ADRENAL GLAND: CORTISOL

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OUTLINE

I) ADRENAL GLAND ANATOMY

(1) In the abdominal cavity

- below the diaphragm
  - The liver is on the right side
  - The spleen is on the left side
- Below them are located the two kidneys

(2) The adrenal glands

- sit on top of the kidneys
  - Also called **suprarenal glands**
  - Have a roughly pyramid shape

(3) Parts of the adrenal gland

- Cortex
  - Has three layers
    - **Zona glomerulosa**
      - Most superficial
    - **Zona fasciculata**
      - In the middle
      - The thickest
    - **Zona reticularis**
      - The deepest
  - All layers are mostly **glandular cuboidal epithelial tissue**
- **Medulla**
  - Has only one layer
  - Made up of **neural tissue**

II) CORTISOL SYNTHESIS

(1) The paraventricular nucleus

- in the hypothalamus secrete **corticotropin-releasing hormone** (CRH)
- CRH goes in the **hypophyseal portal system**
  - ➢ The vascular connection between the hypothalamus and the anterior pituitary (**adenohypophysis**)

(2) CRH stimulates

- specific cells - the **corticotropes** in the adenohypophysis to secrete **adrenocorticotropic hormone** (ACTH) into the bloodstream

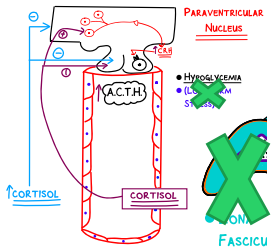

Figure 1 Synthesis of CRH and ACTH

(3) ACTH goes

- to the adrenal cortex
- Binds to a g-protein coupled receptor
  - Triggers an intracellular cascade

(4) It activates a G stimulatory protein

- that goes to an effector enzyme on the cell membrane – Adenylate cyclase
  - The effector enzyme has a specific point of attachment for the Gs protein
  - The effector enzyme becomes very active

(5) Adenylate cyclase

- has a specific enzyme – GTPase
  - GTPase cuts the GTP and turns it into GDP
  - Energy is produced and used to convert ATP to cAMP
  - cAMP activates protein kinase A (pkA)

(6) In the adrenal cortex

- steroid hormones are synthesized
  - This synthesis requires cholesterol as a basic unit
- **Cholesterol** is converted to pregnenolone
  - → **Pregnenolone** is converted to progesterone
  - → **Progesterone** is converted to 17-hydroxy progesterone
  - → **17-hydroxy progesterone** is converted to 11-deoxycortisol
    - by **21-hydroxylase**
  - → **11-deoxycortisol** is converted to **cortisol**
- Each step in this pathway is regulated by specific enzyme

(7) The activated pkA

- activates by phosphorylation the enzymes catalyzing this pathway
  - On multiple steps
- Therefore, ACTH is one of the strong stimuli for cortisol synthesis

(8) Cortisol is released into the bloodstream

- It is a steroid hormone
  - needs to bind to specific proteins for transportation
    - ~75% binds to **corticosteroid binding globulin** (CBG)
      - A.k.a. transcortin
    - ~25% of it binds to **albumin**
      - A protein synthesized by the liver

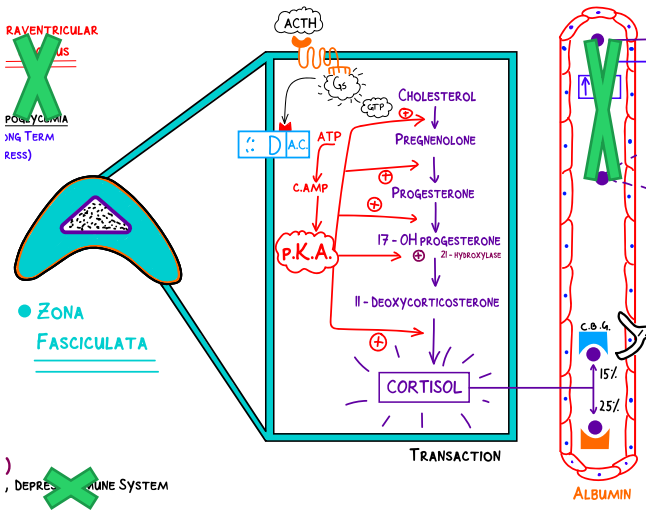

Figure 2 Synthesis of cortisol.

