THYROID GLAND, ADRENAL GLAND, PARARTHYROID HORMONE

11/20/23

THYROID HORMONE SYNTHESIS

1. Iodine Trapping

- Iodine (I^-) is actively transported (as iodide) into the cytosol of follicular cells in response to TSH.

2. Synthesis of thyroglobulin (TGB)

- TGB is produced in the RER and golgi apparatus and packaged in secretory vesicles. Vesicles are released into lumen of follicle via exocytosis.
- N.B. this step happens at the same time as iodine trapping.

3. Oxidation of iodine

- Iodide (I^-) is oxidised to form Iodine (I^0) when it passes through the membrane into the lumen of the follicle.

4. Iodination of tyrosine

- Iodine reacts with the tyrosine amino acids of TGB.
- Binding of a single Iodine forms monoiodotyrosine
- Binding of two Iodines forms diiodotyrosine
- The region of TGB with attached iodine atoms is called colloid

5. Coupling of T1 and T2

- 2 T2 molecules can join to form thyroxine (T4)
- 1 T1 molecule and 1 T2 molecule can join to form triiodothyronine (T3)

6. Pinocytosis and Digestion of Colloid

- Parts of colloid re-enter follicular cells via pinocytosis and merge with lysosomes
- TGB is broken down via digestive enzymes, and T3 and T4 is cleaved off.

7. Secretion of Thyroid Hormones

- T3 and T4 are lipid soluble (despite being amino acid derivatives) so diffuse out of follicular cell into interstitial fluid via plasma membrane, then into blood.

8. Transport into blood

- T3 and T4 bind to thyroxine binding protein in the blood to be transported to target cells.

9. Conversion of T4 to T3

- T4 is secreted in a greater amounts but T3 is more potent.
- T4 is converted to T3 in the liver and kidney.

THYROID HORMONE IN GROWTH AND NEURONAL DEVELOPMENT

- Thyroid hormone stimulates Growth Hormone (GH) secretion and promotes GH effects
- Lack of thyroid hormone → growth retardation but can be reversed by thyroid replacement therapy. Excess thyroid hormone does not produce excessive growth
- Important in promoting growth and development of the brain during foetal and postnatal life
- Thyroid hormone deficiency → mental retardation if therapy is not administered days or weeks after birth

THYROID HORMONE AND METABOLISM

Increase basal metabolic rate (BMR).
BMR = the energy expenditure during rest

Increased heat production

Increase heart rate, BP and force of heartbeat

This is achieved via up-regulating **β**-adrenergic receptors which increases binding of adrenaline and noradrenaline

