Metabolic Regulation
SBCH321

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Module outlines

Title	**Metabolic Regulation**		
Code	**SBCH321**	**Department**	**Biochemistry&Microbiology**
Prerequisites	SBCH212	Co-requisites	None
Aim	The aim of this module is to provide students with comprehensive knowledge of the current concepts and theories of the regulation of metabolic processes.		
Content	Metabolic map. Catabolic and anabolic pathways. Regulation of metabolism. Key enzymes and metabolites. Hormones and neurotransmitters as signals. Signal transduction by intracellular receptors and by cell-surface receptors. Concept of the "second messenger" molecules. Intracellular messenger systems (adenylate cyclase system, calcium/phoshatidylinositol system, calmodulin, nitric oxide) Regulation of glycolysis, gluconeogenesis, glycogen degradation/synthesis. Regulation of Citric Acid Cycle. Inhibitors and activators of the cycle. Regulation of Fatty Acid degradation and synthesis. Synthesis of ketone bodies Regulation of Amino Acid degradation. Transamination and oxidative deamination. Ketogenic and glucogenic amino acids. Urea cycle. Integration of metabolism. Metabolic effects of insulin and glucagon Metabolic regulation in well-fed state and starvation.		
Assessment	40% Continuous Assessment Mark (20% practical assessments; 20% Tests and Assignments 60% Formal end of module exam (3 hours)		
DP Requirement	40% Continuous Assessment Mark 80% Attendance at practical and fieldwork		

Module Units

UNIT 1: Introduction to metabolic regulation

UNIT 2: Introduction to hormones & neurotransmitters

UNIT 3: Signal transduction

UNIT 4: Regulation and Integration of metabolism

UNIT 1: Introduction to metabolic regulation

- Metabolism
- Metabolism: Categories
- Important metabolic pathways
- Metabolic regulation
- Mechanisms of regulation
  - Allosteric regulation
  - Covalent modification
  - Adjustment of enzyme levels
  - Compartmentation
  - Metabolic specialization of organs

UNIT 2: Introduction to hormones/neurotransmitters

- Major systems of human body
- Glands
- Hormones vs neurotransmitters
- Classification of hormones
  - Solubility
  - Where they function
  - Chemical structure
- Briefing on synthesis of hormones/neurotransmitters
- Physiological role of hormones/neurotransmitters

UNIT 3: Signal transduction

- Signal transduction
- Terminology
- G-protein signaling pathway
- Adenylate cyclase signal transduction pathway
- Phosphoinositide signal transduction pathway
- Clinical significance of adenylate cyclase signal transduction pathway
- Alpha subunit of G-proteins
- The signaling gas: Nitric oxide
- Nitric oxide: Signal transduction
- Summary

UNIT 4: Regulation and integration of metabolism

- Glycolysis
- Citric acid cycle/Krebs cycle
- fatty acid synthesis/degradation
- Metabolic fate of Amino acids
- Pentose phosphate pathway
- Gluconeogenesis
- Glycogen metabolism
- urea cycle
- Ketogenesis

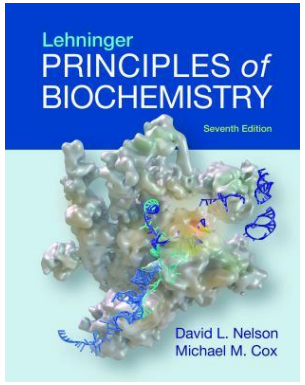
- Metabolic integration
  - Fate of Glucose-6-phosphate
  - Fate of pyruvate
  - Fate of Acetyl-CoA

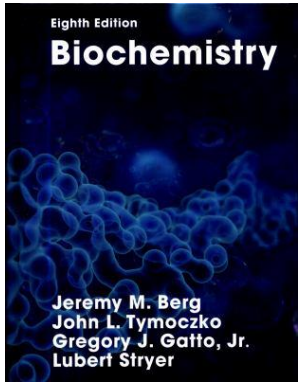
- Effect of hormones on fuel metabolism
  - Fed state and fasted state/stress

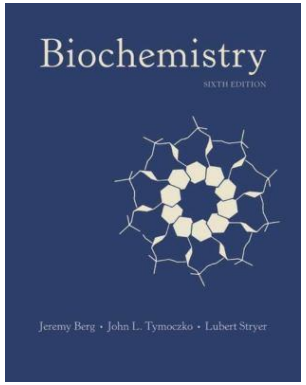
SBCH 321: Assessment

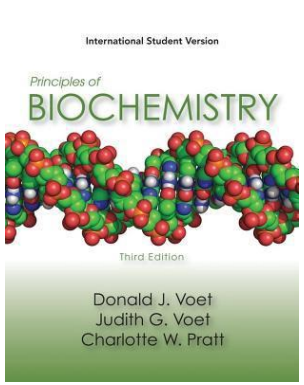
- 40% Continuous Assessment Mark
  - 20% Tests and Assignments (2 tests & 1 assignment)
    - Test 1 : Units 1 & 2 – 40%
    - Test 2 : Units 2 & 3 – 40%
    - Assignment : - 20%
  - 20% Practical assessments (Room no. 203 Department of Biochemistry and Microbiology: Monday 11:30 AM to 4 30 PM)
    - Practical Test – 20%
- 60% Formal end of module exam (3 hours)

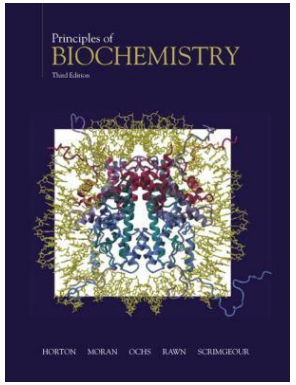
Recommended Books

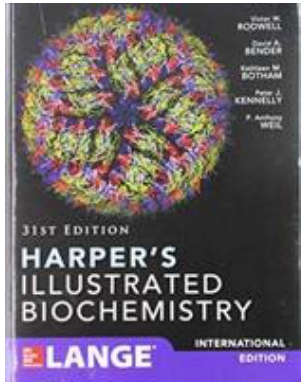


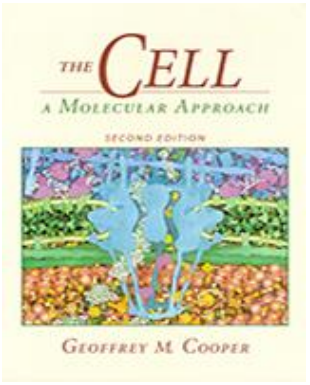












- **Old or latest version of the above books and the Biochemistry books in our library is also fine**
- **Information available on different websites also fine as long as its correct**

You will be fine just try to
understand,
be logical and above all
please use your……

Ways to access Information on SBCH321

- https://ksyed.weebly.com/
  - Page: Teaching

- Google: Type “Khajamohiddin Syed”
  - Click on the first search : Google scholar page
  - Then click on “Homepage”
  - Page: Teaching

- Class representative

UNIT 1: Introduction to metabolic regulation

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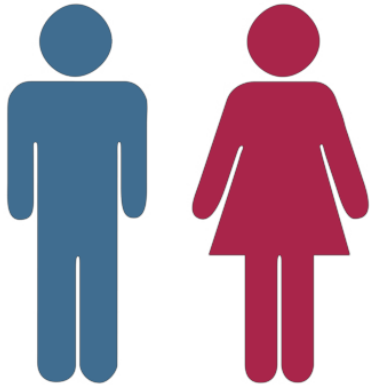
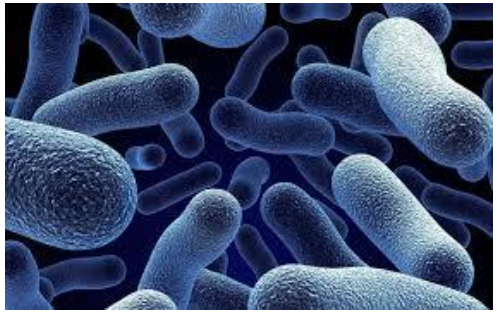
Topics

- Metabolism
- Metabolism: Categories
- Important metabolic pathways
- Metabolic regulation
- Mechanisms of regulation
  - Allosteric regulation
  - Covalent modification
  - Adjustment of enzyme levels
  - Compartmentation
  - Metabolic specialization of organs

Living organisms - energy

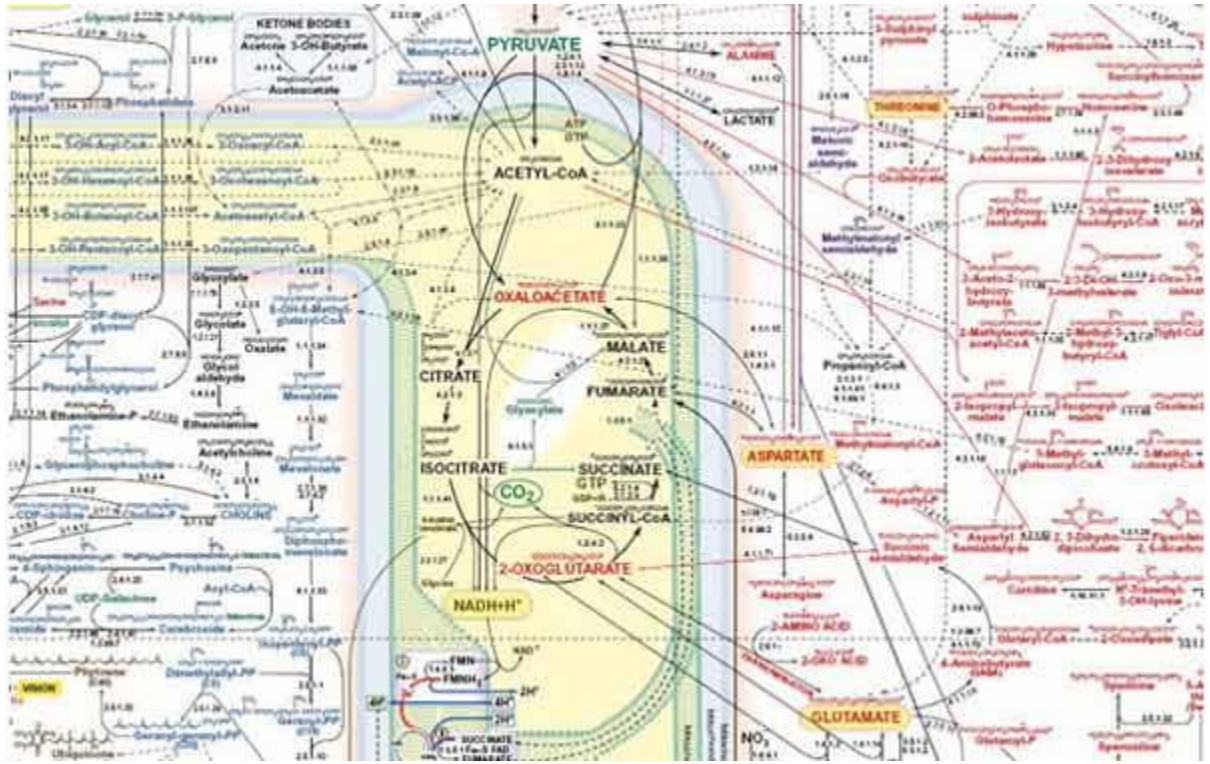




Play videos 1 & 2

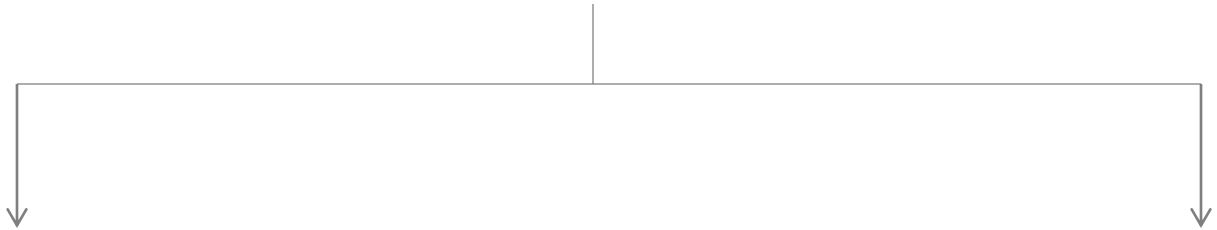
Metabolism

- Metabolism is a term that is used to describe all chemical reactions involved in maintaining the living state of the cells and the organism



Play video 3

Metabolism - categories



Anabolism/
Anabolic pathways

Catabolism/
Catabolic pathways

- Anabolism: The synthesis of all compounds needed by the cells and this process needs energy
- Catabolism: The breakdown of molecules to obtain energy

- Anabolic pathways : characterized by their ability to synthesize molecules with the utilization of energy
- Catabolic pathways : characterized by their ability to break down of complex molecules by releasing energy in the process

Play video 4

Metabolism – Important metabolic pathways

Pathway	Role
Glycolysis	Glucose oxidation in order to obtain ATP
Citric acid cycle (Krebs' cycle)	Acetyl-CoA oxidation in order to obtain GTP and valuable intermediates
Oxidative phosphorylation (electron-transport chain)	Disposal of the electrons released by glycolysis and citric acid cycle. Much of the energy released in this process can be stored as ATP
Pentose phosphate pathway	Synthesis of pentoses and release of the reducing power needed for anabolic reactions
Urea cycle	Disposal of ammonia (NH4+) in less toxic forms
Fatty acid β-oxidation	Fatty acids breakdown into acetyl-CoA, to be used by the Krebs' cycle
Gluconeogenesis	Glucose synthesis from smaller precursors, to be used by the brain

Play video 5

Metabolic regulation

The task of the regulatory machinery is exceptionally complex and difficult

- To maintain cell components in precise and correct amounts (metabolic balance)
- To respond effectively to environmental changes
- To conserve energy and material
- To adjust the need of cell/organisms
- To maximize efficiency of operation by regulating the catabolic and anabolic pathways

Enzymes

Metabolism –
Different mechanisms of Regulation

- Allosteric regulation
- Covalent modification
- Adjustment of enzyme levels
- Compartmentation
- Metabolic specialization of organs

Play videos 6 & 6.1

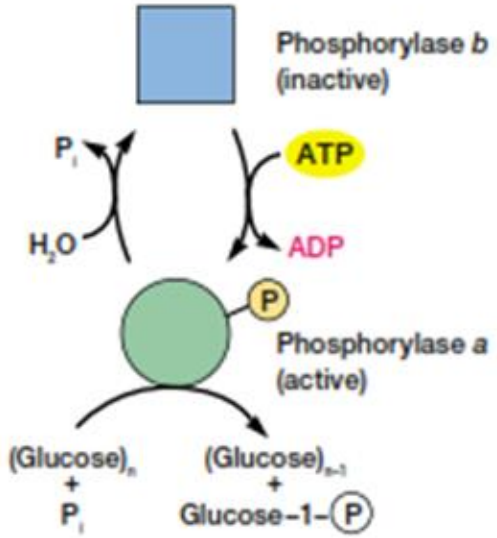
Metabolism – Allosteric regulation

- Allosteric regulation (or allosteric control) is the regulation of an enzyme by binding an effector molecule at a site other than the enzyme's active site.
- The site to which the effector binds is termed the allosteric site.
- Allosteric sites allow effectors to bind to the protein, often resulting in a conformational change involving protein dynamics.
- Effectors that enhance the protein's activity are referred to as allosteric activators, whereas those that decrease the protein's activity are called allosteric inhibitors.

Play video 7 & 8

Metabolism – Covalent modification

- Regulatory enzymes also can be switched on and off by reversible covalent modification
- the addition and removal of a particular group, one form of the enzyme being more active than the other
- Phosphorylation and dephosphorylation are the most common but not the only means of covalent modification



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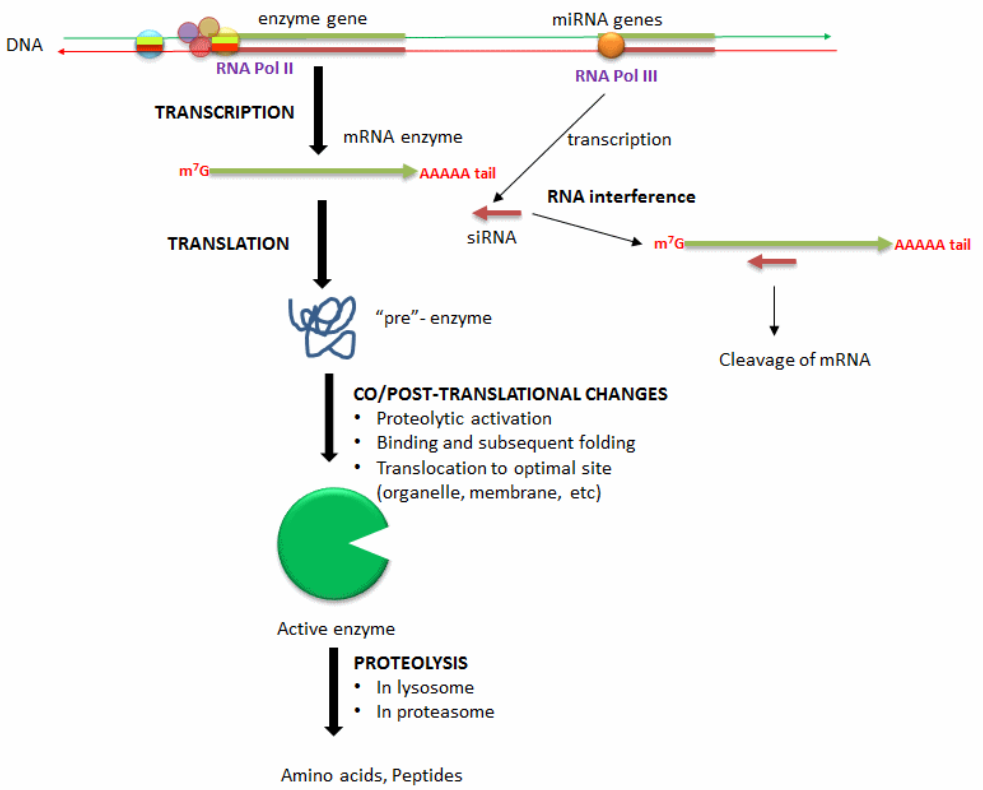
Metabolism – Enzyme levels

- The amount of enzymes, as well as their activities, is controlled
- The rates of synthesis and degradation of many regulatory enzymes are altered by hormones



Metabolism – Compartmentation

All reactions occurring in cells take place in certain space – compartment

Advantages:

(i) Compartmentation helps to separate even chemically quite heterogeneous environments and thus to optimize the course of chemical reactions.

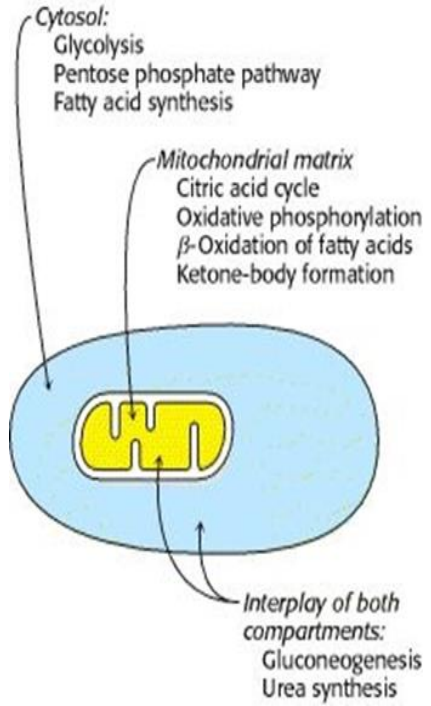
(ii) Compartmentation provides optimal conditions for individual enzymatically catalysed reactions.

(iii) Compartmentation protects cell organelles from the activity of lytic enzymes.

(iv) Compartmentation helps in regulation of metabolic pathways, making them more accurate and targeted and less interfering with one another.

Disadvantage:

Despite its advantages, compartmentation puts greater demand on energy consumption. This arises from a frequent need to use ATP-dependent transporters, transporting substances across membranes against the concentration gradient and thus creating different environments in different compartments.



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Metabolism – Functions of Eukaryotic organelles

Organelle	Major function
Mitochondria	Make energy out of food. Mitochondria are responsible for ATP production
Cytosol	A gel-like environment for the cell's organelles. The cytoplasm is the location for most cellular processes, including metabolism, protein folding, and internal transportation.
Lysosome	Garbage disposal - Enzymatic digestion of cell components and ingested matter
Nucleus	The nucleus houses the cell's DNA and directs the synthesis of proteins and ribosomes. DNA replication, transcription, and RNA processing.
Ribosomes	Responsible for protein synthesis
Golgi apparatus	Sorting of lipids and proteins takes place. Posttranslational processing of membrane and secretory proteins; formation of plasma membrane and secretory vesicles
Endoplasmic reticulum	Modifies proteins and synthesizes lipids
Vesicles	Storage and transport
Peroxisome	Carry out oxidation reactions that break down fatty acids and amino acids and detoxify poisons

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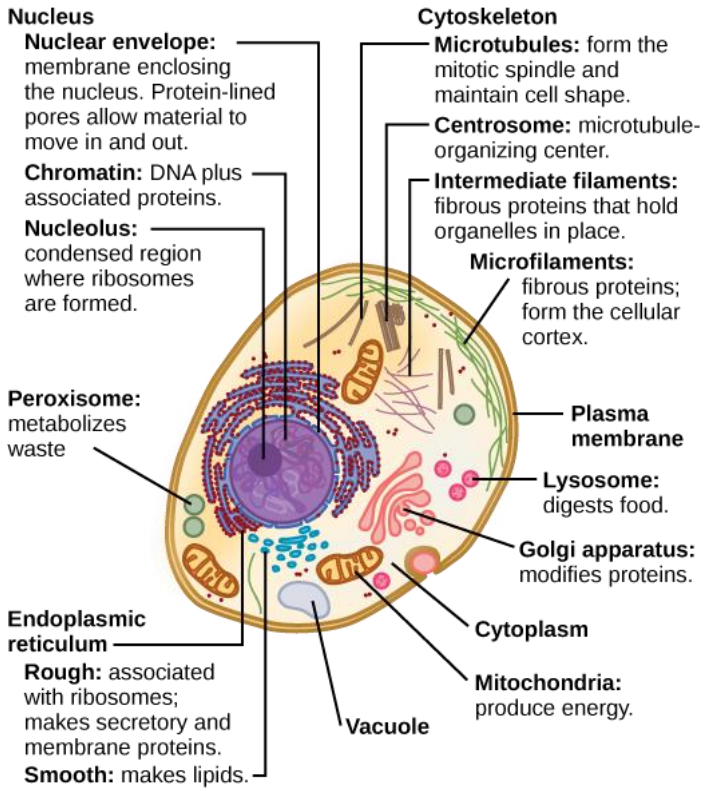
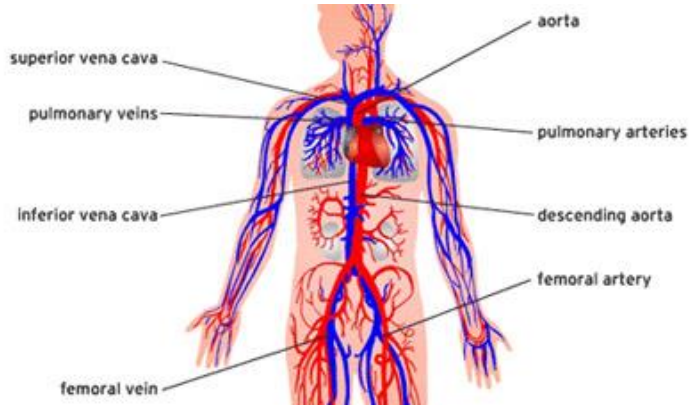
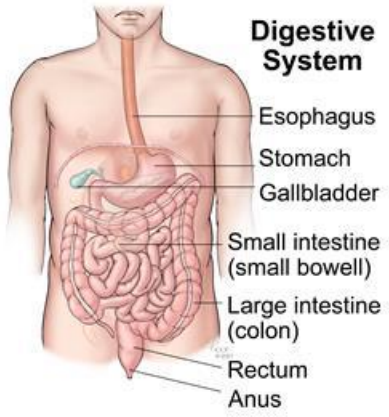


https://courses.lumenlearning.com/boundless-biology/chapter/eukaryotic-cells/

Metabolism – Specialization of organs

- The human body is made up of several organ systems that all work together as a unit to make sure the body keeps functioning. There are ten major organ systems in the body, each of which plays a different role in helping the body work





Circulatory system

Heart, blood, blood vessels and lymphatics

It is the body's delivery system, concerned with circulating blood to deliver oxygen and nutrients to every part of the body

