Glomerular Filtration

Glomerular Membrane

The glomerular basement membrane (GBM) lies between the capillary endothelium and the podocytes. It consists of **three basic layers** :

1) External laminate

2) Lamina densa

3) Internal rail laminate

Thanks to **heparan sulphate proteoglycans** , especially in the lamina densa, GBM has a strongly **negative charge** , which contributes to the barrier, which prevents the passage of larger negatively charged molecules - such as larger **proteins** .

Podocytes are epithelial cells with primary (cytotrabecula) and secondary (cytopodium) **protrusions** that form the **visceral leaf of the Bowman's capsule** (*capsula glomerularis*). The secondary protrusions (often referred to in the Czech literature as **pedicles**) interdigitate each other and thus form an intertwined complex on the basement membrane, which almost completely covers the GBM. **Narrow filter slits** (about 40 nm) remain between the pedicles , but they are covered by a so-called **slit** diaphragm. **The transmembrane protein nephrin** plays a key role in its composition, whose long molecules cover the filter slots and narrow the space to small filter pores. The intracellular domains of nephrin are attached to their actin cytoskeleton in the pedicles. This membrane represents **the main barrier for plasma proteins** , mainly due to its **negative charge** , which also repels negatively charged plasma proteins. The cytoplasmic membrane of the podocyte processes also carries an anionic glycocalyx on the surface, which contributes to the overall negative charge of the barrier.

The endothelium of glomerular capillaries, its basement membrane and podocyte protrusions together form the so-called **glomerular filtration barrier** (**blood / urine barrier**), through which due to high filtration pressure in capillaries water and low molecular weight substances pass from plasma to Bowman space between visceral and parietal renal leaf. capsules.

Glomerular filtration

The volume of liquid filtered per unit time in all glomeruli can be expressed as the **glomerular filtration rate** (**GFR**). Its physiological value is **120 ml/min/1,73m2 body surface area**, thus **180 l/day**. About **99 % of the filtrate gets reabsorbed by the tubular resorption** to the extracellular fluid (back into the body), leaving only 1.5-2 l of urine per day. Movement of the fluid through the filtration membrane is controlled and determined by the ratio of the hydrostatic pressure in the capillaries and oncotic pressure of plasma proteins (less by the hydrostatic pressure of the interstitial fluid and oncotic pressure in the filtrate). These forces are called **Starling´s forces** and there are a few differences from the general principles:

1) Fluid is not exchanged between the capillary and the interstitium, but between the capillary and the fluid of Bowman’s capsule

2) Hydrostatic pressure in the capillaries is different, the movement is thus only one-sided (in the direction of filtration)

3) Filtration barrier (see above) has a unique structure and properties which do not allow passage of proteins into the filtrate (primary urine)

GFR is therefore dependent on the **renal blood flow**, the **filtration pressure**, the **plasma oncotic pressure**, and the **size of the filtration area**.

Control of glomerular filtration

Its main determinant is the **renal blood flow** that is directly proportional to the pressure difference between renal artery and renal vein and inversely proportional to the peripheral resistance of the afferent and efferent arteriole and the interlobular artery. We distinguish **local** and **central regulatory mechanisms**.

Local regulatory mechanisms

Local regulatory mechanisms consist mainly of **myogenic autoregulation** and **tubuloglomerular feedback**.

Myogenic autoregulation

Elevated blood pressure leads to the contraction of renal blood vessels, thereby increasing peripheral resistance. The reverse process occurs when the blood pressure decreases. Thanks to this regulatory mechanism remains the renal blood flow (and thus the GFR) relatively unchanged during normal fluctuations of the mean arterial blood pressure (80-180 mmHg).

Tubuloglomerular feedback

A decrease in GFR is registers by macula densa (part of the juxtaglomerular apparatus). As an answer to the detection of a low flow of tubular fluid or a reduced amount of sodium ions it sends paracrine chemical signal that causes vasodilation of the afferent arteriole, leading to an increase in a hydrostatic pressure and to a restoration of normal GFR.

Central regulatory mechanisms

The central regulatory mechanisms are less important. They are represented by the **sympathetic nervous system**, **epinephrine**, **angiotensin II**, **prostaglandins** and **adenosine**.

Postganglionic neurotransmitter of the sympathetic nervous system **norepinephrine** causes particularly in the afferent arteriole vasoconstriction, thereby reducing the renal blood flow (and thus the GFR) It is important especially in stressful situations, including pain and bleeding. **Epinephrine** has a similar effect.

Angiotensin II (via angiotensin receptor AT1) acts on both the afferent arteriole and the efferent arteriole in similar way as sympathetic nervous system and epinephrine.

Locally produced prostaglandins (especially E2 and I2) reduce the effects of sympathetic nervous system and angiotensin II on both the afferent arteriole and the efferent arteriole.

Adenosine is generally effective vasodilator, in afferent arteriole but acting as vasoconstrictor.

Furthermore, the renal blood flow is increased by **atrial natriuretic peptide** (ANP), **glucocorticoids**, **nitric oxide** or **kinins**, whereas **antidiuretic hormone** (ADH), **ATP** and **endothelin** cause a reduction in the renal blood flow.

References

Dusíková, Kristýna et al. "2. Renal blood circulation • Functions Of Cells And Human Body". *Fblt.Cz*, http://fblt.cz/skripta/vii-vylucovaci-soustava-a-acidobazicka-rovnovaha/2-krevni-obeh-v-ledvinach/.

Dusíková, Kristýna et al. "3. Urine Formation • Functions Of Cells And Human Body". *Fblt.Cz*, http://fblt.cz/en/skripta/vii-vylucovaci-soustava-a-acidobazicka-rovnovaha/3-tvorba-moci/.