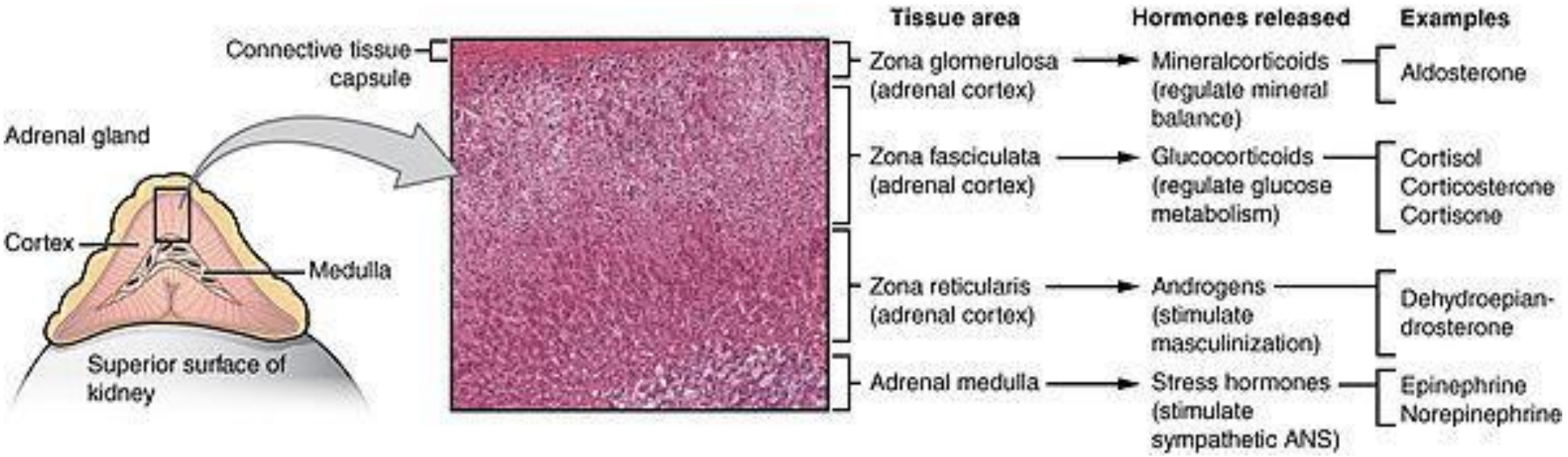
T3/T4 DEFICIENCY

- **Hypothyroidism**– under production of thyroid hormone
- Thyroid hormone **deficiency at infancy can lead to severe mental retardation and stunted bone growth**

CAUSES	SIGNS	SYMPTOMS
Autoimmune thyroiditis	Goitre – swelling at front of neck due to swollen thyroid	Fatigue/lethargy
Iodine 131 treatment	Bradycardia	Weakness
Pituitary deficiencies	Non-pitting oedema	Mental slowness/depression
	Dry skin	Constipation
	Hypertension	Irregular menses
	Slow speech/movements	Infertility
	Hoarse voice	Mild weight gain

Symptoms are **subjective** and can be **perceived only by the person affected.**
Signs are **objective** findings that **can be seen or measured**.

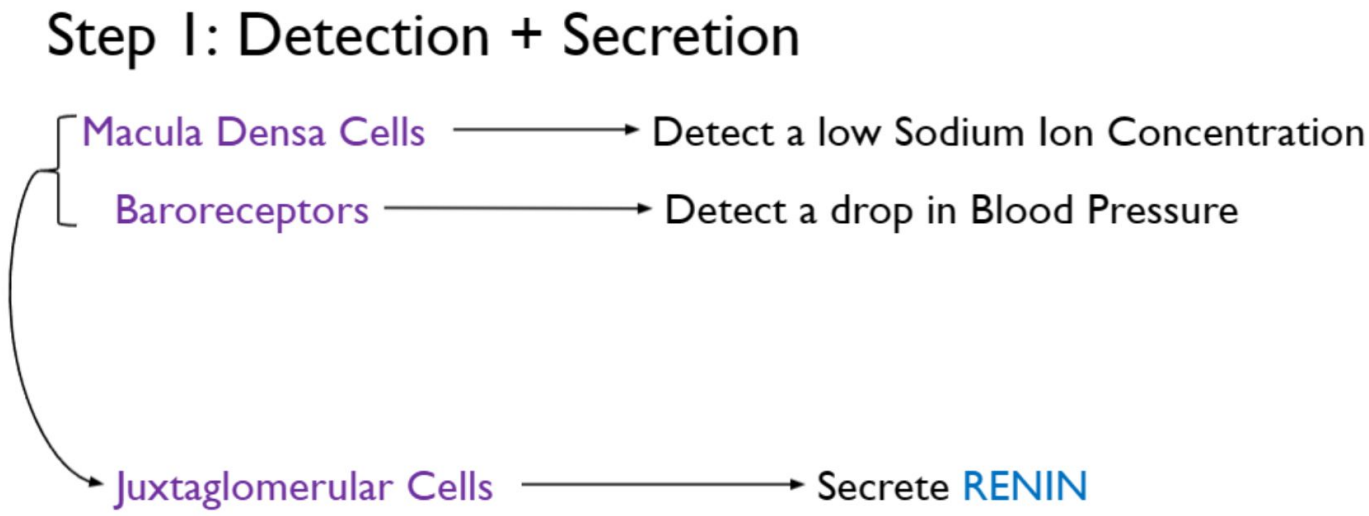
Layers of Adrenal Gland



How to remember: salt, sugar, sex

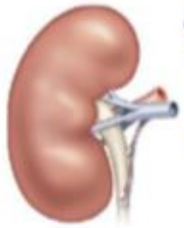
RAAS Pathway

- RAAS (Renin Angiotensin Aldosterone System) helps to regulate aldosterone. This in turn helps regulate sodium (salt) concentration and blood pressure.

