18/MHS01/271

MEDICAL LABORATORY SCIENCE

RENAL FUNCTION OF DESERT DWELLERS AND THE ANATOMICAL BASIS OF THEIR UNIQUE ADAPTATION.

Desert mammals do not readily find water, hence they must excrete very less amount of water. They are able to produce highly concentrated urine. The henle’s loops of juxtamedullary nephrons along the counter flowing blood vessels called vasa recta, help in the 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 the 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 the filtrate. The kidneys prevent water loss in the desert by concentrating urine therby reducing water loss in the summer when the diet provides very little water. To excret nitrogenous waste products, mammals and most amphibians excrete urea diluted in water. Such xerocoles have adapted to make their own urine as concentrated as possible( i.e use the least amount of water) to dissolve urea. The anatomical structures for urine concentration found in animals living in desert or arid environments, although not all occurring in one particular animal, are wide medullae, long loops of henle, long proximal tubules, long collecting tubules, small renal corpuscles, extension of the renal pelvis, well developed elongated papillae, occurance of giant vascular bundles, specialized ultrastructure of henle’s loops, epithelial changes in the collecting tubule, zonation of the vasa recta and perculiarity of the arterial supply of the kidney. The renal rennin content is moderately high in these species. The rennin-angiotensin-aldosterone system is very active, retaining sodium with water. The urine is concentrated at the expense of other electrolytes. Both the renal blood and urinary flow rates are lower than in species with access to unlimited water supply. The juxtaglomerular apparatus components are topographically intimate for effective tubuloglomerular autoregulation of renal blood flow.

CLINICAL IMPORTANCE OF THE GLOMERULAR FILTERATION BARRIER

The glomerular filtration barrier is a highly specialized blood filtration interface that displays a high conductance to small and midsized solutes in plasma but retains relative impermeability to macromolecules. The glomerular filteration barrier has many layers. The first is the glycocalyx 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. Podocyte foot processes line the epithelial side of the GBM; the intercellular junctions between adjacent foot processes are closed by the slit diaphragm, a specialized intercellular junction that acts as a molecular sieve and the final component of the filtration barrier. The slit diaphragm comprises several proteins, including nephrin, CD-associated protein (CD2AP), podocin, the tight junction protein ZO-1 (zonula occludens 1), P-cadherin, catenins, and the calcium channel TRPC6 (transient receptor potential cation channel, subfamily C, member 6), each of which is required for slit diaphragm integrity. Slit diaphragm proteins are supported by the highly dynamic podocyte actin cytoskeleton that in turn is anchored to an integrin complex that fastens each podocyte foot process to the GBM.

The glomerular filtration barrier consists of the fenestrated endothelium, the glomerular basement membrane, and the podocyte foot processes, which are connected by a slit-diaphragm. The filtration barrier normally acts to retain protein inside the lumen of the capillaries separate from the urinary space; however, defects in the podocytes affecting the feet, tight junction (podocin, nephrin), and the slit diaphragm signaling, actin cytoskeleton, and cell matrix interactions have been identified in causing a breakdown of this barrier.In MCD, there is effacement of the foot processes but minimal other changes observed on renal biopsy. In other forms of NS, immune system activation has been proposed as one of the disease mechanisms, and it has been proposed that there is an unidentified circulating factor or that the hyperlipidemia may activate the immune system. The presence of clonal T cell populations and increased production of T cell-mediated cytokines indicate abnormal T cell activation. In addition, direct or indirect B cell activation in association with T cell dysfunction has been suggested to play a role in mediating increased permeability of the glomerular basement membrane.In infantile NS, recent studies have identified these abnormalities of the glomerular basement membrane, which result in increased permeability and excessive protein loss into the urinary tract, to be critical to the pathogenesis of NS.Another mechanism has been proposed in which protein loss activates plasma proteinases, which results in sodium and fluid retention and edema. Increased serum and urinary microRNAs have been identified in children with NS and, although the mechanism for this is unclear, it has been suggested that these may be useful disease biomarkers.

Normally, a healthy glomerular filtration barrier will freely pass water and small molecules, but filtration of larger molecules depends on glomerular surface area and the glomerular capillary wall permeability.

Damage in the glomerular filtration barrier leading to even small excretion of albumin into the urine (microalbuminuria) can easily be measured using the urine albumin creatinine ratio (UACR) from a urine sample. In a recent meta-analysis including 45 population cohorts comprising 105,872 individuals, UACR was associated with all-cause mortality and cardiovascular mortality independently of glomerular filtration rate and traditional risk factors even down to levels of 1.1 mg/mmol . The hypothesis is that increase in UACR reflects general endothelial damage . The Strong Heart Study included 2,391 individuals from American Indian communities free of cardiovascular and renal disease and examined the predictive value of UACR with regard to the incidence of ischemic stroke.

The glomerular filtration barrier determines the composition of the plasma ultrafiltrate. It restricts the filtration of molecules primarily on the basis of size.