correspond relative stationary values of volume and composition of body fluid, varying in admissible limits.

These particular functions of kidneys are performed by its excretory capability based on elimination of useless substances. The needless, even harmful substances are exctreted by mechanism of glomerular filtration and by tubular mechanisms. Kidney is in fact the only way how to excrete the waste products, the molecules containing nitrogen and sulfur. The most important substances are the products of protein metabolism (urea, aminoacids, uric acid, creatinine, creatine etc.). In renal failure the retention of these substances in organism followed by elevation of their concentrations in blood is developing.

In addition to this excretory function, kidney performes important functions, which could be thought to be endocrine. Kidney is not only the effector organ of several hormones (aldosterone, ADH, parathormone, angiotensin, prostaglandins etc.), but kidney is also the site of production of substances with hormonal or enzymatic activities (renin, renal erythropoietic factor, prostaglandins, kallikrein-kinin system).

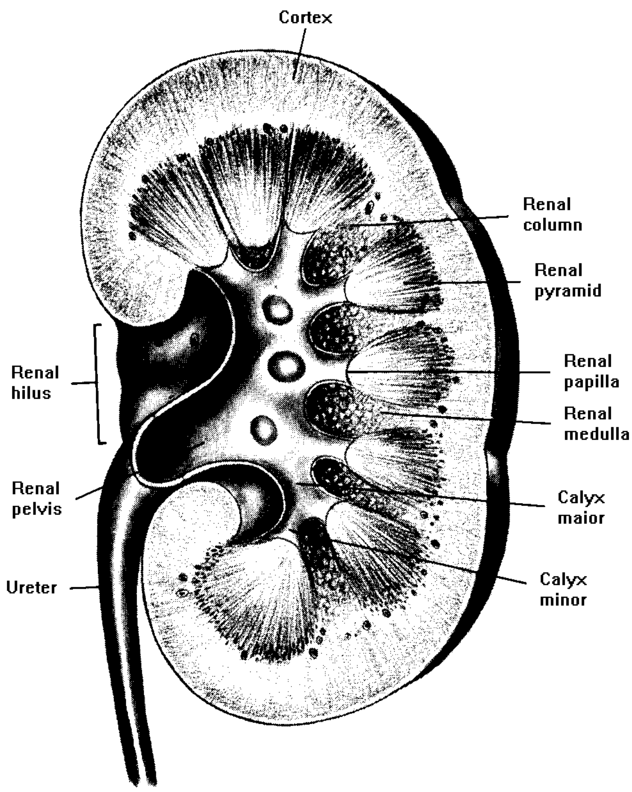

Figure 4.1: Longitudinal section of the kidney

4.2 Basic anatomic notes

Kidneys lies in the abdominal cavity retroperitoneally and paravertebrally, between the twelfth thoracal and third lumbar vertebra. The right kidney lies slightly lower than the left. In adult subjects each kidney weighs 120 to 170 g or more. Kidneys are covered by a thin, but firm fibrous caspsule, adherent to the vessels and renal pelvis in the hilus. The capsule consists mostly of collagenous and less of elastic fibres. In this net of fibres some smooth muscle cells are found. Kidneys are surrounded by a lipid "cushion" - the panniculus. See figure 4.1, page 258.

Renal cortex is about 5 to 15 mm thick, not sharply demarcated from the medulla. The cortical substance forms longitudinal projections – columnae renales, penetrating the medullar substance and reaching the calyces renalles. Medulla renalis consists of 8-20 pyramidal formations separated by cortical projections. The tops of pyramids are oriented towards the renal hilus. Each pyramid with adjacent cortical layer forms the renal lobe – lobus renalis.

A. renalis enters kidney through the **hilus** dividing into 2–3 branches. Accesory arteries with an irregular course can be found sometimes, they can enter the kidney outside the hilus. After entering the kidney the branches of renal artery divide into arteriae interlobares passing between the pyramids into their bases where they branch and join in an arch-like shape, forming the arteriae arcuatae. They lie at the border between the cortex and medulla. From the arcuate arteries are derived the interlobular arteries – arteriae interlobulares – crossing the cortex to its surface. From interlobular arteries arise vertically short afferent arterioles into the glomeruli.

