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The Nephrogenesis in the Human Organism

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Abstract

We wanted to investigate nephrogenesis in its ontogenetic development (in the perinatal periods). This perinatal time interval was divided into five periods. Intrauterine are the early fetal (3–5 months) and late fetal periods, neonates (0–1 months), infants (1–12 months) and young children (1–3 years). We only conducted the analysis until the age of three, because the one million nephron number characteristic of the kidney in adulthood is already developed by the age of three. We found that the structural and functional unit of the kidney is the nephron, which undergoes three initial stages: pro-, meso- and metanephros. There are two periods of accumulation: late fetal and infant age. After birth, the number of incomplete renal corpuscles is negligible. In further periods of ontogenesis, the nephron count remains unchanged, only the volume of the nephrons increases. When modeling kidney function, we found that the body is "resting" some of the nephrons, because it is during this time that the cell walls resulting from cavitation are regenerated.

Keywords: ***nephrogenesis, biophysical modelling, perinatal periods, ontogenetic development of the kidneys***

Introduction

The kidney excretes excess substances through urine: decomposition products of substances foreign to the metabolism and organism (medicines, nutritional supplements). The kidneys also play an important regulatory role [1] (fluid and water balance, pH, blood pressure, hematopoiesis [2], bone metabolism). The kidney regulates certain ions of the body (Na+, K+ and chlorides) and its total water content, and thus regulates the osmotic pressure [3] of the extracellular space. (Table I.)

Table I. The quantity of the filtration and reabsorb matter

Matter	Filtration quantity	Reabsorb quantity	Excretion quantity	Proportion of reabsorb %
glucose (g/day)	180	160	0	0
Bikarkonat mM/day	2160	2159	1	>99,9
Na^+ (mM/day)	25.560	25.410	150	99,4
K^+ (mM/day)	756	664	92	87,8
Cl^- (mM/day)	19.440	19.260	180	99,1
urea (g/day)	46,8	23,4	23,4	50
creatinine (g/day)	1,8	0	1,8	0

In addition to regulating ionic balance, the kidney also plays an important role in the excretion of metabolites resulting from metabolism. The end product of proteolysis is urea (residual nitrogen), while the end product of nucleic acid decomposition is uric acid. Creatinine is the metabolite of muscle metabolism. The kidneys also play an important role in the excretion of many drugs and other foreign substances and in the elimination of red blood cell metabolites (bilirubin) in liver disease. In this article we do not deal with several types renal failure [4, 5], including kidney cancer.

The prenatal periods

Initial signs of the final form of the kidneys are already evident on the 8th week of embryonic development, i.e. they are characteristic of the early fetal period (3–5 intrauterine month). During ontogeny, three renal organs develop relatively sequentially in time and space: pro-, meso- and metanephros. At week 3, the most cranial renal organ developes in the embryo from somite 8–10 on week 3, and it persists for 10 to 14 days. Before the involution of pronephros, mesonephros, which develops from the epithelium of the somatic meso¬nephrine 11–30, appears on week 4. [6] The involution of the mesonephros begins in month 2, progresses in the cranio-caudal direction, and ends in month 4. Metanephros is the renal organ developing in the most caudal way, appearing on week 7–8 on the area of somite 31–32.

At the beginning of the early fetal period there is no clear separation between the cortex and the marrow, and the structure of the lobes in the cortex is incomplete. In the third month, in the cortex - which is approx. one fifth of the marrow - only the outer zone is observed, the inner zone appears only in the fourth month. The outer zone of the cortex contains a large number of small renal corpuscles, the inner zone is characterized by a small number of

large glomeruli, while the middle zone is characterized by transient sized renal corpuscles.

In the outer zone, the differentiation of the metanephrogenic tissue to the tubules and vesicles formed by these cells is observed, i.e. this is the nephrogenic zone. The tubules show intrusions, which are considered to be the initiators of the Malpighian corpuscles. These are called incomplete renal corpuscles. This incomplete form dominates the outer zone of the cortex. These renal corpuscles are grouped multifocally.

The cortex and the marrow is structured for the late fetal period, the linear ratio of the two is 1:4. In the cortex, the three zones can be clearly demarcated. The incomplete renal corpuscles are multifocally located in the outer zone. Transient forms between incomplete and complete renal corpuscles are also observed, in which the Bowman's capsule completely surrounds the glomerulus but the vascular pole has not yet formed. The middle and inner zones are clearly dominated by complete renal corpuscle, in which the capillary loops are fully developed, and their lumen displays red blood cells. The proximal and distal convoluted tubules found near renal corpuscles can be distinguished by staining procedures.

