

Metabolic and endocrine renal function

Endocrine Functions of the Kidneys

The kidneys produce three important hormones: **erythropoietin**, **calcitriol** (1,25- dihydroxycholecalciferol) and **renin**. They also synthesize **prostaglandins**, which affect many processes in the kidneys .

In addition to synthesis , the kidneys also contribute to the **degradation** of certain **hormones** – such as **insulin** (forms **insulinase** – cleaves insulin) or **parathyroid hormone**.

Erythropoietin

Erythropoietin is a peptide hormone which **regulates erythropoiesis**.

Structure and function

Erythropoietin is a **glycoprotein** containing 165 amino acids. Its receptors are present on the membranes of **red blood cell precursors**. Binding of the hormone **reduces apoptosis** of these cells – multiple cells survive and can therefore complete their development into mature erythrocytes.

Synthesis and inactivation

In adults, approximately **90 % of erythropoietin is synthesized in the kidneys** (interstitial cells) , the remaining amount in the **liver** (perivenous hepatocytes) . The liver plays a key role in the production of erythropoietin during the fetal period. But in adulthood, the liver is no longer able to compensate for a potential decrease in production in the kidneys.

Clinical correlations:

For most people in **end-stage renal failure**, **anemia** with erythropoietin deficiency occurs. Doctors can administer **recombinant erythropoietin** to these patients.

Erythropoietin is also abused as **doping substance** – especially in endurance athletics (cycling) .

The main stimulus for the production of erythropoietin is a **decrease in the partial pressure of oxygen** in the blood flowing through the two organs. Hormone production is also supported by **androgens** (testosterone) , and **catecholamines** (β – receptors).

The main location of **inactivation** of erythropoietin is the **liver**.

Calcitriol (1,25- dihydroxycholecalciferol)

Final activation of vitamin D to the active hormone calcitriol takes place in the **kidneys** – 1-hydroxylation of **25-hydroxycholecalciferol** to **1,25- dihydroxycholecalciferol**.

Calcitriol **stimulates the small intestine** for protein synthesis **allowing absorption of Ca^{2+} and phosphates**. This ensures the **availability of Ca^{2+} and phosphate for bone growth**. Calcitriol simultaneously **activates osteoblasts to synthesize collagen**.

Renin

Renin is part of the **renin – angiotensin – aldosterone system (RAAS)** . This system is discussed in detail in Chapter 11 and in subchapter about metabolism of water and minerals. We will only provide a basic overview here.

In the **case of insufficient blood flow** to the kidneys (e.g., decrease in blood volume) cells of the **renal juxtaglomerular apparatus** begin the synthesis of protein **renin**. Renin is an enzyme, which catalyzes the conversion of plasmatic **angiotensinogen to angiotensin I**. Angiotensin I is then converted by **angiotensin converting enzyme** to **angiotensin II**, which stimulates aldosterone synthesis and causes vasoconstriction.

RAAS participates in the regulation of mineral balance and blood pressure.

Role of the Kidneys in the Intermediary Metabolism

Process of urine formation requires a lot of energy (eg for active transport of ions). It is therefore not surprising that kidney cells need very **intense energy metabolism**. This applies especially to **tubular epithelial cells in the renal cortex**, which have **better blood supply** and **more mitochondria**, place for **aerobic processes** (produce

more energy). These cells can utilize **almost all nutrients** – glucose, fatty acids / ketone bodies and amino acids (significance of glutamine). Metabolism of cells in **renal medulla** is limited by an **insufficient oxygen supply**, most ATP molecules is thus obtained in the **anaerobic glycolysis**.

Kidneys represent a significant organ of **gluconeogenesis**.

Metabolism of glutamine

Glutamine (Gln) is produced mainly in **skeletal muscle from branched-chain amino acids** (Leu, Ile, Val). In its molecule body **stores toxic ammonia**:



Cells with rapid turnover rate (tubular cells in kidneys, enterocytes, immune cells) are the **main consumers of glutamine from blood**. It serves as an **energy substrate** and as a **nitrogen donor in some synthetic pathways**.

Glutaminase reaction has a high activity in kidneys. Unused nitrogen from glutamine can be **secreted into the urine** or **incorporated into alanine**, which transports it to the **liver** (nitrogen is used for synthesis of **urea**). Carbon skeleton of glutamine forms **α -ketoglutarate** that can be **oxidized, converted to glucose** or is released as serine or alanine.

References

Fontana, Josef and Lavříková, Petra. "5. Role of the Kidneys in the Intermediary Metabolism • Functions Of Cells And Human Body". *Fblt.Cz*, <http://fb.lt.cz/en/skripta/vii-vylucovaci-soustava-a-acidobazicka-rovnovaha/5-uloha-ledvin-v-intermediarnim-metabolismu/>.

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