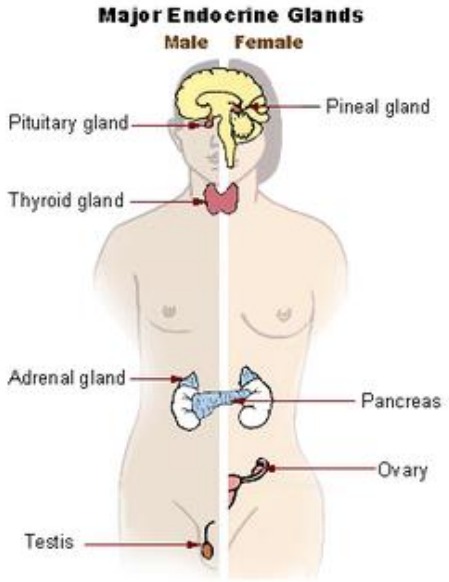
Play video 12

Digestive system

Mouth, stomach and intestines

The purpose of the digestive system is to turn the food you eat into something useful for the body. When you eat, your body uses this system to digest food so your cells can use it to make energy

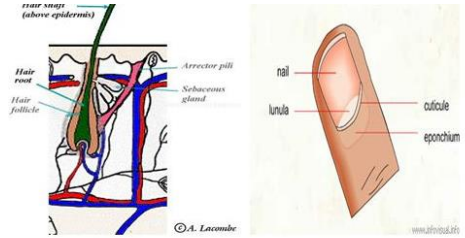
Metabolism – Specialization of organs

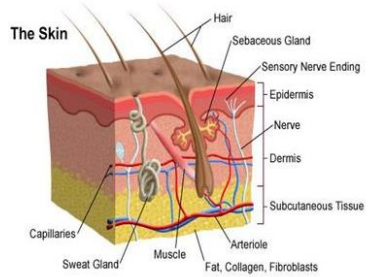


Endocrine system

Collection of glands: Pituitary and thyroid glands, as well as the ovaries and testes

It regulates, coordinates, and controls a number of body functions by secreting chemicals into the bloodstream. These secretions help control moods, growth and development, and metabolism



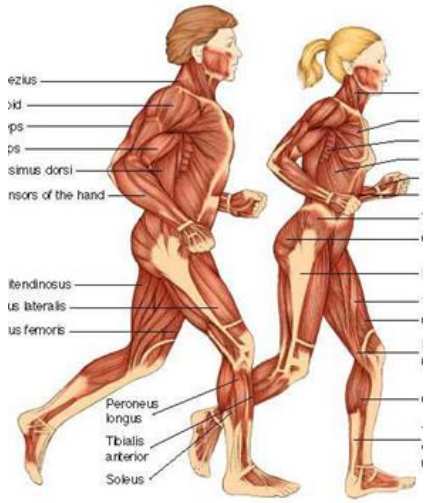


Integumentary system

Skin, hair, nails, and sweat glands

Its main function is to act as a barrier to protect the body from the outside world. It also functions to retain body fluids, protect against disease, eliminate waste products, and regulate body temperature

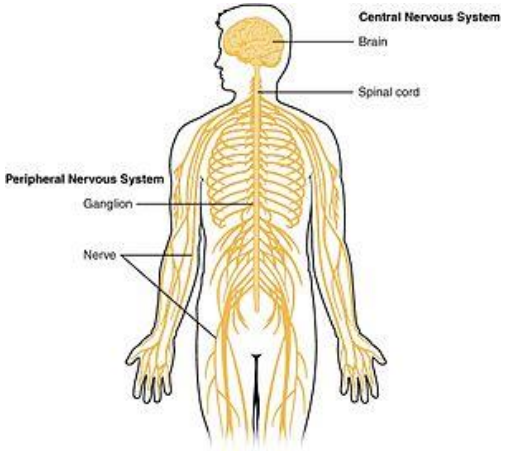
Metabolism – Specialization of organs



Muscular system

Muscle tissue

This system is made up of muscle tissue that helps move the body and move materials through the body. Quite simply, muscles move you. Muscles are bundles of cells and fibers that work in a simple way: they tighten up and relax

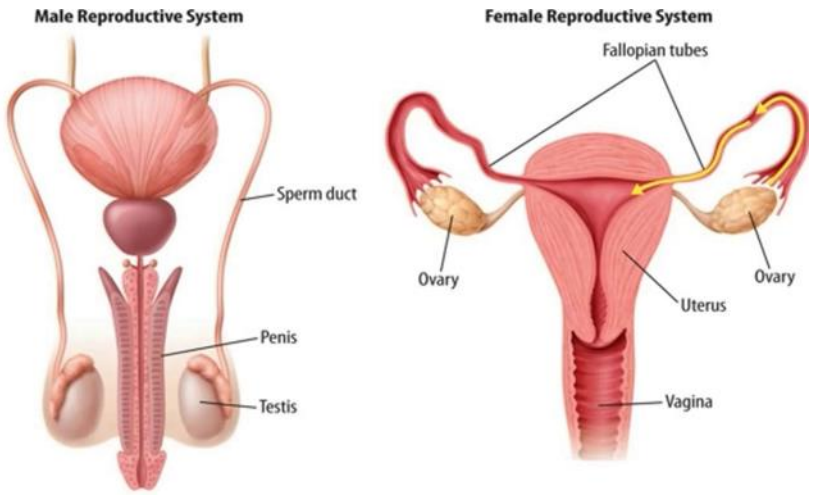


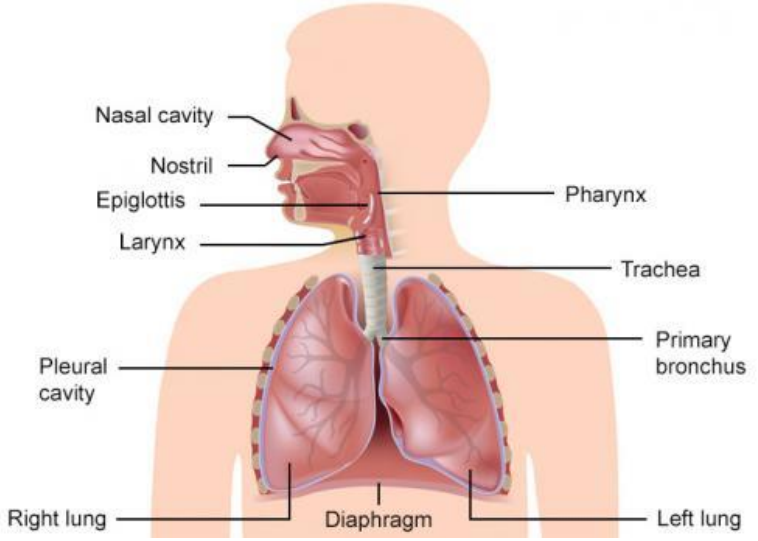
Nervous system

brain, spinal cord, and nerves

The nervous system is the control center of the human body. It receives and interprets stimuli and transmits impulses to organs. Your brain uses the information it receives to coordinate all of your actions and reactions

Metabolism – Specialization of organs





Reproductive system

uterus, penis, ovaries, and testes

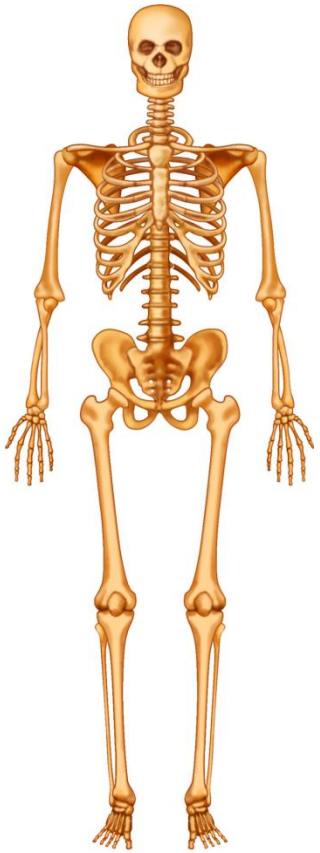
The human reproductive system ensures that humans are able to reproduce and survive as a species

Respiratory system

nose, larynx, trachea, diaphragm, bronchi, and lungs

The primary function of the respiratory system is to supply the blood with oxygen in order for the blood to deliver oxygen to all parts of the body. The respiratory system does this through breathing

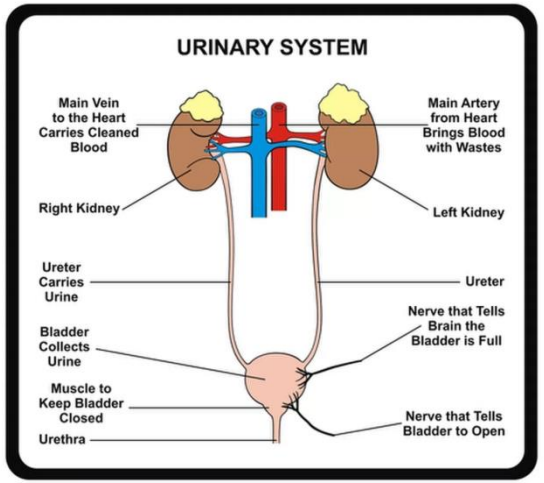
Metabolism – Specialization of organs



Skeletal system

bones, cartilage, and joints

The skeletal system provides the shape and form for our bodies in addition to supporting and protecting our bodies, allowing bodily movement, producing blood cells, and storing minerals



Urinary system

kidneys, ureters, urinary bladder, and urethra

The purpose of the urinary system is to filter out excess fluid and other substances from your bloodstream. Some fluid gets reabsorbed by your body but most gets expelled as urine

Sources

Video 1: Living things need energy: https://www.youtube.com/watch?v=x99snLJBhts
Video 2: Why do living things need energy? https://www.youtube.com/watch?v=m-DykNG-lMg
Video 3: Metabolism: https://www.youtube.com/watch?v=0kZLQGByXN4
Video 4: Overview of metabolism: Anabolism and catabolism | Biomolecules | MCAT | Khan Academy
https://www.youtube.com/watch?v=ST1UWnenOo0
Video 5: Video on my website
Video 6: Metabolic Regulation: https://www.youtube.com/watch?v=GRkL2WToSCo
Video 6.1: Enzyme regulation: https://www.youtube.com/watch?v=0jy6m-LGr1s
Video 7: Enzymes, Feedback Inhibition, and Allosteric Regulation: https://www.youtube.com/watch?v=LKiXfqaWNHI
Video 8: Enzymes -Allosteric Enzymes: https://www.youtube.com/watch?v=fyww37XOrXo
Video 9: Role of glycogen phosphorylase: https://www.youtube.com/watch?v=cWziKUftOc4
Video 10: 145-Regulation through Compartmentation: https://www.youtube.com/watch?v=BUhdgFskWs4
Video 11: Biology: Cell Structure I Nucleus Medical Media : https://www.youtube.com/watch?v=URUJD5NEXC8
Video 12: Human Body Systems and Functions: https://www.youtube.com/watch?v=qhajGKS5thQ

Useful video links:
Biochemistry introduction to metabolism tutorial by Prof. P M Bingham
https://www.youtube.com/watch?v=FgAuslfreKs
Basics of metabolism | MCAT | Khan Academy
https://www.youtube.com/watch?v=wQ1QGZ6gJ8w
A general overview of the major metabolic pathways by Prof. D. P. Silva
http://homepage.ufp.pt/pedros/bq/integration.htm

UNIT 2: Introduction to hormones & neurotransmitters

Prof K Syed

Department of Biochemistry & Microbiology

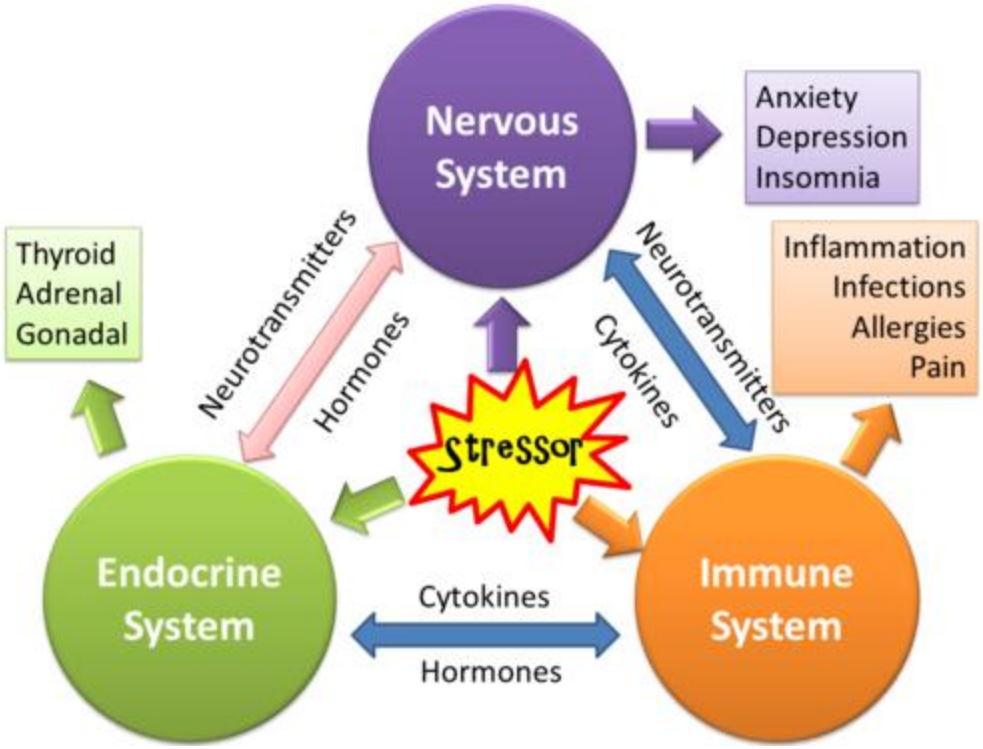
University of Zululand

Room no. 247

Topics

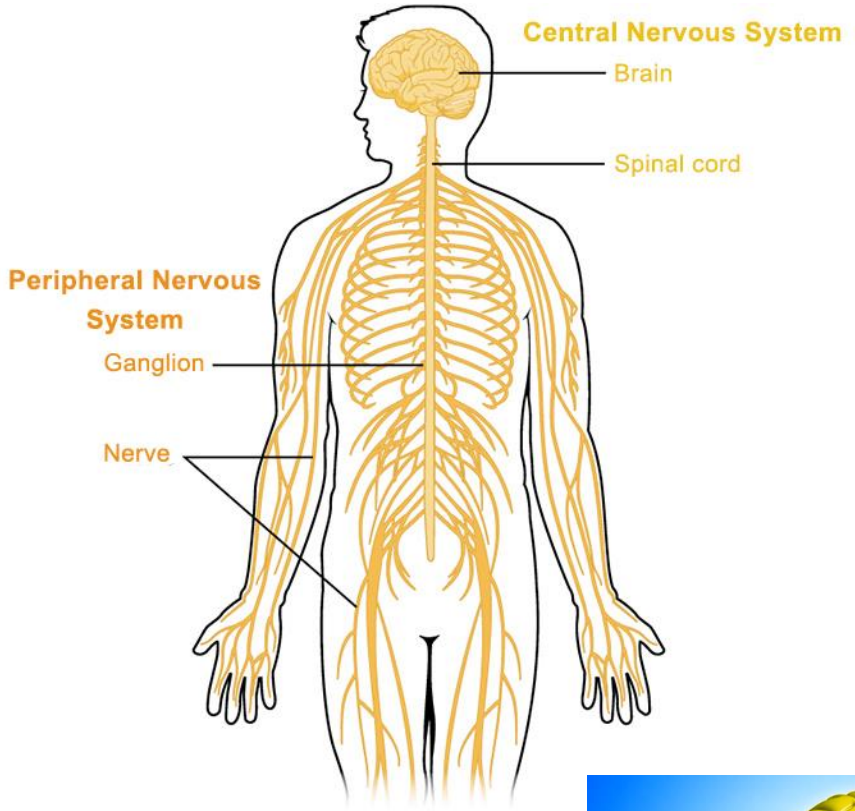
- Major systems of human body
- Glands
- Hormones vs neurotransmitters
- Classification of hormones
  - Solubility
  - Where they function
  - Chemical structure
- Briefing on synthesis of hormones/neurotransmitters
- Physiological role of hormones/neurotransmitters

Major system of human body

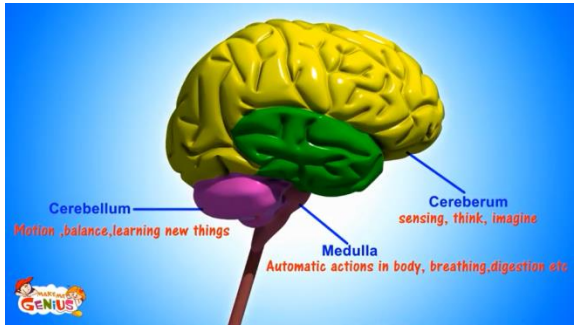


https://www.quora.com/What-is-the-difference-between-hormones-and-neurotransmitters

Nervous system – Central Nervous system



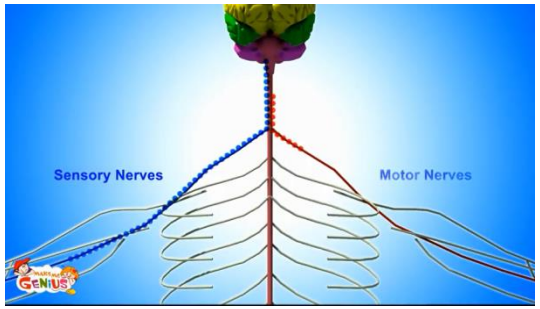
- Controls all the actions of our body
- Our nervous system is divided in two components:
  - central nervous system - brain and spinal cord
  - peripheral nervous system - which encompasses nerves outside the brain and spinal cord.
- These two components cooperate at all times to ensure our lively functions: we are nothing without our nervous system
- Brian has 3 major parts
  - Cereberum – sensing, thinking & imagination
  - Cerebellum – motion, balance & learning new things
  - Medulla – involuntary actions in the body (digestion, heart beat and breathing etc.,)

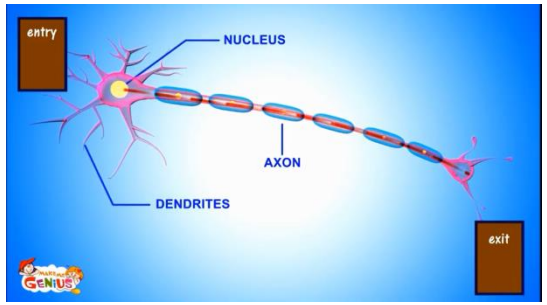


Video 1

https://qbi.uq.edu.au/brain/brain-anatomy/peripheral-nervous-system

Nervous system – peripheral nervous system





- Peripheral nervous system - which encompasses nerves outside the brain and spinal cord.
- Two functions
  - Sensory nerves – carry messages from body (senses) to the brain
  - Motor nerves - carry messages from brain to the body
- Nerves are made of neurons
- Neuron has three major parts
  - Cell body – contains nucleus, maintain the neuron's structure and provide energy to drive activities
  - Dendrites – receive stimulation and pass to cell body
  - Axon – conducts electrical impulses away from nerve cell body

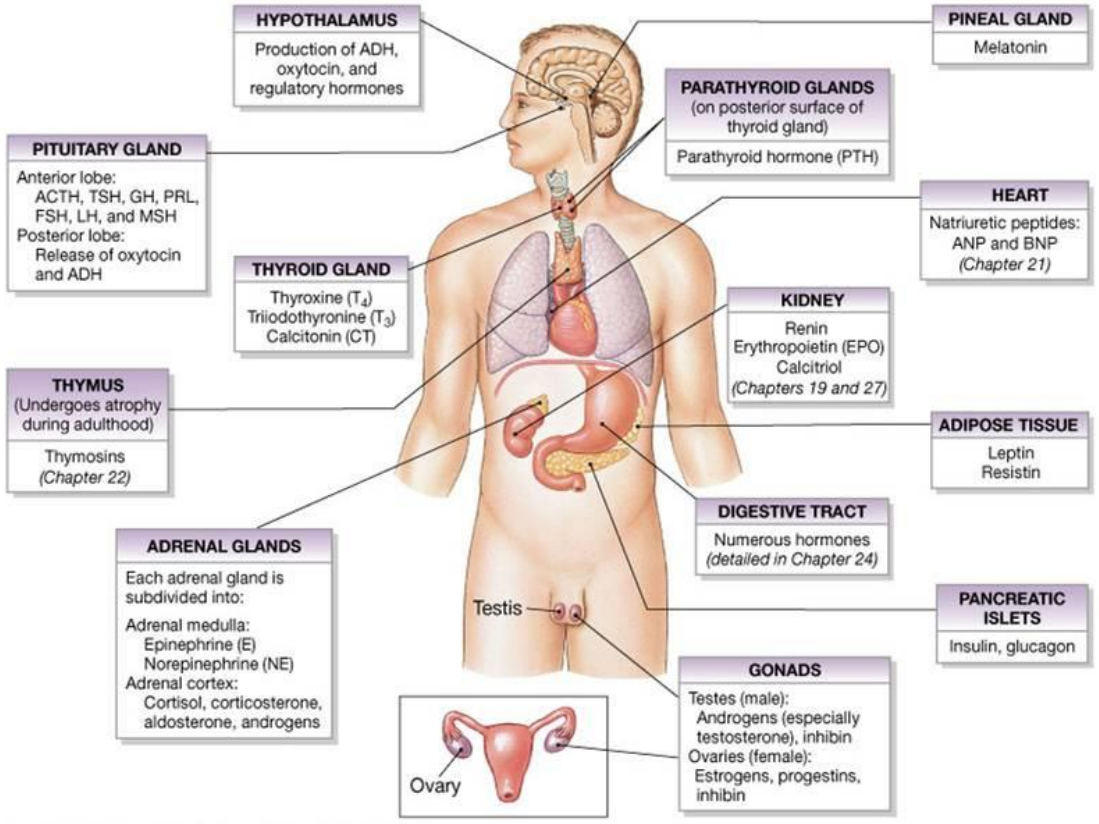
https://qbi.uq.edu.au/brain/brain-anatomy/peripheral-nervous-system

Neurotransmitters functions

Neurotransmitters	Major known function/diseases
Dopamine	• Critical for memory and motor skills. • Deficiency in dopamine production is associated with Parkinson's disease, a degenerative condition causing "shaking palsy"
Norepinephrine (also a hormone)	• Neuromodulator optimizes brain function. • As part of bodies fight or flight hormone. • Norepinephrine quickly provides an accurate assessment of danger or stressful situations.
Epinephrine (also a hormone)	• Activates muscle adenylate cyclase, thereby stimulates glycogen breakdown. • Promotes lipolysis in adipose tissue. • Promotes Glycogenolysis and Gluconeogenesis in Liver.
Histamine	• Involved in allergic responses as well as in the control of acid secretion by the stomach
Serotonin	• It is popularly through to be a contributor to feelings of well-being and happiness. • Important factor in mood, depression, anxiety, sleep quality, emotions and regulation of appetite and body temperature. However, biological functional role of serotonin is not clear.
Acetylcholine	• Its basic functions involve the control of skeletal muscles via activation of the motor neurons as well as stimulating the muscles of the body
Gamma-aminobutyric acid or GABA	• The role of GABA is to inhibit or reduce the activity of the neurons or nerve cells. • People with too little GABA tend to suffer from anxiety disorders. • If GABA is lacking in certain parts of the brain, epilepsy results.
Glutamate	• Glutamate is the principal excitatory neurotransmitter in the brain.
Nitric oxide	• Plays a role in affecting smooth muscles, relaxing them to allow blood vessels to dilate and increase blood flow to certain areas of the body.

