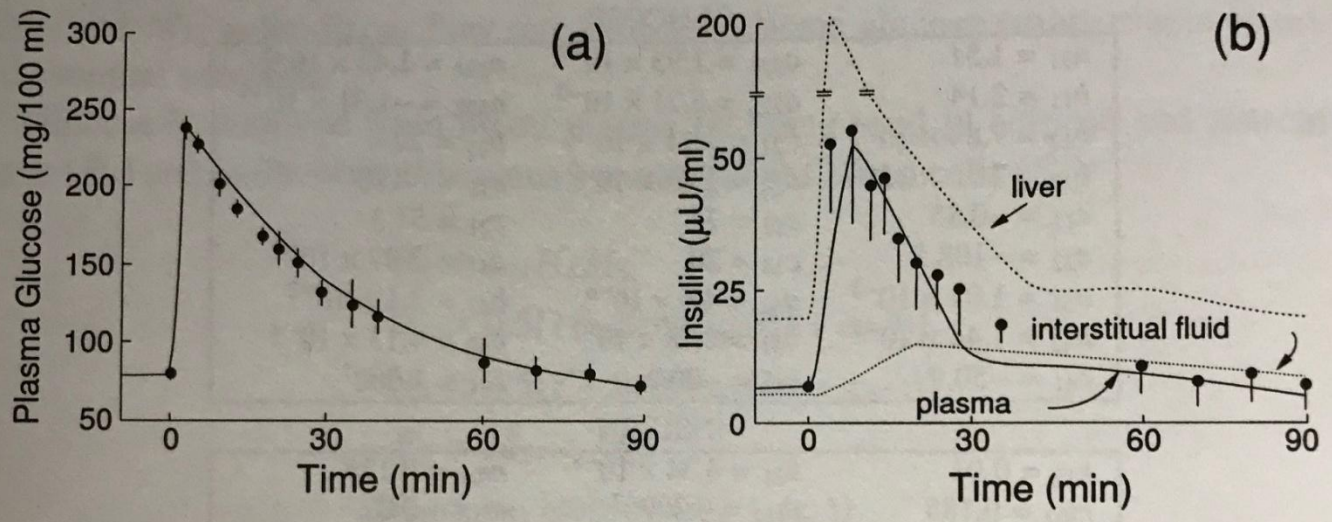


Figure 12.4: Simulated and average observed glucose (a) and insulin (b) responses of a normal individual following an intravenous pulse of glucose (IVGTT). Error bars are ±1 standard error, $n = 5$ patients. In (b), the solid line is plasma insulin (p), the dashed line is liver insulin (l), and the dotted line is interstitial insulin (i). Points are observations. (Reprinted by permission of the publisher from Cobelli et al. 1982, Figs. 6 and 7. © 1982 by Elsevier Science, Inc.)