One of the most characteristic features of the late fetal period is the significant increase in the number of nephrons, so this stage of the ontogeny of methanephros can be called the first accumulation period. [7]

The postnatal periods

The postnatal periods are next: neonates (0–1 months), infants (1–12 months) and young children (1–3 years). We only conducted the analysis until the age of three, because the one million nephron number characteristic of the kidney in adulthood is already developed by the age of three.

Birth is the only compatible big leap in an individual's life. In the neonatal period, the ontogenesis of metanephros represents a tremendous change in quality, since during the intrauterine development, besides the kidney, the placenta also played a role, whereas after birth, the kidney alone fulfills this function. In the functional realization of the homeostasis of the internal environment, the hydroelectrolytic balance is substantially modified, taking into account that the newborn must adapt to the gaseous medium rather than the liquid medium. During this period, the water balance is extremely unstable, as the kidney has not reached full maturity, neither structurally nor functionally, and its antidiuretic hormone response is also poor. The regulatory mechanisms that regulate fluid balance are extremely fragile, and diseases that disrupt fluid balance are more common. It follows from this that the newborn has to adapt to the changed conditions extremely quickly after birth, and that is why functional changes are far more significant than anatomical changes.

The maturation process of the nephrons accelerates over time, which explains why the proportion of incomplete renal corpuscles is significantly reduced compared to the previous period. This morphological structuring of the kidney can be understood as a response to altered functional requirements.

During this period, the linear ratio of the cortex to the marrow is 1:3, and the lobes and lobuli are clearly structured. The diameter of the lumen of the canals increases from the outside to the inside of the marrow, whereas in earlier periods it was characterized by an approximately uniform diameter. One of the most important features of this period is that this is the last stage in which incomplete renal corpuscles are still present. [8]

Infant age is characterized primarily by morphological changes, including easily distinguishable cortical zones, well-structured lobes and lobuli, and the exclusive presence of complete renal corpuscles. Table II

Table II: The characteristics data of kidney.

Periods	Kidney-volum (cm^3)	Ratio of cortex/marrow	Nefron number
Neonatals	6,5	1,37/1	300.000
Infancy	21,0	1,37/1	650.000
Little child	55,0	2/1	1000.000

Despite the fact that only complete renal corpuscles exist, kidney development has not yet been completed. The reasons for the apparent absence of incomplete renal corpuscles are: the relative long duration of infancy (330 days) compared to the maturation time of the nephrons (approximately 1-2 days); the large number of pre-existing renal corpuscles compared to the developing ones (approx. 1,000: 1). So, out of 500,000 to 1,000,000 renal corpuscles, only 1 to 10 are in an incomplete state at a given moment. [9]

This period is characterized by a significant increase in the number of nephrons per unit area, so this period can be called the second accumulation phase. This accumulation is of such extent that it represents a significant increase compared to the former, but the kidney mass triples only by the age 3 compared to the newborn kidney, while the body weight triples by the age of 1.

During the infant period, the period is primarily characterized by dimensional growth of the nephrons, while numerical growth is secondary. At this age, microscopic images of the kidney show a striking resemblance to those of the adult kidney.

The cortex and marrow and their elements are well structured and clearly distinguishable. The ratio of cortex to marrow is 1:2, which is characteristic of adulthood as well.

In this period, the total number of nephrons in the kidneys reaches one million, and this number does not change in adulthood, but after the age of 60, the total number of nephrons decreases by approx. 1% per year. [10]

Nephrons are formed in a multifocal, asynchronous, spatially and temporally unequal manner. Asynchronism of nephrogenesis is indicated by two accumulation periods of nephron growth. Multifocal character and asynchronism, as well as sequential location, indicate the morphological heterogeneity of the kidney, resulting in functional heterogeneity. [11]

Human kidney development in perinatal periods is influenced by three important parameters: periods of ontogenesis, gender and zone-based localization. [12] The ontogenetic development of the kidney, in the light of the nephron number, in the perinatal periods is strongly influenced by age (ontogenetic periods), moderately influenced by the distribution based on zones, while gender has a less significant effect on nephrogenesis.

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