According their localization **two types of glomeruli** can be distinguished in kidneys. Most of them are localized superficially, designated as glomeruli corticales. Nearer to the medulla are the glomeruli juxtamedullares. From the cortical glomeruli arise the vasa efferentia (vessels of arteriolar type) forming the peritubular capillary network, from where the blood is flowing into the venae stellatae corticales and further into the venae interlobulares. At the margin between the cortex and medulla the venae interlobulares join into the vv.arcuatae, further with vv. interlobares, forming finally v. renalis.

From juxtamedullar glomeruli arise the vasa efferentia with a larger luminal diameter. They do not form such a capillary network like around the cortical glomeruli, but they form some smaller branches only. Greater part passes into the vasa recta (arteriolae rectae medullares spuriae) entering the medulla and returning from medulla as thin venulae to the cortico-medullar margin, where they drain the venae arcuatae. The peritubular capillaries have a similar structure as the glomerular capillaries, but they do not contain the podocytes. Vas efferens of juxtamedullar glomerulus branches into the capillaries which can supply several different nephrons. Lymphatic vessels are present in the capsule and in renal parenchyma. They drain into the lymph nodes along the vena cava inferior.

Sympathetic, parasympathetic and sensitive nerve fibres enter the kidney innervating mainly the afferent arterioles. Glomeruli have no special innervation.

4.2.1 Nephron

Basic functional unit of kidney is the nephron. Each kidney contains about 1 200 000 nephrons. Nephron consists of glomerulus, Bowman's capsule, proximal tubule, the loop of Henle and of distal tubule. The glomeruli lie in the renal cortex, the tubules in the cortex and in the medulla. The system of collecting and discharging ducts crosses the medulla and lead into the papillary apices as canaliculi renales. Nephrons are separated from each other by only a thin layer of interstitial tissue. Glomeruli of the cortical nephrons lie in cortex, their loops of Henle reach the medulla. Glomeruli of the juxtamedullar nephrons lie at the margin between the cortex and medulla (near to medulla). The loops of Henle of these nephrons course deeply into the medulla, or to the papillae.

4.2.1.1 Glomerulus

The mean diameter of glomerulus is close to 200 μm. It is a tuft of capillaries inserted into the mesangium and lying in the Bowman's capsule. Glomerular capillaries have a rather simple structure: the inner layer consists of endothelial cells, the medial layer of basement membrane and the outer layer oriented towards the Bowman's capsule consists of epithelial cells – podocytes. The space between the capillaries is filled with mesangial cells and mesangial extracellular substance - the matrix. The parietal part of Bowman's capsule consists of basement membrane and flattened epithelial cell lining oriented towards the glomerulus. (See the figure 4.2, page 260).

Endothelial cells The thickness of the endothelial cells measures only 50-60 nm and their nuclei bulge into the capillary lumen. The layer of endothelial cells is not continuous, it is breached in intervals by holes and covered with a very thin mucopolysaccharide membrane - forming membrana fenestrata. The whole surface area of human glomerular capillary endothelium measures approximately 1,5 m^2.

Basement membrane is the basis of the capillary wall. Basement membrane of glomerular capillaries is in fact the continuation of vas afferens basement membrane. It is continuous with the basemnet membrane of vas efferens and of basement membrane of Bowman's capsule. At several sites it is connected with mesangial cells and mesangial substance. Basement membrane consists of glycoproteins and of collagen, measuring about 300–330 nm in thickness. Three layers can be observed in basement membrane: the medial, the inner and the outer layers. The medial layer is the thickest and the most consistent of them - lamina densa. The layer lying under the endothelial cells is the - lamina rara interna and the layer under the podocytes is - the lamina rara externa.

