**NAME:** BASHIR AL-AMIN MOHAMMED

**COURSECODE/NAME:** ANA 204/ SYSTEMIC HISTOLOGY

**DEPARTMENT:** PHYSIOLOGY

**MATRIC NUMBER:** 18/MHS01/108

**ASSIGNMENT**

**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 AND THE ANATOMICAL BASIS OF THEIR UNIQUE ADAPTATION**

Desert dwellers also known as Bedouin maintain a mild state of dehydration, have low concentration of urine outputs, high incidence of kidney disease and high hematocrit ratio all characterize this population. In renal function, the deserts Bedouins show no special adaptations.

10 (ten) healthy subjects were picked for a series of various experiments/tests from residents of Negev desert in Israel

For phase one, two and three respectively; for a week, the normal voluntary water intake was doubled with salt supplements (50mM NaCl, 20Mm KCl). After all these phases, significant increase in body masses, decreased concentration of serum proteins, hemoglobin, hematocrit ratios and serum osmolalities were found.

The subjects were asked to exercise on a bicycle for 60 min in heated chamber at 450C. Experiments were terminated if and when heart rate exceeds 180bpm.

Observation

It was noticed that the subjects increased tolerance to heat, extending exercise periods by 25% and 30%.

In adjusting to the hot climates, the functioning of the kidney was a subject in this area. Tests of heat tolerance and sweat capacity were carried out and the glomerular filtration rate was greater compared to a resident of relatively low humidity.

Compared with their starting levels; concentration of serum proteins, hemoglobin, hematocrit ratios. It is suggested that spontaneous voluntary water drinking in desert dwellers is not enough to achieve a true state of euhydration, being the normal state of body water content; absence of absolute or relative hydration or dehydration.

Anatomical structures found in mammals living in desert or environments although not all occurring in a particular animal:

The wide medullae, long loops of Henle, Long proximal tubules, long collecting tubules, small renal corpuscles, extension of renal pelvis well developed elongated papillae, occurrence of giant vascular bundles specialized ultrastructure of Henle’s loops epithelial change in the collecting tubule, rotation of vasa recta.

**2. CLINICAL IMPORTANCE OF GLOMERULAR FILTERATION BARRIER**

What is the Glomerular Filtration Barrier?

The glomerular filteration barrier has several layers. The first is a glocalyx made up of proteoglycans and an adsorbed layer of plasma proteins that is located between the endothelial cells and the capillary lumen. Fenestrated endothelial cells form the next layer. Next is the thick glomerular basement membrane (GBM) which is synthesized by podocytes and endothelial cells and has an inner layer composed of collagen type IV and laminin sandwiched between layers of heparin sulfate.

The epithelial side of the GFB is lined by podocyte foot processes, the intercellular junctions between adjacent foot processes are closed by the slit diaphragm. This is a specialized intercellular junction that acts as a molecular sieve and a final component of the filtration barrier. The slit diaphragm consists of several proteins, including nephrin, poducin, zonula occludens-1, P-cadherins, catenins, CD-associated protein (CD2AP), calcium channel TRPC6 (Transient receptor potential cation subfamilyC member 6), each of which is required for the integrity of the slit diaphragm. Slit diaphragm proteins are supported by the highly dynamic podocyte actin cytoskeleton that in turn is anchored to an integrin complex that factors each podocyte foot processes to the GBM.

CLINICAL IMPORTANCE

A reduction in GFR in disease states is most often due to decreases in the ultrafiltration coefficient (Kf) because of the loss of filtration surface area. The GFR also changes in pathophysiologic conditions because of changes in the hydrostatic pressure in the glomerular capillary (PGC), oncotic pressure in the glomerular capillary (πGC), and hydrostatic pressure in Bowman’s space (PBS).

1. Changes in Kf: An increased Kf enhances the GFR, whereas a decreased Kf reduces the GFR. Some kidney diseases reduce the Kf by decreasing the number of filtering glomeruli (i.e., diminished surface area). Some drugs and hormones that dilate the glomerular arterioles also increase the Kf. Similarly, drugs and hormones that constrict the glomerular arterioles also decrease the Kf.
2. Changes in PGC: With decreased renal perfusion, the GFR declines because the PGC decreases. As previously discussed, a reduction in the PGC is caused by a decline in renal arterial pressure, an increase in afferent arteriolar resistance, or a decrease in efferent arteriolar resistance.
3. Changes in πGC: An inverse relationship exists between the πGC and the GFR. Alterations in the πGC result from changes in protein synthesis outside the kidneys. In addition, protein loss in the urine caused by some renal diseases can lead to a decrease in the plasma protein concentration and thus in the πGC.
4. Changes in PBS: An increased PBS reduces the GFR, whereas a decreased PBS enhances the GFR. Acute obstruction of the urinary tract (e.g., a kidney stone occluding the ureter) increases the PBS.
* Nephrotic Syndrome

The nephrotic syndrome is a set of symptoms that include the following:

1. Protein in the urine;
2. Low blood protein levels;
3. Swelling or edema.
4. It may also include elevated levels of serum lipids, anemia, and vitamin D deficiency, All because of loss of plasma proteins into the urine. This can have multiple causes, but all involve defects in the glomerular barrier to proteins so that excess proteins are filtered and thereby excreted in the final urine. The three barriers were discussed in the text: the fenestrated endothelial cell layer, the GBM, and the podocyte and slit diaphragm.

Nephrotic syndrome can be primary or secondary. Primary causes are described by their histological changes: minimal change disease, focal segmented glomerulosclerosis, and membranous nephropathy. Secondary causes are described by their underlying cause, which include diabetes mellitus, sarcoidosis, hepatitis B, hepatitis C, bacterial infections, parasitic infections, and more.

All of the diseases are characterized by protein in the urine, at least 3.5 g per 24 h. The loss of protein can cause hypoalbuminemia, with resulting edema that may show as puffiness around the eyes, pitting edema in the legs, and pleural effusion. Loss of proteins stimulates liver synthesis, including lipoproteins. Because lipoprotein lipase levels fall, lipoprotein levels increase. Loss of vitamin D binding protein can lead to vitamin D deficiency diseases, with calcium malabsorption and bone disease.

Mutations of nephrin, a protein of the filtration slit can cause nephrotic syndrome. Mutations of podocin also cause nephrotic syndrome that is insensitive to steroid treatment. Podocin is an integral protein of the podocyte cell membrane that segregates into lipid rafts and is required to recruit nephrin into those rafts. Current thought is that podocin and nephrin form a signaling complex that activates protein kinases involved in glomerular structural integrity. These mutations cause minimal change diseases in which structural changes are evident only at the electron microscope level and not at the histological level. Until recently, these were part of the set of nephrotic syndrome called idiopathic nephrotic syndrome.

Membranous glomerulonephritis is one of the more common causes of nephrotic syndrome in adults. It is an inflammatory disease, believed to be caused by binding of antibodies to antigens in the GBM that triggers the formation of a membrane attack complex from complement.

Treatment depends on etiology. For all nephrotic syndromes, monitoring and maintaining normal fluid levels and distribution among the body compartments are the goal. This could include restriction of fluid intake, restriction of salt intake, regular monitoring of blood pressure and urine output, and the use of diuretics. Inflammatory causes of nephrotic syndrome are treated with immunosuppressants such as prednisolone and dietary modificaton.