III) EFFECTS OF CORTISOL

(A) EFFECTS ON THE SKELETAL MUSCLES

(1) In the muscles

- there are a lot of proteins
  - Made up of amino acids
  - Have an **amino terminus** and a **carboxyl terminus**

(2) As a steroid hormone

- cortisol passes through the lipid bilayer of the cell membrane
- Binds to an intracytosolic receptor
  - Activates it

(3) The activated receptor activates specific genes

- expressed in the nucleus
- Those genes are transcribed
  - Producing mRNA
- mRNA goes into the cytoplasm
  - The ribosomes translate it into proteins - proteases

(4) The proteases break

- the peptide bonds inside the proteins
  - Produce amino acids
    - Released into the bloodstream
    - Go to the liver
- The process is called **protein catabolism**
  - It is stimulated by cortisol
- Cortisol also stimulates catabolism within the bones

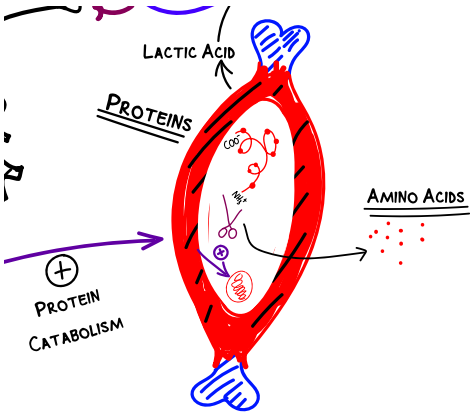

Figure 3 Effects of cortisol on the skeletal muscles.

(B) EFFECTS ON THE ADIPOSE TISSUE

(1) Cortisol affects

- the adipocytes of the adipose tissue
  - Main component – triglycerides

(2) As a steroid hormone

- cortisol passes through the lipid bilayer of the cell membrane
- Binds to an intracytosolic receptor
  - Activates it

(3) The activated receptor activates specific genes

- expressed in the nucleus
- Those genes are transcribed
  - Producing mRNA
- mRNA goes into the cytoplasm
  - The ribosomes translate it into proteins

(4) These proteins break down

- the triglycerides into
  - Fatty acids
    - Utilized by the muscles or redistributed and relocated to different parts of the body
  - Glycerol
    - Goes to the liver
- The process is called **lipolysis**

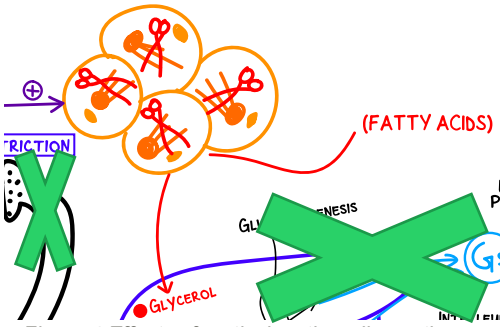

Figure 4 Effects of cortisol on the adipose tissue.

(C) EFFECTS ON THE LIVER

(1) As a steroid hormone

- cortisol passes through the lipid bilayer of the cell membrane
- Binds to an intracytosolic receptor
  Activates it

(2) The activated receptor activates specific genes

- expressed in the nucleus
- Those genes are transcribed
  - Producing mRNA
- mRNA goes into the cytoplasm
  - The ribosomes translate it into proteins
    - These proteins stimulate the processes **gluconeogenesis** and **glycogenesis**

(3) Gluconeogenesis is

- a process where glucose is produced from non-carbohydrate sources
  - From the muscles
    - Amino acids
    - Lactic acid
  - From the adipose tissue
    - Glycerol
    - Odd chain fatty acids

(4) Glycogenesis is

- a process where glucose is converted into glycogen
  - Glycogen is a polymer of glucose
    - A storage molecule for glucose

(5) Cortisol enhances

- the sympathetic nervous system
- Acts on many different tissues sensitive to norepinephrine
  - There are **adrenergic receptors** on the liver
    - They bind norepinephrine

(6) As a steroid hormone

- cortisol passes through the lipid bilayer of the cell membrane
- Binds to an intracytosolic receptor
  - Activates it

(7) The activated receptor activates specific genes

- expressed in the nucleus
- Those genes are transcribed
  - Producing mRNA
- mRNA goes into the cytoplasm
  - The ribosomes translate it into proteins