Podocytes are the epithelial cells covering the external surface of the basement membrane. Under great and spatial magnification they have a octopus-like shape with thick foot processes branching into less-sized pedicels attached to the basement membrane by fine fibrils. Network of these pedicels forms a variable interpedicular split (pores) which can vary or disapear. They are permeable for smaller molecules than those passing through the membrana fenestrata. The penetration of molecules through the capillary membrane is determinated, besides their

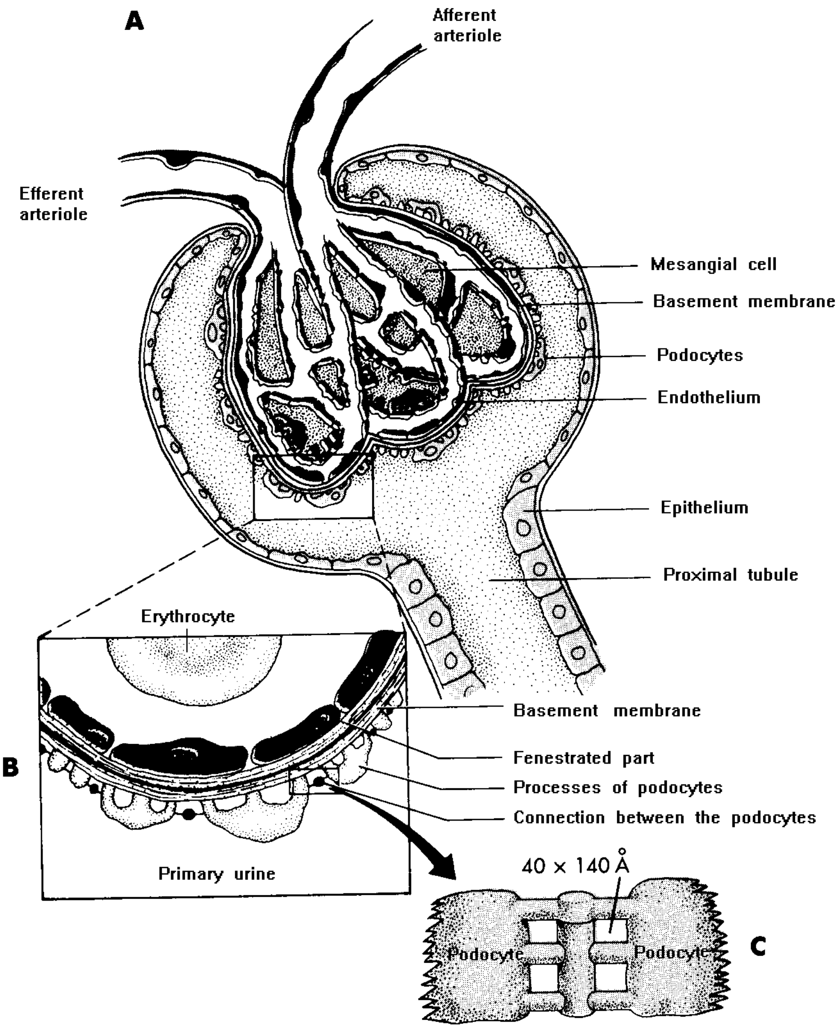

Figure 4.2: Structure of glomerulus (A – cross-section through glomerulus; B – capillary wall; C – connection between the podocytes; from McCance KL, Huether SE: Pathophysiology, 1990)

size, also by electrical charge of molecules. The sialoproteins form a polyanionic gel covering the cytoplasmic membranes of pedicels and are present in the peripedicelar splits. This polyanionic gel suppresses the penetration of negatively charged molecules of albumin (See figure 4.3, page 261).

Mesangial cells and mesangial substance fill the space between the glomerular capillaries. Mesangial substance is similar with the basement membranes. Mesangial cells are dispersed in the mesangial substance. They are more numerous at site where the arterioles enter and leave the glomerulus. Here they have a closer connection with the the juxtaglomerular apparatus. Mesangial cells are star-shaped cells with several thin processes penetrating the surrounding tissue.