Video 2

Glands and their secreted hormones

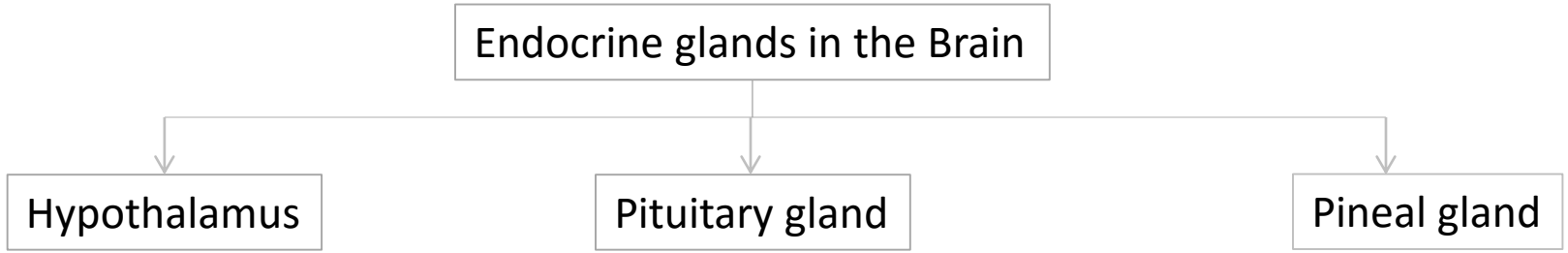


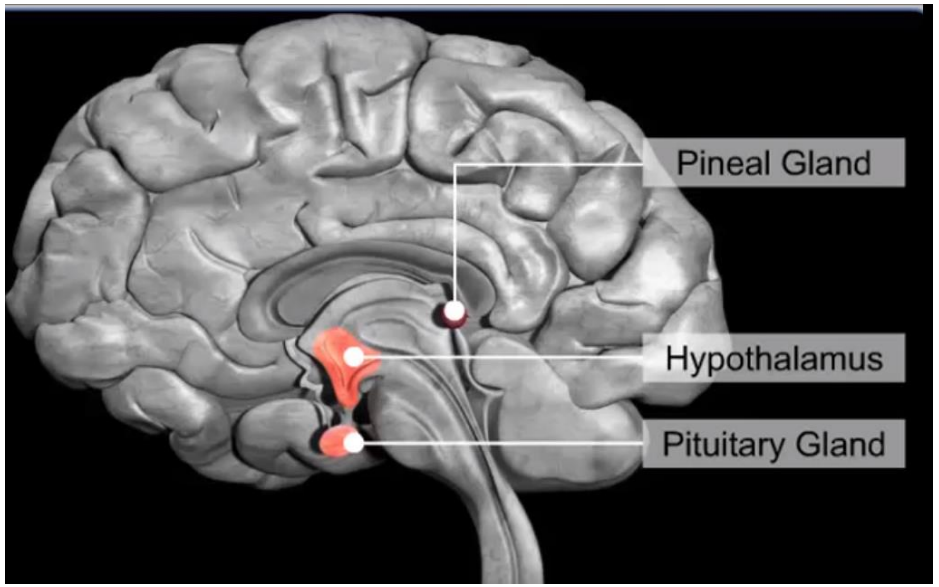
- A gland is a just any structure that makes and secrets a hormone

http://www.austincc.edu/apreview/PhysText/Endocrine.html

Video 3

Hypothalamus, Pituitary and Pineal glands



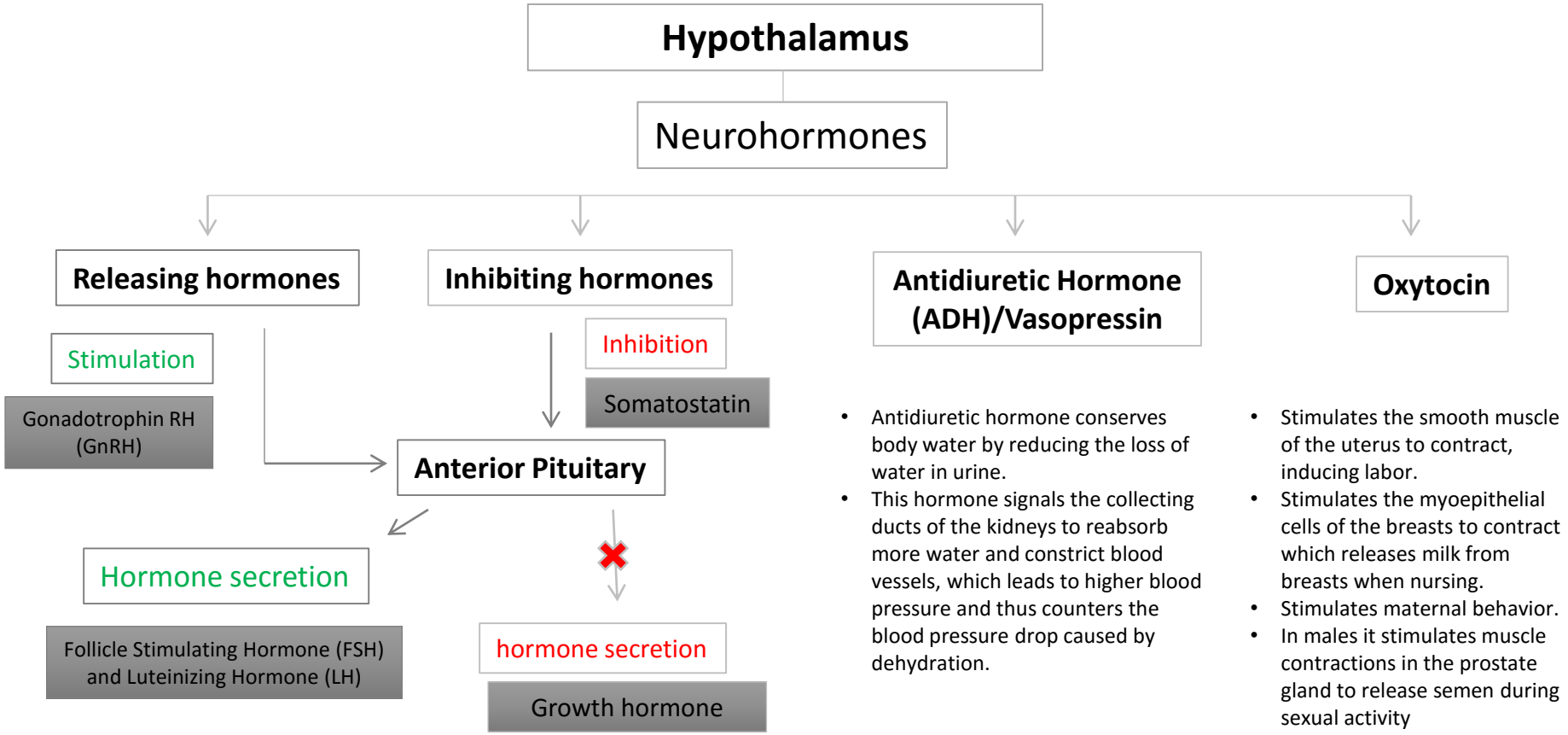


The endocrine glands of the brain are crucial in regulating mood, growth and development, metabolism, sexual functions & reproductive processes in the human body.

Video 4 & http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html#hypothal

http://www.austincc.edu/apreview/PhysText/Endocrine.html

Hypothalamus

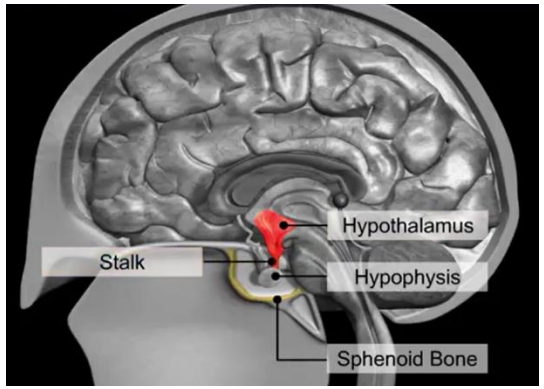


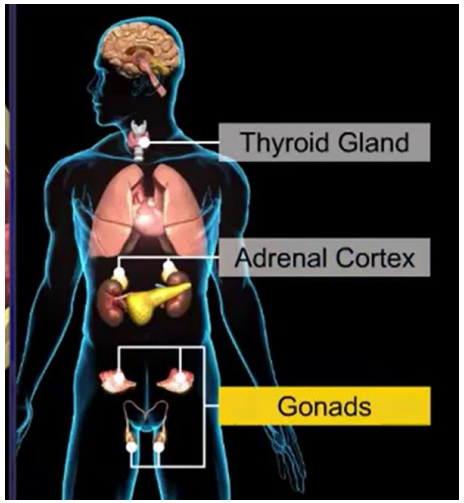
- Neurohormones – regulate the synthesis and secretion of Pituitary hormones
- These hypothalamic hormones pass through the exons and are released from their nerve endings into the Pituitary and into the portal circulatory system
- This hypothalamus and pituitary system is direct proof of coordination between the hormonal and nervous system
- Maintains homeostasis inside the body and regulates most of its physiological activities.

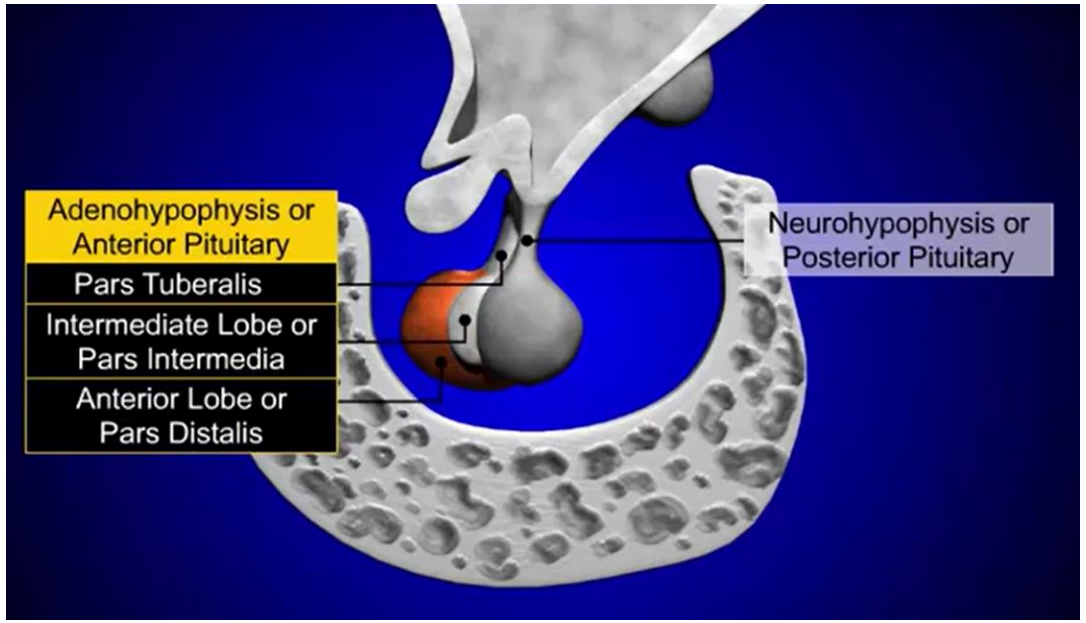
Video 4 & http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html#hypothal

http://www.austincc.edu/apreview/PhysText/Endocrine.html

Pituitary gland



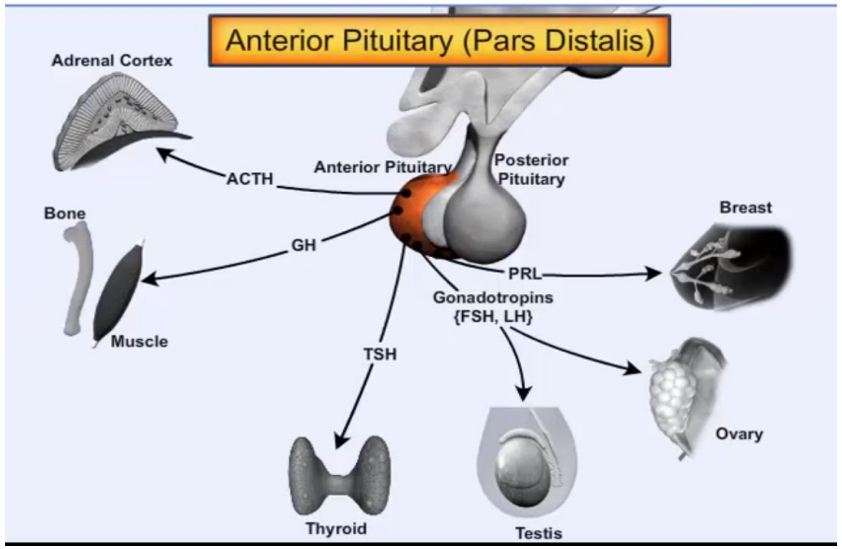


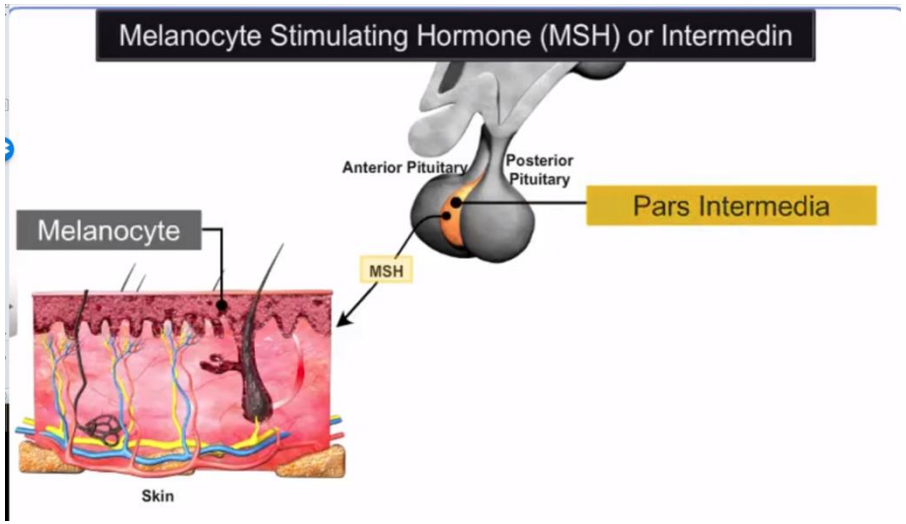


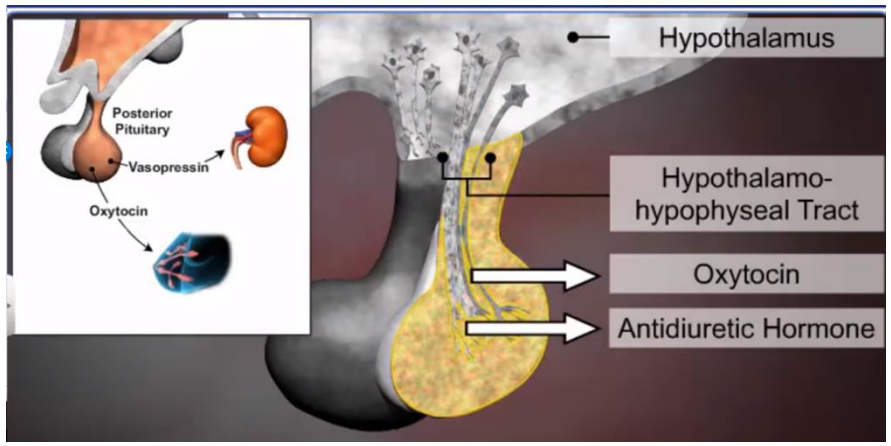
- Pituitary gland is the smallest endocrine gland yet it is called the master of endocrine glands because it produces the hormones that control the thyroid gland, adrenal cortex and gonads.

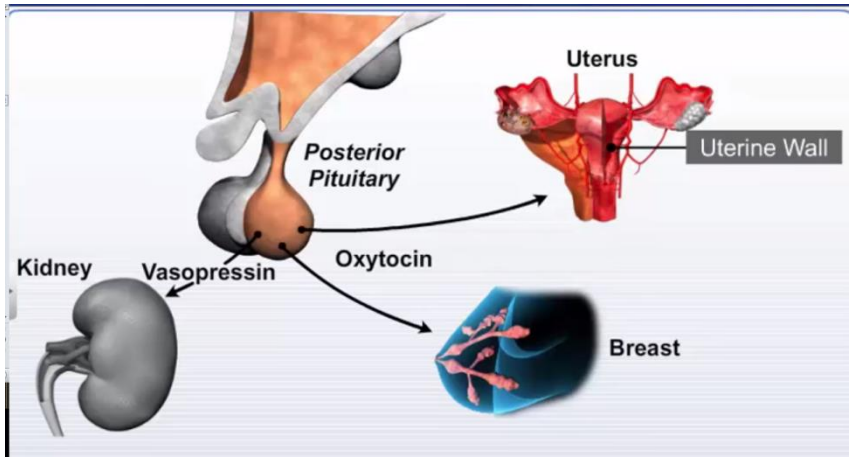
Video 4 & http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html#hypothal

Pituitary gland







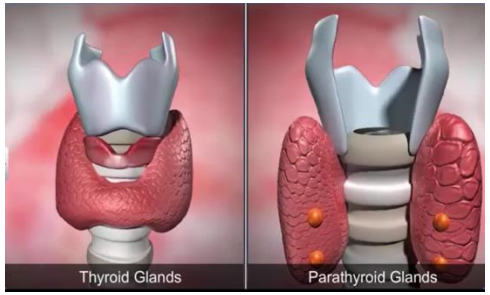


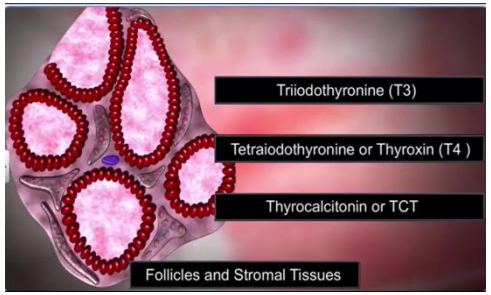
Video 4 & http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html#hypothal

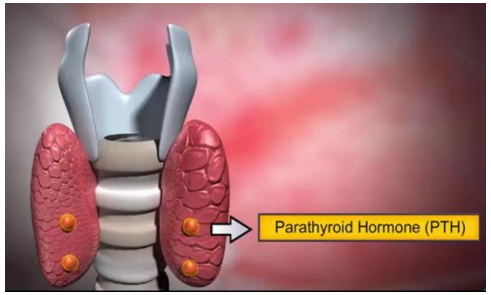
Pituitary gland hormones and their functions

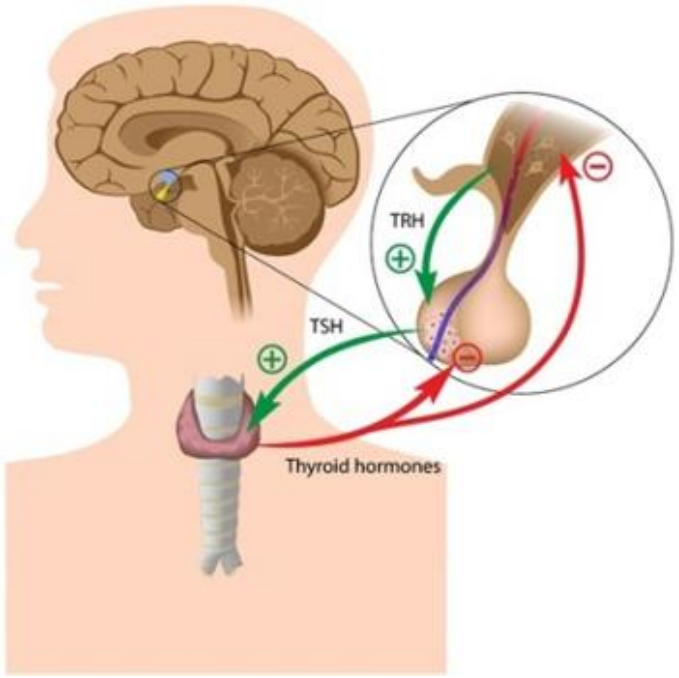
Pituitary gland parts	Hormones	Functions
Anterior pituitary gland	Growth hormone (GH) or Somatotropin	Regulates growth, metabolism and body composition
	Prolactin (PL)	Stimulates milk production
	Luteinizing hormone (LH) and Follicle Stimulating Hormone (FSH) (gonadotrophins)	Act on the ovaries or testes to stimulate sex hormone production, and egg and sperm maturity
	Adrenocorticotropic Hormone (ACTH) or Corticotropin	Stimulates the adrenal glands to secrete steroid hormones, principally cortisol
	Thyroid Stimulating Hormone (TSH) or Thryotropin	Travels to the thyroid gland (target cells) where it stimulates the release of thyroid hormones in response to low temperatures, stress, and pregnancy
Intermediate pituitary gland	Melanocyte-stimulating hormone (MSH)	Acts on cells in the skin to stimulate the production of melanin
Posterior pituitary	Anti-diuretic hormone (ADH) (also called vasopressin)	Controls water balance and blood pressure
	Oxytocin	Stimulates uterine contractions during labour and milk secretion during breastfeeding

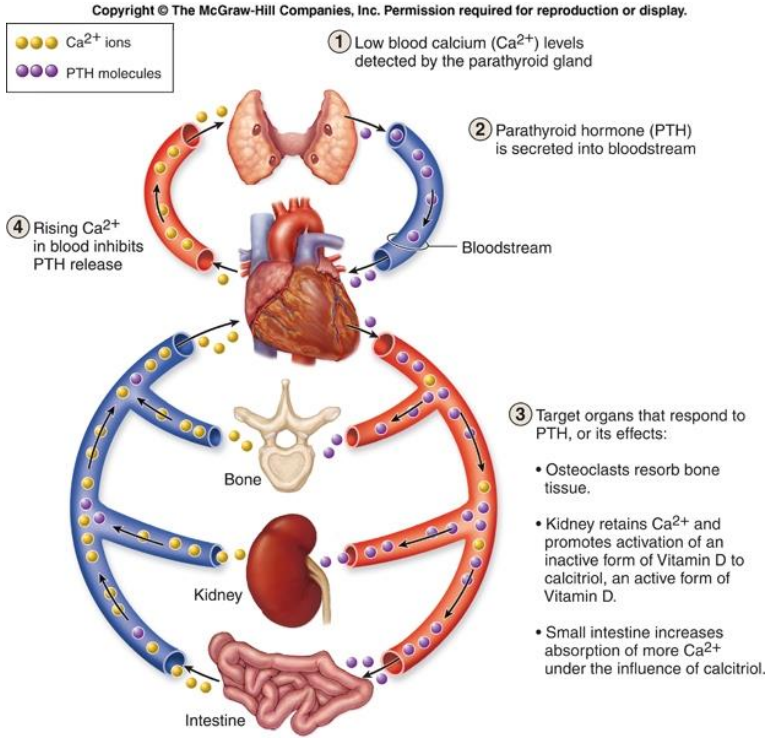
Thyroid and parathyroid glands











http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html#parathyroid

Video 5

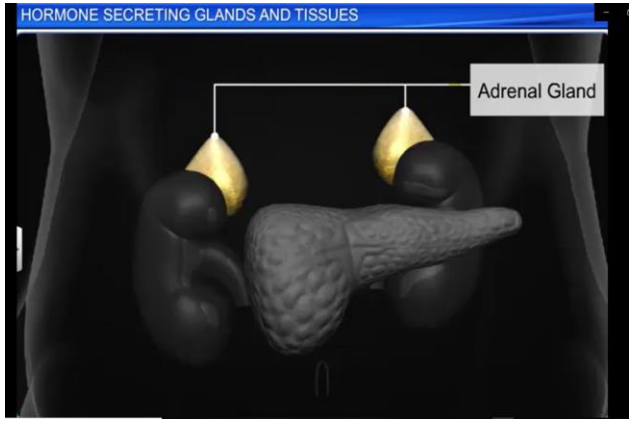
Thyroid and parathyroid glands

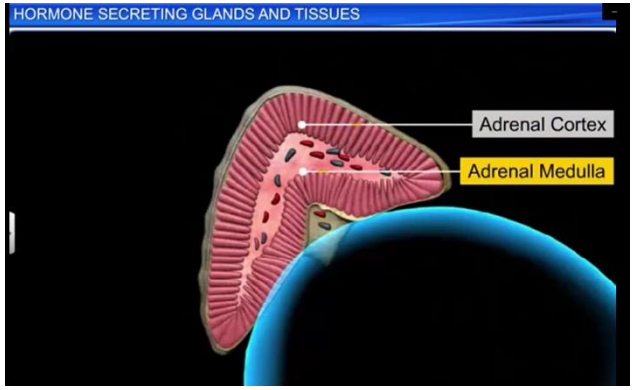
Gland	Hormones	Functions/diseases	
Thyroid	Triiodothyronine (T3) Thyroxine (T4)	• Help regulate tissue growth and development • Support the formation of red blood cells • Control the metabolism of proteins carbohydrates and fats • Maintain the water and electrolyte balance and regulate the basal metabolic rate (BMR)	
		Hyperthyroidism • High metabolic rate • Weight loss • Hyperactivity • Heat intolerance • Goiter	**Hypothyroidism** • Low metabolic rate • Weight gain • Sluggishness • Sensitivity to cold
	Calcitonin	• Regulate calcium concentration in body fluids. Calcitonin decreases the concentration of calcium in the blood where most of it is stored in the bones; it stimulates osteoblast activity and inhibits osteoclast activity, resulting in new bone matrix formation.	
Parathyroid	Parathyroid hormone (PTH)	• Regulator of calcium and phosphorus concentration in extracellular fluid. PTH has the opposite effect of calcitonin. • PTH stimulates osteoclasts which increases blood calcium levels. • PTH causes reabsorption of Ca^{+2} from kidneys so it is not excreted in the urine • PTH stimulates synthesis of calcitriol (hormone made in the kidney which the active form of Vitamin D which increases Ca+2 absorption from small intestine)	

http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html#parathyroid

Video 5

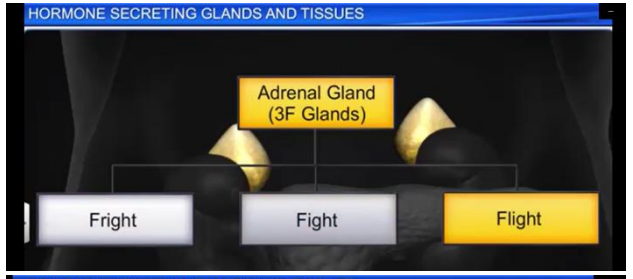
Adrenal glands





- The yellowish triangular shaped glands are also called supra-renal glands because they are situated on the top of the anterior part of the kidneys.
- The adrenal glands are also known as 3F glands. The 3F's stands for fright, fight or flight.

