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HISTOLOGY OF RENAL PYRAMIDS WITH SPECIAL REGARD TO CHANGES DUE TO AGEING

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Among the investigations into the pathology of the kidneys few have dealt with the histology and physiology of the renal pyramids. Most of the recent works touch upon this subject only in connection with the pathogenesis of nephroliths. Although profound histological changes are well-known to occur in the renal pyramids especially of old people, the nature and pathomechanism of these changes are mostly obscure.

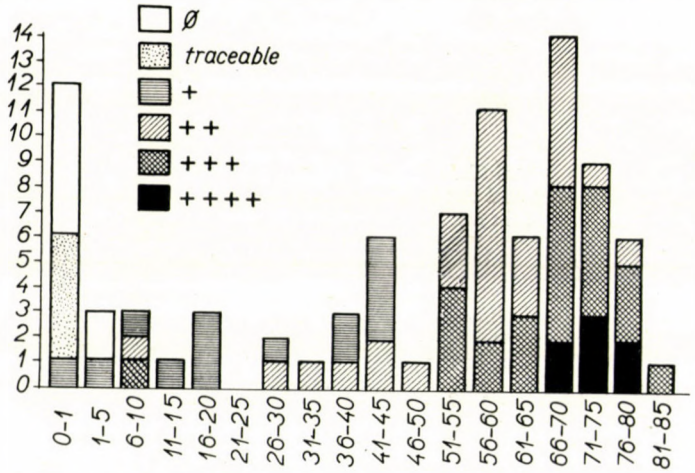

Fig. 1. Age distribution of the material, and intensity of pyramidal sclerosis in the age groups. The number of cases is indicated on the ordinate, the age on the abscissa

With a view to studying geriatric changes in the renal pyramids 89 kidneys from necropsy material were examined. The cadavers belonged to all age groups, the majority to that of over 50 years. The age distribution is shown in Fig. 1. Kidneys of cadavers necropsied more than 24 hours after death were not included in the material.

Material and methods

As a rule, 2 or 3 pyramids, together with the cortex, were excised from both kidneys. Two sections were fixed in 10 per cent formalin, one in Carnoy's fluid. Frozen preparations were made from one of the formalin-fixed sections, 59 in number; these were stained with Sudan III. The other sections were embedded in paraffin and stained with haematoxylin-eosin, van Gieson's and for elastic fibers, some impregnated with silver according to Gomori. Von Kossa's reaction was performed in 31 cases, when gross examination had revealed greyish stripes in the pyramids or if the microscopic examination of section stained with other methods had revealed the presence of calcium. The following histochemical reactions were performed in special cases: PAS, Ritter-Oleson; acetylated PAS; Schiff's alloxan; tetrazolium benzidine; Millons' reaction. Thus, of 59 cadavers we examined at least 4, and of 30 at least 3, sections from pyramids. These figures do not include some selected cases treated with special methods. These cases either showed pictures characteristic of certain age groups or else pyramids obtained mostly from old persons with exceptionally grave changes.

Morphology

The collecting tubules of the medulla converge towards the renal pelvis, and the papillary ducts open into the minor calyces in the area cribrosa. The tubules are lined distally with high epithelium, while columnar epithelium is found in the papillary ducts. The former are surrounded by a connective tissue of collagen fibres. Most of the connective tissue is in the so-called vascular zone. Most of the interstitium is found in the medulla, especially in its inner zone, where the bulk of connective tissue is interlobar.

Arterial blood is supplied to the medullary substance by the true and spurious straight arterioles. The former issue partly from the interlobar and partly from the arciform arteries, the latter consist of juxtaglomerular efferent vessels. Arterial blood flows from the base to the apex of the pyramids, venous blood takes the opposite course and flows into the interlobular and the arciform veins. The renal papillae appear, therefore, to be less supplied with blood than the other parts of the pyramids. In general, the course of the lymphatics corresponds to that of the blood vessels.