The parietal wall of Bowman's capsule consists of basement membrane with identical structure as the basement membrane of glomerular capillaries. The epithelium covering the parietal wall of Bowman's

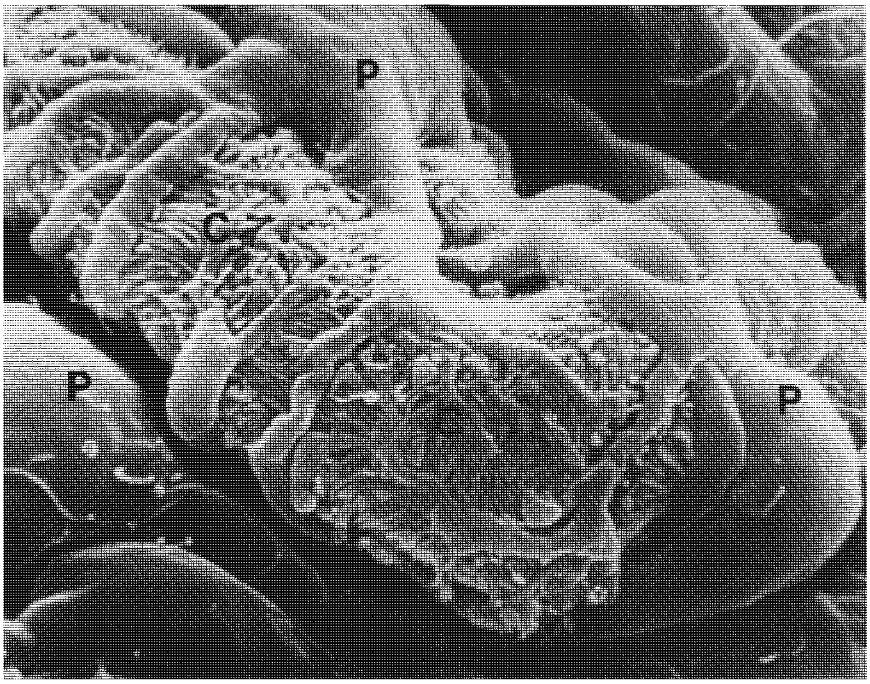

Figure 4.3: Glomerular capillary (P – podocytes; from Kissane JM: Anderson's Pathology, 1985)

capsule passes at the vascular pole to the podocytes.

4.2.1.2 Tubules

The basic structure of tubules is the basement membrane which in fact, is a continuation of the Bownam's capsule basement membrane.

Proximal tubule is about 15 mm long and its diameter measures 5 mm. It is lined by a single layer of cuboidal cells containing numerous elongated mitochondria and enzymes of anaerobic metabolism. Numerous processes at the basal portion of tubular cells increase the surface area and forms a labyrint at the basement membrane which contains a great amount of canaliculi communicating with extracellular space. The border between the tubular epithelium and the epithelial cells of peritubular capillaries is formed only by the basement membrane of similar qualities as the basement membrane of glomerular capillaries. The proper intercellular dividing line is formed by cytoplasmic membrane provided with brush border at the apical cell surface. This lipoprotein membrane enables a selective choice and transfer of various substances. The lipid component of the membrane acts as isolating layer, being permeable for liposoluble substances.

Convoluted portion of proximal tubule (pars convoluta) continues in the straight portion (pars recta) forming the beginning of Henle's loop. The proximal convoluted tubule is lined by low cells provided with brush border at their apical surface. It continues in descending limb of Henle's loop. The nephrons derived from glomeruli lying in outer renal cortex have short loops of Henle, while the nephrons derived from juxtamedullar glomeruli have long Henle's loops extending to the medullary pyramids. The thin segment of Henle's loop having a lenght of 2 to 14 mm continues in the thick segment of ascending limb being about 12 mm in lenght.

