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AGE RELATED ANATOMICAL AND FUNCTIONAL CHARACTERISTICS OF HUMAN KIDNEY

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Summary. *Development of the human kidney begins at the end of the first month, and the kidney becomes functional in the course of the second month of antenatal life. In the last trimester, the fetal kidney already manifests first involutive changes. From then on to its adult maturity, the kidney is characterised by intensive processes of maturation, but also evident involutive changes. The dynamism of these changes, however, is different in certain life ages. The antenatal period is characterised by intensive processes of nephrogenesis, realised in three successive phases of renal development: pronephros, mesonephros, and metanephros. The first two changes represent a temporary system, while the third stands for a permanent system of excretion, that is, a definitive kidney. The functioning of kidneys, though not necessary in the antenatal stadium, indicates their excretory, homeostatic and endocrine roles, and signifies the maturation process. After birth, there is a further process of structural and functional maturation of the kidneys. With a definitive number of nephrones at birth, renal mass increases at the expense of growth of certain nephrone structures and interstitium. The kidney reaches its full anatomical and functional maturity by the end of the third decade of life. From then on, the kidney is characterised by involutive changes of varying intensity. By the end of the sixth decade these changes are slow; afterwards, to the end of life, they show a trend of very rapid progression, and are a consequence primarily of the reduced renal perfusion. In spite of that, under normal conditions they do not show signs of renal insufficiency even in a well-advanced age. The involutive renal changes can be separate, but they can coincide with corresponding renal diseases. In some individuals this can result in a progressive failure of renal functions in an advanced age.*

Key words: *Age, anatomy, function, human kidney*

Introduction

One of the oldest definitions of ageing states that it is: "a gradual weakening of cell reactivity based on the biophysical and biochemical changes of cell matter, on the changes in its physico-chemical structure, on the gradual loss of the cell capacity for reproduction and regeneration of its biochemical structural elements" (1). Another definition states that "ageing represents an inevitable process conditioned by natural laws, a process of limiting the adaptive capacity of the organism, of increasing death probability, of shortening the life span, which allows for the development of age-related pathology." (1). There have been since various definitions of ageing which, in their specific ways, contribute to the understanding of ageing as a complex phenomenon relevant to each living organism. Theories which conceive of ageing as of a global all-encompassing process have been recently replaced by the idea that the ageing of an organism represents a sum of its ageing individual cells. It is supported by the fact that age-induced dysfunction of organs and tissues in man, such as brain or subcutaneous fat tissue, is closely related to the reduction of cell number (2). The same author quotes the genetic theory of ageing which assumes that it is a result of a genetic programme determining the progressive manifestation of various age-related phenotype changes. "The theory of telomere-shortening" holds that the cells do not replicate the chromosomes in their entirety during the cycle of partition so that their DNA sequences replicating late are lost due to the age-related loss of the telomerasis. Current research shows that the shortening of the telomere may be a phenomenon related to development and not only ageing (3).

The research carried on animal and human kidneys shows that in the course of ageing there is a progressive loss of renal parenchyma so that one third to one half of renal nephrones are lost by old age (4). It has been established that the processes of hialinosis and sclerosis of glomeruli in man begin as early as the seventh month of antenatal life with juxtamedullary nephrons, and in the ninth with cortical ones. Although these processes develop very slowly, there is a clear correlation between the age and the number of affected glomeruli. The regression curve drops from 95% of normal glomeruli at the age below 40 to 63% at the age of 90 (5). These involutive kidney structural changes are also accompanied by a progressive reduction of its function (6).

These data clearly illustrate how the kidney changes from the moment of its budding in the embryonic period to the well-advanced age of man. There are numerous and dynamic changes from the emergence of pronephros to an aged kidney, and they are characterised by the processes of maturation and involution, occasionally overlapping in certain ages of life.

Kidney in an Embryo and Fetus

Anatomical Characteristics

The antenatal life of man, including pre-embryonic, embryonic and fetal periods of development is characterised by the development of three successive, bilateral, excretory systems: pronephros, mesonephros and metanephros. All of them develop from the so-called nephrogenic cord, which take rise from intermediate mesoderm (Fig. 1A). Pronephros and mesonephros are temporary, while metanephros is a permanent excretory organ (7-14).