Physiology

Literature seems to contain hardly any data concerning the physiology of the renal medulla. Reabsorption of water and recovery of electrolytes occur in the distal portions of the tubules and, according to certain authors, in the papillary ducts. This process is governed by the antidiuretic hormone.

Results

Renal pyramids may, according to the literature, undergo three kinds of change: proliferation of the interstitial tissue and the ground substance; accumulation of fat; deposition of calcium. The first we tried to ascertain was the nature of histological changes in the renal pyramids due to ageing and to determine whether they were physiological changes, or changes correlated with atherosclerosis.

The histological structure of the renal pyramids undergoes considerable alterations during life. Interstitial connective tissue, rich in cells, fills the space between the densely packed collecting tubules in the newborn and the infant (Fig. 2). The amount of intercellular substance increases gradually from childhood and becomes predominant at about the age of 50. It is red and apparently homogeneous in sections stained with haematoxylin-eosin, van Gieson's, and elastic stain. It may accumulate to such an extent that HELPAP [4] is

justified in suggesting the term "medullary sclerosis". To characterize the appearance and gravity of this phenomenon, we established different degrees on the evidence of 3 to 4 sections per case. Zero represented the stage at which the pyramids contained no intercellular substance; the amount of such substance was indicated by 1, 2, 3 and 4 crosses. When making this scale, we took into account the condition of the collecting tubules and the appearance of lime granules in the interstitial tissue.

Fig. 1 shows the results of our observations. It can be seen that intercellular substance appeared in about 50 per cent of our material as early as the first year of life, while its amount increased markedly in young adults. It became

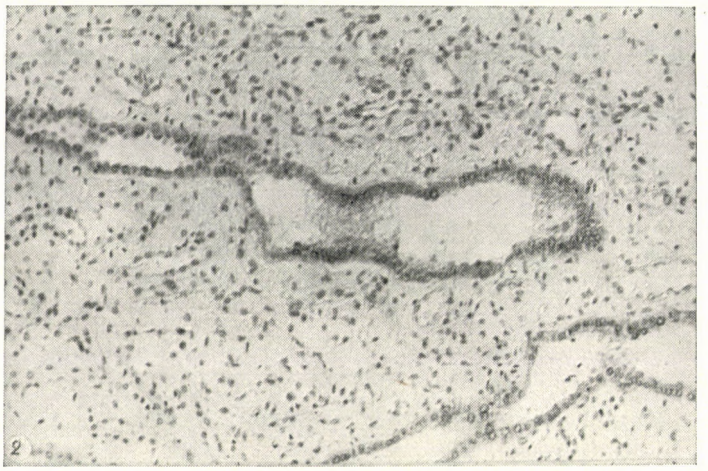

Fig. 2. Cell-rich interstitial tissue in the pyramid of a middle-aged subject. HE. ×200 (Male, 38 years; ulcerative tbc, coecal cancer, +)

so extensive from the 50th year as to dominate the histological picture, while its gravest form became increasingly frequent above 65 years. Increase of intercellular substance seemed to go hand in hand with a decrease in the number of cells, although scattered connective-tissue cells were still present even with the gravest sclerosis. The number of collagen fibres in the interstitial tissue seemed to increase with advancing sclerosis. We also found slightly argyrophile, fragmentary somewhat undulating fibres. Elastic fibres were noted in the mucosa of the renal pelvis only. With van Gieson's stain, the accumulated homogeneous substance became unevenly red in patches, intensively in the papillary region.

