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18/MHS06/058
Medical laboratory science
Histology of special senses and neuro histology
ANA 204

Question
1. Critically examine the renal function of desert dwellers and the anatomical basis of their unique adaptation

2. Write extensively on the clinical importance of the glomerular filtration barrier.

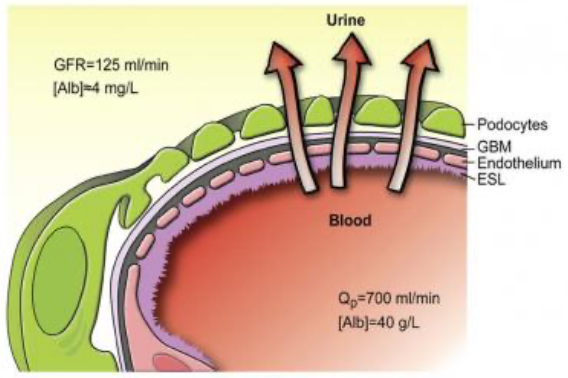
1. Renal function of desert dwellers

The kidney is made of the cortex and medulla. The cortex and medulla are seen to be composed of masses of tiny tubes. These are called kidney tubules or nephrons. A human kidney consists of over a million of them.
At one end of each nephron, in the cortex of the kidney, is a cup shaped structure called the (Bowman's or renal) capsule. It surrounds a tuft of capillaries called the glomerulus that carries high-pressure blood. Together the glomerulus and capsule act as a blood-filtering device. The holes in the filter allow most of the contents of the blood through except the red and white cells and large protein molecules. The fluid flowing from the capsule into the rest of the kidney tubule is therefore very similar to blood plasma and contains many useful substances like water, glucose, salt and amino acids. It also contains waste products like urea.
After entering the glomerulus the filtered fluid flows along a coiled part of the tubule (the proximal convoluted tubule) to a looped portion (the Loop of Henle) and then to the collecting tube via a second length of coiled tube (the distal convoluted tubule). From the collecting ducts the urine flows into the renal pelvis and enters the ureter.
Note that the glomerulus, capsule and both coiled parts of the tubule are all situated in the cortex of the kidney while the loops of Henle and collecting ducts make up the medulla.
As the fluid flows along the proximal convoluted tubule useful substances like glucose, water, salts, potassium ions, calcium ions and amino acids are reabsorbed into the blood capillaries that form a network around the tubules. Many of these substances are transported by active transport and energy is required. In a separate process, some substances, particularly potassium, ammonium and hydrogen ions, and drugs like penicillin, are actively secreted into the distal convoluted tubule.
By the time the fluid has reached the collecting ducts these processes of absorption and secretion have changed the fluid originally filtered into the Bowman's capsule into urine. The main function of the collecting ducts is then to remove more water from the urine if necessary.
Normal urine consists of water, in which waste products such as urea and salts such as sodium chloride are dissolved. Pigments from the breakdown of red blood cells give urine its yellow colour.
For desert dwellers, there's very little availability of water and therefore the need to conserve it. Their urine is mostly concentrated.
Because of the high pressure of the blood in the glomerulus and the large size of the pores in the glomerulus/capsule-filtering device, an enormous volume of fluid passes into the kidney tubules. If this fluid were left as it is, the animal's body would be drained dry in 30 minutes. In fact, as the fluid flows down the tubule, over 90% of the water in it is reabsorbed. The main part of this reabsorption takes place in the collecting tubes.
The amount of water removed from the collecting ducts is controlled by a hormone called antidiuretic hormone (ADH) produced by the pituitary gland, situated at the base of the brain. When the blood becomes more concentrated, as happens when an animal is deprived of water, ADH is secreted and causes more water to be absorbed from the collecting ducts so that concentrated urine is produced.

