MASSIVE PROTEINURIA: PATHOPHYSIOLOGY AND TREATMENT

How does the glomerulus prevent protein excretion?
• Old view: glomerular basement membrane was the main site of charge and size selectivity.
• New view: the slit diaphragm is the key player in preventing proteinuria.
• Slit diaphragm is basically a super-specialized epithelial tight junction that exists between podocytes.
• As you are reading this coversheet, scientists around the world are discovering new proteins that play a role in the slit diaphragm! Nephrin, CD2-associated protein, Neph1, and Podocin are just a few (absence of any of these proteins causes severe congenital nephrotic syndrome).

Are nephrotic syndrome patients at increased risk for infection?
• Yes; this is thought to be due to decreased levels of IgG and alternative complement factor B.
• These patients are at increased risk for infections with encapsulated organisms (humoral immunodeficiency).
• Uncontrolled studies have shown positive results with IV IgG.

What are specific treatments for proteinuria?
• ACE-inhibitor, angiotensin-receptor blocker (ARB)
• Cyclosporine (CsA) to combat the “immune” side of disease (as well as potent afferent vasoconstrictor)
• “Medical nephrectomy”: high-dose NSAIDs, CsA/ACE-I used in past; now bilateral renal artery embolization is the usual approach.

How do ACE-inhibitors decrease proteinuria?
• Old view: ACE-I decreases glomerular pressure by dilating efferent arteriole
• New view: ACE-I increases nephrin levels, alters and re-aligns proteins in the slit diaphragm in addition to hemodynamic effects