Diabetic Response to IVGTT

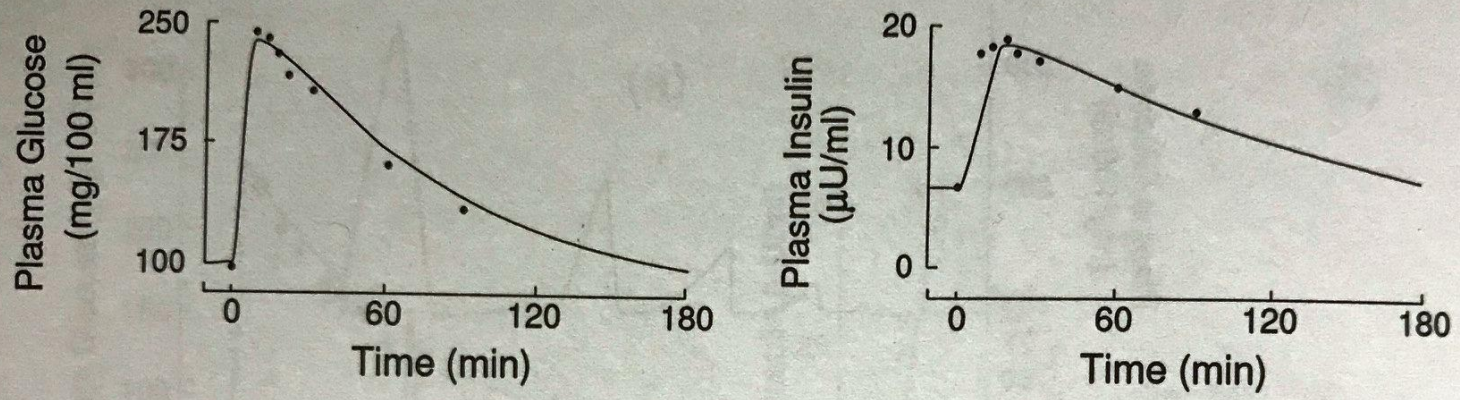
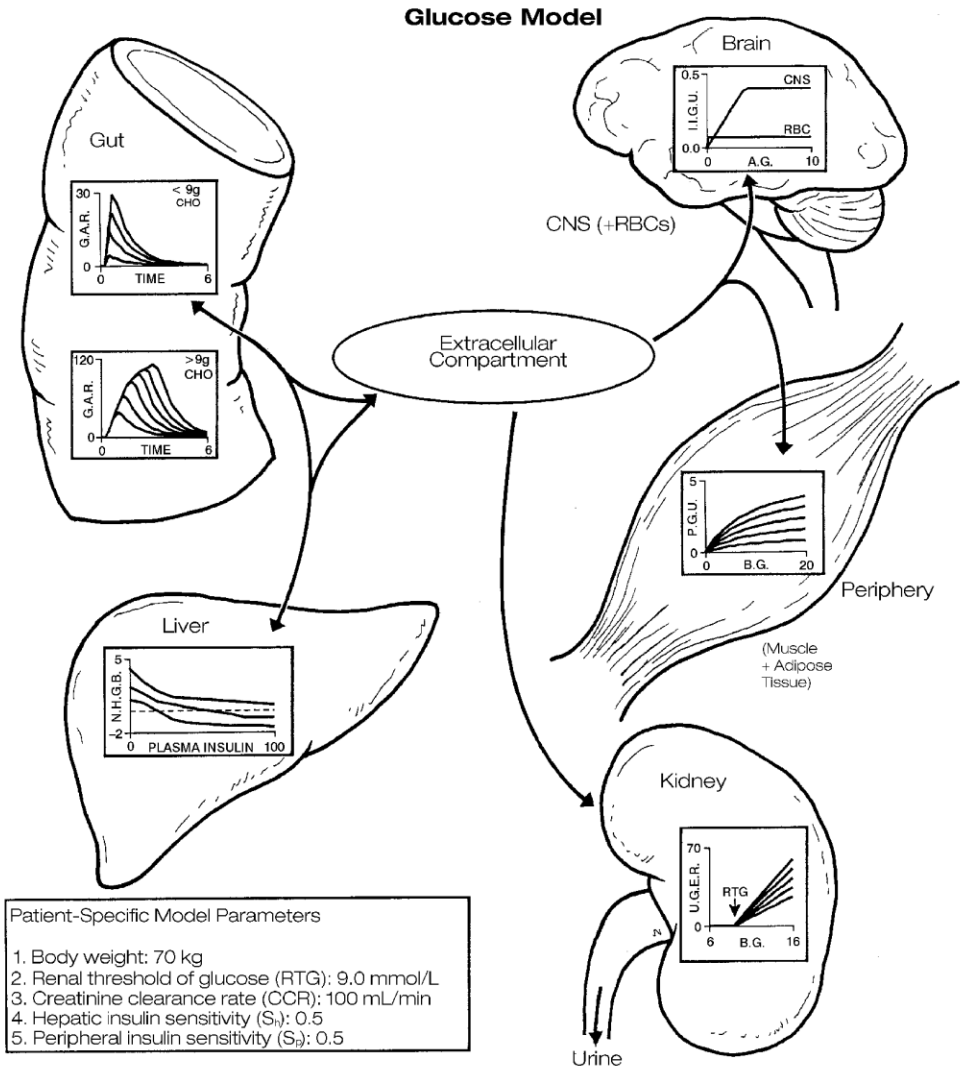
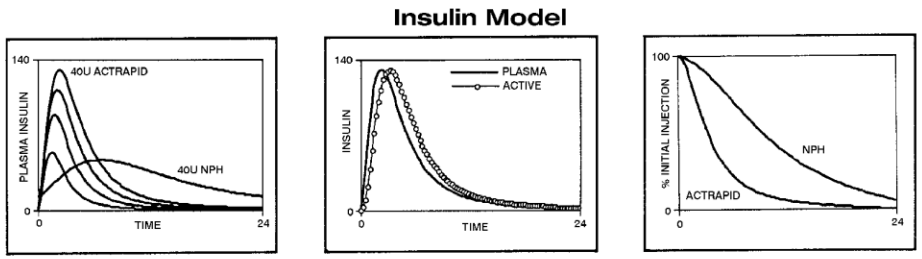