(8) These proteins increase

- the sensitivity of the G protein-coupled adrenergic receptors of the cell
  - The overall effect of norepinephrine on the vessels is **glycogenolysis**
    - The conversion of glycogen into glucose

(9) Cortisol

- **Directly** stimulates glycogenesis
  - The conversion of glucose into glycogen
- **Indirectly** stimulates glycogenolysis
  - The conversion of glycogen into glucose
  - By increasing the sensitivity of the adrenergic receptors for norepinephrine

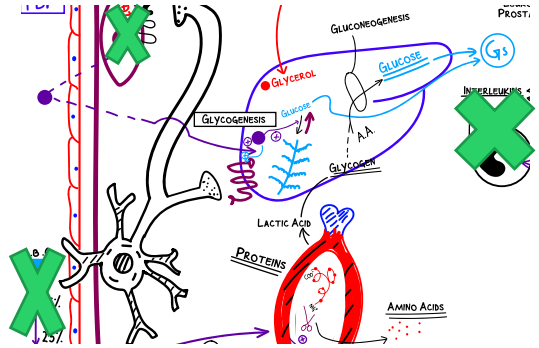

Figure 5 Effects of cortisol on the liver.

(D) EFFECTS ON THE BLOOD VESSELS

(1) Cortisol enhances

- the sympathetic nervous system
- Acts on many different tissues sensitive to norepinephrine
  - There are **adrenergic receptors** in the smooth muscle cells within the tunica media of the vessels
    - They bind norepinephrine

(2) As a steroid hormone

- cortisol passes through the lipid bilayer of the cell membrane
- Binds to an intracytosolic receptor
  - Activates it

(3) The activated receptor activates specific genes

- expressed in the nucleus
- Those genes are transcribed
  - Producing mRNA
- mRNA goes into the cytoplasm
  - The ribosomes translate it into proteins

(4) These proteins increase

- the sensitivity of the G protein-coupled adrenergic receptors of the cell
  - The overall effect of norepinephrine on the vessels is **vasoconstriction**
    → ↑ resistance in the blood vessels
    → ↑ **blood pressure**
  - Cortisol amplifies the vasoconstriction

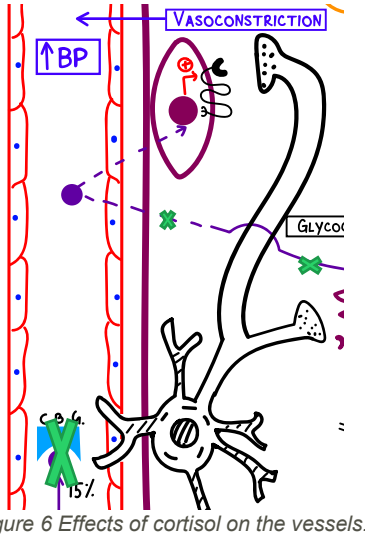

Figure 6 Effects of cortisol on the vessels.

(E) EFFECTS ON THE IMMUNE SYSTEM

(1) Cortisol can inhibit specific processes

- inside the immune cells
  - **Basophils** are responsible for secreting
    - Histamines
    - Leukotrienes
    - Prostaglandins
  - **Lymphocytes** and **monocytes** are responsible for secreting
    - Interleukins
      - (IL1, IL2, IL4, etc.)
    - Cytokines
- This is the **inflammatory immune response**
  - Cortisol inhibits it
    - By preventing the immune cells from producing those chemicals

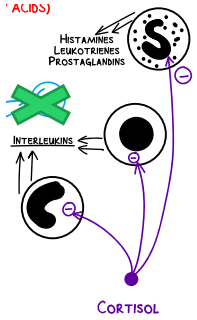

Figure 7 Effects of cortisol on the immune system.