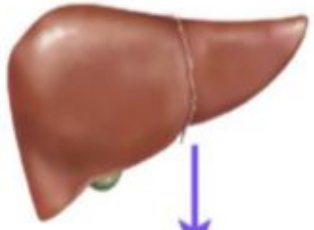


Renin-angiotensin system

Drop in blood pressure
Drop in fluid volume

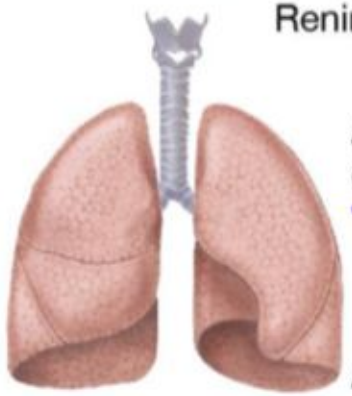


Renin release from kidney



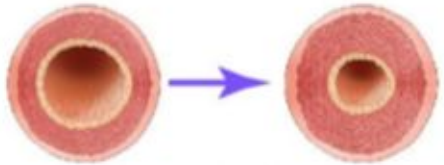
angiotensinogen

Renin acts on angiotensinogen to form **angiotensin I.**

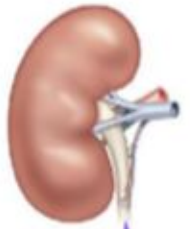


ACE (angiotensin-converting enzyme) release from lungs

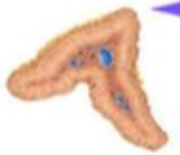
ACE acts on angiotensin I to form **angiotensin II.**



Angiotensin II also acts directly on blood vessels, stimulating vasoconstriction (narrowing).



NaCl
H_2O



Angiotensin II acts on the adrenal gland to stimulate release of **aldosterone.**

Aldosterone acts on the kidneys to stimulate reabsorption of salt (NaCl) and water (H_2O).

Angiotensin II:

- Aldosterone production
- Stimulates ADH release
- Arterial vasoconstriction
- Degrades Bradykinin

Aldosterone:

- Helps increase blood pressure Because ……. more Na+ is reabsorbed and so more water is retained.
- Decreases K+ levels in blood

BRADYKININ

- Bradykinin synthesizes nitric oxide (NO)
- NO is a vasodilator
- ACE degrades bradykinin
- Thus, less vasodilation so more vasoconstriction