Staining with Sudan III revealed finely distributed patches of fat in the interstitial tissue of most of the sclerosed pyramids (Fig. 3). The amount of Sudan-positive fatty substance seemed to be proportionate with the degree of pyramidal sclerosis and was almost invariably present

in ++ and +++ cases, although in some of these the pyramids contained no or hardly any fat. There was only one case of incipient sclerosis (+) displaying a considerable amount of Sudan-positive substance; the majority of such specimens did not take fat stains. The presence of sudanophile matter in the interstitial tissue is not connected with fatty degeneration in the epithelium of the collecting tubules. There were several instances of grave tubular fatty degeneration without deposits of fat in the interstitial tissue. Fat appeared in the form of fine droplets or pale, diffuse sudanophilia; as a rule no large drops occurred. Occasionally there were marked fat deposits

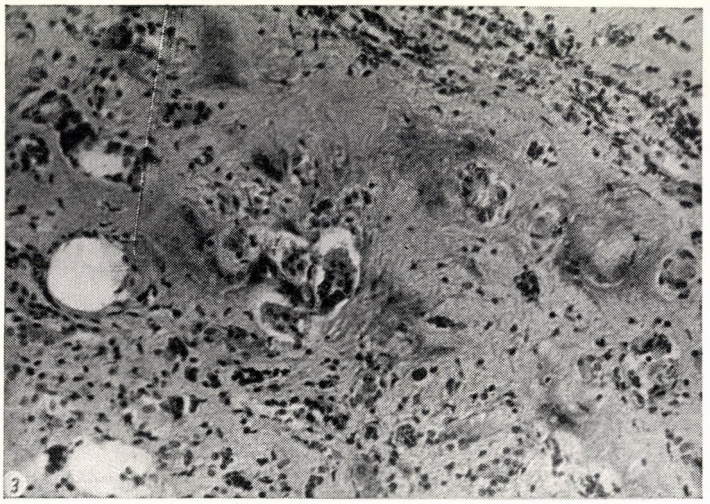

Fig. 3. Deposit of fat in the interstitial intercellular substance. Sudan III-haemalum. ×100 (Male, 74 years; cerebral haemorrhage, ++++)

in the basement membrane of the tubules (Fig. 4) when there was no fat in the interstitial tissue.

Histochemical reactions were performed in a few selected cases in which a considerable accumulation of interstitial tissue was noted. The PAS reaction was slightly positive in a few occasional areas of the homogeneous substance; Ritter—Oleson's reaction gave a blue focal colouring in all sections; acetylation eliminated the PAS positivity; the tetrazolium benzidine reaction was diffusely positive, with more intensive foci in the homogeneous area; Schiff's alloxan reaction yielded small, pale, irregular positive spots in the interstitial tissue; Millon's test gave a slight diffusely positive reaction. Calcium deposits were found in the pyramids in 34 cases out of 89. We regarded a case as calcium-positive even if only a single small focus of lime was present. Granules of calcium in the epithelium of the collecting tubules, in the basement membrane, or the interstitial tissue were noted in 32.3 per cent of the cases below 50 years

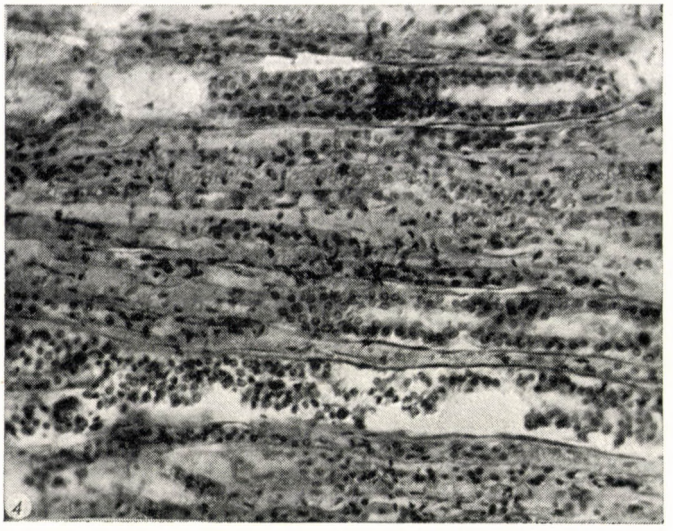

Fig. 4. Deposit of fat in the basement membrane of collecting tubules, indicated by dark lines in the picture. Sudan III-haemalum. ×100 (Female, 56 years; mitral stenosis, ++)

of age and in 41.8 per cent of these above that age (Fig. 5). Rarely also calcium casts occurred. Deposition of calcium and pyramidal sclerosis must not be regarded as parallel processes: deposits of calcium were observed in an infant 7 months of age who had died of subdural haemorrhage, as also in 30 to 40 year-old persons with + pyramidal sclerosis or in the kidney of old persons with ++++ sclerosis. Old age and grave sclerosis are, no doubt, more