Pronephros. The development of pronephros begins at the end of the third week of preembryonic period, from the first five cranial segments (nephrotomes) of the nephrogenic cord (Fig. 1B). Pronephros in a human embryo is first represented by seven to ten solid cell clusters. These cell clusters then become vesicular. Vesicles then elongate and form tubules. The tips of the lateral

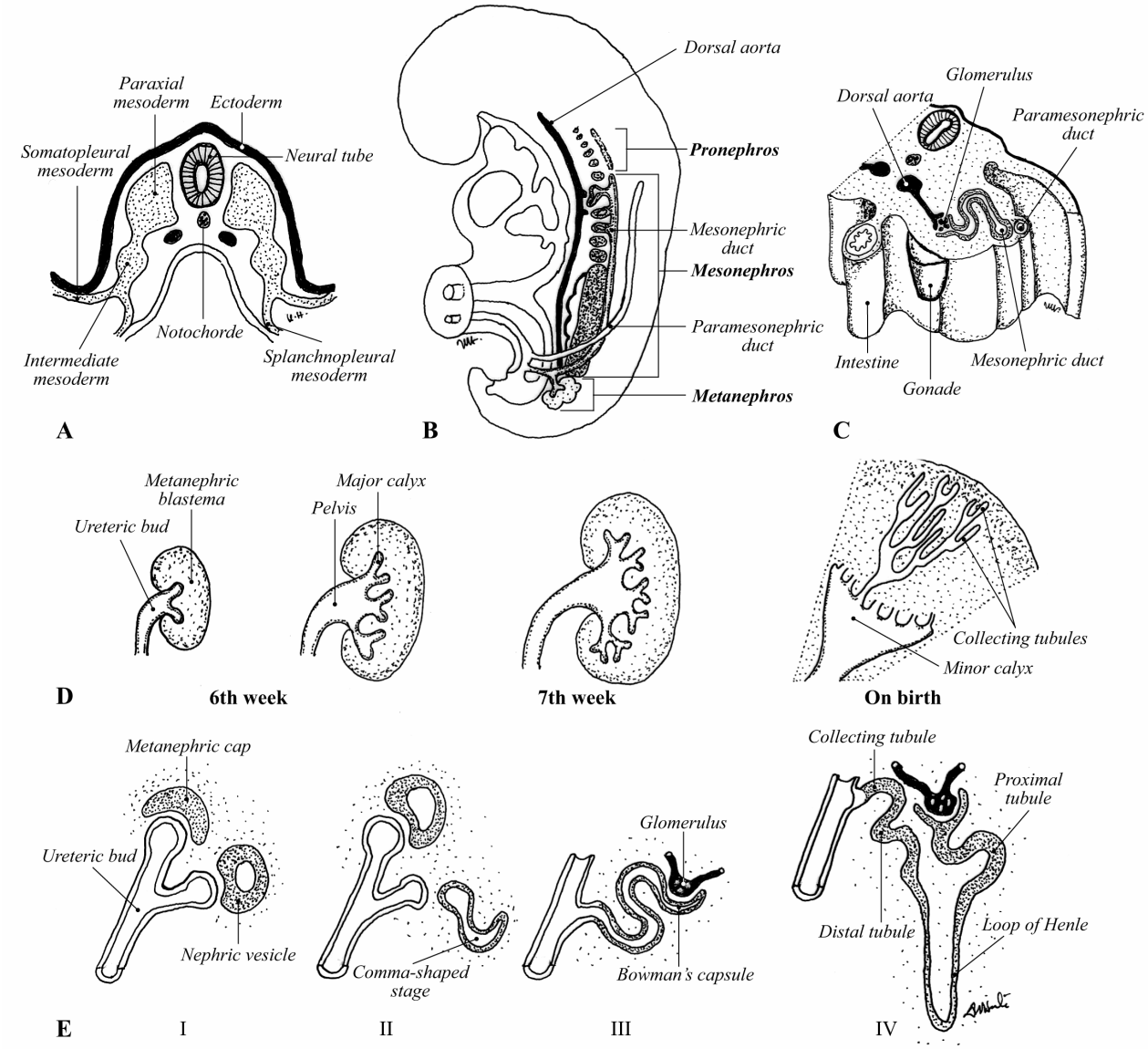


Fig. 1. Kidney development: A – differentiation of mesoderm, at the end of 3th week of developmet; B – pronephros, mesonephros and metanephros in the 5th week of development; C – mesonephros in the 5th week of development; D – metanephros: prenetration of the ureteric bud in metanephric blastema and development of excretory system of kidney; E – nephron development: I – branching of ureteric bud, II – comma-shaped stage, III – S-form, IV – ending of nephrogenesis.
(Adapted from Nikolić et al., Embriologija čoveka. Dečje novine, Beograd, 1988; 199-207 (in Serbian)).

tubule ends extend caudally so that they soon reach the nearest tubule below and connect with it. In this way tubules form the pronephric duct which elongates caudally. At their medial ends these tubules have holes (nephrostomes) used for communication with the coelomic cavity. Pronephric tubules are not fully differentiated, they are short, the aorta does not branch into them, so that glomeruli are not developed either. The regression of pronephric tubules begins very early, so that cranial tubules disappear before the caudal ones appear (7). On the disappearance of the pronephric tubules, the pronephric duct made by them also disintegrates. By the end of the fourth week of the embryonic development of man, pronephros almost completely disappears (8).