ARTERIAL VASOCONSTRICTION

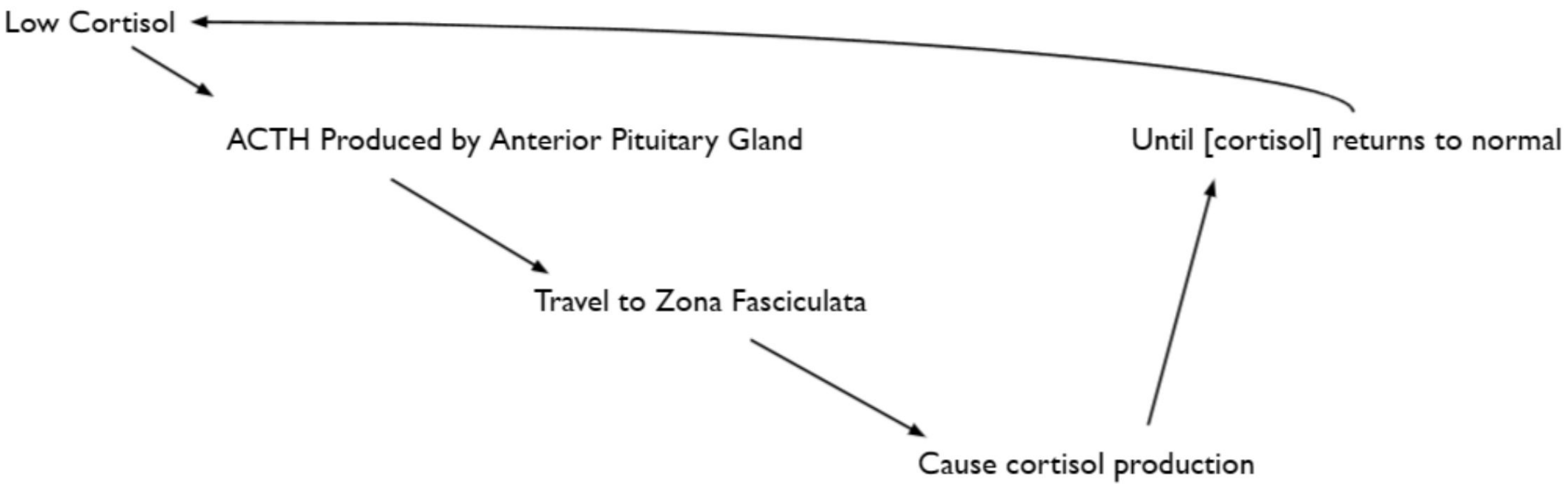
- Angiotensin 2 also acts on kidney
- Causes vasoconstriction of arterioles
- Narrower vessel = more pressure

GLUCOCORTICOIDS: CORTISOL

Effects of Cortisol (key in a fight or flight situation) Ie key in **sympathetic nervous system**.

1. Glucose
   - Gluconeogenesis
   - Hepatic Glycogen synthesis
   - Inhibit peripheral glucose uptake
2. Lipids
   - Increased Appetite
   - Fat Deposition
3. Proteins
   - Protein Breakdown
   - Decreased Protein Production
4. Ions
   - Sodium Retention
   - Increased Potassium Loss
   - Anti-Inflammatory effects

REGULATION OF CORTISOL



What type of feedback? Negative

ACTH = Adrenocorticotropic hormone

ANDROGENS

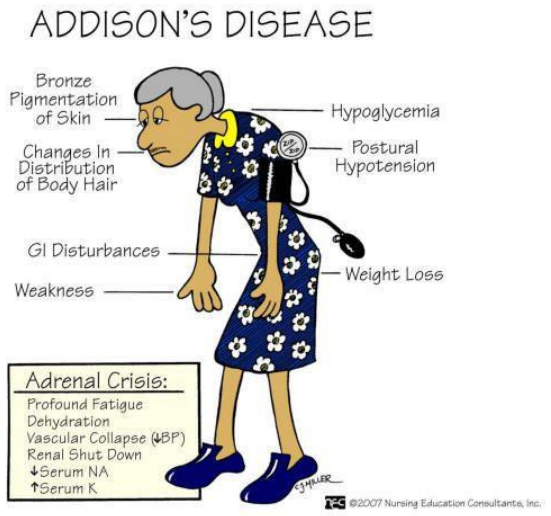
- In females promote libido (sex drive) and are converted into oestrogens (feminizing sex steroids) by other body tissues
- After menopause, when ovarian secretion of oestrogens ceases, all female oestrogens come from conversion of adrenal androgens
- Adrenal androgens also stimulate growth of axillary and pubic hair in boys and girls and contribute to the prepubertal growth spurt