Figure 12.6: The response of a diabetic subject to the IVGTT test. Points are a single patient; the line is model predictions. Parameters as in Table 12.3. Note the slow recovery period. (Reprinted by permission of the publisher from Cobelli et al. 1982, Fig. 21. © 1982 by Elsevier Science, Inc.)

AIDA Model:


Glucose Model
Brain
0.5
I.I.G.U.
CNS
RBC
0.0
0
A.G.
10
CNS (+RBCs)
Gut
30
G.A.R.
< 9g CHO
0
TIME
6
120
>9g CHO
Extracellular Compartment
5
P.G.U.
0
B.G.
20
Periphery
(Muscle + Adipose Tissue)
Liver
5
N.H.G.B.
2
0
PLASMA INSULIN
100
Kidney
70
U.G.E.R.
RTG
6
16
N
Urine
Patient-Specific Model Parameters
1. Body weight: 70 kg
2. Renal threshold of glucose (RTG): 9.0 mmol/L
3. Creatinine clearance rate (CCR): 100 mL/min
4. Hepatic insulin sensitivity (S_h): 0.5
5. Peripheral insulin sensitivity (S_p): 0.5


Insulin Model
140
PLASMA INSULIN
40U ACTRAPID
40U NPH
0
TIME
24
140
INSULIN
PLASMA
ACTIVE
0
TIME
24
100
% INITIAL INJECTION
NPH
ACTRAPID
0
24

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  - Use to Design a Control System for Manipulating Hormones
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    - http://www.2aida.org/
  - Thought Experiments
    - Normal Glucose Metabolism
    - Diabetes
      - 1x (Daily insulin injection) vs
      - 2x (Daily finger prick and test using glucose monitor, then inject)
      - Continuous monitoring and glucose/glucogon pump

Future of Endocrinology

- Endocrine Society President on the Future of Endocrinology
  - https://www.youtube.com/watch?v=FkID8Z0DDIo
- Genetics and the Future of Endocrinology
  - https://www.youtube.com/watch?v=ky0Jp8ko2D8

Videos from: https://www.news-medical.net/health/Future-of-Endocrinology.aspx

Endocrine System Books and Websites

- Aroused by Randi Hutter Epstein
  - The history of hormones and how they control just about everything
- The Endocrine System by Stephanie Watson and Kelli Miller
  - Fact filled and easy to read by a lay person
- Modeling Biological Systems by James W. Haefner
  - Chapter 12 on Hormonal Control in Mammals
- American Association of Clinical Endocrinologists
  - www.aace.com
- Endocrine Society (US)
  - www.endo-society.org
- Society for Endocrinology (UK)
  - www.endocrinology.org

Additional Slides

- Based on Member Requests Here are Slides for:
  - Placebo Effect
  - Stress Impacts on the Endocrine System per Robert Sapolsky

Placebo Effect

- Placebo Effects are Real
  - Observed in animals and babies
  - “More expensive" works better
  - There is a dose response relationship
  - Injections work better than pills
  - Ability to overpower real drug effects
  - May actually get *stronger* over time
  - May be transferable from other believers
  - Typically sugar pill or saline injection
- Statistics on Cures
  - 50% Western Science Based Medicine
  - 33% Placebo Effect
  - 17% Unknown