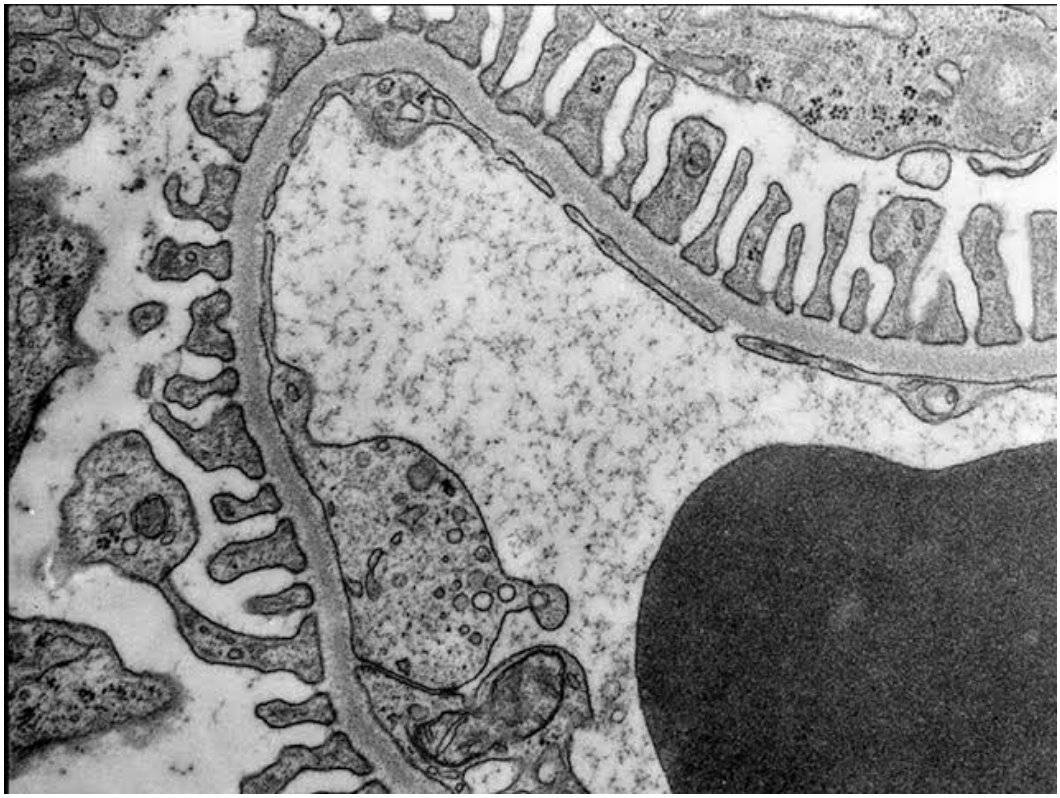
ANATOMICAL BASIS OF THEIR UNIQUE ADAPTATION
Desert dwellers do not readily find water, hence they must excrete very less amount of water. They are able to produce highly concentrated urine.
The nephrons in desert dwellers (Camel) are equipped with well developed Henle's loop and number of juxtamedullary nephrons in kidneys is very high, about 35% (in man this number is about 15%).
The Henle's loop of juxtamedullary nephron goes deep down into the medulla. This is why medulla of camel's kidney is thicker than that of other mammals, but it is most well developed in another desert dwellers, e.g the kangaroo rats.
The Henle's loops of juxtamedullary nephrons along with counter flowing blood vessels, called vasa recta, help in conservation of water.
Blood first flows along ascending limb of Henle, which is impermeable to water. Solutes can leave the filtrate and enter the blood along this stretch. When this blood flows along descending limb, water is reabsorbed from filtrate but not the solutes. Longer the Henle's loop, more amount of solute will be reabsorbed and hence more amount of water could be removed from filtrate.

2. Glomerular filtration barrier (GFR)

The glomerulus is a highly irrigated structure that performs selective filtration of the plasma. Inside the Bowman's capsule, several tortuous arterioles receive the blood and filtrate it forming the primary urine, which then passes to the proximal tubule. The glomerular capillaries are lined by a fenestrated endothelium that sits on the glomerular basement membrane, which in turn is covered by glomerular epithelium, or podocytes, which envelops the capillaries with cellular extensions called foot processes. In between the foot processes are the filtration slits. Together, the endothelial cells, the basement membrane, and the podocytes form the glomerular filtration barrier.



The glomerular filtration barrier is highly permeable to water and small molecules. Moreover, it is slightly permeable to macromolecules and acts as a physical and electrical barrier for the filtration process. These characteristics are dependent of the cellular structures, and its function is influenced by factors such as molecular weight and electric charge. Moreover, changes in the cell junctions of the glomerular barrier prejudice the glomerular function.