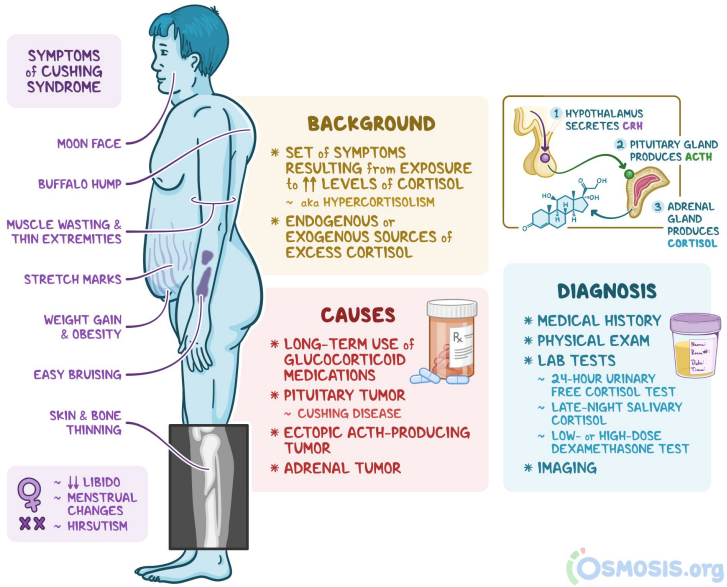
Adrenal Medulla

- Catecholamine production = adrenaline + noradrenaline (epinephrine + norepinephrine)
- Catecholamines bind to G protein coupled receptors – GPCR
- Prepare the body for the sympathetic fight-or-flight response
    - Breakdown of glycogen to glucose
    - Breakdown of fats – fatty acids
    - Increase rate and force of cardiac muscle contraction
    - This all enables the body to deal with physical and physiological stress

OVER/UNDER PRODUCTION OF ADRENAL HORMONES

- Overproduction: Cushing's Syndrome (over production of cortisol) and Conn's Syndrome (over production of aldosterone)
- Underproduction: Addison's disease (under production of cortisol and aldosterone)





PHOSPHATE

Nucleic acid synthesis

ATP production

CALCIUM

Cell division

Cell adhesion

Plasma membrane integrity

Protein Secretion

Muscle contraction including cardiac muscle

Neuronal excitability

Glycogen metabolism

Blood coagulation

REGULATION OF CALCIUM AND PHOSPHATE

Low blood calcium is detected

PTH is released from chief cells of the parathyroid gland

This has 3 different major effects

The effect of PTH on bone:
Stimulates osteoclasts and inhibits osteoblasts (breaks down bone) - releases calcium and phosphate into the blood

The effect of PTH on kidneys:
Stimulates retention of Calcium or loss of Phosphate (or vice versa)
Stimulates release of Calcitriol (active vitamin D)

The effect of PTH on the intestine:
This is an indirect effect. This is because the calcitriol from the kidneys is what stimulates absorption of calcium from food.

High blood calcium is detected

Calcitonin is released from the parafollicular cells of the thyroid gland

This has the effect of stimulating osteoblasts and inhibiting osteoblasts (builds bone) - reduces the amount of calcium and phosphate circulating in the blood

HYPERPARATHYROIDISM

OVERPRODUCTION OF PARATHYROID HORMONE

Primary Hyperparathyroidism

- ◦ Abnormality of parathyroid glands themselves
- ◦ Excessive parathyroid hormone production leads to loss of bone tissue

Secondary hyperparathyroidism

- ◦ Excessive secretion of PTH in response to hypocalcaemia (low calcium)