The distal tubule is only 5 mm in lenght. The ascending part of Henle's loop and the convoluted part of distal tubule have a nearly identical microscopic structure. The cells are shorter than in proximal tubule, the brush border is absent, the basal

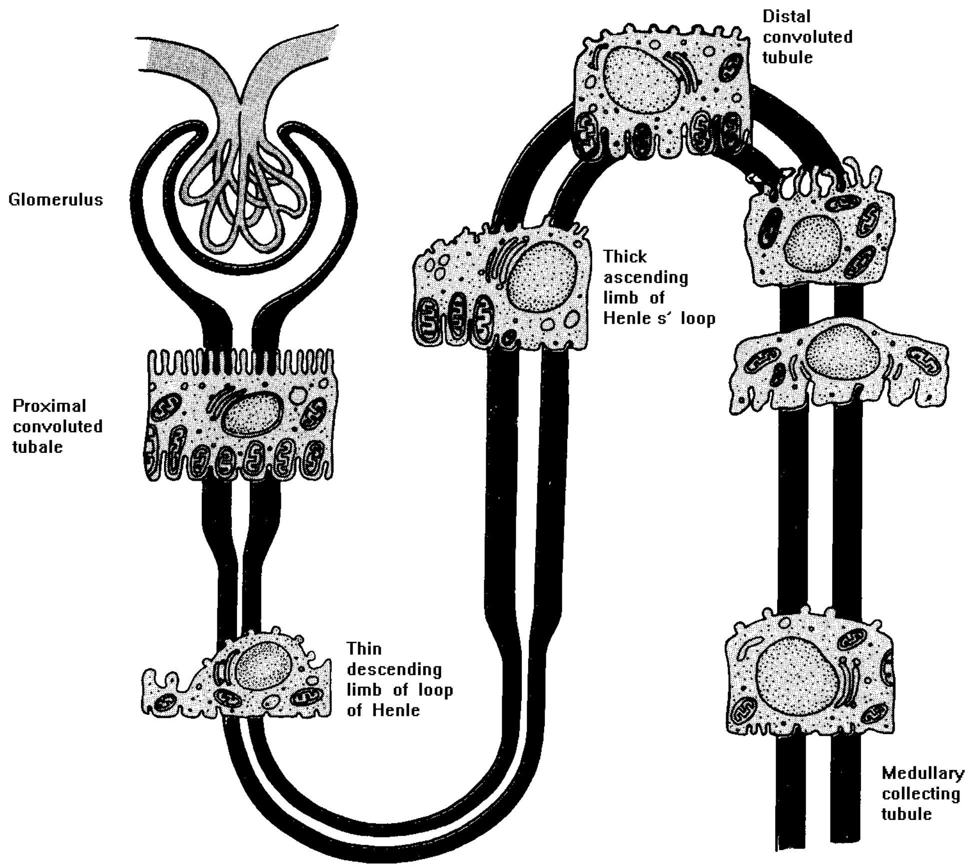

Figure 4.4: The epithelial cells of the tubules (from Berne RM, Levy MN: Physiology, 1988)

labyrinth is not so pronounced. They are cuboid in their shape and have few processes covered by acid mucopolysaccharide. In the luminal portion of these cells numerous vesicles can be found. They contain fewer mitochondria and enzymes than the cells of ascending limb of Henle's loop.

Macula densa is a portion of the distal tubule closely adjacent to the glomeruli at the vascular pole.

The collecting tubules are about 20 mm in lenght. The lining of the collecting tubules consists of relatively large cells named the light and dark cyllindrical cells. At their basal site are numerous pseudopodia and many enzymes of anaerobic metabolism. Several collecting tubules join the neighbouring ones to form finely papillary ducts which drain at the papillary tips of kidneys.

The entire nephron with the collecting tubule is about 45-65 mm in lenght (see figure 4.4, page 262).