Mesonephros. Mesonephros appears starting with the fourth week of the embryonic life (9). It stretches from the sixth cranial to the third lumbar segment of the nephrogenic cord (Fig. 1B). It is considerably larger and of more complex structure than its predecessor.

The formation of mesonephros begins with the successive differentiation of solid cell clusters from the nephrogenic cord, caudally from pronephros. They soon become vesicular. The vesicles then elongate and form tubules. The mesonephric tubule (in the S shape) consists of the medial expanded and invaginated end (Bowman capsule) with which they enclose aortic capillaries and form Malpighi corpuscles; the proximal segment which has a secretory function; and distal segment which through connection creates the mesonephric duct (a continuation of the pronephric duct).

The mesonephric duct elongates caudally, and then curves ventrally and opens into a cloaca. It is believed that about 70 to 80 glomeruli and tubules develop in the mesonephros, but not all of them develop at the same time. The maximum number of these glomerular tubular units (nephrones) in each mesonephros amounts to 30 and they are identified in the fifth and sixth weeks of age (10). It is at that time that the mesonephros reaches is maximum length and represents a large, oval, bilateral organ lying by the dorsal wall of the body cavity, on both sides of the middle line (11). The Malpighi corpuscles and the curves of mesonephric tubules are located in its medial part, while the mesonephric (Wolffian) collecting duct are in the lateral one. The mesonephros, unlike the pronephros, is not related to the body cavity, and it is considerably longer with greater tubule curvature (Fig. 1C).

The mesonephros mainly disappears by the end of the eighth week of antenatal life. Degeneration of cranial tubules and glomeruli begins before the appearance of the caudal ones. In female foetuses, the few remaining caudal tubules become non-functional structures (epoöphorone and paroöphorone), situated in the broad ligaments of the uterus; the mesonephric duct completely disappears. In male foetuses, the remaining mesophrenic tubules build up the efferent ductules of the testis, the rostral and caudal aberrant ductules, and the paradidymis, while the mesonephric duct develops into the canal of the epididymis, ductus deferens, seminal vesicle and ejaculatory duct (9).

Metanephros (definitive kidney). The metanephros represents the final developmental stage of mammal kidney, whose development begins in the fifth week of embryonic life. It develops from three sources: an evagination of the mesonephric duct, the *ureteric bud*, and a local condensation of mesenchyme termed the *metanephric blastema* form the nephric structure, while *angiogenic mesenchyme* migrates into the metanephric blastema slightly later to produce the glomeruli and vasa recta. It may also be the case that innervation is necessary for metanephric kidney induction (11).

The ureteric bud, the ureter to be, develops with the second month of the embryonic development from the lower part of the mesonephric duct, in the close vicinity of its connection with the cloaca (Fig. 1B). It grows dorsocranially and penetrates into the metanephric blastema with its loose cranial end (11). Further development of the metanephros is a result of the reciprocal inductive interaction of the ureteric bud and the metanephric blastema. Immediately upon the penetration of the metanephric blastema, the ureteric bud spreads into the primary renal pelvis and then begins to branch dichotomally and produces the next fifteen generations of side-branches which will produce calyces and colleting ducts (12). Thus the whole excretory renal system is formed (Fig. 1D). The contact between the ureteric bud and the metanephric blastema is also the moment when the latter begins to differentiate into two types of cells: nephrogenic and stromagenic ones. The first ones differentiate in the form of compact cell clusters (metanephric caps) around the growing ends of ureteric bud side-branches (Fig. 1E). They will develop into nephrones, the basic structural and functional renal units. During the process, the condensed mass first becomes vesicular, then forms in the shape of a comma, and finally progressively extends and forms a tubular structure in the shape of an S. The proximal end of this S structure will along with the capillaries from the nearby blood vessels form the renal corpuscle, while the remaining part builds up the proximal and distal tubules as well as Henley's loop. The distal tubule connects with the collecting duct and establishes the connection between the secretory (nephrone) and the excretory renal components. Stromagenic cells are not clearly defined and they will make the renal connective tissue.