Tertiary Hyperparathyroidism

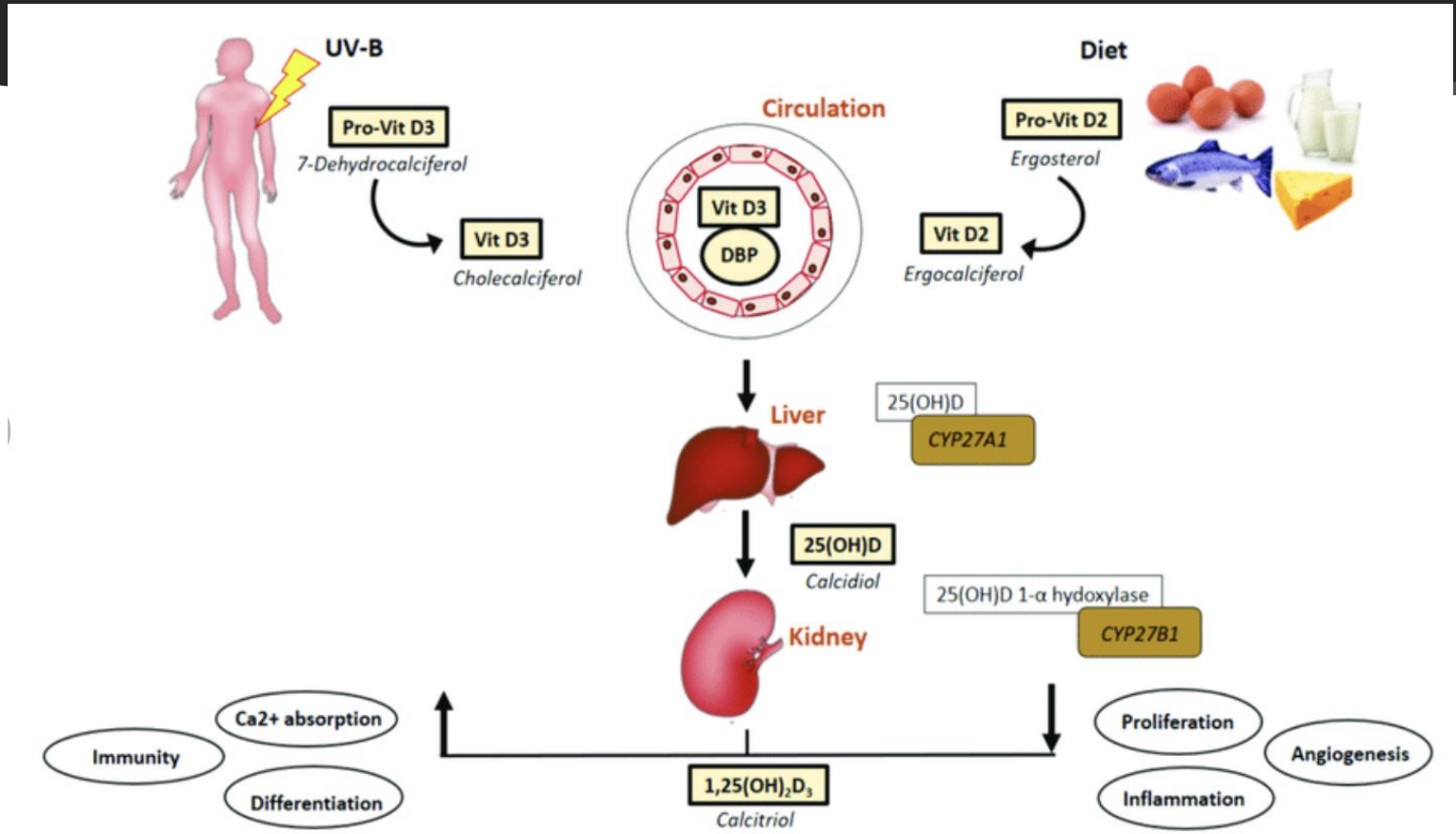
- ◦ Excessive secretion of PTH AFTER secondary hyperparathyroidism treatment
- ◦ Extremely rare

HYPOPARATHYROIDISM

Underproduction of parathyroid hormone.

- Results in low PTH and low Ca^{2+} levels.
- Most caused by autoimmune disorders

VITAMIN D SYNTHESIS



- Vitamin D increases osteoclast activity and increases osteoclast uptake from the GI tract.

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2. Overproduction of aldosterone
3. Underproduction of androgens
4. Underproduction of cortisol
5. Overproduction of adrenaline

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2. Leydig cell
3. Sertoli cell
4. Macula Densa cell
5. Chief cell

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3. Kidney
4. Thyroid gland
5. Liver

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Which mineral is involved in nucleic acid synthesis?

1. Magnesium
2. Calcium
3. Phosphate
4. Zinc
5. Iron

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- Zona glomerulosa
- Zona fasciculata
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