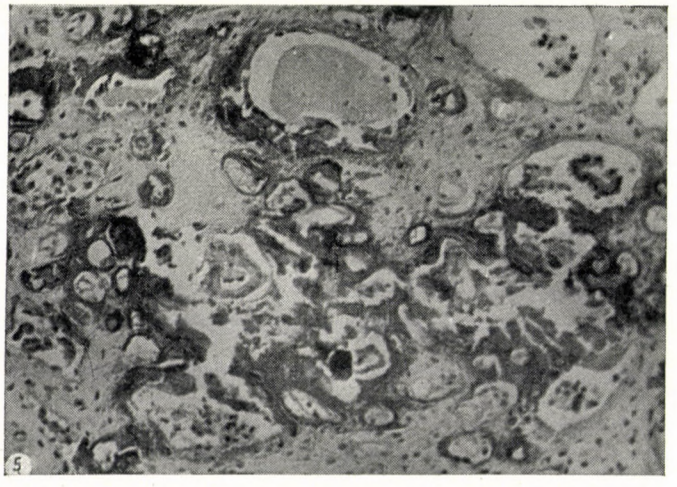

Fig. 5. Extensive calcium deposit in the interstitial tissue of a pyramid. HE. ×100 (Female, 53 years; meningeoma; +++)

frequently associated with nephrocalcinosis. The calcium foci were scattered; they were widely spread in two cases of renal damage due to shock, and pronounced in the kidney of an 8 year-old child who had succumbed to miliary tuberculosis. In our opinion they have no special significance. The presence of calcium did not seem to be correlated with nephrolithiasis: renal calculi or sand were found in no case. Greyish-white stripes on the pyramids usually termed calcium infarction, were visibile in 14 instances, but in 5 of them calcification could be detected in none of several sections. The term calcium infarction seems to be incorrect; the pale greyish colour may be due to ischaemia, since the appearance of the stripes showed no close correlation with the degree of pyramidal sclerosis. Fixation in Carnoy's fluid for 3 to 4 hours or the preparation of thick frozen sections after a short fixation in formalin appear to be the methods of choice for the demonstration of calcification.

A comparatively rich vascularization of the pyramids and their apexes appeared also in cases of serious pyramidal sclerosis. Dystrophic processes in this area are obviously due to insufficient blood supply rather than vascular occlusion. The vessels are of the capillary type, frequently dilated and well supplied with blood. We saw no obstructed vessels but encountered the remnants of the basement membrane of disintegrated tubules in the homogeneous interstitial tissue also in cases of sclerosis (Fig. 6).

With a view to ascertaining whether there existed a connection between nephrosclerosis and pyramidal sclerosis, we studied microscopical changes in the cortical vessels and always took into account general atherosclerosis if it figured in the autopsy record. Our material comprised 55 cases of the age group over 50 years; most of them showed ++, +++ and ++++ pyramidal sclerosis, and pronounced nephrosclerosis was absent in only 10 of them. On the other hand, grave nephrosclerosis is always accompanied by grave pyramidal sclerosis. Slight pyramidal sclerosis occurred in the age group under 50 years even when there were no signs of nephrosclerosis. Careful examination of the renal pelvis disclosed no correlation between its histological condition and the changes in the pyramids.