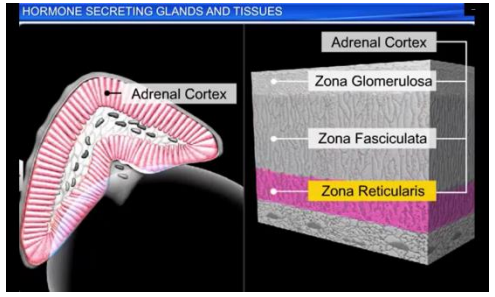
- These glands also called 4S glands where the four S stands for sugar metabolism, salt metabolism, sex hormones and source of energy.

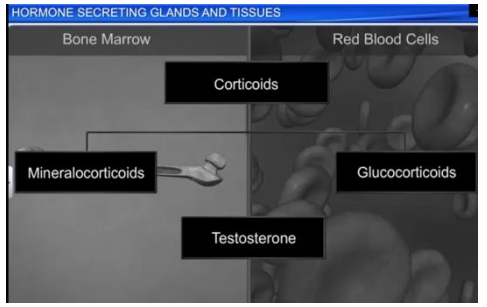


http://www.austincc.edu/apreview/PhysText/Endocrine.html

Video 6 (from 0:58 to 6:29)

Adrenal glands : Adrenal cortex hormones & their functions



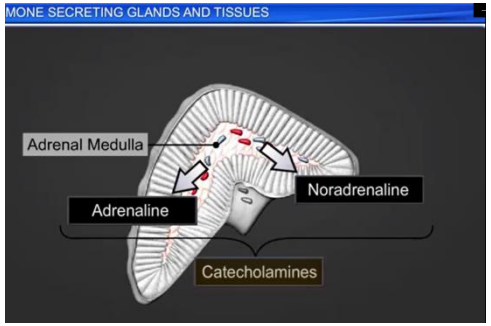


Mineralocorticoids		**The primary function of mineralocorticoids is to regulate the balance of water and electrolytes in our body.**
	Aldosterone	• Acts on the renal tubules on the kidneys and stimulates the reabsorption of sodium and water and the removal of potassium and phosphate ions. • Also helps to maintain the body fluid volume, electrolytes, osmotic pressure and blood pressure
Glucocorticoids		• Involved in carbohydrate metabolism • Chief function is to stimulate Gluconeogenesis, Lipolysis and Proteolysis. • Also inhibit the utilization of amino acids and cellular uptake.
	Cortisol	• Provides anti-inflammatory reactions, helps to maintain the cardiovascular system and the functions of the kidneys • Cortisol stimulate red blood cell production and suppresses the immune response
Testosterone (male hormone)		• Stimulate the development of secondary sexual characters such as axial hair, pubic hair, facial hair and deepening of the voice.

http://www.austincc.edu/apreview/PhysText/Endocrine.html

Video 6 (from 0:58 to 6:29)

Adrenal glands : Adrenal medulla hormones & their functions

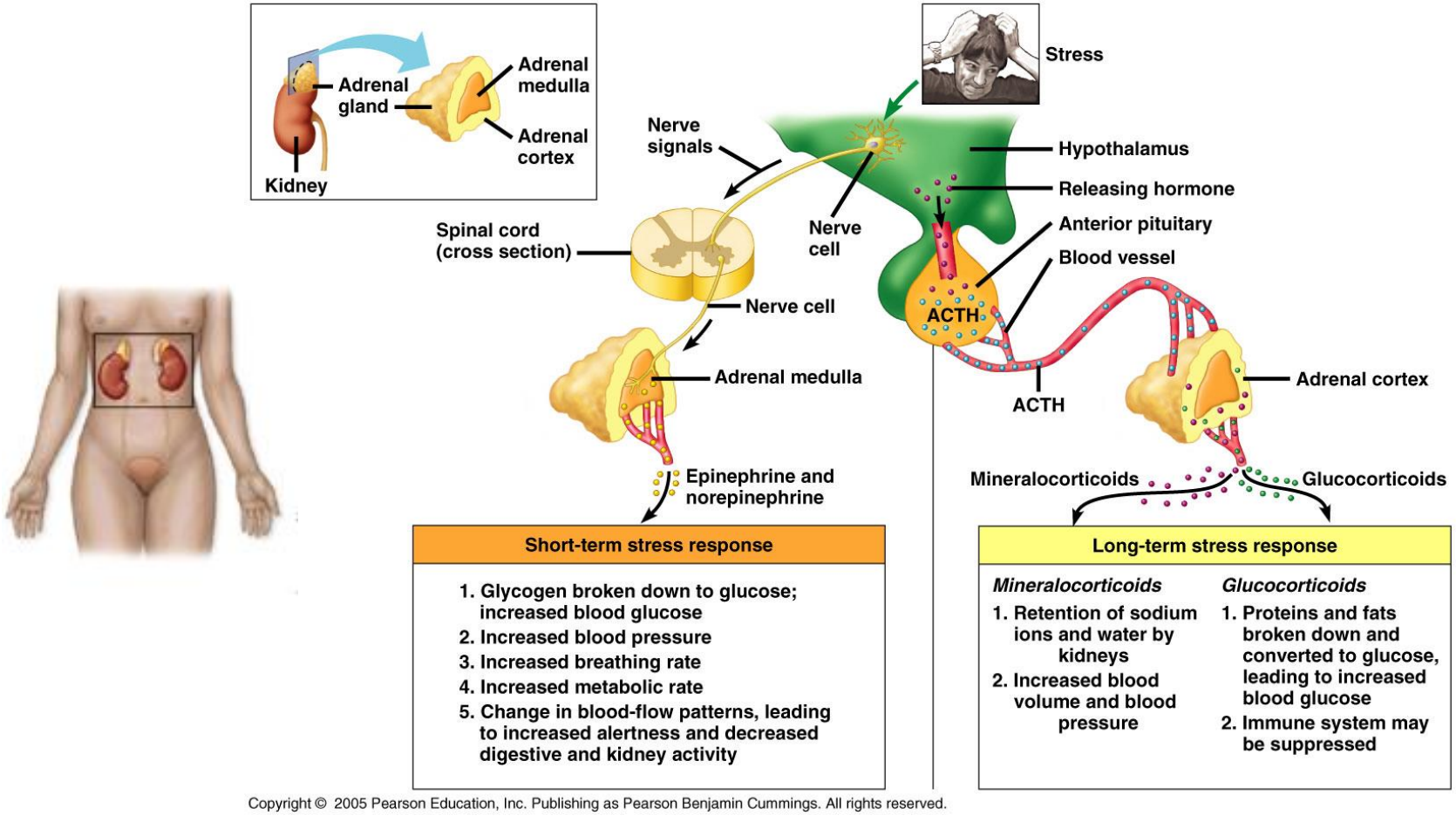


Catecholamine's	• **Increase the strength of heart contractions, heart beat and rate of respiration** • **Also increase alertness, sweating and papillary dilation** • **Stimulates the breakdown of glycogen, proteins and lipids** • **In short, catecholamine's are rapidly secreted in response to stress and emergency situations and or thus also called emergency hormones or hormones of flight or fight.**

http://www.austincc.edu/apreview/PhysText/Endocrine.html

Video 6 (from 0:58 to 6:29)

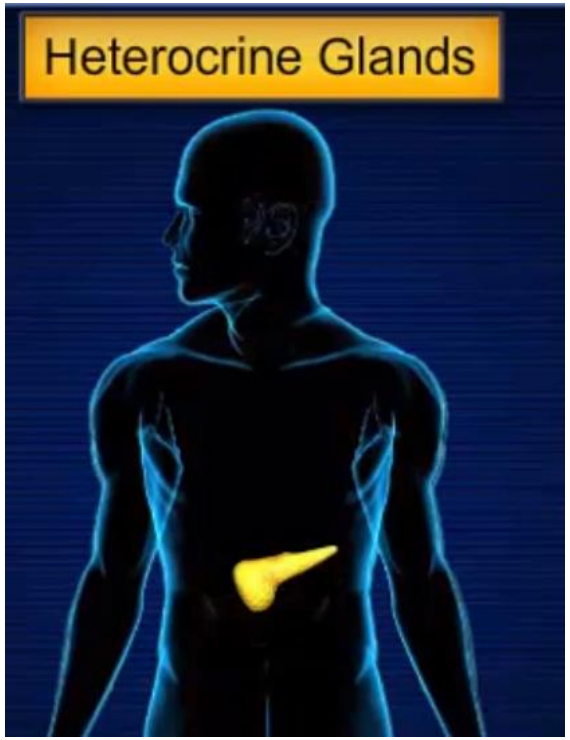
Adrenal glands : over-view

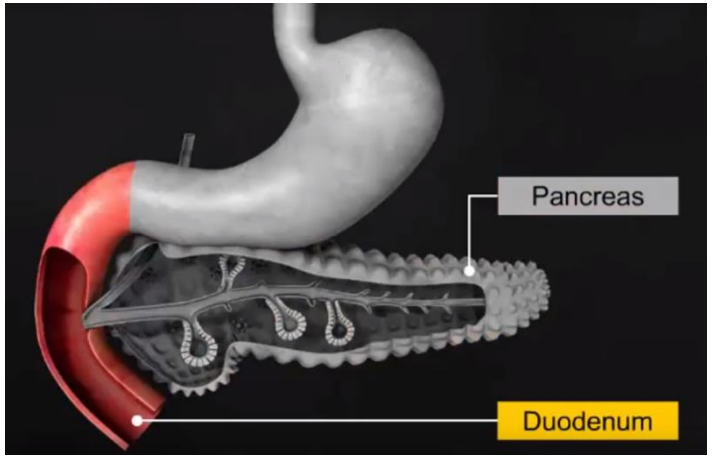


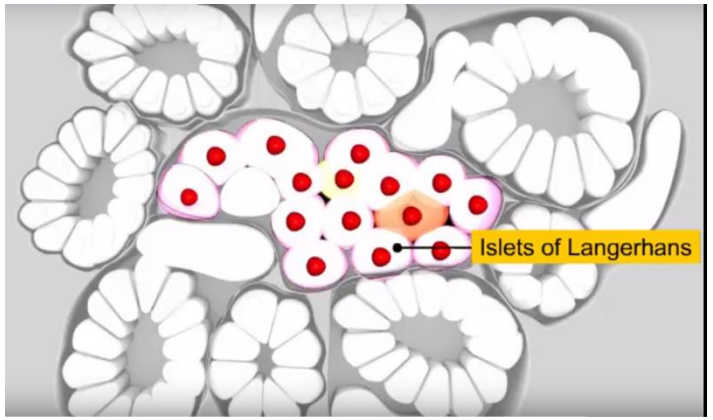
http://www.austincc.edu/apreview/PhysText/Endocrine.html

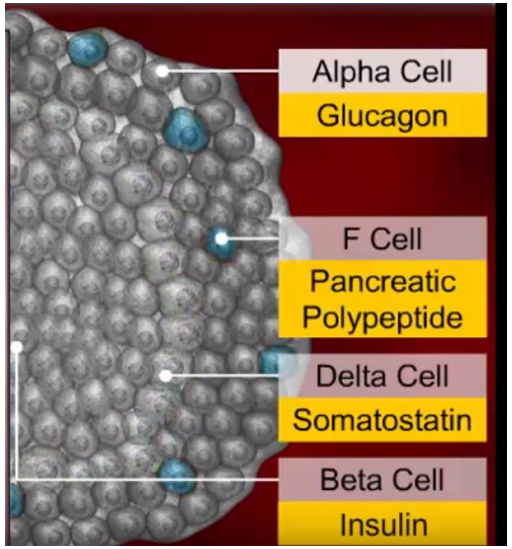
Video 6 (from 0:58 to 6:29)

Pancreas





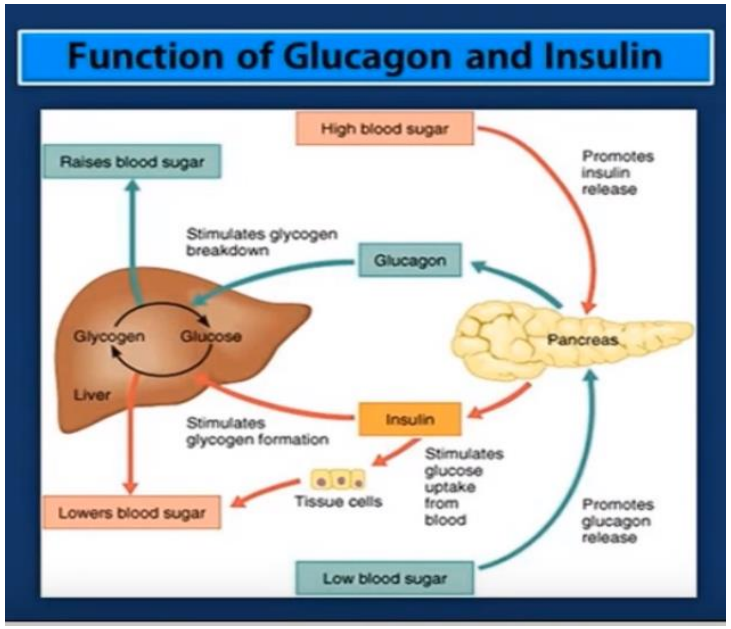




http://www.austincc.edu/apreview/PhysText/Endocrine.html

Video 7 (from 0:28 to 1:30) & Video 8

Pancreas

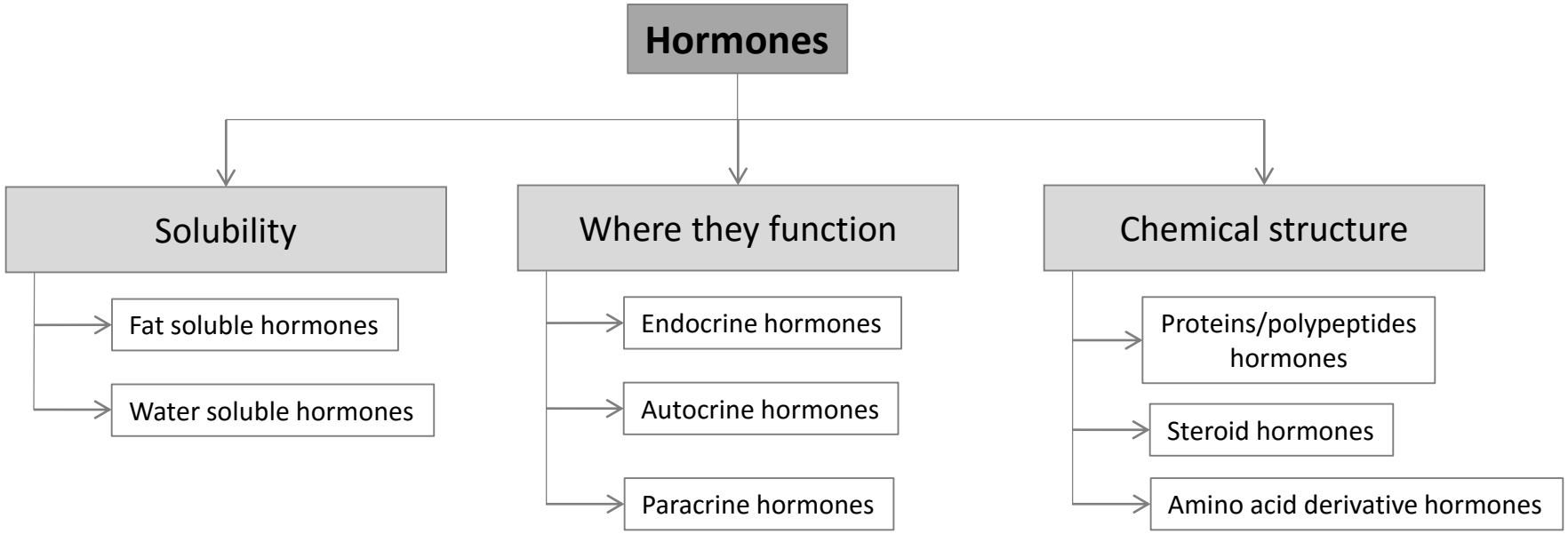


Insulin	• **Reduces the blood glucose concentration** • **In liver it promotes glycogen synthesis and stops glucose production** • **Promotes glucose uptake by muscle cells to use it for energy and store glucose as glycogen (glycogen synthesis)** • **Promotes glucose uptake by adipose tissue to store it as fat (lipogenesis)** • **Overall, it stimulates cell growth and differentiation by increasing the synthesis of glycogen, proteins and triacylglycerol** • **Hormone releases when glucose concentration is high in blood**
Glucagon	• Increases blood glucose concentration • In liver it promotes glycogen breakdown to release as glucose (Glycogenolysis) and also synthesis of glucose (Gluconeogenesis) • Hormone releases when glucose concentration is low in blood
Somatostatin	• Somatostatin, also known as growth hormone-inhibiting hormone (GHIH) or by several other names, is a peptide hormone that regulates the endocrine system and affects neurotransmission and cell proliferation via interaction with G protein-coupled somatostatin receptors and inhibition of the release of numerous secondary hormones. Somatostatin inhibits insulin and glucagon secretion