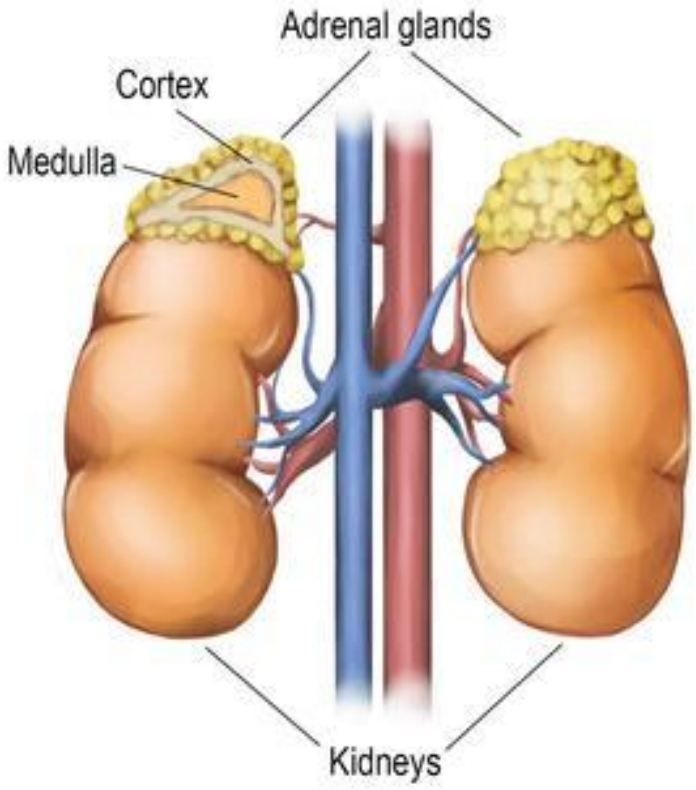
- Definition
  - The **placebo effect** is a psychosomatic phenomenon in which symptoms of a disease or condition lessen — or even appear to be cured completely — from the patient being merely exposed to a treatment, as a result of the body releasing endorphins. Believing that their condition will be improved, they will begin to feel better and perhaps identifiable symptoms may disappear, irrespective of whether the treatment has any chemical or pharmacological effect. Because of this, controlling for the placebo effect is an essential part of medicine.

Placebo Effect Video: https://www.youtube.com/watch?v=cwYjTfCoofE

Stress, Portrait of a Killer

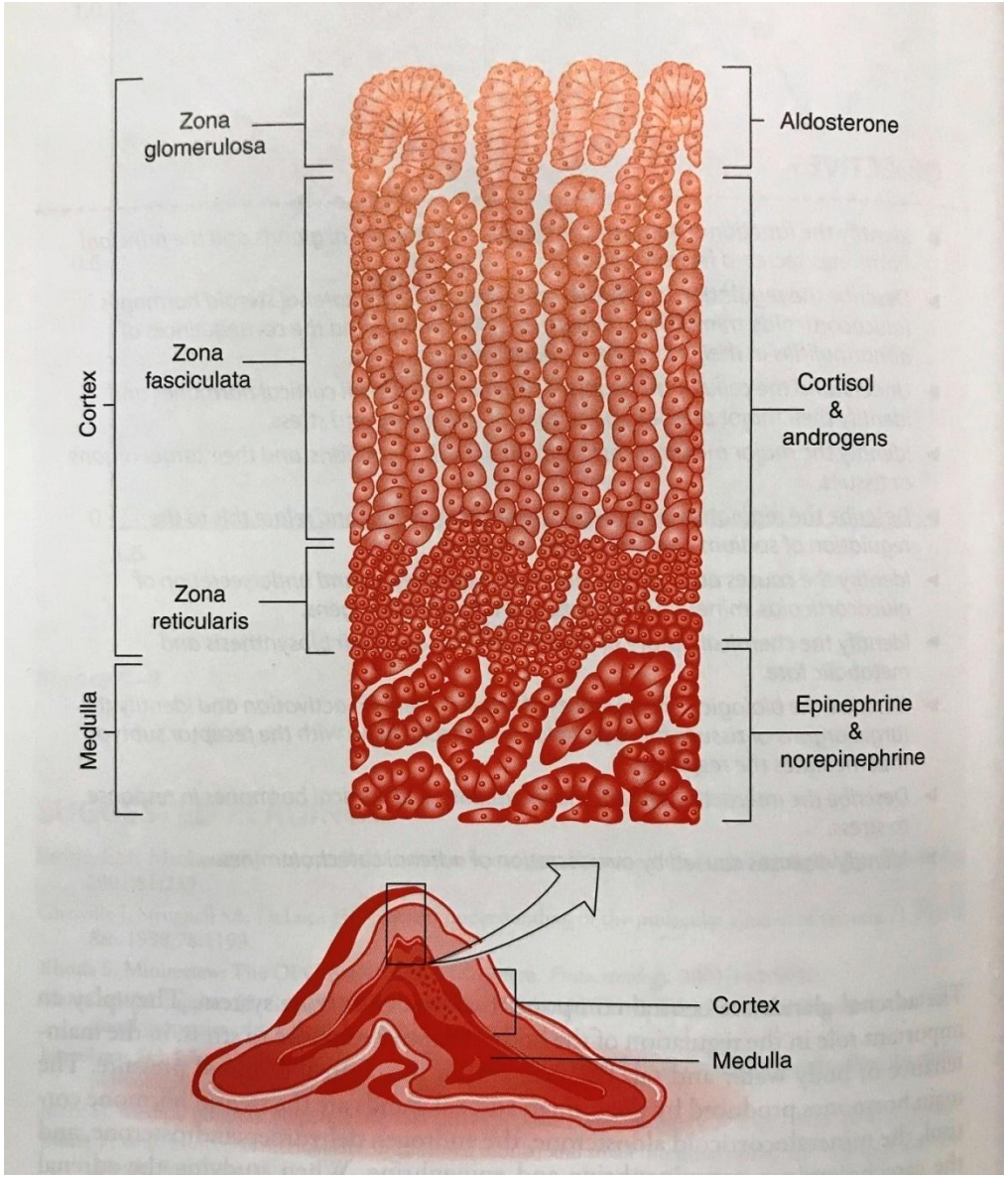
- Stress Triggers an Endocrine System Response
  - Hypothalmus to Pituitary to Adrenal (HPA) Axis
  - Good News when you need it to avoid tigers
  - Bad News when you don’t and it persists