Various growth factors regulating cell proliferation, transformation, differentiation, morphogenesis and motogenesis along with their surface receptors take part in the processes of induction as well as in the later phases of nephrogenesis. The presence of the nerve growth factor (NGF) as well as NGF receptors is of essential importance for the induction of the metanephros kidney. Research done on mice identified a protein family, "formins", which has a critical role in the early processes during the nephrogenesis. Renal agenesis and hypoplasia are explained by the mutation of its genes (13).

Nephrones are being formed throughout the fetal life. Out of 15 successive nephrone generations, each successive one is closer to the outward surface of the cortex in relation to the previous one. The formation of new nephrones is completed in the period between the 28th and 36th week of gestation so that the number of nephrones is definite at birth (13,14). Each of man's kidneys contains at birth about one million of nephrones, at different stages of development. The greatest number of mature nephrones is located close to the medulla, and their maturity decreases in the direction of the outward cortex. Structural and functional maturation of the nephrones continues after birth.

A fetal kidney normally consists of lobes, and the number of lobes increases from 3 – 4 in the eighth week of development, to 40 – 50 in the 34th week. Each lobe consists of a group of papillary ducts, their branches and accompanied nephrones (8). The number of lobes decreases with time, so that the normal kidney of an adult is of a smooth surface.

Definitive kidneys begin their development in the small pelvis, laterally from the aorta. During their development, they migrate upwards due to the growth of their basement in the cranial direction (ascensus renis). In the course of this migration, the kidneys move laterally, while their hiluses originally located ventrally now rotate medially. During their pelvic position, the kidneys are vascularised by the branches of the common iliac artery. When the kidneys migrate upwards, the renal arteries develop from the corresponding segments of the aorta, while the more caudal branches disappear. Due to the position change of the kidneys, 25% of the population may have two or more renal arteries (15).

Percentagewise, the kidneys grow most rapidly between the 14th and 16th week of the antenatal life, when they increase in volume three times. Certain kidney structures (cortex, medulla and sinus) grow continually, but unevenly (16).

Several studies emphasized the relation of fetal kidney development to adult renal diseases. It has been proposed that kidney disease may be determined by events that occurred during fetal development (17,18). Brenner et al. (19) suggested that congenital nephron deficits predispose individuals to hypertension later in life. It has been also documented that any disturbance of the ureteric bud outgrowth and/or its branching pattern may lead to renal malformation and various degrees of oligonephronia (20).