http://www.austincc.edu/apreview/PhysText/Endocrine.html

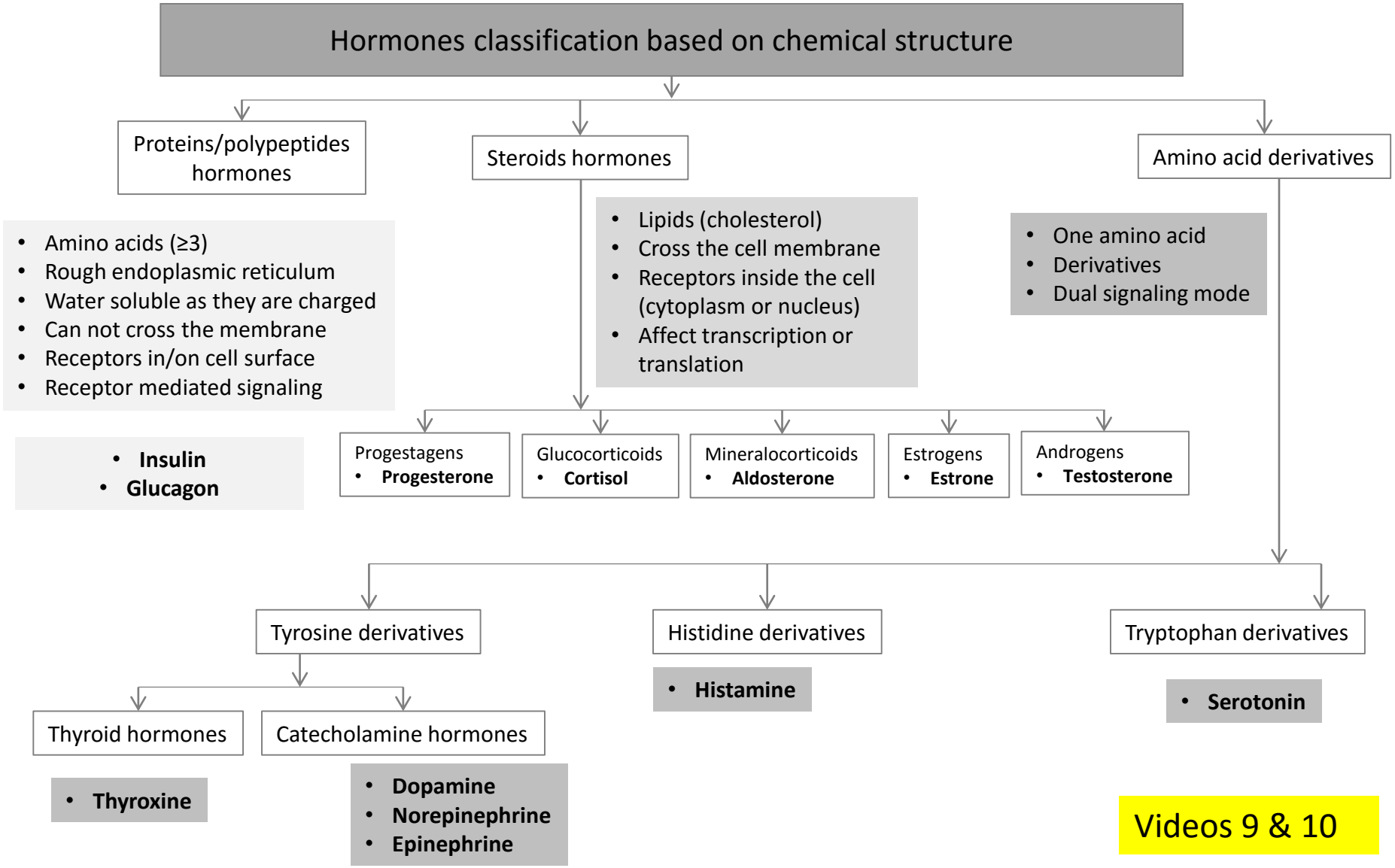
Video 7 (from 0:28 to 1:30) & Video 8

Classification



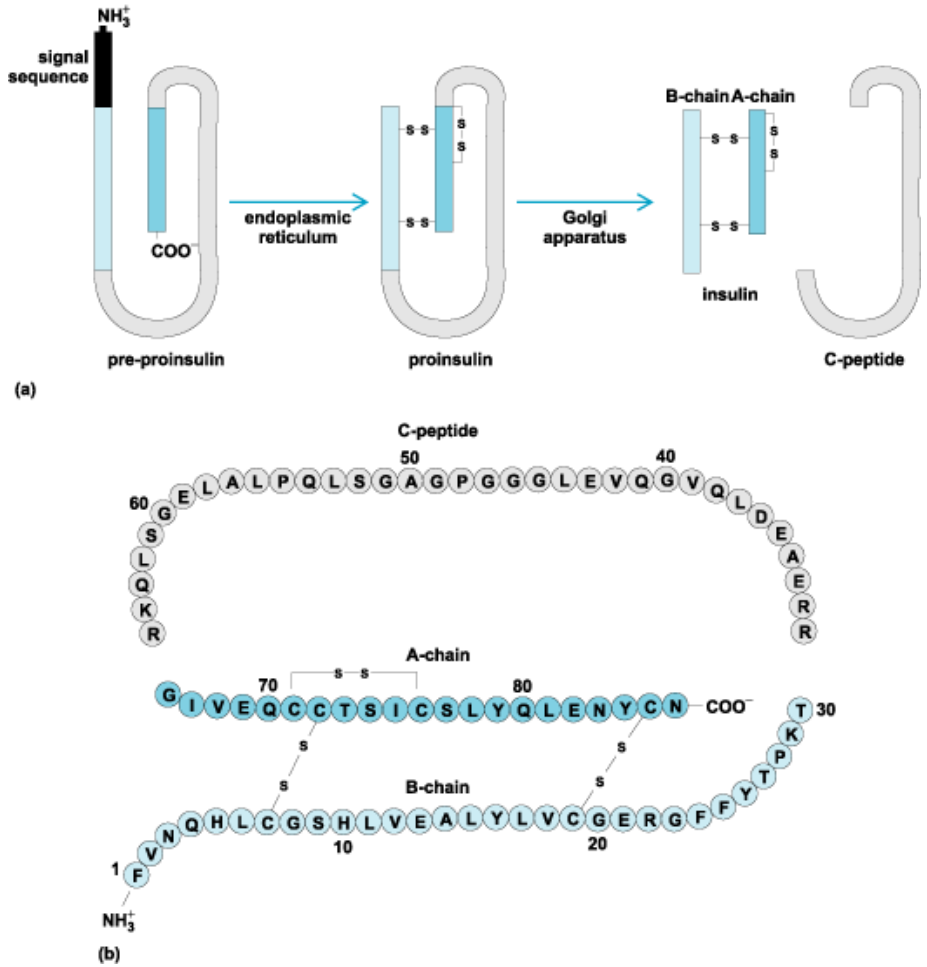
Videos 9 & 10

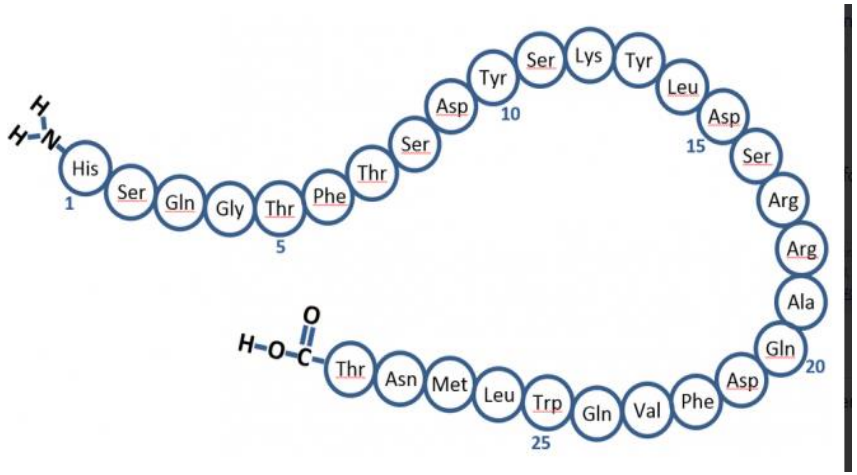
Hormones classification



Videos 9 & 10

Insulin & Glucagon

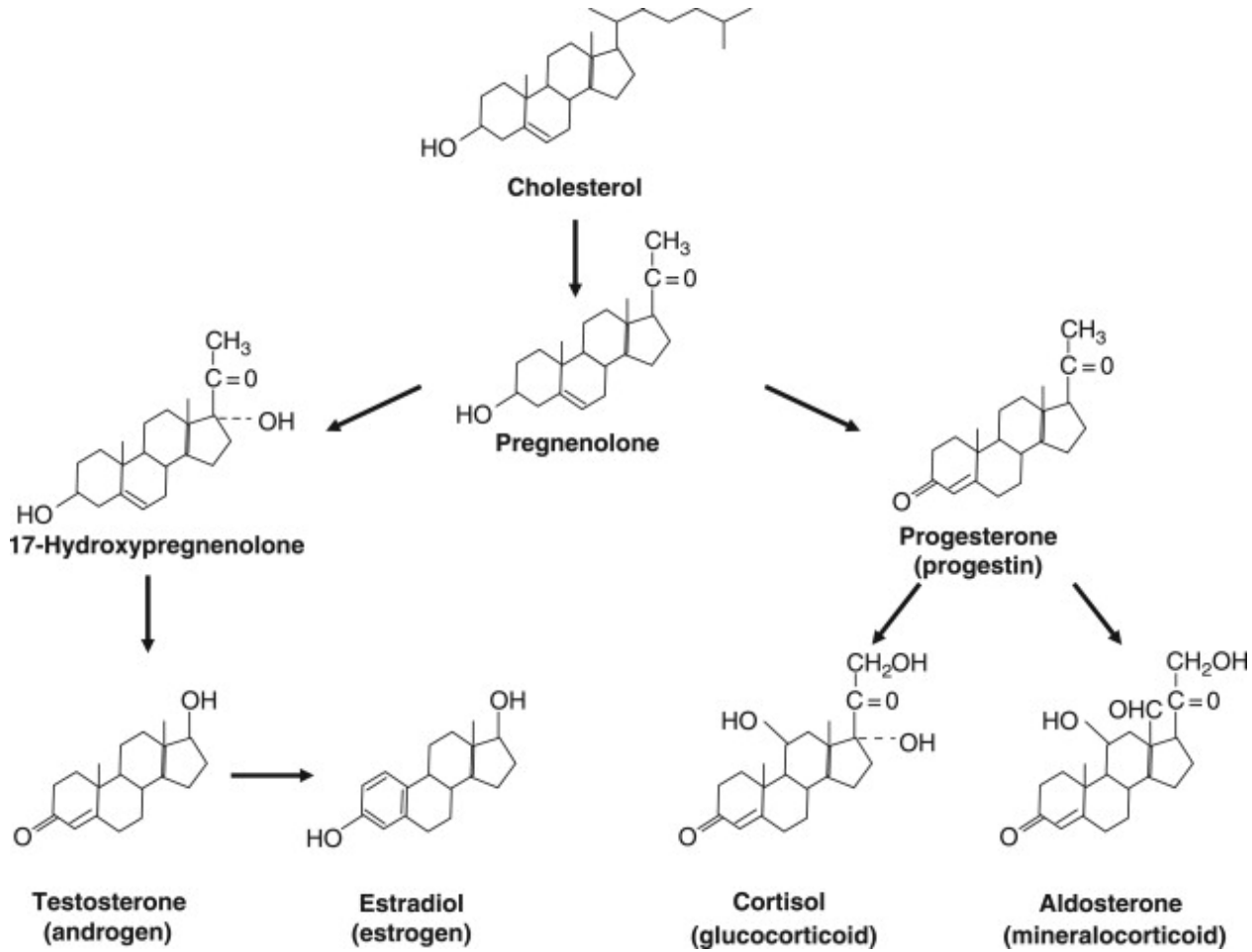




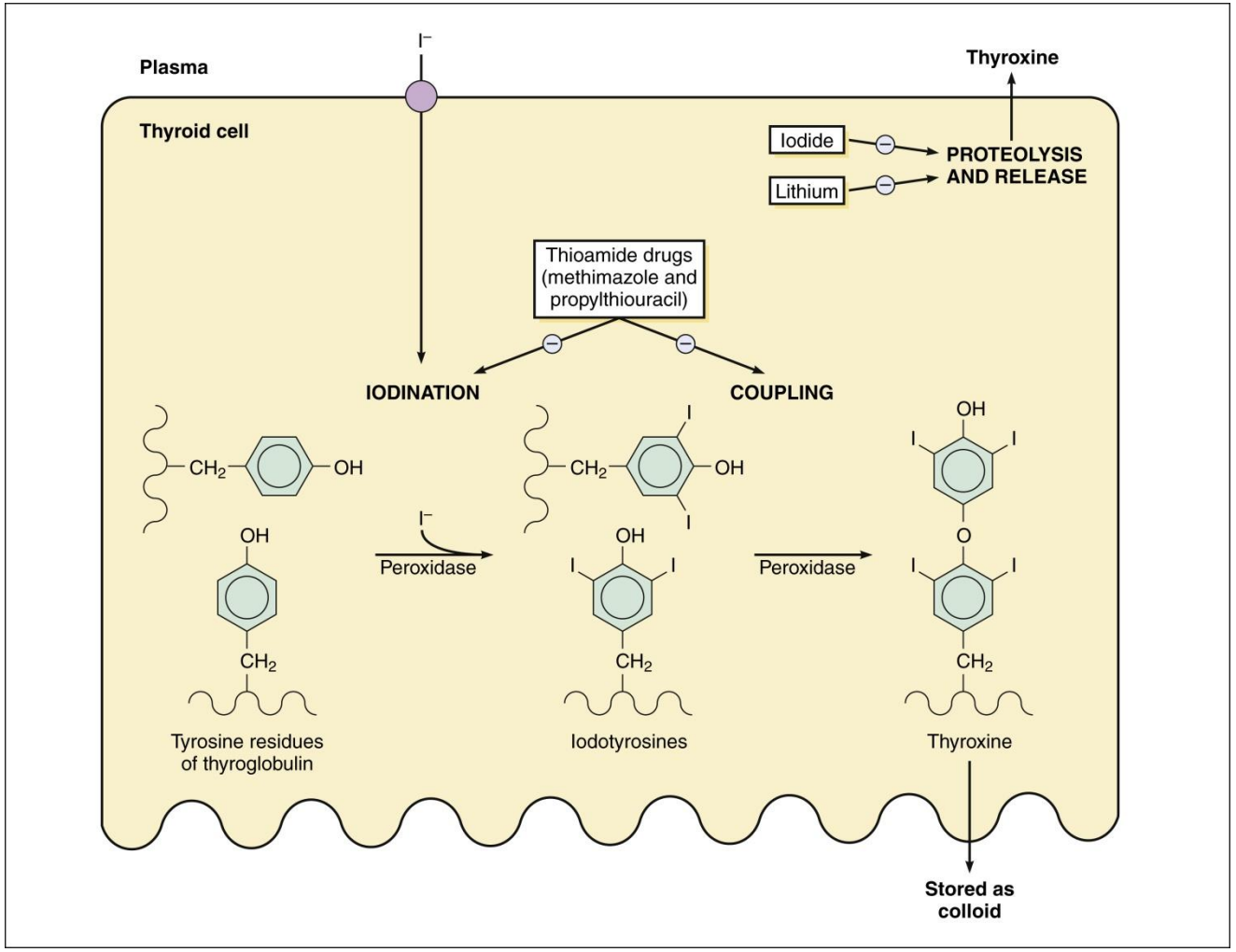
http://www.namrata.co/insulin-biosynthesis-secretion-and-action/

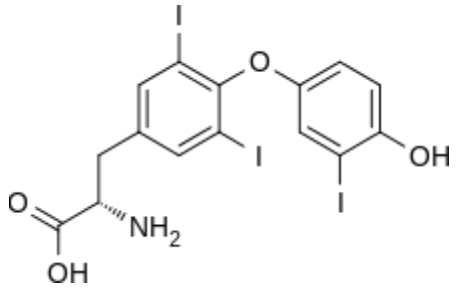
https://www.diapedia.org/metabolism-insulin-and-other-hormones/51040851520/glucagon

Steroid hormones

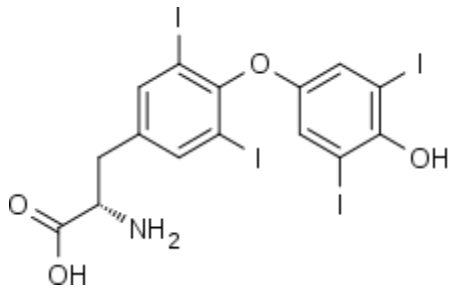


Amino acid derivatives: Thyroid hormones





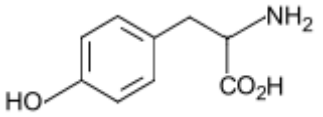
Triiodothyronine (T3) – 20%



Tetraiodothyronine (T4) – 80%

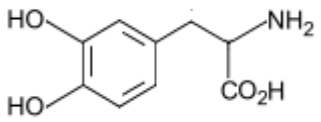
https://basicmedicalkey.com/thyroid-drugs-2/

Amino acid derivatives: Catecholamine



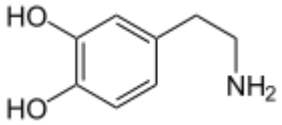
Tyrosine

Tyrosine hydroxylase



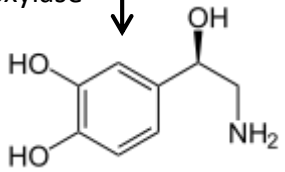
DOPA

DOPA decarboxylase



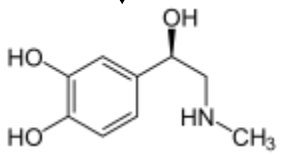
Dopamine

DOPA β-hydroxylase



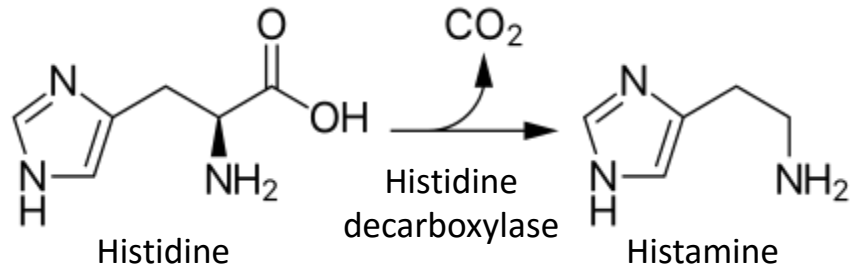
Norepinephrine

Phenylethanolamine *N*-methyltransferase

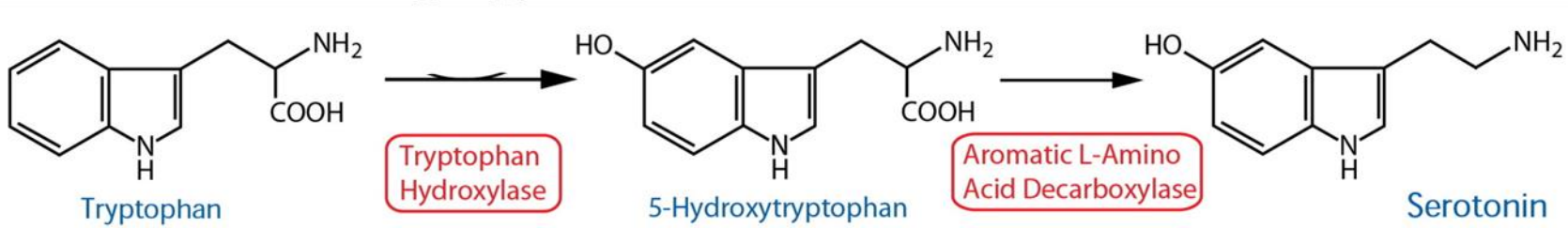


Epinephrine

Amino acid derivatives: Histamine & Serotonin



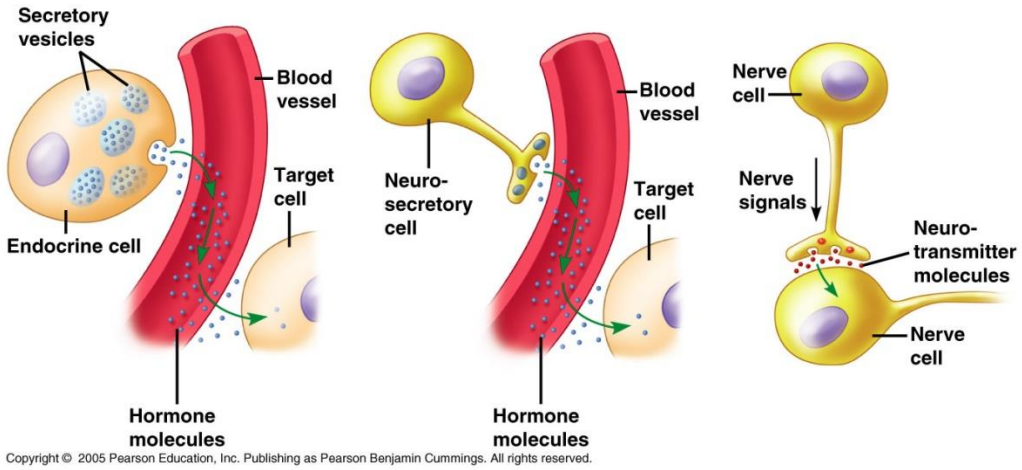
Histamine is derived from the decarboxylation of the amino acid histidine, a reaction catalyzed by the enzyme L-histidine decarboxylase



http://www.wormatlas.org/neurotransmitterstable.htm

Hormones vs neurotransmitters

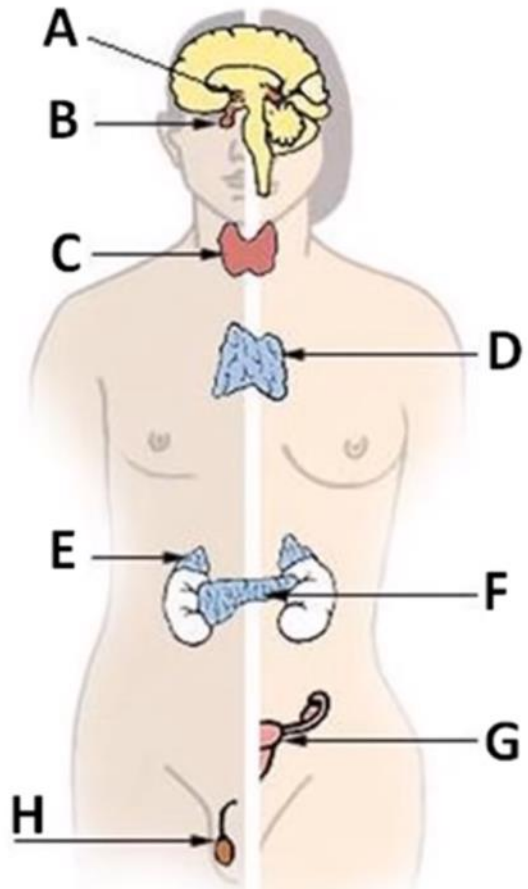
- A hormone is any member of a class of signaling molecules produced by glands in multicellular organisms that are transported by the circulatory system to target distant organs to regulate physiology and behavior.
- Neurotransmitters, also known as chemical messengers, are endogenous chemicals that enable neurotransmission.

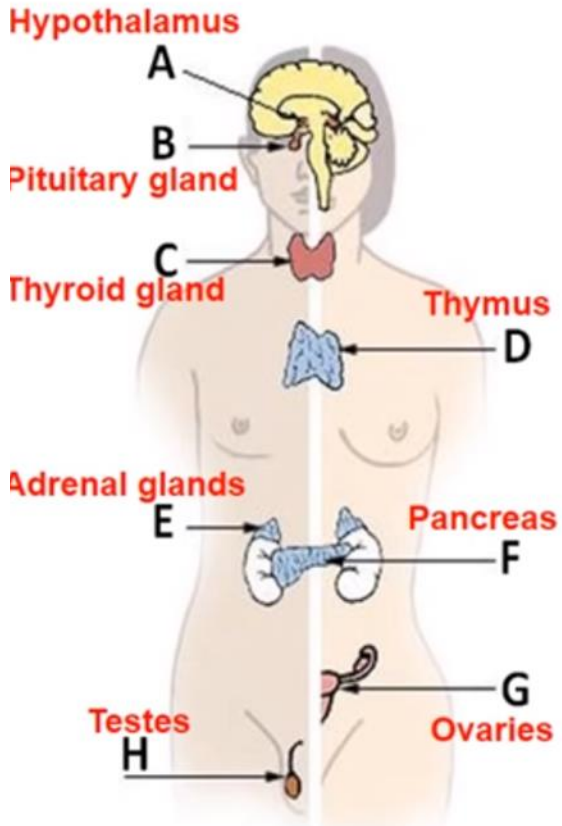


Nervous System	Endocrine System
Neurons release neurotransmitters	Endocrine cells release hormones
A neurotransmitter acts on specific cell right next to it.	Hormones travel to another nearby cell or act on cell in another part of the body.
Neurotransmitters have their effects within milliseconds.	Hormones take minutes or days to have their effects.
The effects of neurotransmitters are short-lived.	The effects of hormones can last hours, days, or years.
Performs short term crisis management	Regulates long term ongoing metabolic function

https://www.quora.com/What-is-the-difference-between-hormones-and-neurotransmitters

http://www.wormatlas.org/neurotransmitterstable.htm





Hormones & the Endocrine system (updated): https://www.youtube.com/watch?v=7STDtdryYTI

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- Video 1: The Nervous System Functions and Facts -Animation video: https://www.youtube.com/watch?v=NALZwb-_YO4

- Video 2:Neurotransmitters - What Are Neurotransmitters And What Do They Do In The Body? : https://www.youtube.com/watch?v=Mz3PIvyu3ew

- Video 3:CBSE Class 11 Biology, Chemical Coordination and integration – 1, Human Endocrine System https://www.youtube.com/watch?v=OECzHqH_mGA
- Video 4: CBSE Class 11 Biology, Chemical Coordination and integration– 2, Hypothalamus, Pituitary Gland & Pineal gland: https://www.youtube.com/watch?v=qMCWQ2LnLsg
- Video 5: CBSE Class 11 Biology, Chemical Coordination and integration – 3, Thyroid and Parathyroid Glands: https://www.youtube.com/watch?v=3BWUp5XwrQI
- Video 6: CBSE Class 11 Biology, Chemical Coordination and integration – 4, Hormone Secreting Glands & Tissues: https://www.youtube.com/watch?v=aQc_e4R1L2s (from 0:58 to 6:29)
- Video 7: CBSE Class 11 Biology, Chemical Coordination and integration – 5, Heterocrine Glands Pancreas: https://www.youtube.com/watch?v=PF_VKS4D4qM (from 0:28 to 1:30)
- Video 8: Endocrine pancreas | Gastrointestinal system physiology | NCLEX-RN | Khan Academy: https://www.youtube.com/watch?v=xNf--q0YMq8

- Video 9: Types of hormones/overview of cell signaling: https://www.youtube.com/watch?v=FQFBygnIONU
- Video 10: Types of hormones | Endocrine system physiology | NCLEX-RN | Khan Academy https://www.youtube.com/watch?v=KSclrkk_Ako

- Endocrine gland hormone review | Endocrine system physiology | NCLEX-RN | Khan Academy: https://www.youtube.com/watch?v=ER49EweKwW8

- Hormones and the endocrine systems: https://www.youtube.com/watch?v=WMVEGAVdEoc
- Good videos: http://www.austincc.edu/apreview/NursingPics/NursingAnimationsWebPage.html

- Textual information: http://www.austincc.edu/apreview/PhysText/Endocrine.html

UNIT 3: Signal transduction

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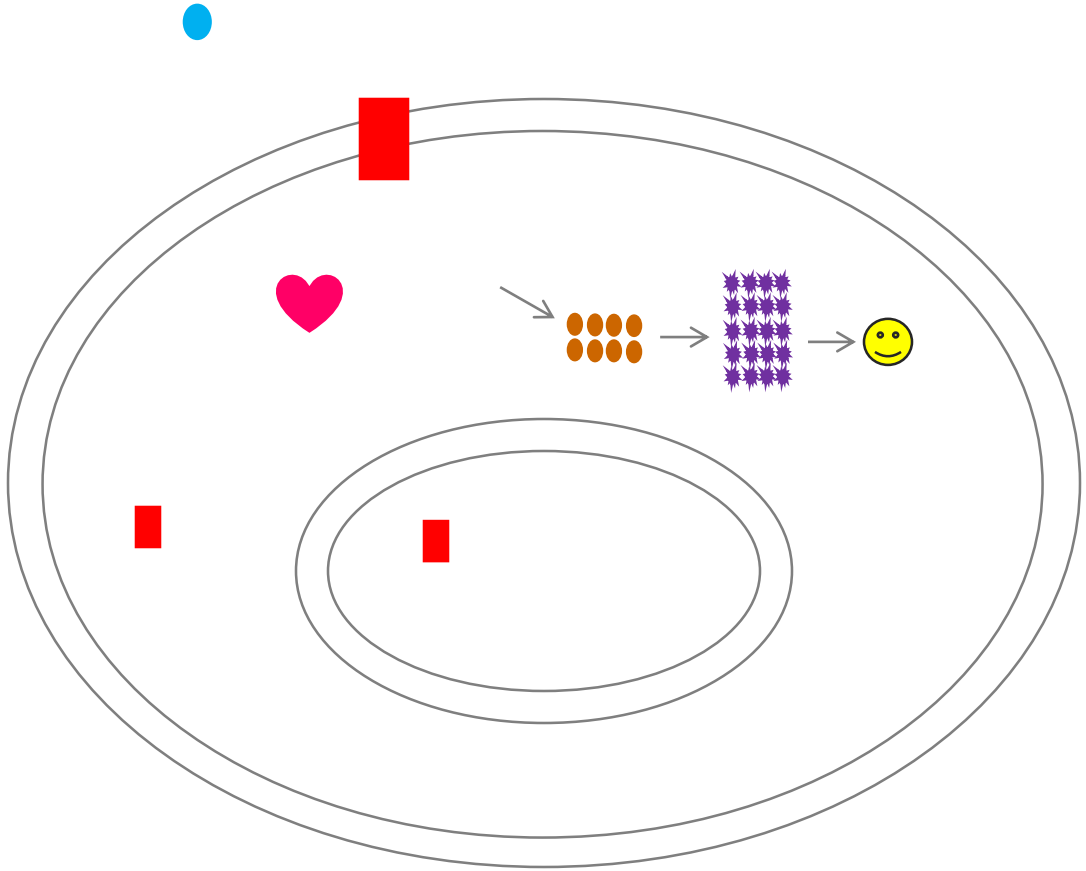
Topics

- Signal transduction
- Terminology
- G-protein signaling pathway
- Adenylate cyclase signal transduction pathway
- Phosphoinositide signal transduction pathway
- Clinical significance of adenylate cyclase signal transduction pathway
- Alpha subunit of G-proteins
- The signaling gas: Nitric oxide
- Nitric oxide: Signal transduction
- Summary

Signal transduction

- Molecular events or pathways whereby intercellular signals are converted (transduced) to intracellular signals are known as “signal transduction” **or**
- Signal transduction is the process by which a chemical or physical signal is transmitted through a cell as a series of molecular events, most commonly protein phosphorylation catalyzed by protein kinases, which ultimately results in cellular response.