The Adrenal Glands



Adrenals secrete:

Epinephrine (Adrenaline)
Norepinephrine
Cortisol & Androgens
Aldosterone



Fight or Flight Response

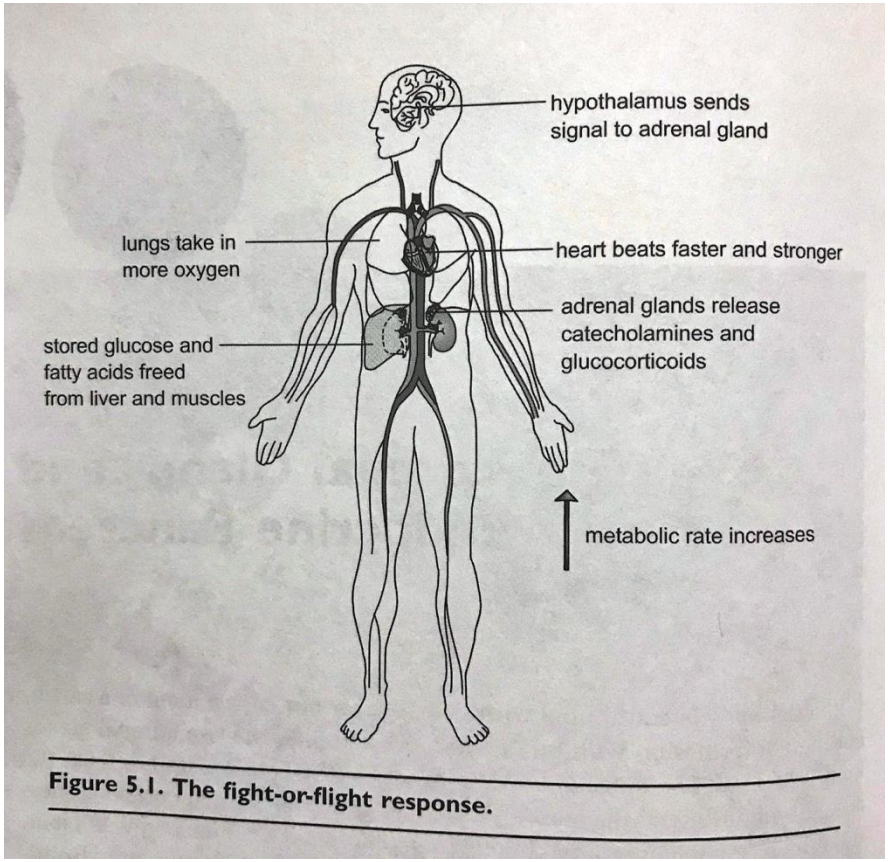
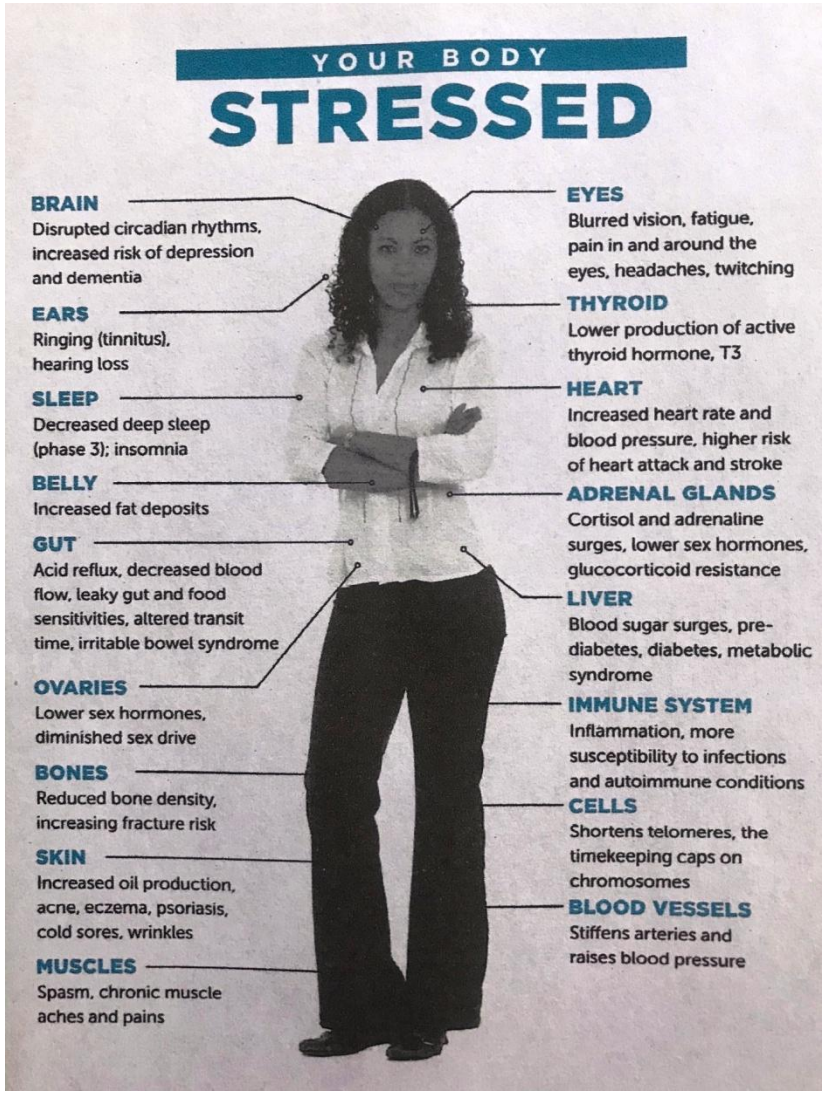


Figure 5.1. The fight-or-flight response.

- Cascade of events
  - You see the Tiger
  - Brain signals the Hypothalamus to release CRH which signals Pituitary to release ACTH to adrenals
  - Adrenal gland releases epinephrine, cortisol causing the response
  - Heart rate and breathing increases
  - Pancreas releases glucagon
  - Liver releases stored energy
  - Fat cells release stored energy
  - Immune system shuts down
  - Reproductive system shuts down
  - You outran the Tiger <u>this time</u> !!!

ACTH = adrenocorticotropic hormone
Cortisol – helps cells release stored food particles.
Epinephrine – increases blood flow to the muscles

Chronic Stress Response



- Compromised Immune System
- Ulcers
- Heart Attack
- Memory Loss
- Depression
- Obesity
- Sapolsky PBS Video
  - Stress, Portrait of a Killer
  - Watch 20:18 to 29:55
  - https://www.youtube.com/watch?v=eYG0ZuTv5rs

Stress Reduction

- Take a Break
  - Walk, listen to music, snack, nap, read a poem
  - Take a hot shower or bath
- Personal Time Management
  - Do more and fret less, get over it
- Meditate
- Exercise
- Take a Rest Day
  - Avoid screen time, Hide phone, Get a hobby
  - Spend time with family and friends
  - Go to a museum, movie, play, concert