

# Edema in Nephrotic Syndrome

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# Nephrotic Syndrome

- Protein excretion  $> 3.5$  gr/24h
- Hypoalbuminemia ( $< 3$ gr/dl)
- Peripheral edema
- Hyperlipidemia
- Thrombotic disease

# Etiology of Nephrotic Syndrome

- Children: minimal change disease
- Adults: systemic disease and primary renal disease

# Mechanism of Proteinuria

- Podocytopathy and podocyte depletion
- Foot process effacement
- Slit diaphragm dysruption

# Definition of Edema

- Palpable swelling produced by expansion of the interstitial fluid volume
- Anasarca: massive and generalized edema

# Underfill vs. Overfill Hypothesis

- Secondary sodium retention
- Primary sodium retention

# Starling`s law

- Unit permeability (porosity)
- Surface area available for fluid movement
- Capillary and interstitial hydraulic pressure
- Capillary and interstitial oncotic pressure
- Reflection coefficient
- Lymphatic flow

# KF vs. $\delta$

- LPS (KF) : Filtration coefficient
- Decrease in  $\delta$  (increase in pore size) necessitates an increase in KF



# Hypoalbuminemia and Interstitial Albumin

- Wash down mechanism
- Wash out mechanism

# Neurohormonal changes

- RAAS
- SNS
- AVP
- ANP

# Primary Renal Sodium Retention

- High Na-K ATPase activity
- High ENaC activation

# Regulation of ENaC

- Regulation of channel density
- Regulation of open channel probability

# ENaC Receptor Density

- Aldosterone
- Vasopressin

# open channel probability

- Proteolytic processing
- Anionic phospholipids

# ENaC Subunits

- $\alpha$ ,  $\beta$ ,  $\gamma$ ,
- $\alpha$  and  $\gamma$ , have regulatory roles

# Activators of ENaC (1)

- Plasmin
- Prostasin
- Matriptase-2
- Elastase
- Kallilrein-1



# Activators of ENaC (2)

- Cysteine
- Metalloproteases
- Transmembrane protease serine 4
- Chemotrypsin

# Role of Urokinase-type Plasminogen activator

- Convert plasminogen to plasmin

# Role of Plasmin

- Removal of inhibitory  $\gamma$  chain domain
- Activating prostatesin

# Proteinuria and ENaC activation

- Primary Renal Sodium Retention
- Active in all patients with nephrotic syndrome