Ligand

Receptor

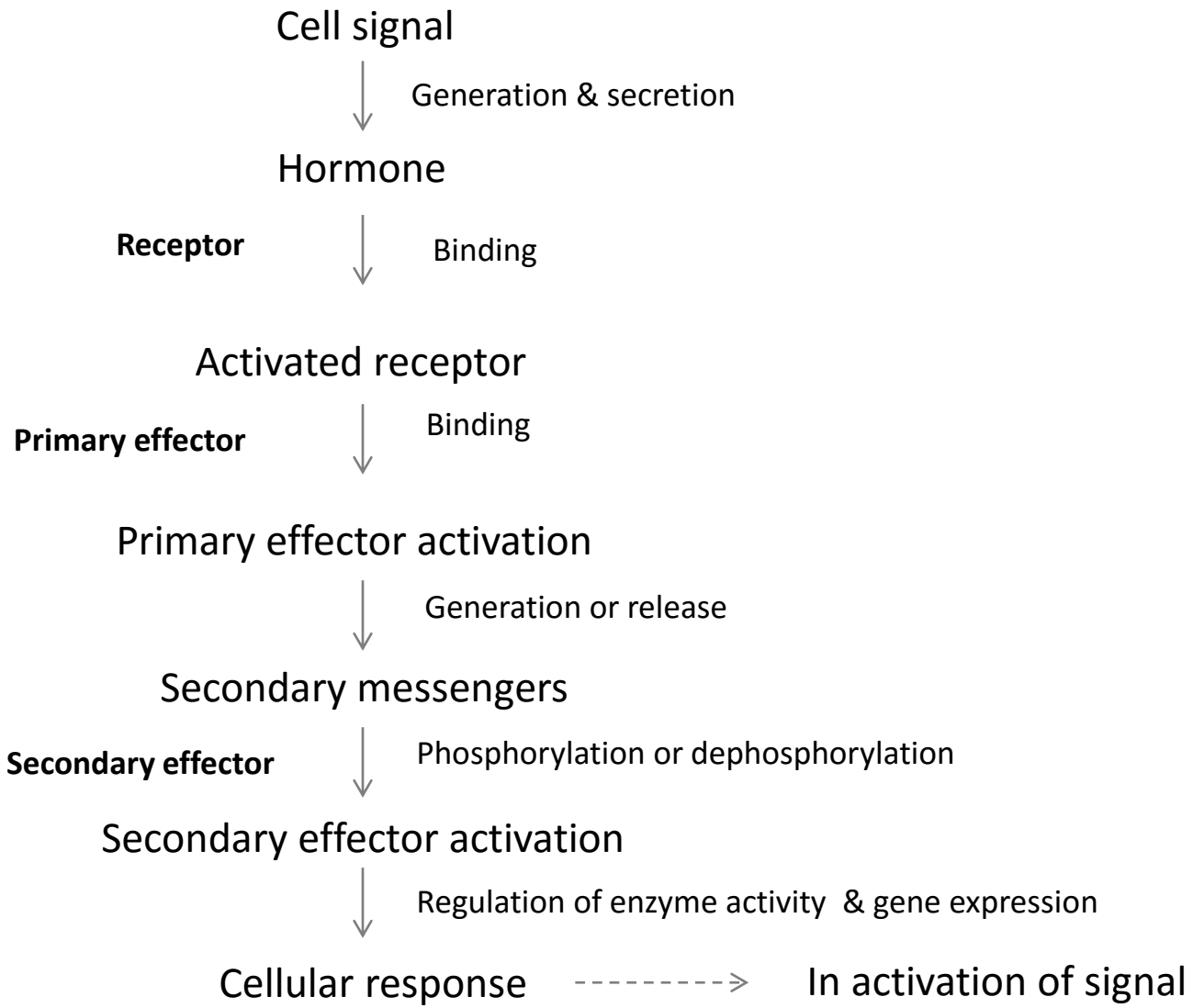
Primary effector

Second messengers

Secondary effectors

Cellular response

Signal transduction



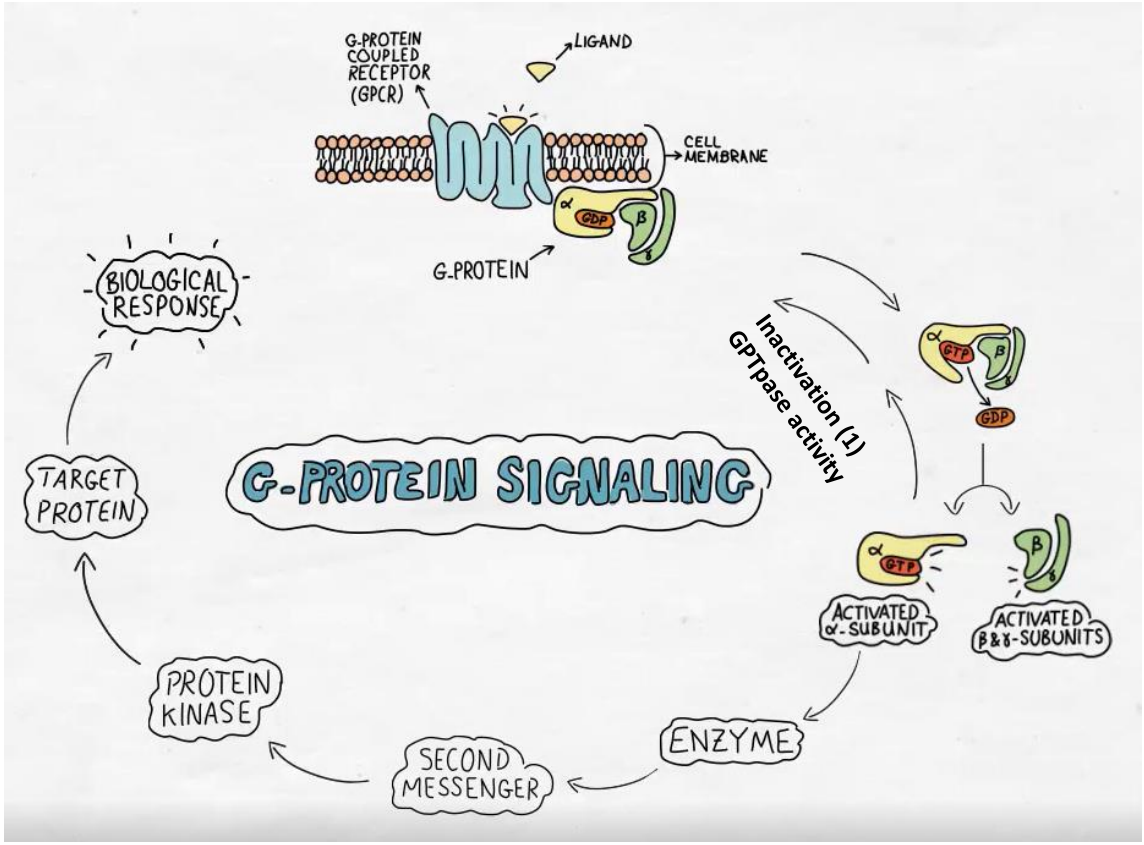
Signal transduction

Component	Description
Ligands	Ligands are first messengers that are released in response to stimuli by specialized glands. Ligands can be classified roughly into two categories based on permeability across cellular membrane: permeable and non-permeable
Receptor	Proteins that bind to the ligands are known to be receptors. Thus, receptors considered as signal transducers as they transfer the information that ligand has bound to the cell's interior. The binding of a ligand with receptor causes a change in the confirmation of the receptor, known as receptor activation. Receptors can be roughly divided into two major classes: Extracellular and Intracellular
Primary effector	The activated receptor interacts and activates another component of the signal transduction pathway which is known as primary effector. Primary effectors are linked to generation of second messengers.
Second messenger	An intracellular substance that mediates cell activity by relaying a signal from an extracellular molecule (as of a hormone or neurotransmitter) bound to the cells surface. Second messengers further activate secondar effectors and so on.
Secondary effector	Components of signal transduction pathways activated by second messengers are known as secondary effectors. Secondary effectors responsible for activating different genes/proteins and thus generating the cellular response.

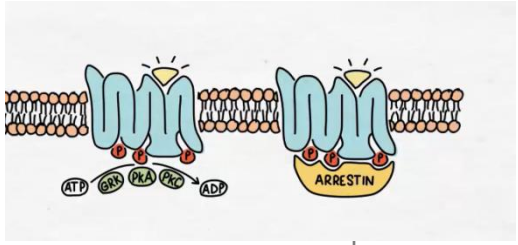
Signal transduction

Component	Example
Ligands	Hormones including neurotransmitters. Permeable hormones: steroid hormones Non-permeable hormones: proteins/polypeptide hormones
Receptor	Extracellular receptors: G protein-coupled receptors (GPCR) Intracellular receptors: cytoplasmic (NOD-like receptors) and nuclear receptors (retinoic acid receptors)
Primary effector	Adenylate cyclase & Phospholipase C
Second messenger	Cyclic AMP (cAMP) Cyclic GMP (cGMP) Calcium ion (Ca2+) Inositol 1,4,5-triphosphate (IP3) Diacylglycerol (DAG)
Secondary effector	Proteins kinases, phosphatases and calmodulin

Signal transduction: G-protein signaling pathway



Inactivation (2)

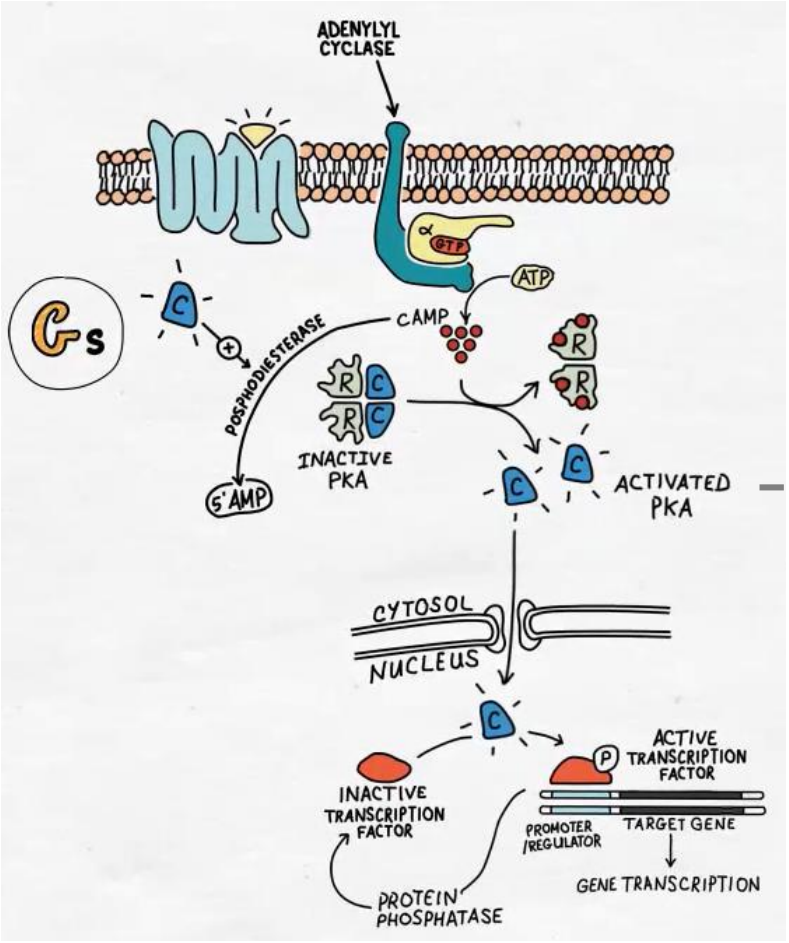


Endocytosis

Stop at 3:20
Start at 8:13

G Protein Signaling - Handwritten Cell & Molecular Biology.mp4

Adenylate cyclase signal transduction pathway



Glycogen phosphorylase activation

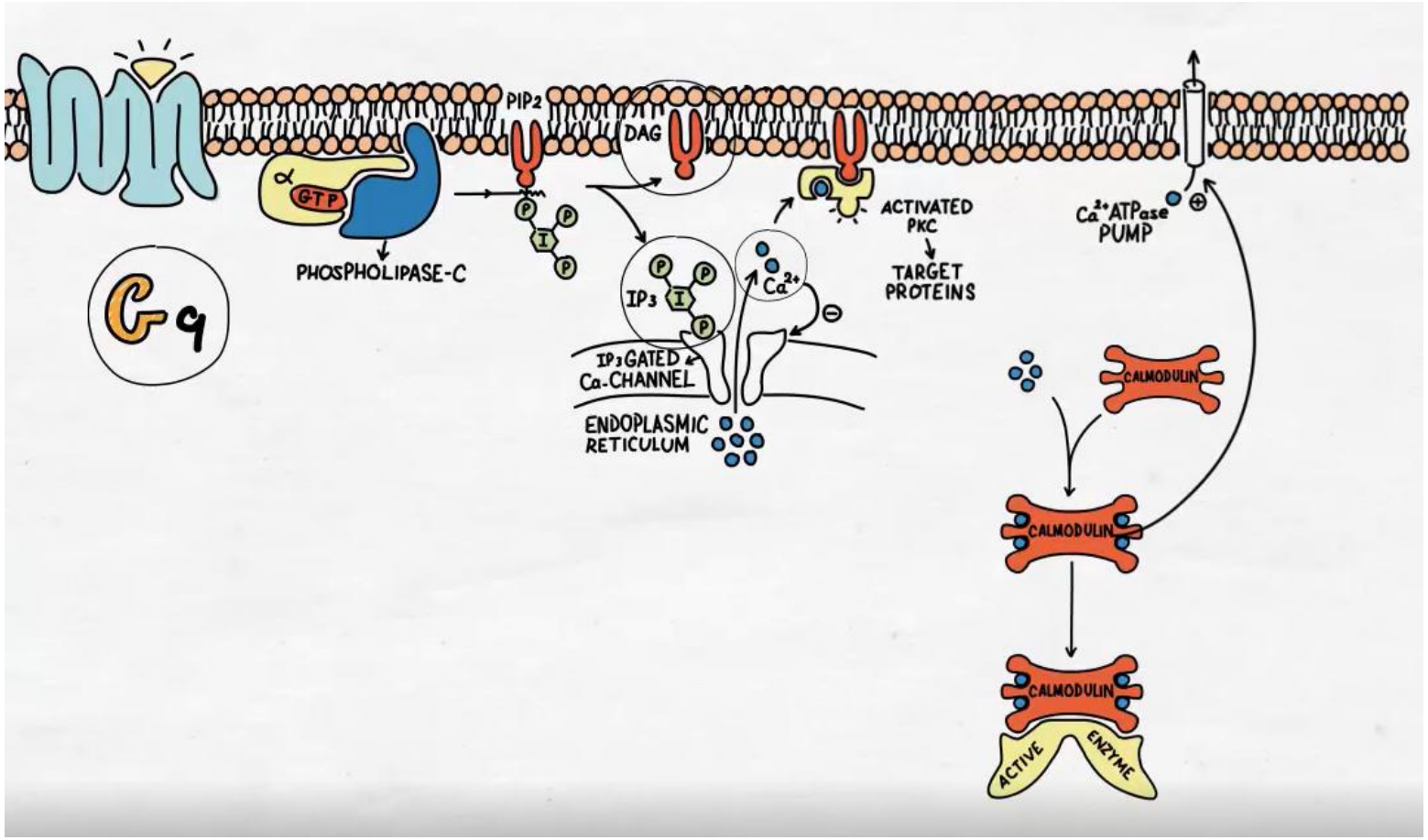
↓

Glycogen breakdown

Start at 3:31; Stop at 5:20

G Protein Signaling - Handwritten Cell & Molecular Biology.mp4

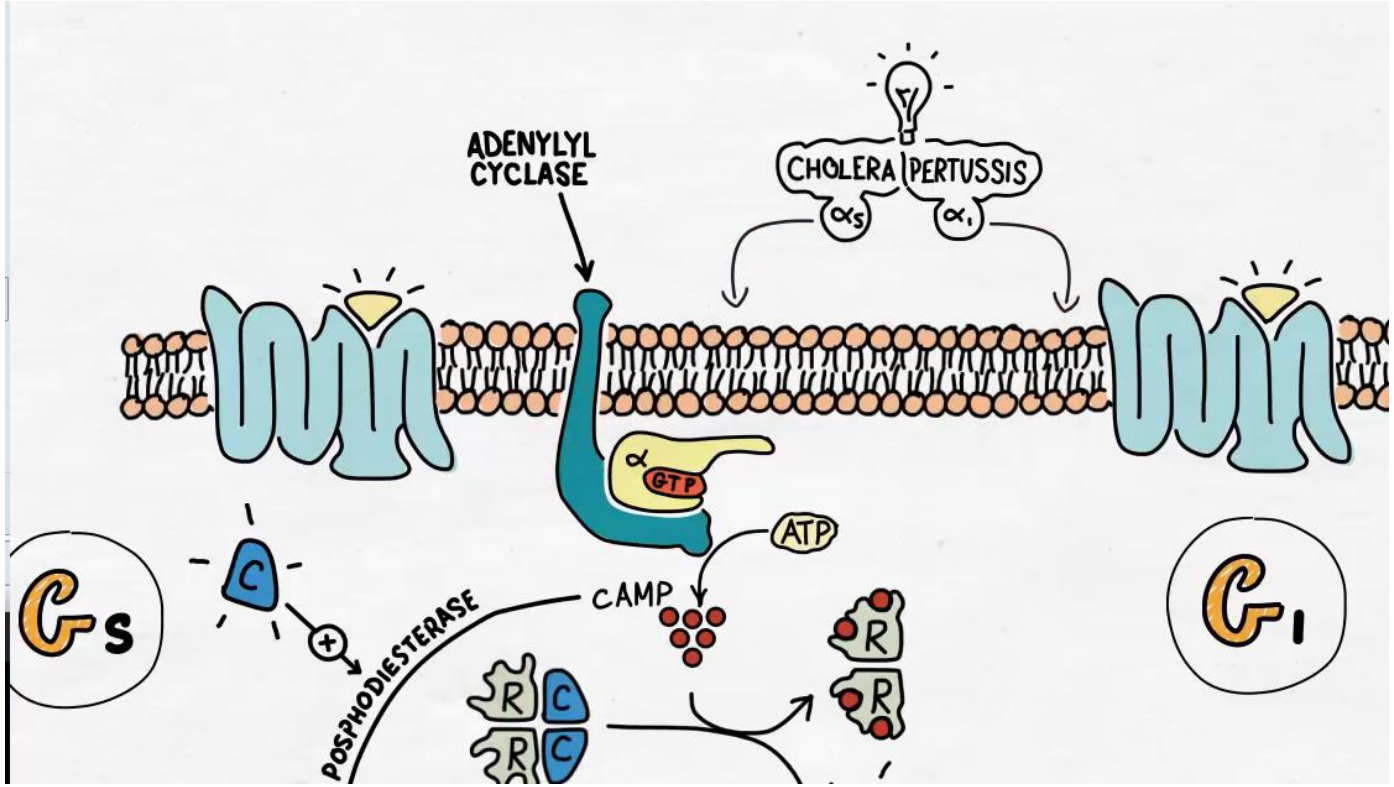
Phosphoinositide signal transduction pathway



Start at 5:59; Stop at 8:09

G Protein Signaling - Handwritten Cell & Molecular Biology.mp4

Clinical significance of adenylate cyclase signal transduction pathway



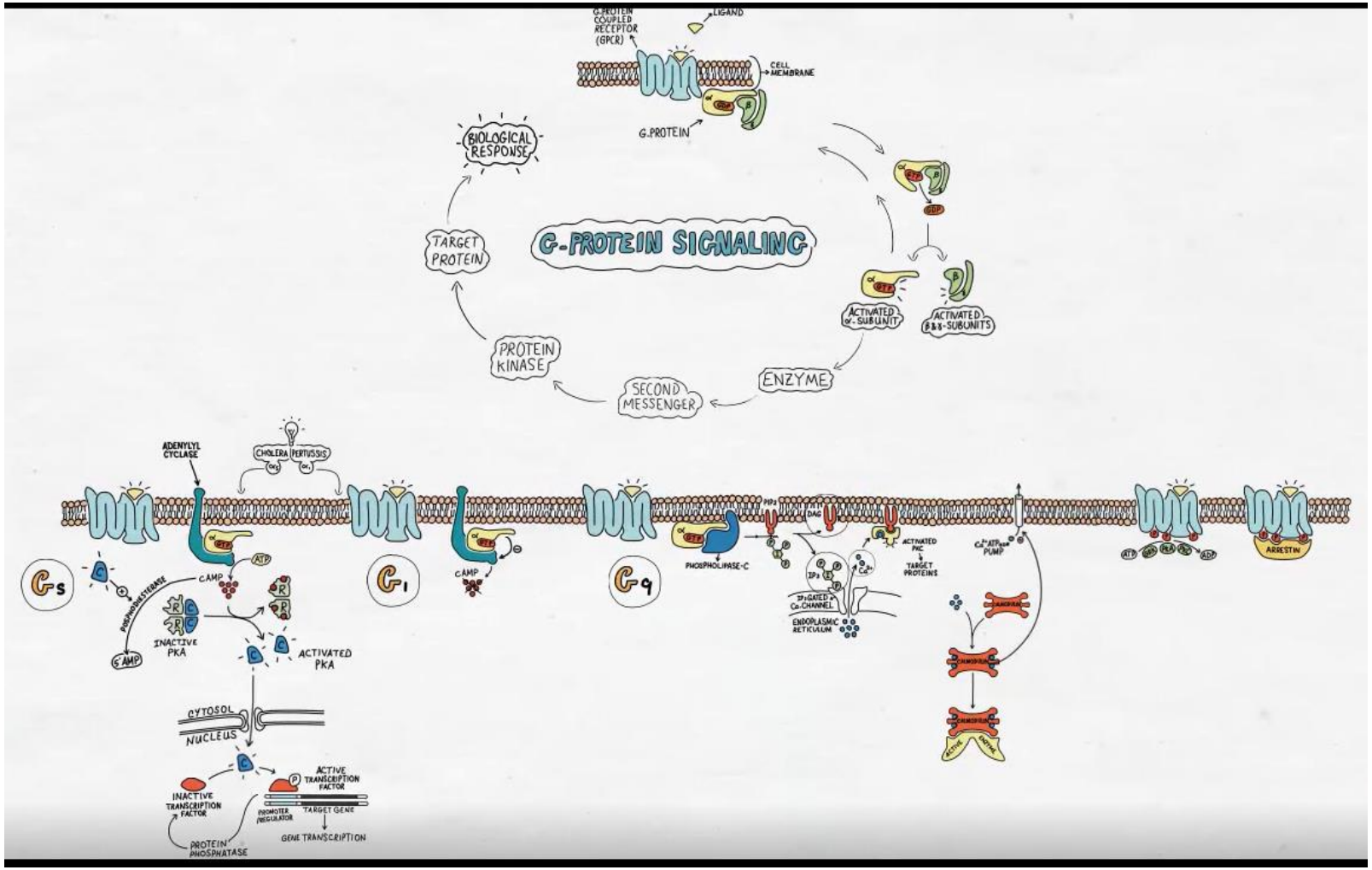
Start at 9:34

G Protein Signaling - Handwritten Cell & Molecular Biology.mp4

Alpha subunit of G-proteins : Role in signal transduction pathways

Alpha subunit	G-protein	Importance
S-type (stimulatory)	Gs-protein	Stimulates adenylate cyclase
I-type (inhibitor)	Gi-protein	Inhibits adenylate cyclase
q-type	Gq-protein	Stimulates phospholipase C

Signal transduction: Summary



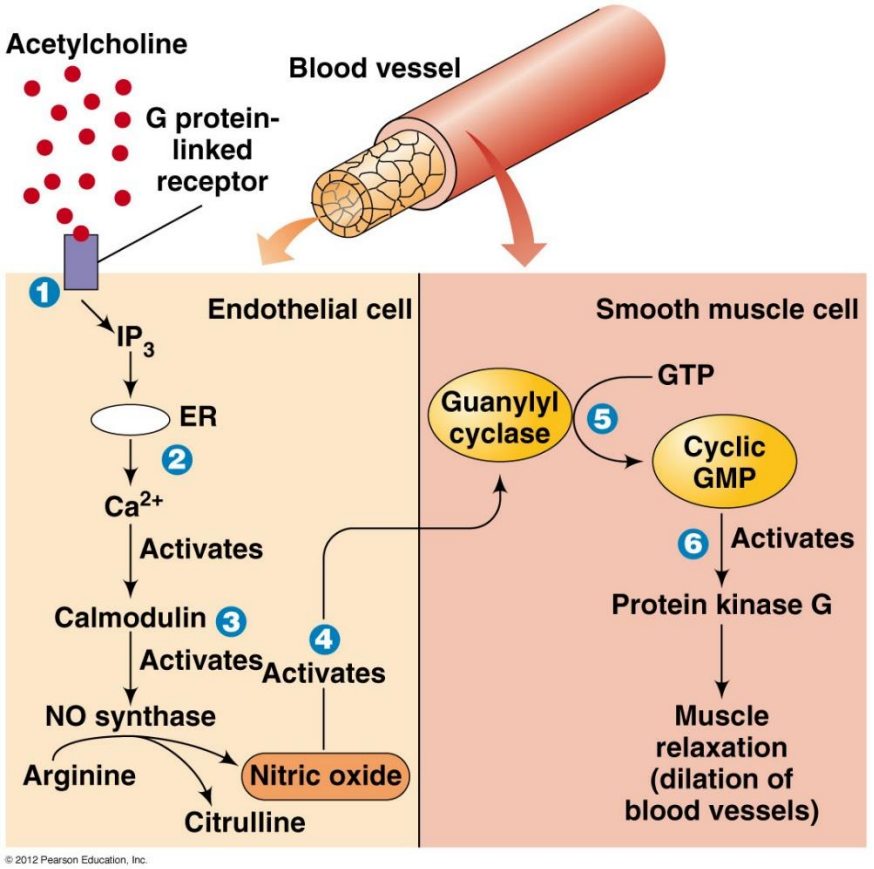
The signaling gas : Nitric oxide

Nitric oxide is an important messenger in many vertebrate signal transduction processes. Nitric oxide is a stable free radical gas. It diffuses across the cell membranes, although it's high reactivity (half-life ~5 seconds) prevents it from acting much further than ~1 mm from its site of synthesis. Nitric oxide is produced endogenously from arginine in a complex reaction that is catalyzed by nitric oxide synthase.

