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Session Topic : Perspective on the Pathophysiology of Glomerular Diseases

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Insight into Glomerular Filtration and Albuminuria

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This presentation will cover current insights, based on classic studies that defined the size- and charge-selective properties of the glomerular filter, to help explain how the unique structure and composition of the glomerular capillary wall maintain highly selective filtration properties when healthy, and how it changes with kidney disease. The glomerular filter enables the filtration of approximately 180 liters/day of water and small solutes while restraining the passage of albumin and other macromolecules. This ability is closely tied to the normal structure and composition of the glomerular capillary wall. Podocytes form both a structural barrier to albumin leakage as well as a buttressing force against the distending high intra-glomerular capillary pressure, thereby maintaining glomerular (GBM) compression and resisting transmural passage of albumin. Repulsive forces established by the net negative charge of cell surface molecules maintain the patency of the filtration slits and together with negatively charged proteoglycans on the endothelial cell surfaces and within the GBM serve as a charge barrier to restrict the permeation of negatively charged albumin. This construct allows us to explain how one can have a reduction in GFR at the same time as increased albumin leakage. Podocyte effacement reduces the area available for filtration of water and small solutes and at the same time increases permeability to albumin by reducing the compressive force on the GBM. During development, podocytes mature from cuboidal cells with apical occluding junctions to become highly complex cells with interdigitating foot processes that form complex cell-matrix connections with GBM constituents. They also form a mutually supporting relationship with their neighboring foot processes through the actin-linked slit diaphragms. Congenital or acquired alterations in any of these carefully orchestrated relationships will lead to loss of selective permeability and may impair the rate of glomerular filtration.



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