4.2.1.3 The juxtaglomerular apparatus

The juxtaglomerular apparatus is located in the region where vas afferens enters the glomerulus. It is spacially confined by afferens and efferens glomerular arterioles and the wall of distal tubule. The centre of this triangle is filled with special cells being related with smooth muscle cells of arterioles and connected through the vascular pole with glomerular mesangial cells. In afferent arterioles occur the juxtaglomerular cells having properties of myoepithelioid cells. A few dispersed cells of this type occur also on other parts of renal arteries. Juxtaglomerular cells contain numerous ribosomes, well developed Golgi complexes and endoplasmic reticulum and secretory granules. Some of these granules are considered to be specific secretory granules containing renin the other granules do not contain renin, but it is suggested, that renin could be deposited in these cells in a non granular form.

In the juxtaglomerular triangle cells called lacis cells occur designated also as extraglomerular mesangial, or Goormaghtig's cells. They have numerous microvilli forming a fine network.

The interstitium consists of cells and cell-free substance. Interstitial cells resemble in their structure to fibroblasts. They contain lipoid drops of prostaglandin precursors and a system of fibrils, probably identical with elastic fibrils. The thicker fibres cross the juxtaglomerular cells entering the Bowman's capsule and the podocytes.

4.2.2 The urinary outflow tract

Urine from collecting ducts is excreted into the renal pelvis, passing calyces renales minores et maiores. From the renal pelvis is the urine transported into the urinary bladder by the contractive activity of ureters. The wall of the urinary excretory system has in all its segments almost the same structure. It cosits of three coats: mucous, muscularis nad fibrous. The mucosa is lined by transitional epithelium. In the proximal parts of urinary outflow tract 2-3 cellular layers in the more distal portion 5-7 layers can be found. Lamina propria mucosae lying beneath the epithelium consists of collagenous connective tissue.

The middle coat of urinary tract excretory system consists of an inner longitudinal and an outer circular layer of smooth muscle. **Calyces renales** have two muscle layers enabling contraction waves wich aid the urine transport into the renal pelvis. The renal pelvis has the same structure, consisting of two muscle layers. The distal third of ureters consists of three muscle coats – the thirth, outer coat is formed of longitudinally oriented smooth muscle layer. The peristaltic waves of ureter occur 1-5/min. shifting the urine towards the urinary bladder. The stimulus initiating these movements is not understood till now. It could be a certain filling pressure in renal pelvis. The oblique "entrance" of ureters into the urinary bladder inhibits the urine reflux, though ureters are not provided with sfincters at their terminal portion.

Urinary bladder is the reservoir for urine. Its physiologic capacity is variable, it varies about 300 ml. The urinary bladder wall consists of three muscle coats, the lining of a superfiacial layer of flat cells, and a deep layer of cuboid cells. In the region of trigonum vesicae urinariae is an inner sfincter.

The man **urethra** is divisible into three portions: prostatic, membranous and cavernous. The female urethra is short. It's lining consists of pavement epithelium.

4.3 Peculiarities of renal blood flow

Concerning the blood flow the kidneys are exeptional organs. The peculiarity of renal haemodynamics is a consequence of the fact, that the kidneys have 100 times greater blood flow than other organs and tissues in human organism. The arteriovenous difference in blood oxygen content is low in renal blood vessels. In healthy adult man at rest the renal blood flow is about 1200 ml per minute representing 25 per cent of cardiac output. In fact, almost the whole blood flows through the glomeruli, only 5-10 per cent of it courses trhough the paraglomerular anastomoses.

It was found that the **blood pressure whitin the glomerular capillaries** is about 50-60 per cent of the blood pressure in systemic arteries – 10 kPa (80 torr). The blood pressure in peritubular capillaries is about 1,9 kPa (15 torr) and in **vena renalis** about 0,8 kPa (6 torr). The glomerular capillary network can be so considered to be a high – pressure capillary network in contrast to the low – pressure peritubular capillary network. The striking difference in pressure between the glomerular and peritubular capillaries is caused by the high resistance within the vas efferens.

The **high-pressure region of cortical glomerular network** resembles the arterial end of capillaries. In the low-pressure peritubular capillary network prevails the retrograde diffusion of fluids according to Starling's law, thus the peritubular capillary bed functions as the venous end of capillaries. Blood flowing through the peritubular capillary network is deprived of the water volume which has been filtered