The renal pyramids seem to undergo a physiological change in the course of life: the interstitial connective tissue is first rich, and becomes gradually poor, in cells; the amount of intercellular substance increases; the number of tubules becomes less and the distance between them increases. This process is more pronounced if the vascular apparatus of kidney is atherosclerotic, and may assume a grave form also owing to other — presumably metabolic — factors. The renal pyramid is, as regards blood supply, a relatively bradytrophic tissue in which dystrophic calcification is frequent. (Pathologic changes due to disturbed calcium metabolism did not occur in our material.) We found the matter deposited in the interstitial tissue to consist of a considerable amount of chiefly acid mucopolysaccharides, certain proteins and lipids. The protein

component contained much histidine and a lesser amount of tyrosine and tryptophan.

Very grave pyramidal sclerosis may be accompanied by a cystic dilatation or atrophy of the collecting tubules. The structure of the pyramids is completely disorganized in such cases, a phenomenon that has been termed by us "phthisis pyramidis renis" (Fig. 7). It should be noted that we saw several cases of grave pyramidal sclerosis in which the cortical substance was well preserved so that the process need not lead to lethal renal damage. In some instances, cardiac

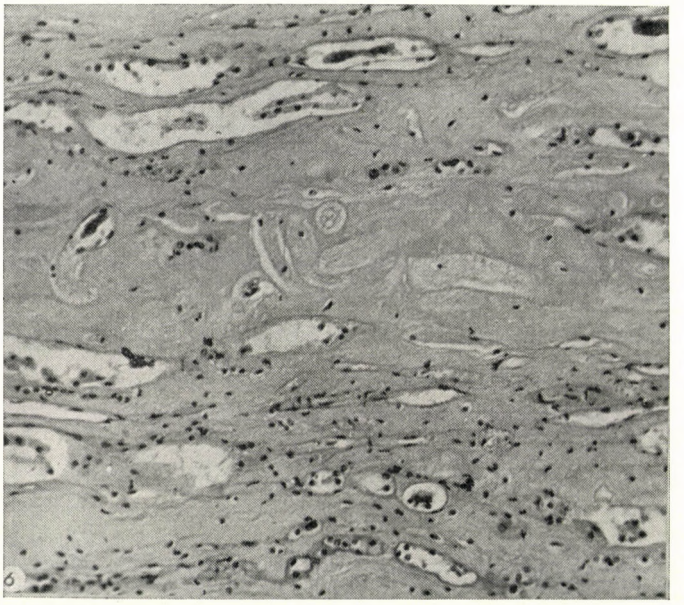

Fig. 6. Remnants of the basement membrane of disintegrated collecting tubules in the accumulated acellular interstitial tissue. PAS. ×100 (Male, 74 years; cerebral haemorrhage; ++++

insufficiency did not induce grave pyramidal sclerosis. Sometimes in old persons there is scarcely any intercellular substance in the pyramids. Sclerosis is usually diffuse but may occur in foci. The apex of gravely sclerotic pyramids may be tapering or retracted (Fig. 8). Calcification is most frequent in sclerotic pyramids, but does not necessarily depend on the degree of sclerosis and may occur at any age, presumably as a consequence of metabolic disturbances and sometimes of therapeutic interventions. In a newborn child who had died with uratic infarction, the collecting tubules were occluded by casts, while the interstitial tissue seemed to be unimpaired. The accumulation of intercellular substance in the interstitial tissue of the pyramids seemed to be preceded usually by a thickening of the basement membrane in the tubules (as demonstrated by the PAS reaction) and its lipoid infiltration.

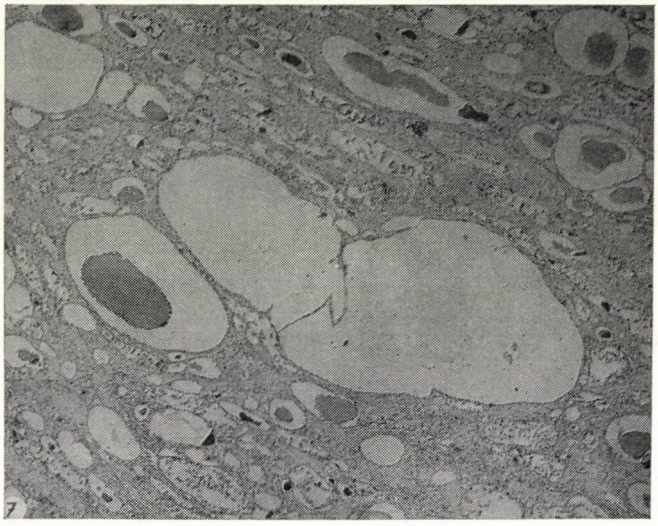

Fig. 7. Dilated collecting tubules. HE. Microtar. (Male, 75 years; emphysema, bronchiectasis; ++++)