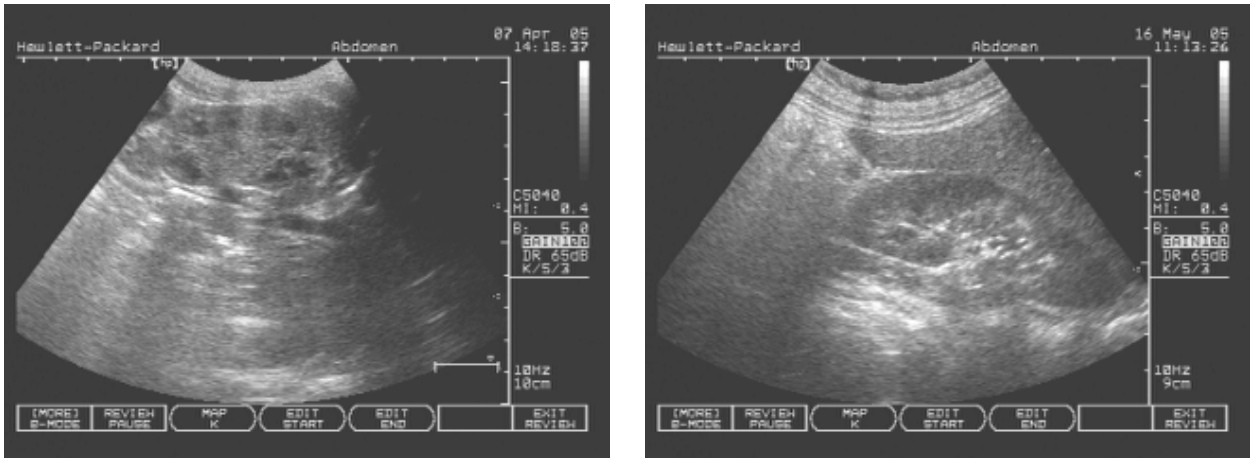
Functional Characteristics

Pronephros does not function in man as an excretory organ. *Mesonephros* represents the organ which temporarily takes part in the creation of urine and maintenance of the electrolytic balance. *Metanephros* begins to function in the ninth week of the antenatal life, reaching its maximum after birth. The homeostatic role of fetal kidneys has not been well researched so far, but it is evident that they are necessary for a normal growth of the fetus. The kidneys in a foetus begin to function when the waste materials from the mother reach the blood of the fetus via the umbilical vessels through the placenta. The fetal kidney filtrates the blood and makes very diluted urine. The urine is excreted into the amniotic cavity surrounding the foetus and blends with the amniotic liquid. The urine (filtrate) in fact represents the main ingredient of the amniotic liquid (21). The foetus by reflex swallows a few hundred millilitres of the amniotic liquid every day; it is absorbed from the intestines and again transported through circulation back to the kidneys where it is filtrated. That filtration, though, is not necessary for the elimination of the waste materials because they are transported into the mother's blood through the placental membrane. The glomerular filtration as well as the consequential presence of the tubule liquid in the fetal kidney are a precondition for its normal maturation (13). The same authors claim evidence that the fetal kidney takes part in the synthesis of vitamin D and the production of hormones with autocrine and paracrine effects, such as angiotensin, prostaglandin and kallikrein-kinin system, which are active in the second half of the gestational period.

Kidney in a Newborn and Suckling Infant

Anatomical Characteristics

The kidney of a newborn infant continues its growth and development without a clear boundary in relation to the fetal period. The weight of both kidneys at birth is about 23 g. There is a considerable difference between the left and the right neonatal kidney with respect to length and width. Namely, the left kidney is considerably longer (4.32 cm) than the right one (4.21 cm), but the right one is considerably wider (2.23 cm) than the left one (2.14 cm) (22). The dimensions of both kidneys are larger in newborns with greater body mass (23). Under normal conditions, the cortex is mature at birth, and all layers of glomeruli are fully formed (24). The kidney glomeruli occupy a much larger cortex volume during the first two months of life (18%) in comparison with an adult (8.6%) (25). The main characteristic of the neonatal glomeruli is conspicuous polymorphism regarding both shape and size (26). The cellular glomerular component of the neonatal kidney is much larger than in an adult, and there are present 20% of all Henley's loops in the cortex (27). The medulla takes up a larger percentage of the volume in the neonatal than in the adult kidney. The neonatal kidney is also characterised by a marked echogenic cortex and hypoechogenic kidney pyramid (27,28). Afterwards, there is a decline in the cortex echogenic and in the prominence of the kidney pyramids (Fig. 2). These changes occur between the first and the sixth month of life, so that as early as the seventh month, the renal parenchyma shares the characteristics of the adult one (29). The fetal lobulation gradually disappears and it is much more frequent in the newborns with the body mass below 2000 g. During the first year of life, the nephrones grow, while tubular structures extend. It is possible to make an early diagno-



A B

Fig. 2. Echosonography of the kidney: A – newborn infant, 8th day; B – suckling infant, 10th month
(with kindness of Predrag Miljković, MD, Children's Clinic, Clinical Center, Niš)

sis of kidney anomalies and vesicoureteral reflux by ultrasonographic evaluation (30).

Functional Characteristics

The neonatal kidneys are structurally and functionally immature. Immediately after birth, the newborn infant adapts to the new conditions of living. It begins to maintain its homeostasis on its own, since there is a rapid structural and functional maturation of its kidneys. Upon the completion of nephrogenesis, the mature juxtamedullary nephrones manifest a greater filtration capacity than the immature superficial cortical nephrones, which, on the other hand, grow intensively and contribute to the greater renal blood flow in this part of the cortex (31). The decline of vascular resistance leads to the increased kidney perfusion and the intensity of glomerular filtration (13). The increase of glomerular filtration is very fast in the first three months of life, and then gets slower till the adult level is reached at the end of the second year. The level of glomerular filtration in a newborn is about 30% of its value in an adult. A relatively low blood flow in the fetal and neonatal kidney is explained by the minute volume of the heart (the fetal kidney receives only 2% – 3% of the minute heart volume in comparison to 15% – 18% of the adult heart) (31). The adult values of the renal blood flow are reached by the kidney by the end of the first year of life. One of the significant characteristics of the neonatal kidney is its reduced urine concentration capacity which increases the risk of dehydration at the restricted intake of liquids. The human kidney reaches the concentration capacity of the adult level at the age of 18 months (13). The same authors state that the reduced renal concentration capacity under normal conditions does not handicap the newborn and the suckling infant since they take higher quantities of liquid in any case. One of the reasons for the reduced renal concentration capacity in newborns is the reduced glomerular filtration as well as the lower sensitivity of the distal tubule to the antidiuretic hormone. There is also a reduced excretion capacity of the liquid surplus at this age, which brings about a tendency towards developing of dilution hyponatremia (31). The suckling infant's kidney is also characterised by a much lower excretion of potassium and the resorption of amino-acids in comparison to the adult kidney. The activity of plasma renin and angiotensin II is higher than in adults (13).