Some biological role of nitric oxide is listed below:

- Nitric oxide stimulates mitochondrial biogenesis.
- Nitric oxide is essential for the function of the central nervous system.
- Nitric oxide is well known as vasodilator of endothelial cells and neurons. One of the most highlighted nitric oxide effects is relieving chest pain and penile erection. The wonder drug Viagra acts by producing nitric oxide and thus improving the penile erection in man.
- Nitric oxide in leukocytes acts as anti-bacterial. In Leukocytes nitric oxide combines with superoxide and produce highly reactive hydroxyl radical which kills invading bacteria.

Nitric oxide Signal transduction



https://www.youtube.com/watch?v=On-jTcLLP9o

Sources

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- Video 2: Signal Transduction Pathways 1: https://www.youtube.com/watch?v=-U2dBURQbjk
- Video 3: G-protein receptor activation video: https://www.youtube.com/watch?v=2_nGMd0COH4
- Video 4: Signaltransduktion: https://www.youtube.com/watch?v=V-z415c6eOU
- Video 5:How Hormones Use G-protein Signaling Pathways: A Video Review of the Basics: https://www.youtube.com/watch?v=wC2_7Ror3qY&t=159s
- Video 6: G Protein Signaling - Handwritten Cell & Molecular Biology: https://www.youtube.com/watch?v=9Bq6qHJaSJs
- Video 7: G Protein linked 2nd Messengers, G protein coupled receptors, GPCRs: https://www.youtube.com/watch?v=3qR9B2JCT_s
- Video 8: Nitric oxide - benefits and side effects: https://www.youtube.com/watch?v=On-jTcLLP9o

UNIT 4: Regulation and Integration of metabolism

Prof K Syed

Department of Biochemistry & Microbiology

University of Zululand

Room no. 247

Topics

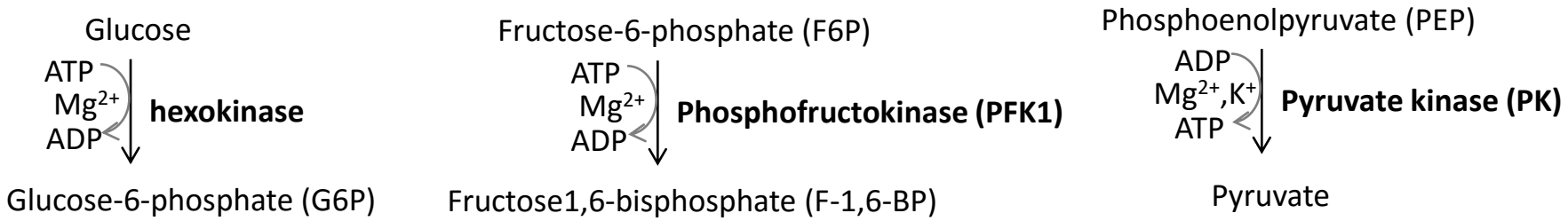
- Glycolysis
- Citric acid cycle/Krebs cycle
- fatty acid synthesis/degradation
- Metabolic fate of Amino acids
- Pentose phosphate pathway
- Gluconeogenesis
- Glycogen metabolism
- urea cycle
- Ketogenesis

- Metabolic integration
  - Fate of Glucose-6-phosphate
  - Fate of pyruvate
  - Fate of Acetyl-CoA

- Effect of hormones on fuel metabolism
  - Fed state and fasted state/stress

Regulation of Glycolysis

- Allosteric regulation at 3 steps – Irreversible reactions
- PFK1 – Committed step

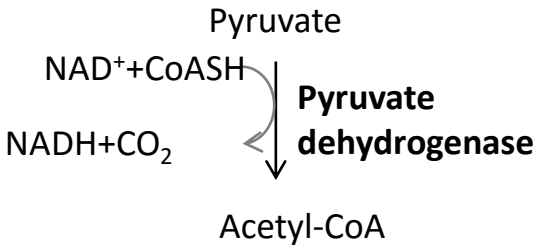


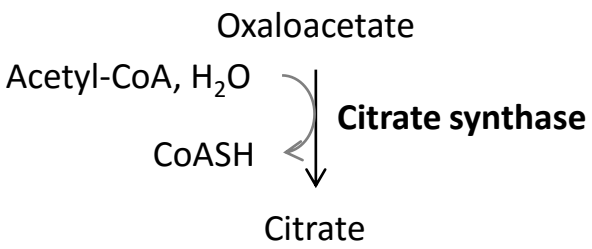
Enzyme	Hexokinase (HK)	Phosphofructokinase (PFK1)	Pyruvate kinase (PK)
Allosteric Activator(s)	-	↑ ADP ↑ AMP ↑ F-2,6-BP	↑ F-1,6-BP
Allosteric Inhibitor(s)	G6P	↑ ATP ↑ PEP	↑ ATP ↑ Acetyl-CoA ↑ Alanine

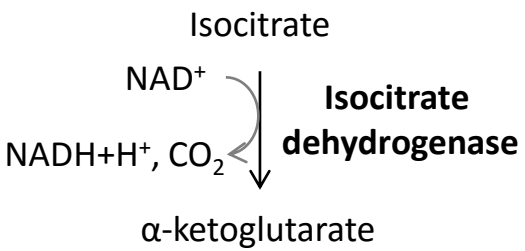
PLAY VIDEO 1

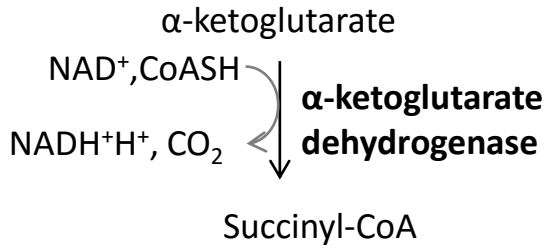
Regulation of citric acid cycle/Krebs cycle

- Allosteric regulation (three simple ways)
- 3 steps
- Pyruvate dehydrogenase
- Citrate synthase – Committed step





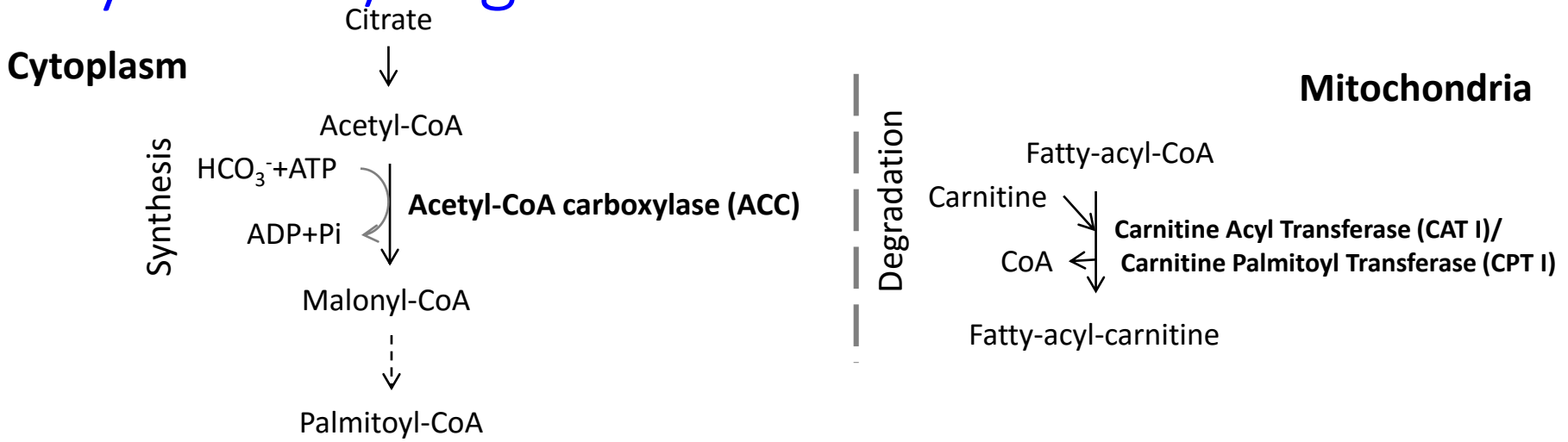


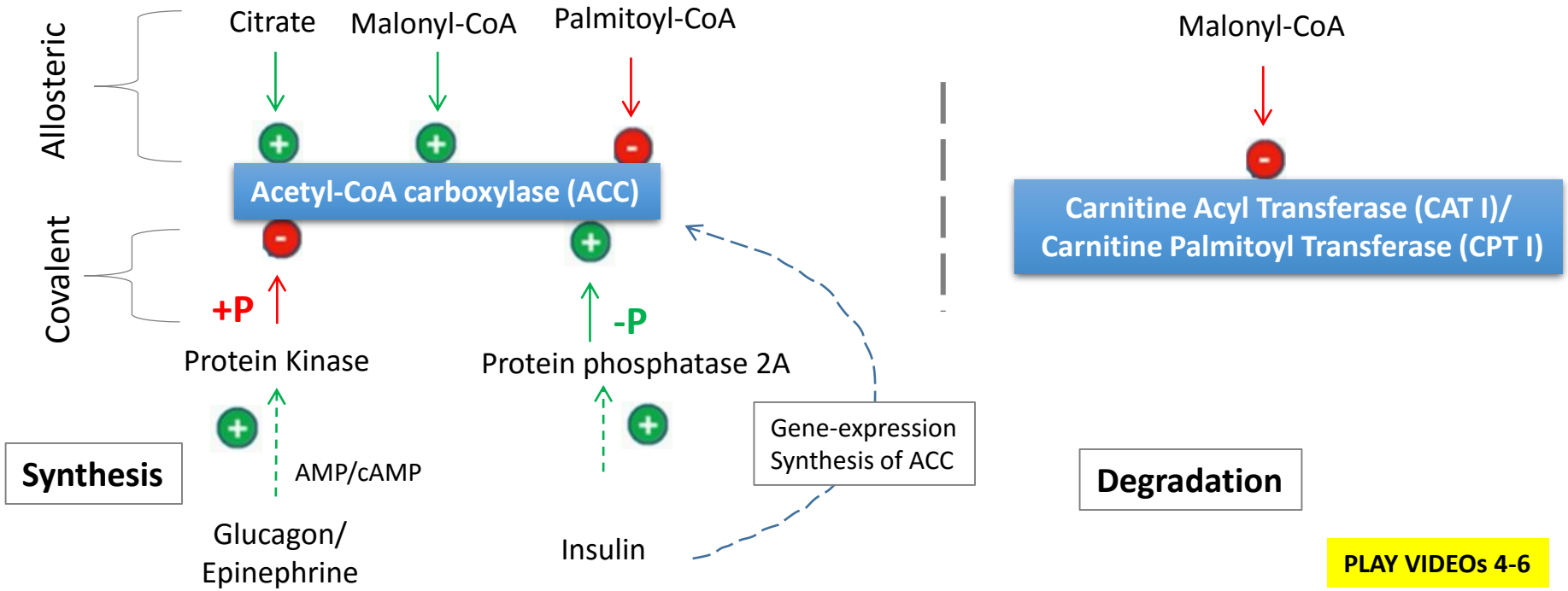


Enzyme	Citrate synthase	Isocitrate dehydrogenase	α-ketoglutarate dehydrogenase	Pyruvate dehydrogenase
Allosteric Activator(s)	-	↑ ADP ↑Ca^{2+} ↑ NAD^+	↑Ca^{2+}	↑Ca^{2+}
Allosteric Inhibitor(s)	↑ ATP ↑ NADH ↑ Succinyl-CoA ↑ Citrate	↑ ATP ↑ NADH	↑ ATP ↑ NAHD ↑ Succinyl-CoA	↑ATP ↑Acetyl-CoA ↑NADH

PLAY VIDEOs 2 & 3

Regulation of fatty acid synthesis/degradation



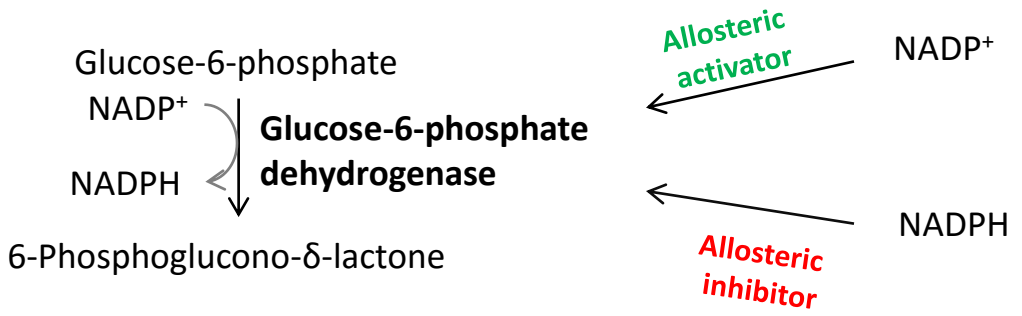


PLAY VIDEOs 4-6

Regulation of Pentose Phosphate Pathway

- Response to metabolic needs
- Oxidative: equal amount of NADPH and Ribulose-5-phosphate
- Non-oxidative phase: Need lots of Ribulose-5-phosphate and don't need NADPH

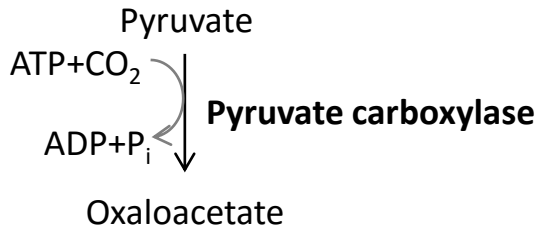
- Oxidative phase – allosteric regulation
- Glucose-6-phosphate dehydrogenase – committed step

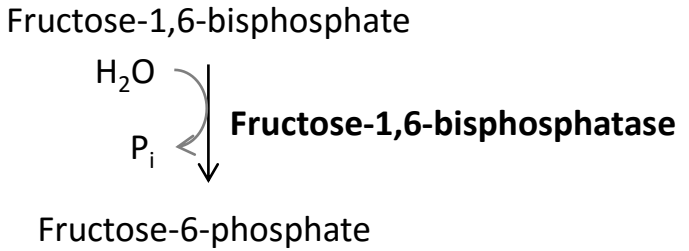


PLAY VIDEO 9

Regulation of Gluconeogenesis

- Two steps



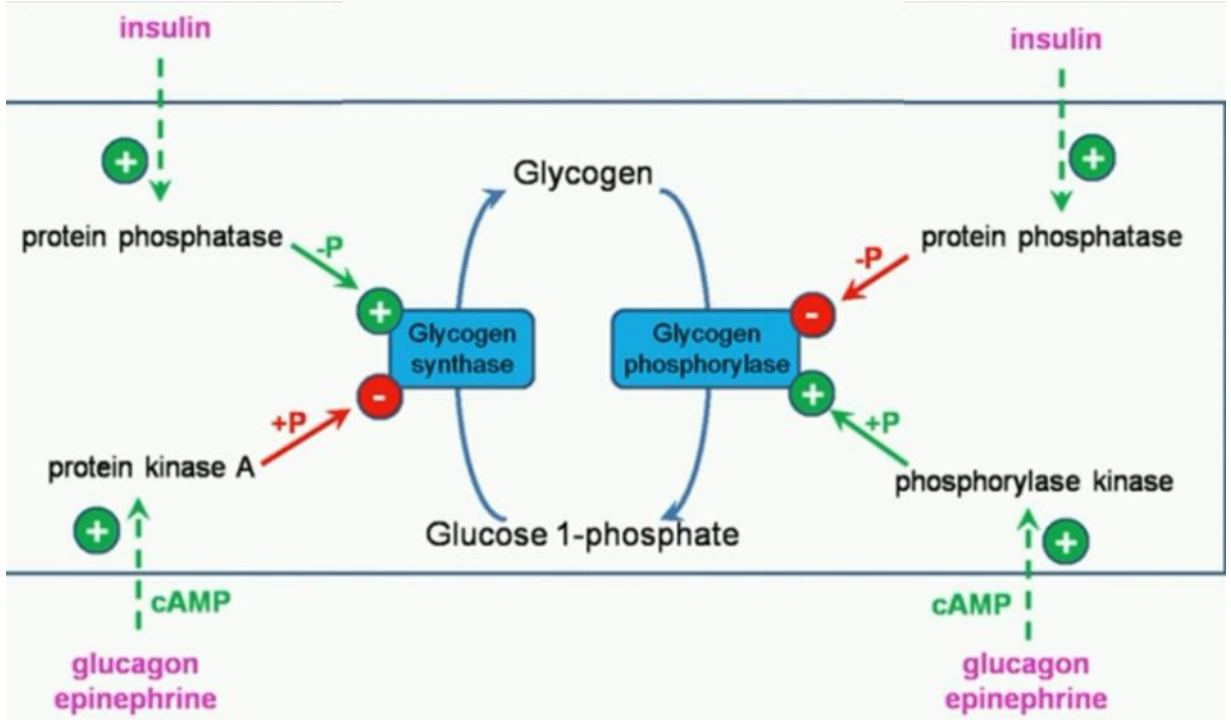


Enzyme	Pyruvate carboxylase	Fructose-1,6-bisphosphatase
Allosteric Activator(s)	↑ Acetyl-CoA	↑ ATP
Allosteric Inhibitor(s)	-	↑ AMP ↑ Fructose-2,6-bisphosphate

PLAY VIDEO 10

Regulation of Glycogen metabolism

- Covalent modification & hormonal control
- Insulin and Glucagon steps
- Two enzymes: Glycogen synthase & Glycogen phosphorylase



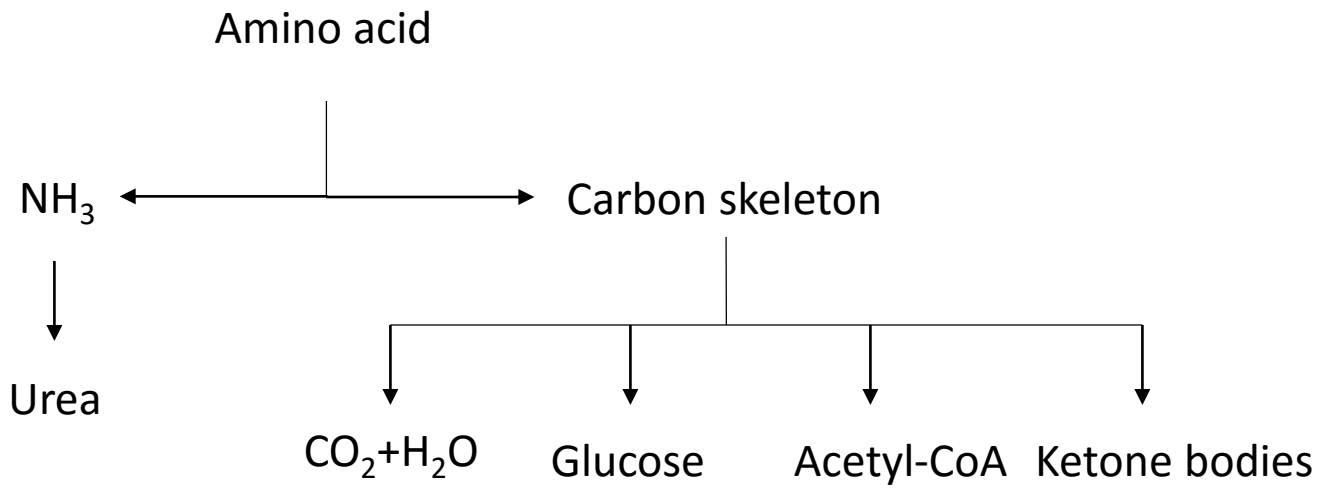
PLAY VIDEOs 11 & 12

Hormonal effects on fuel metabolism

Tissue	Insulin	Glucagon	Epinephrine
Muscle	↑ Glucose uptake	No effect	↑ Glycogenolysis
	↑ Glycogen synthesis		
Adipose tissue	↑ Glucose uptake	↑ Lipolysis	↑ Lipolysis
	↑ Lipogenesis		
	↓ Lipolysis		
Liver	↑ Glycogen synthesis	↓ Glycogen synthesis	↓ Glycogen synthesis
	↑ Lipogenesis	↑ Glycogenolysis	↑ Glycogenolysis
	↓ Gluconeogenesis		↑ Gluconeogenesis

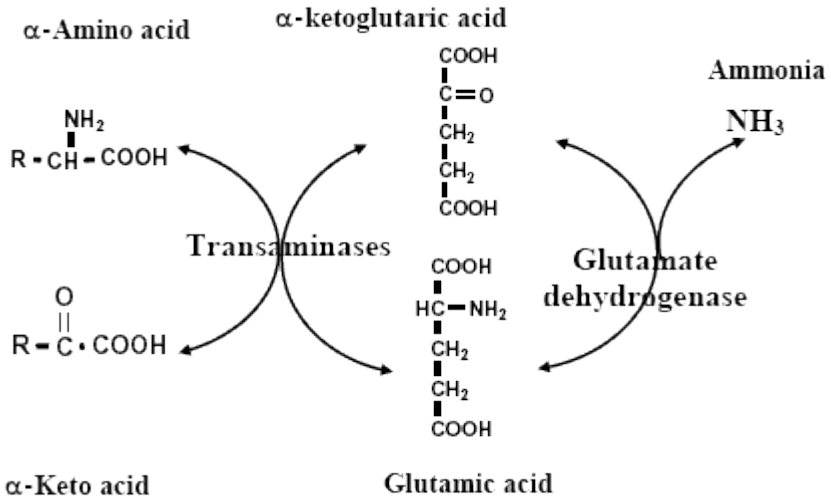
PLAY VIDEO 16

Overview of amino acid catabolism



- **Amino acid deamination**
  - Transamination
  - Deamination
  - Lysine – no transamination