Damage to the glomerulus by disease can allow passage through the glomerular filtration barrier of red blood cells, white blood cells, platelets, and blood proteins such as albumin and globulin. Underlying causes for glomerular injury can be inflammatory, toxic or metabolic. These can be seen in the urine (urinalysis) on microscopic and chemical (dipstick) examination. Examples are diabetic kidney disease, glomerulonephritis, and IgA nephropathy.
Due to the connection between the glomerulus and the GFR, the GFR is of clinical significance when suspecting a kidney disease, or when following up a case with known kidney disease, or when risking a development of renal damage such as beginning medications with known nephrotoxicity.
Several diseases affect the glomerular filtration barrier. Some conditions such as sa as diabetes mellitus, hypertension, and maternal nutritional changes during critical periods of development, known as fetal programming, are well recognized as important risk factors for developing chronic kidney disease.
Diabetes mellitus is one of the most chronic diseases emerging on twenty-first century, in which hyperglycemia is a major indicator, generating microvascular damage such as retinopathy, neuropathy, and kidney disease. Diabetic nephropathy is a chronic progressive disease that affects 20–40% of patients with diabetes mellitus. Histopathologically, this disease in humans courses with the thickening of glomerular and tubular glomerular basement membrane, podocytopenia, mesangial expansion, glomerular, and arteriolar hyalinosis. The earliest clinical manifestation of diabetic nephropathy is microalbuminuria, a strong predictor of renal and cardiovascular disease in patients with type 1 and type 2 diabetes mellitus. These modifications contribute to the abnormal stimulation of resident kidney cells, which increases the production of TGF-β1 and causes collagen (types I, IV, V, and VI), fibronectin, and laminin depositions in the extracellular matrix of the glomerulus. Thus, this structural disorganization of the glomerular slit diaphragm enhances renal damage and chronic kidney disease progression.
Likewise, hypertension is directly related to renal failure. Hypertensive nephropathy, a consequence of chronic increase of blood pressure, is secondary to diabetic nephropathy in terms of diagnosis and is considered the last stage of renal disease. Some complications are associated with hypertensive nephropathy such as glomerular damage resulting in impaired renal function. Hypertension causes an increase of numerous local factors, such as angiotensin II, which may contribute to the development of renal fibrosis. It is reported that angiotensin II stimulates the gene expression of TGF-β1 and the release of this protein. The presence of TGF-β1 activates the conversion of fibroblasts into myofibroblasts, producing large amounts of extracellular matrix components, and induces renal fibrosis.

Moreover, angiotensin II regulates the number and integrity of podocyte. In high quantities, it promotes the disintegration and breakup of these highly specialized cells and causes glomerular endothelial cells hypertrophy since it raises intraglomerular pressure, preferably affecting the afferent glomerular arterioles. The increase of blood volume is also capable to reduce the levels of podocin (abundant protein in the podocyte body) and nephrin (a structural component of the slit diaphragm) in the glomerulus, which enhances the glomerular podocyte injury and albuminuria.
Recently, experimental and epidemiological studies report that several metabolic disorders manifested in adulthood have their roots dating embryonic periods. Protein or energy restriction during pregnancy induces low birth weight and, consequently, the injury of nephrogenesis, increasing the incidence of chronic kidney disease in adulthood. As previously mentioned, the glomerulus (the most important filtering apparatus in the body) is a highly specialized structure formed by four types of cells: mesangial, endothelial, visceral (podocytes), and parietal epithelial cells. Accordingly, the intrauterine growth restriction induced by maternal protein restriction may cause morphological and functional changes in the glomerulus, thereby decreasing the filtration barrier efficiency with consequent glomerulosclerosis.
Just as occurs in diabetic nephropathy, low birth weight promotes glomerulosclerosis, expansion of mesangial matrix, hyalinosis, and podocytopenia, which compromises glomerular filtration and facilitates progressive kidney dysfunction. The loss of podocytes may represent the starting point for an irreversible glomerular injury, characterized by proteinuria and glomerular scarring.
Transmission electron microscopy analysis revealed that the offspring from maternal low protein diets at 26 weeks of age and at 16 weeks old and presents the effacement of pedicels, the absence of the slit diaphragm, and an increase of glomerular basement membrane thickness, denoting a reduced of barrier efficiency filtration.
Another metabolic programming model related to the occurrence of chronic kidney disease in adult life is maternal vitamin D restriction. This vitamin is essential for the development of the nervous system, immune function, skeletal formation, and fetal kidney. Studies in rats showed that vitamin D restriction during critical periods of development has increased the number of glomerulus, reduced the size of renal corpuscles, and delayed glomerular maturation, further lower expression of WT1 and podocin in adult offspring. These structural and functional adaptations in the glomerulus may progress to chronic kidney disease.