The renal immaturity of a healthy newborn and suckling infant is not a hazard under normal circumstances, but may be causing problems in cases of certain illnesses, inadequate liquid balance and exogenous pharmacological stress. Besides, such a kidney is more prone to pyelonephritis and calculosis than an adult kidney (32).

Kidney in Children, Adolescents and Young Adults

Anatomical Characteristics

During this period of life there is a full maturation of all renal structures. The corticomedullar index (cortex:medulla ratio) increases from 1.64:1 in the newborn infant (due to cortical immaturity) to 2.59:1 in adults (27). The glomeruli begin to degenerate as early as the seventh month of the intrauterine life and by the seventh year of life there are clearly visible degenerated juxtamedullary glomeruli (33).

Regarding the kidney dimensions, there is a prominent correlation between the kidney length and volume and the age of children, their height, weight and body surface. It has been established that the kidney length correlates best with the height of the child, and that the left kidney is somewhat longer and larger. There were not sex differences established. Possible pathological kidney changes in children mainly affect its volume (30,34).

The adult kidney is 10-12 cm in length, 5-6 cm in width, and it is about 3 cm thick. The weight of a single male adult kidney is about 150 g, while in women it is

about 135 g (35). The maximum length is reached between the 20th and 30th year of age (the left one is longer than the right one on average for about 2 mm) (36).

For more on the anatomy of the mature kidney please consult relevant course books and scientific journals.

Functional Characteristics

During the infant age as well as the age of adolescents and young adults there is a full functional renal maturation. A functionally and anatomically mature kidney is fully functional in all its activities, and the basic ones are: 1. Excretion of the final metabolic products and surplus water, 2. Maintenance of the constant composition of body liquids, 3. Preservation of the acid-base balance, and 4. Endocrinal function manifested as the production and release of erythropoietin, renin and 1,25 dihydroxycholecalciferol (35).

Estimates of glomerular filtration rate (GFR) are the best overall indices of the level of kidney function. The level of GFR should be estimated from prediction equations that take into account the serum creatinine concentration and some or all of the following variables: age, gender, race, and body size. Normal GFR in young adults is approximately 120-130 ml/min/1.73m^2 and declines with age (37).

For more on the functioning of a mature kidney please consult relevant course books and scientific journals.

The Kidney in the Elderly

Anatomical Characteristics

Age-related renal changes are similar to those identified in chronic kidney diseases and in experimental models with progressive chronic renal failure and surgical reduction of kidney mass. Old age is in man accompanied by a progressive loss of kidney mass. The weight of both kidneys declines from 250 g – 270 g in early adulthood down to 180 g – 200 g in the eighth decade of life. The loss of kidney mass is primarily evident in the cortex (there may be cortex reduction to less than a half of its maximum value), while the medulla is relatively spared (38). The atrophy of renal cortex is characterised by a reduction in the number of functional nephrones (2). The glomeruli suffer a progressive enlargement of the mesangial matrix, basement membrane gets thicker, while the arterioles are hyalinized (39,40). There is an irregular fusion of foot-like extensions (2). The number of renal corpuscles is gradually decreased, while their average surface increases with age (41). Some structures of renal tubules are reduced, that is, there is a disballance in the parenchyma/stroma ratio at the expense of the first component. The number of hyalinized or sclerosed glomeruli increases from 1% – 2% in the period from the third to the fifth decade of life, to even 30% in some apparently healthy 80-year-olds (38). It has been determined that all individuals under normal conditions have at least 50% of normal glomeruli to the age of 80 (33). The loss of the glomeruli is not necessarily followed by the degeneration of the tubules. The glomerular volume decreases with age, tubule volume is dilated, while the cell number in both structures declines although the glomerular cells tend to atrophy and the tubular cells tend to hypertrophy (42). Not only does the number of nephrones decline with age but also the volume of the remaining ones (33). In the course of ageing, there is a slight decrease of absolute kidney weight starting at the age of 30 to the age of 59, to be followed by a considerable weight loss from the age of 60 to the age of 70 and onwards (36). The same authors state that the relative kidney length measured by KBR index (kidney:body ratio) reaches the highest values from the age of 20 to the age of 30, to start slightly decreasing till the age of 59, and get considerably lower in the well-advanced age.