Fig. 8. Atrophied pyramid. Von Kossa. Mikrotar. (Male, 75 years; cancer of stomach; ++++)

Discussion

Interstitial hyperplasia is regarded by PRYM [7] as a physiological process which progresses with advancing age. He observed it in persons above 40 years, and his finding agrees with our results. HELPAP [4] found the intermedullary tissue so much extended at certain points that it had induced tubular atrophy and led to ascending nephrosclerosis. Relying on earlier data, he revived the idea of a connection between medullary sclerosis and arteriosclerosis but could not accept it as a regular phenomenon on the evidence of his own observations. We, too, failed to find an unequivocal connection between the two kinds of sclerosis, although its existence often seemed to be evident. STAEMMLER [9] described oedema and subsequent medullary sclerosis in atrophied kidneys. ZOLLINGER [13] suggests that interstitial scarring may be induced by the absorption of urates from obstructed urinary channels into the interstitial tissue and the lymph vessels of the medulla. He regards arteriosclerosis as a significant factor in the pathogenesis of interstitial changes.

PRYM [7] ascribed the appearance of fat in the medullary interstitial tissue to circulatory disturbances; the theory is supported by the fact that it is around the capillaries that fat deposition begins. HELPAP [4] observed fat in the renal medulla mostly in association with arteriosclerosis; in spite of this he found no correlation between arteriosclerosis and the deposition of fat. Fat infarction is the term applied by STAEMMLER [9] to the fatty infiltration of the connective tissue of renal papillae. We encountered patches of fat in the interstitial tissue of strongly sclerosed pyramids, and the phenomenon seemed to be independent of tubular fatty degeneration. Noteworthy was the occasional fatty degeneration of the basement membrane. Sudanophilia was invariably observable in the sclerosed pyramids of young persons; from the intensity and fine distribution of the staining we concluded that lipids, before being deposited, are bound to some other substance, perhaps to protein. This problem requires further investigation.

Precipitation of calcium in the pyramids is connected with a change of the ground substance as also with fatty infiltration. Calcification begins, according to STAEMMLER [9], with the precipitation of phosphorus and carbonic lime salts in the basement membranes and the interstitial tissue; he attributed the process to hyaline degeneration. Coincidentally, calcareous casts appear in the tubules. Chronic serous and inflammatory processes ascending from the renal pelvis may lead to latent medullary oedema and then to sclerosis which promotes the precipitation of calcium. GOLDSCHMID [3] found calcium infarction in the kidneys in 44 out of 48 cases of hepatic cirrhosis; he suggested, on the strength of literary data, the possibility of a correlation between disturbed protein metabolism and calcification. KÜHN [6] rejected this possibility, attaching importance to local renal lesions and disturbances in calcium metabolism.

STOUT et al. [10], too, attribute calcification to local processes. JACCOTTET [5] distinguished two types of renal calcification, (i) nephrocalcinosis which includes metastatic calcifications in the widest sense of the term; (ii) calcium nephrosis, a collective term for dystrophic calcifications, where the process is mainly limited to the cortex. STOUT et al. [10], VERMOOTEN [12] and RANDALL [8] regard calcification of the renal pyramids as a factor of nephrolithiasis. TAKÁCS-NAGY and ENDES [11], further STOUT et al. [10] repeatedly observed a state of shock in cases of nephrocalcinosis. The latter authors hold that a damage of the lower nephron is a preliminary condition of nephrocalcinosis. Our material included tow cases which confirmed this view.