IV) STIMULI

(1) Hypoglycemia

- is one of the main stimuli of cortisol
  - Low blood glucose levels
- In response to it cortisol
  - Indirectly stimulates glycogenolysis
    - The conversion of glycogen into glucose
    - By increasing the sensitivity of adrenergic receptors to norepinephrine
  - Directly stimulates gluconeogenesis
    - The production of glucose from non-carbohydrate sources.
  - Directly stimulates glycogenesis
    - The conversion of glucose into glycogen

(2) Long term (chronic) stress

- is another stimulus
  - May be caused by trauma or starvation
- Long term stress causes a direct release of CRH
  → excessive release of ACTH
  → ↑ production of cortisol
- In response cortisol
  - ↑ the sensitivity of adrenergic receptors for NE in the smooth muscle cells of the vessels
    → Vasoconstriction
    → ↑ blood pressure
    → allows the cells to get more nutrients, glucose, amino acids, etc.
  - ↑ muscle catabolism
    - Provides nutrients
  - Depresses the immune system

- Glycogenolysis (indirectly)
  – ↑sensitivity to NE
- Gluconeogenesis
- Glycogenesis (direct effect)

Protein Catabolism, Blood Pressure, Depresses Imune System

Figure 8 Responses of cortisol to stimuli.

- Preparing for finals is a type of long term stress
  - Due to it the immune system is depressed and microorganisms can cause damage (infections)
  - That's why people tend to get sick before finals

- Cortisol is used to treat **leukemia**
  - It depresses the bone marrow and inhibits the white blood cells
  - Prevents the already formed cells from producing **inflammatory cytokines**

V) FEEDBACK

- ↑ **levels of cortisol** in the blood
  - Exert a **negative feedback** on the hypothalamus → ↓ the production of CRH
  - Inhibit the adenohypophysis production of ACTH → ↓ the production of cortisol
- ↓ **levels of cortisol** in the blood
  - Not enough is going to the hypothalamus and the adenohypophysis to exert an inhibitory effect
    - The nuclei are **stimulated** to produce more CRH
    - The pituitary is **stimulated** to produce more ACTH
      - The synthesis of cortisol is stimulated

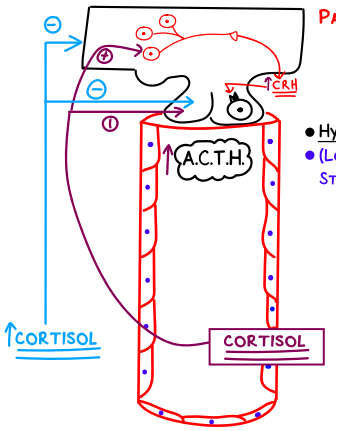

Figure 9 Feedback of cortisol.

VI) REVIEW QUESTIONS

1) What is the inner layer of the adrenal gland?
a) Zona glomerulosa
b) Zona fasciculata
c) Zona reticularis
d) None of the above

2) What does zona fasciculata secrete?
a) Cholesterol
b) Aldosterone
c) Progesterone
d) Cortisol

3) How does the low level of cortisol affect ACTH production?
a) Stimulates ACTH production
b) Inhibits ACTH production
c) Both
d) Neither

4) Which of the following is an effect of cortisol?
a) Protein synthesis
b) Decrease in blood pressure
c) Immunosuppression
d) Stimulating glycolysis

5) What is the effect of cortisol on the liver?
a) Stimulating gluconeogenesis
b) Stimulating glycogenesis
c) Inhibiting glycogenesis
d) a) + b)

6) How does cortisol affect the blood vessels?
a) Increases the sensitivity of the adrenergic receptors of the cells
b) Vasoconstriction
c) ↑ blood pressure
d) Everything of the above

7) What are the main stimuli of cortisol secretion?
a) Chronic stress
b) Hypoglycemia
c) a) + b)
d) Hyperglycemia

8) How does the high level of cortisol affect CRH production?
a) Stimulates CRH production
b) Inhibits CRH production
c) Both
d) Neither

9) Which of the following as a WRONG effect of cortisol on the human organism?
a) Direct stimulation of glycogenolysis
b) Vasoconstriction
c) Protein catabolism
d) Immunosuppression

10) Having in mind the effects of cortisol, in which cases we can use it for treatment?
a) Autoimmune disorders
b) Leukemia
c) Allergic reactions
d) Everything is true

CHECK YOUR ANSWERS

VII) REFRENCES

Use style "Ref"

(example)
- APA citation guide. (2016). http://www.bibme.org/citation-guide/apa/
- Lipson, C. (2011). *Cite right: A quick guide to citation styles – MLA, APA, Chicago, the sciences, professions, and more* (2nd ed). United States of America: The University of Chicago Press, Ltd., London.
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