In the course of ageing there are changes in the vasculature, regardless of the hypertension or other health conditions. There are various normal sclerotic changes in the walls of the kidney arteries, which can under certain circumstances significantly compromise the kidney perfusion and result in the ischaemic nephropathy, a fairly recent clinical entity (43, 44). As a result of ageing, the kidney arteries extend, lose their rectilinear shape, and later tend to curve spirally. This applies especially to aa. arcuatae et aa. interlobulares. These changes take place despite the arterial branching geometric optimisation which occurs in all arteries in advanced age (45). The biochemical substrate of artery ageing has been researched in the last few years which resulted in the discovery of increased creation of matter such as Endothelin-1 and nitric oxide- synthase (46), reactive oxygen species (47), or accumulation of calcium (48) in the artery walls of elderly persons. With regard to microvasculature, there may be twofold changes. In the first type of changes, hyalinization and the glomerular collapse are related to the obliteration of the afferent arteriole which is primarily the case with the glomeruli in the cortical area. The second type is typical for the juxtamedullary glomeruli, when the above cited glomerular changes lead to the creation of shunt – an anatomical continuity between the afferent and efferent arterioles. This is the reason why a considerable part of the blood flow in an aged kidney is transferred from the cortex onto the medullar area. At birth, shunts are identified in 9% of juxtamedullar glomeruli, and their number steadily increases reaching 100% in the ninth decade of life (49).

The process of ageing leads to a considerable increase of the interstitial tissue (2,50). That process takes place not so much in the cortex as in the renal pyramids. It is believed that it is caused by a reduction of blood quantity, and not so much by the vascular occlusion (33).

Regarding the biochemical aspect, in the renal medulla, there is with age the accumulation of acid mucopolysaccharides, and the reduction in the water content

(especially after the age of 50). There is an increase in the quantity of heparin sulphate and hyaluronic acid. The glomerular basement membrane manifests a concentration decrease of certain amino acids: threonine, methionine, isoleucine, leucine, histidine, tyrosine, phenylalanine and hydroxylysine (51). Also, there is an age-related intensified hydroxylation of proline and lysine in the glomerular basement membrane. The most important biochemical change induced by age consists in an increased collagen content. The increase of collagen I and III occurs only in areas with interstitial fibrosis, while the glomerular basement membrane exhibits an increased content of various laminin isoforms (52).

Functional Characteristics

The functioning of the kidney is rather stable in the period between early adulthood and the middle years, but with further ageing there are certain functional disorders in the kidney. Fortunately, in healthy individuals these old age-related changes develop very slowly so that even an old kidney functionally meet the needs of the organism. An old kidney becomes vulnerable and more sensitive to the toxicity of medicines and their metabolites, which should be taken into account during treatment of the elderly (53). These authors claim that there is also significant sex-related dimorphism as a response of the kidney to ageing – women are more protected from kidney chemodynamic changes and structural impairment in old age. As a result of ageing, there is a progressive reduction in renal blood flow of about 10% per a decade of life; from 600 ml/min/1.73m^2 in the third decade of life to 300 ml/min/1.73m^2 in the ninth. This reduction is related to a significant increase of vascular resistance in the afferent and efferent arterioles, which may also explain age-related increase of filtration fraction (54). After the fourth decade of life there is also an old age-related progressive decline of the intensity of glomerular filtration. In persons older than 55, it is 22% lower than in persons younger than 40 (55). The creatinin clearance progressively decreases on the average for about 0.8 ml/min/1.73m^2 per year (56). Despite the lower intensity of the glomerular filtration, the serum creatinine does not change with age, which is explained by a proportional decrease of the muscle tissue (2). It is interesting that one third of the elderly do not manifest the decline of renal plasma flow nor of the intensity of glomerular filtration (56). The permeability of the glomerular filtration barrier is only slightly changed with age (2). The average arterial blood pressure significantly rises in the course of ageing (57). The capacity of an old kidney to preserve Na^+ as a response to its insufficient intake is lowered. The elderly show a lower capacity of the distal tubule for the reabsorption of Na^+, which is explained by interstitial fibrosis or by a lower activity of the renin-angiotensin-aldosterone system. Related to that, the lower concentration of plasma renin of 30% to 50% has been noticed in the elderly. The plasma volume is also decreased in the elderly due to increase of ANP-related excretion of Na^+ and water, as well as due to the translocation of liquids into intercellular space caused by the higher permeability of the capillaries – the so-called edematogene effect (38). The metabolism of the atrial natriuretic peptide (ANP) is intensified because of its reduced clearance and longer half-life as well as because of its increased amount in the circulation. The renal capacity for concentration and dilution of urine decreases with age (33,58). The kidneys of the elderly can maintain the acid-base balance within normal limits just like the kidneys of the younger persons, as long as they are not provoked by an acute intake of acids. In that case, the acid excretion does not rise to the degree it reaches in the kidneys of the young (59). As a consequence of ageing, there is also a lower metabolism of potassium, calcium, phosphorus, and vitamin D (1-α hydroxylase deficit) (38). The process of ageing is also characterised by a reduced synthesis of renin and by its lower concentration in the plasma, despite the normal concentration of its substrates (2).