It is known that hypercalcaemia is accompanied by the presence of marked calcium deposits in the kidney. BAKER et al. [2] observed that a depolymerisation of the ground substance was necessary for calcium to be precipitated. By blocking the reactive groups with toluidine blue, they succeeded in preventing calcification; they suggested that inflammations, renal trauma, tubular injury in hydronephrosis, prolonged administration of uric acid in cases of gout, certain hormones (parathormone, cortisone) and prolonged dehydration may depolymerise the ground substance. KÜHN [6] attached importance to the accumulation of fat as a forerunner of calcification. According to ANDERSON at al. [1] the concentration of calcium is usually higher in the medullary interstitial tissue than elsewhere. We observed interstitial calcification but did not regard it as being connected with pyramidal sclerosis, although the process might develop with advancing age. We failed to establish its correlation with nephrolithiasis. The precense of calcium in renal pyramids is connected with the relatively bradytrophic character of the tissue and generally shows the picture of dystrophic calcification.

Summary

The renal pyramids in 89 kidneys obtained from cadavers have been studied. In agreement with the data in the literature it has been found that the renal pyramids undergo essential structural changes in the course of life, in the form of a "sclerotic" transformation of the interstitial tissue. The process is characterized by a hyperplasia of the intercellular substance; this contains few fibers, and consists mostly of acid mucopolysaccharides in addition to fat and proteins. These components seemed to occur in the form of complexes. The process need not be accompanied by atherosclerosis of renal vessels and even its grave form do not essentially impair renal functions.

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ГИСТОЛОГИЧЕСКОЕ ИССЛЕДОВАНИЕ ПОЧЕЧНЫХ ПИРАМИД С ОСОБЫМ ВНИМАНИЕМ НА ВОЗРАСТНЫЕ ИЗМЕНЕНИЯ

Ш. КЕРЕСТУРИ и Л. МЕДЬЕРИ

На 89 случаях вскрытия трупов, авторы исследовали почечные пирамиды. Они установили, что в полном согласовании с литературными данными, почечные пирамиды в течение жизни подвергаются значительным структурным изменениям, состоящим из «склеротического» преобразования интерстиция. Последний процесс характеризуется значительным размножением межклеточного состава. Размножающееся вещество содержит сравнительно мало волокон, и большое количество гомогенного внутриклеточного вещества, в котором при помощи гистологического метода исследования удалось выявить много — преимущественно кислых — мукополисахаридов, жиров и белков. Вышеназванные компоненты присутствуют предположительно в виде комплексных соединений. Этот процесс может наступать также без атеросклеротического изменения почечных сосудов, и, вероятно, даже его тяжелые формы не обусловливают значительного поражения почечной функции.

ÜBER DIE HISTOLOGIE DER NIERENPYRAMIDEN, MIT BESONDERER BERÜCKSICHTIGUNG DER ALTERVERÄNDERUNGEN

S. KERESZTURY und L. MEGYERI

Die Pyramiden von 89 Nieren aus Sektionsmaterial wurden untersucht. Es wurde festgestellt, daß in Übereinstimmung mit den literarischen Daten die Nierenpyramiden im Laufe des Lebens eine wesentliche strukturelle Veränderung durchmachen, die in eine "sklerotischen" Umwandlung des Interstitiums besteht. Der letztere Prozeß wird durch eine bedeutende Vermehrung der interzellulären Substanz gekennzeichnet. Das vermehrte Gewebe hält verhältnismäßig wenig Fasern. In der homogenen interzellulären Substanz konnten histochemisch hauptsächlich saure Mukopolysaccharide, Fett und Eiweiß nachgewiesen werden. Diese Bestandteile sind aller Wahrscheinlichkeit nach in der Komplexverbindungen anwesend. Der Vorgang kann ohne der atherosklerotischen Veränderung der Nierenarterien zustandekommen, und wahrscheinlich führen auch schwere Formen zu keiner bedeutenden funktionellen Nierenschädigung.

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