Case Scenario 1: The GBM and Disease

A 10-year-old boy is brought to the clinic with puffy eyes (periorbital edema) and frothy urine. Urinalysis reveals massive proteinuria (3+ protein) but no red blood cells or glucose. Blood tests show low serum albumin. A renal biopsy is performed. Under electron microscopy, the pathologist notes that the glomerular capillary loops appear normal, and the podocyte foot processes are intact and interdigitating. However, the glomerular basement membrane (GBM) appears uniformly and significantly thinned compared to normal controls.

Question: Based on the histology and the clinical presentation, which specific component of the glomerular filtration barrier is most likely structurally defective? How does this defect explain the presence of protein in the urine (proteinuria) but the absence of blood or glucose?

Answer:

The defective component is the **Glomerular Basement Membrane (GBM)**, specifically its structural integrity.

the GBM is "the most substantial part of the filtration barrier" and acts as the "first, coarser filtration barrier; it blocks the passage of molecules larger than 70 kD." A pathologically thinned GBM would lose its normal sieving properties, allowing medium-sized plasma proteins (like albumin, ~66 kD) to pass through into Bowman's space, leading to **proteinuria**. Glucose is a much smaller molecule that is freely filtered and normally reabsorbed, so its absence in the urine is expected. Red blood cells are physically blocked by the **fenestrated endothelium**, which remains intact in this case.

Case Scenario 2: The Podocyte and the Slit Diaphragm

A 45-year-old woman presents with swelling in her legs and fatigue. A kidney biopsy is done for diagnosis. Electron microscopy reveals a striking finding: the podocytes' foot processes are effaced (flattened and fused together), blurring the distinct interdigitating pattern. The filtration slit diaphragms between the pedicels are poorly defined.

Question 1: What is the name of the specialized junctional complex that is disrupted between the effaced foot processes?

Question 2: Why is alteration in this structure a common finding in many kidney diseases?

Answer 1: The disrupted structure is the **slit diaphragm**.

Answer 2: the slit diaphragm molecular complex is "associated with the actin cytoskeleton" of the contractile podocyte foot processes. It is a "specialized occluding junction" critical for the final, selective filter.

"Alterations in composition and/or arrangement of these complexes are found in many forms of human and experimental diseases." Disruption of these diaphragms destroys the final layer of selectivity, allowing proteins to leak into the urine, which is a hallmark of many glomerular diseases (glomerulopathies).

Case Scenario 3: The Mesangium in Immune Complex Disease

A patient with long-standing systemic lupus erythematosus (SLE) develops signs of kidney involvement (lupus nephritis). A renal biopsy is evaluated with light microscopy, immunofluorescence, and electron microscopy. The pathologist's report highlights a significant increase in the number of cells and extracellular matrix within the central, supportive regions of the glomerular tuft (the mesangium). Immune complex deposits are noted in this same area.

Question: Identify the cells that are proliferating and describe **two** of their normal functions that are relevant to this pathological scenario

Answer:

The proliferating cells are **mesangial cells**.

Two relevant normal functions are:

1. **Phagocytosis of protein aggregates... including antibody-antigen complexes:** This is directly pertinent, as SLE is characterized by circulating immune complexes (antibody-antigen). The mesangium is attempting to clear these pathological deposits that have become trapped in the glomerulus.

2. **Secretion of several cytokines, prostaglandins, and other factors important for immune defense and repair:** The proliferative and inflammatory response seen in lupus nephritis is likely driven, in part, by cytokines released by activated mesangial cells.

Case Scenario 4: Compensatory Hypertrophy Post-Donation

A healthy 32-year-old man donates his left kidney to his sibling. One year after the successful transplant, a follow-up MRI scan of the donor shows that his remaining right kidney has increased in size. A research study analyzing blood and urine from the donor shows that his glomerular filtration rate (GFR) is about 70-80% of the normal pre-donation value for two kidneys, which is considered excellent single-kidney function.

Question: Based on the histological changes described , what is the primary microscopic adaptation in the remaining kidney that allows for this maintenance of near-normal function? In which specific part of the nephron does this occur?

Answer:

The primary adaptation is **cellular hypertrophy** (increase in cell size, not number). According to the lecture, this occurs specifically in **the proximal parts of the nephron tubules** (i.e., the proximal tubules). This hypertrophy, along with functional adaptations like increased filtration rate per nephron, allows the remaining kidney to compensate for the loss of its partner and maintain adequate overall renal function.