Age Related Renal Diseases

The kidney of the elderly is sensitive to numerous influences coming from the environment (high temperatures, insufficient intake of liquids, physical exhaustion etc.), as well as to various diseases accompanied by high temperatures, a considerable loss of liquids, or a great cell destruction. Because of this, certain renal diseases manifest specific etiopathogenetic characteristics in the elderly.

Vascular renal diseases. The main cause of renal insufficiency in the elderly is the atheromatose renal disease (60, 61). It can be manifested as the stenosis of the renal artery, a complex of intrarenal lesions with multiple stenoses, and as the cholesterol embolism. The atheromatose renal disease is responsible for renal insufficiency in 14% of the patients older than 50 in the terminal stage (62).

Acute glomerulonephritis. Its most common form in the elderly is a rapid progressive glomerulonephritis, with a progressive loss of renal function in the period of a few weeks up to a few months (32).

Nephritic syndrome. It is the most frequently diagnosed renal disease in the elderly. It is confirmed that it may be related to malignity (63).

Renal cysts. Ordinary renal cysts are quite common in the advanced age. At least one cyst has been postmortally found in over 50% of people older than 50. The prevalence of at least one cyst has been diagnosed ultrasonographically; it progressively grows from 0% in persons between 15 and 29 years of age up to 22.1% in persons over 70 years of age (38).

Acute renal insufficiency. The main cause for its development in the elderly is prerenal insufficiency, that is the decreased renal perfusion which may lead to the irreversible type of acute renal insufficiency (38).

Chronic renal insufficiency. It is manifested in many forms because it is a consequence of other old age related diseases: atherosclerosis of kidneys, diabetes,

hypertension, chronic glomerulonephritis, hydronephrosis due to prostate hypertrophy etc. The number of the elderly on dialysis is on the increase every year because of the longer life-span and the growing number of patients suffering from terminal renal failure (64).

Urinary tract infections. They are a serious problem for the elderly. Their frequency is related to the functional changes of the bladder, pelvic muscle system, prostate size, impaired immune response etc. The reduced level of oestrogen in menopausal women causes a higher frequency of urinary tract infections (38).

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UZRASNE ANATOMSKE I FUNKCIONALNE KARAKTERISTIKE BUBREGA ČOVEKA

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Kratak sadržaj: *Razviće bubrega čoveka započinje krajem prvog, a njegove prve funkcije već u toku drugog meseca prenatalnog života. U zadnjem trimestru fetalni bubreg pokazuje i prve involutivne promene. Nadalje, sve do dostizanja adultnosti, bubreg karakterišu intenzivni procesi maturacije ali i evidentne involutivne promene. Dinamika ovih procesa se, međutim, razlikuje u pojedinim uzrasnim dobima. Prenatalni period karakterišu intenzivni procesi nefrogeneze, koji se ostvaruju kroz tri sukcesivne razvojne forme bubrega: pronefros, mezonefros i metanefros. Prve dve forme predstavljaju privremene, a treća trajni ekskretorni sistem, tj. definitivni bubreg. Funkcionisanje bubrega, iako nije neophodno u prenatalnom stadijumu, ukazuje na njihovu ekskretornu, homeostatsku i endokrinu ulogu i odraz je procesa sazrevanja. Po rođenju, bubrezi se odlikuju daljim procesima strukturne i funkcionalne maturacije. Sa, na rođenju, definitivnim brojem nefrona oni uvećavaju svoju masu na račun rasta pojedinih struktura nefrona i intersticijuma. Punu anatomsku i funkcionalnu zrelost bubreg dostiže krajem treće decenije života. Nadalje bubreg odlikuju involutivne promene različitog intenziteta. Do kraja šeste decenije ove promene su spore; potom, sve do kraja života imaju trend veoma ubrzane progresije i posledica su, pre svega, smanjene perfuzije bubrega. Uprkos tome, u normalnim uslovima i u najdubljoj starosti ne pokazuju znake funkcionalne insuficijencije. Involutivne promene na bubrezima mogu biti zasebne, a mogu se i superponirati sa odgovarajućim bubrežnim bolestima, što kod izvesnog broja osoba u poodmaklim godinama može dovesti do progresivnog gubitka bubrežnih funkcija.*

Ključne reči: *Uzrast, anatomija, funkcija, bubreg čoveka*