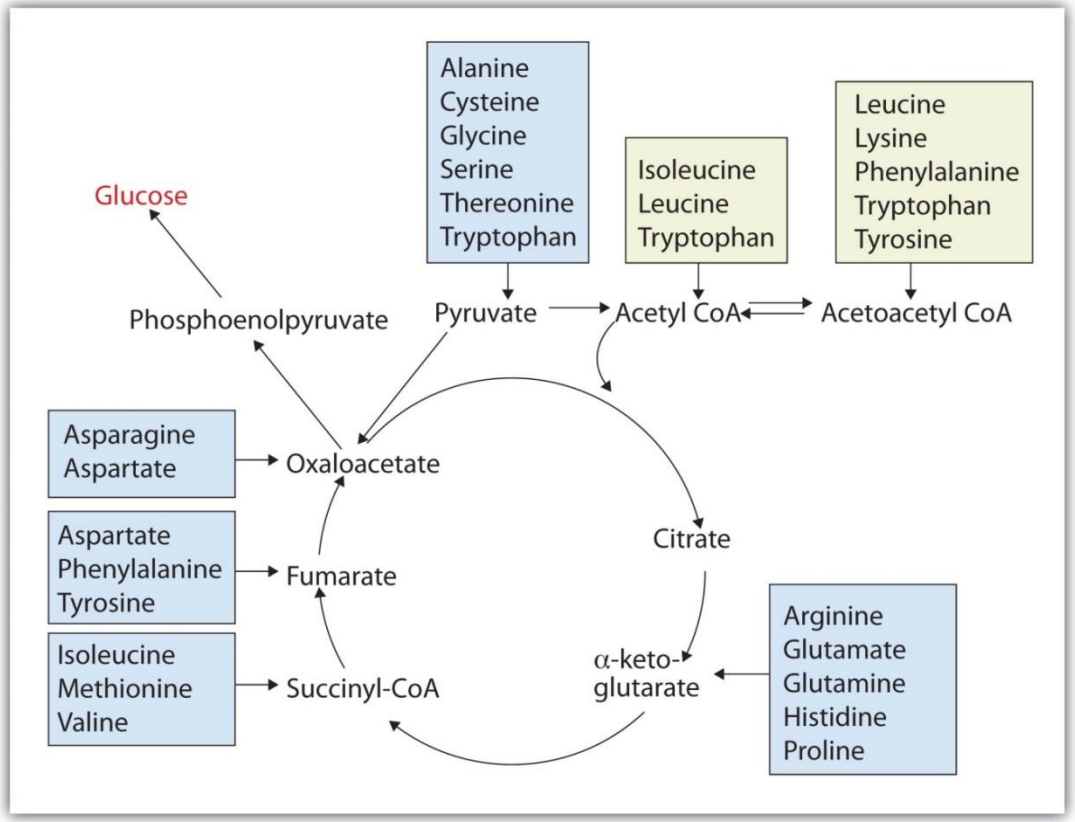
Glutamate dehydrogenase (allosteric regulation	
Inhibitor: GTP & NADH	Signaling abundant metabolic energy
Activators: ADP & NAD^+	Signaling the need to generate ATP



PLAY VIDEOs 7 & 8

Metabolic fate of Amino acids

Strategy: transform the carbon skeletons into major metabolic intermediates that can be converted into glucose or oxidized citric acid cycle



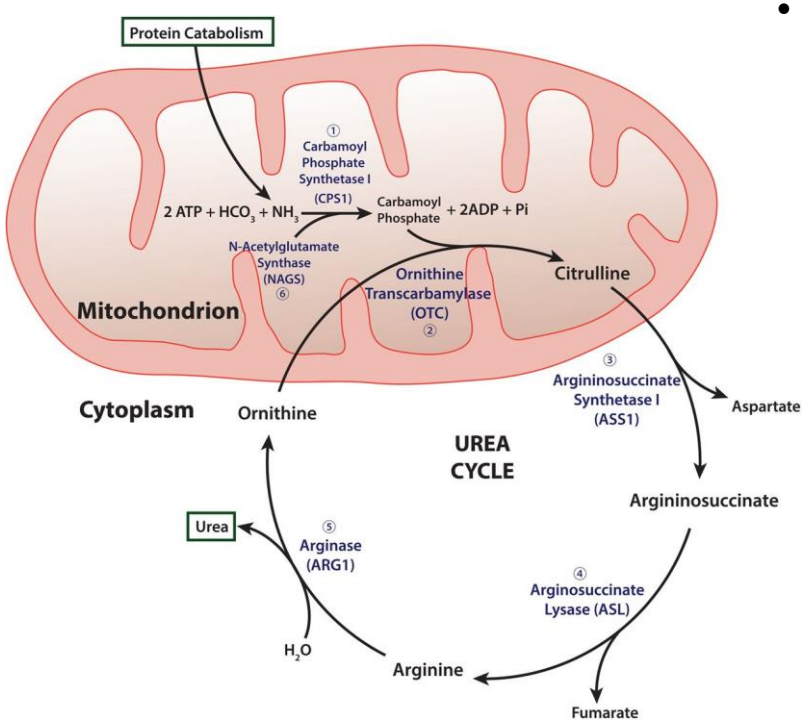
Ketogenic:
Leucine & Lysine - LL

Keto and Glucogenic:
Phenylalanine, Isoleucine
Threonine, Tryptophan
Tyrosine
(PITTT)

Glucogenic:
Alanine
Arginine
Asparagine
Aspartic acid
Cysteine
Glutamic acid
Glutamine
Glycine
Histidine
Methionine
Proline
Serine
Valine
(AAAACGGGHMPSV)

PLAY VIDEOs 7 & 8

Regulation of urea cycle : Adjustment of enzyme levels (Long term regulation)



- All five enzymes involved in regulation of urea synthesis
- Based on N flux (substrate availability)
- Gene-expression and enzyme production

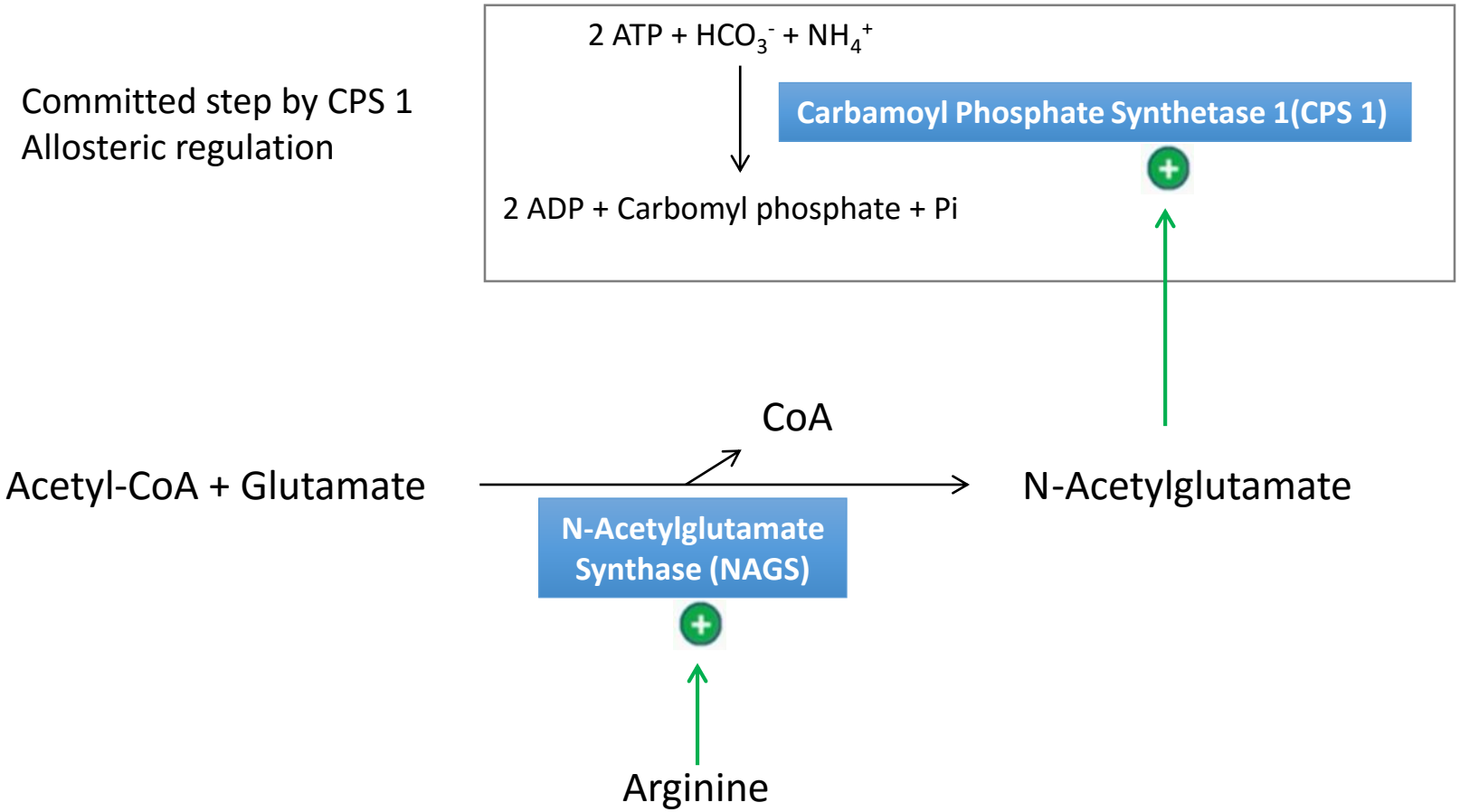
N Flux	Synthesis of enzymes	Urea production
↑	↑	↑
↓	↓	↓

High protein diet: ↑ **N Flux**
Low protein diet: ↓ **N Flux**
Starvation: ↑ **N Flux**

PLAY VIDEOs 13 & 14

Regulation of urea cycle : Allosteric regulation (Short term)

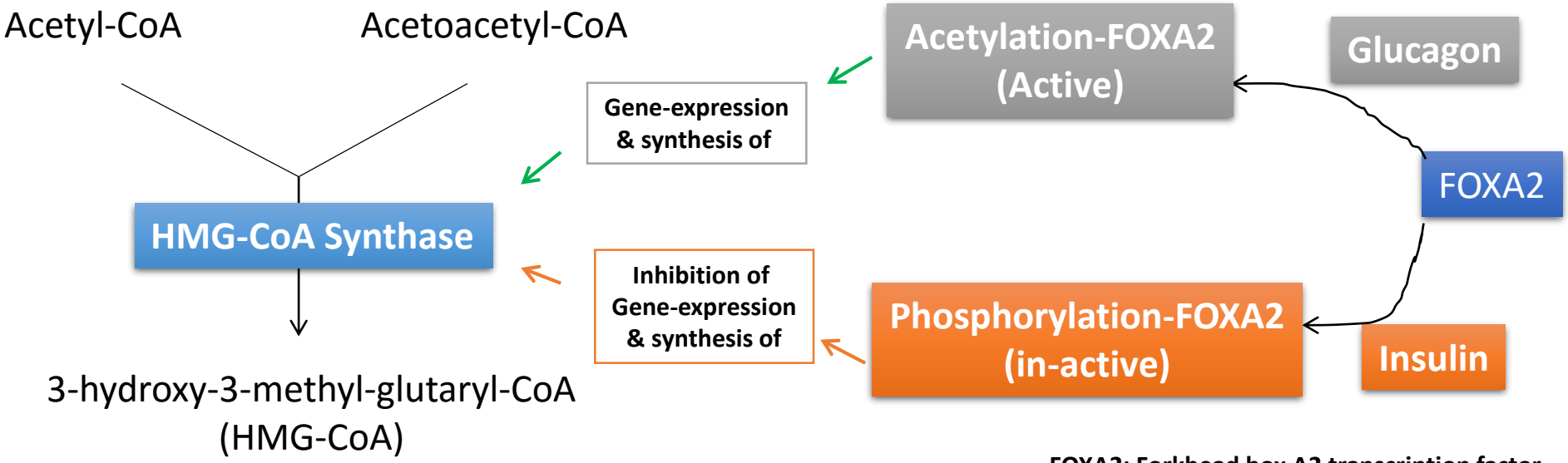
- Committed step by CPS 1
- Allosteric regulation



- ↑ Arginine indicates high amount of amino acids and thus high amount of N flux
- Arginine indirectly activate CPS 1 via N-Acetylglutamate

PLAY VIDEOs 13 & 14

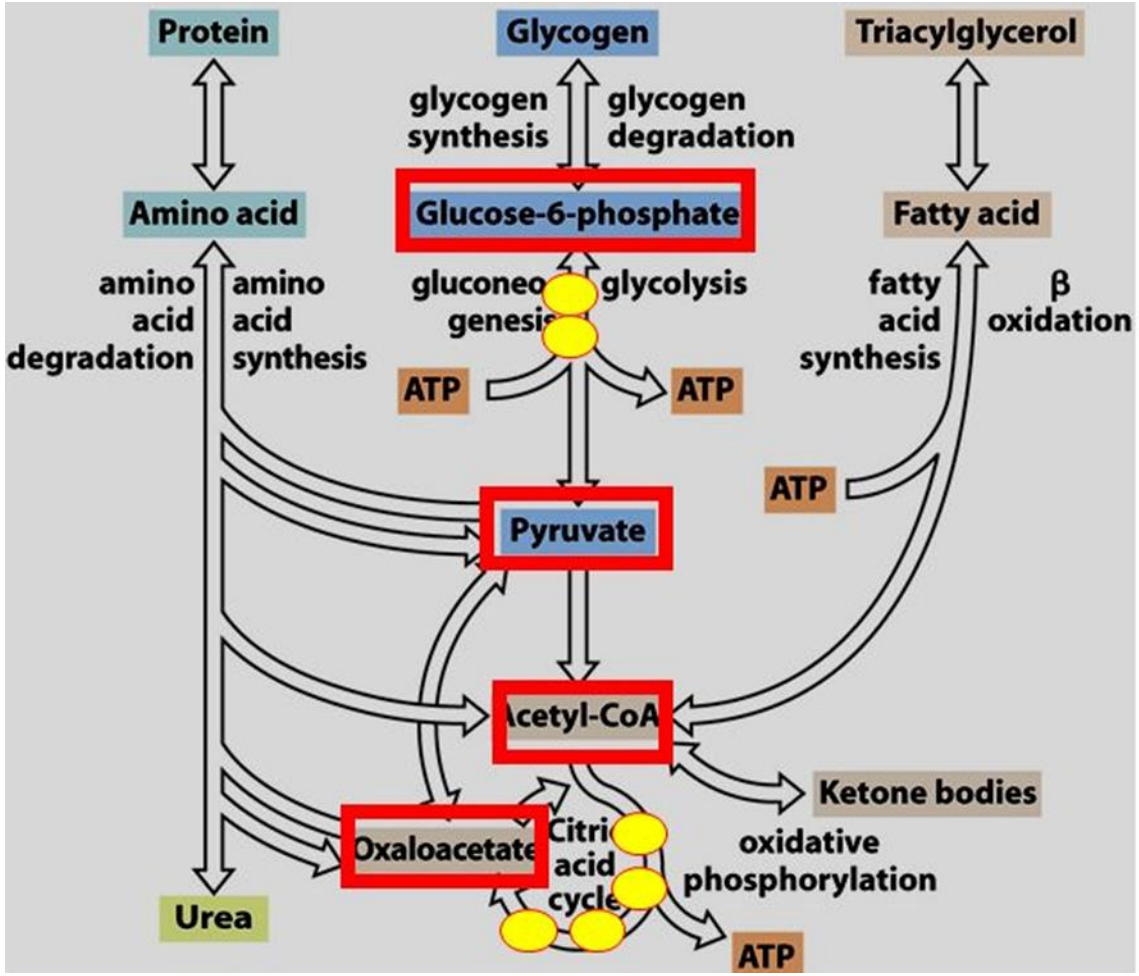
Regulation of ketogenesis: Adjustment of HMG-CoA synthase under hormonal control



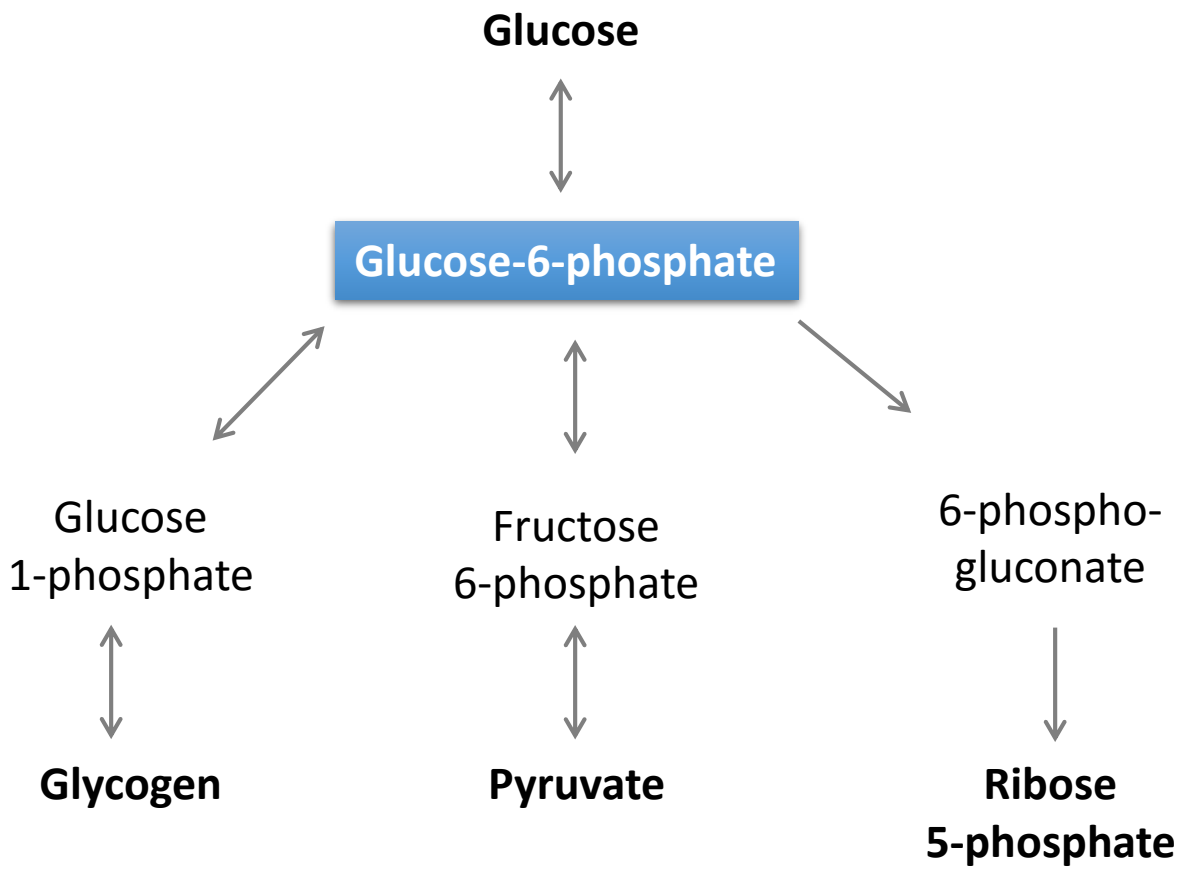
FOXA2: Forkhead box A2 transcription factor

PLAY VIDEO 15

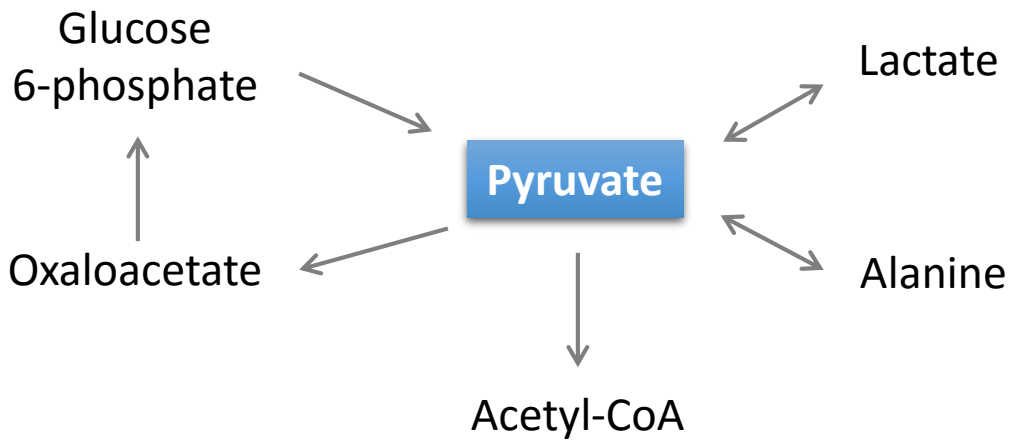
Metabolic pathways integration



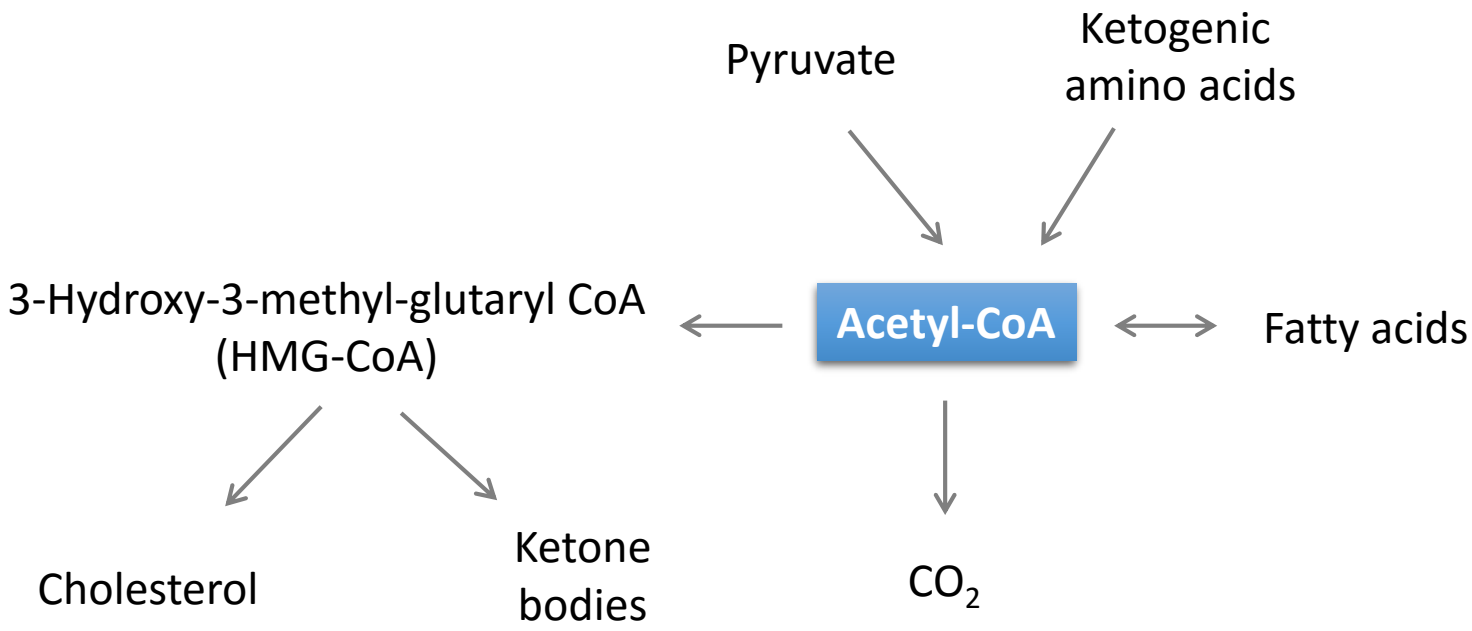
Metabolic fates of Glucose-6-phosphate



Metabolic fates of Pyruvate



Metabolic fates of Acetyl-CoA



Sources

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  - Video 2: https://www.youtube.com/watch?v=gQkfwq0DaiI
  - Video 3: https://www.youtube.com/watch?v=w47MiUnhbGM
- fatty acid synthesis/degradation
  - Video 4: https://www.youtube.com/watch?v=A2mQPCtKA6U
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  - Video 7: https://www.youtube.com/watch?v=Sy-rfy5Mdc0
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