

# Nephrotic Syndrome In Children



# Idiopathic Nephrotic Syndrome

An illustration of a person in a dark suit and tie, holding a white certificate that says "CERTIFICATE". To the left, a hand holds a smartphone. To the right, a yellow pencil is positioned near a tablet displaying a bar chart. The background is teal with light blue circles.

- (NS) is characterized by the triad of:
  - Proteinuria
  - Hypoalbuminemia
  - Oedema
    - $\pm$  *Hypercholesterolemia*

# Definition & Classification

An illustration of a person in a dark suit and tie, holding a white certificate that says "CERTIFICATE". The background is teal and features various icons: a smartphone, a pen, a tablet, and a pencil.

- Idiopathic NS can be classified on *the basis* of:
  - Response to steroid therapy,
  - Pattern of relapse,
  - Histopathology,
  - By genetic mutations.

## Relevant definitions in nephrotic syndrome

- ***Nephrotic Range Proteinuria:***
  - protein excretion  $>40$  mg/m<sup>2</sup> per h
  - Urine protein:creatinine ratio  $\geq 2000$  mg/g ( $\geq 200$  mg/mmol) ( $>2$ )
  - $>3+$  proteinuria on dipstick with serum albumin  $<2.5$  g/dL (25 g/L)
  - $>50$ mg/kg/day
  - $>1-2$ gm/m<sup>2</sup>/day



## Relevant definitions in nephrotic syndrome

- **Remission**
  - Urine albumin trace or negative on dipstick
  - proteinuria  $<4 \text{ mg/m}^2$  per h
  - urinary protein:creatinine ratio  $<200 \text{ mg/g}$  ( $20 \text{ mg/mmol}$ ) for 3 consecutive days
- **Relapse**
  - Urine albumin 3+ or 4+ or proteinuria  $>40 \text{ mg/m}^2$  per h
  - urinary protein:creatinine ratio  $>200 \text{ mg/g}$  ( $20 \text{ mg/mmol}$ ) for 3 consecutive days



## Relevant definitions in nephrotic syndrome

- ***Frequently relapsing NS***
  - $\geq 2$  relapses within 6 months of initial response
  - $\geq 4$  in any 12 month period
- ***Steroid-dependent NS***
  - 2 consecutive relapses occurring while weaning to alternate day steroids or within 2 weeks of steroid discontinuation
- ***Steroid-resistant NS***
  - Persistent proteinuria despite  $60 \text{ mg/m}^2$  or  $2 \text{ mg/kg}$  for 8 weeks, after ensuring no infection or non-adherence to medication



## Mechanisms of Disease

- It is suspected that dysfunction or dysregulation of T lymphocytes are involved in the pathogenesis of NS.
  - A recent molecular candidate for the cause of podocytopathies and proteinuric states is CD80 (B7-1).
  - CD80, is a protein expressed on antigen-presenting cells that provides the primary co-stimulatory signal for T-cell activation via receptors on the T-cell surface.
- A circulating glomerular permeability factor has been hypothesised to cause NS, however, defining a single putative factor remains elusive. The majority of studies favour a circulating factor in SRNS or FSGS

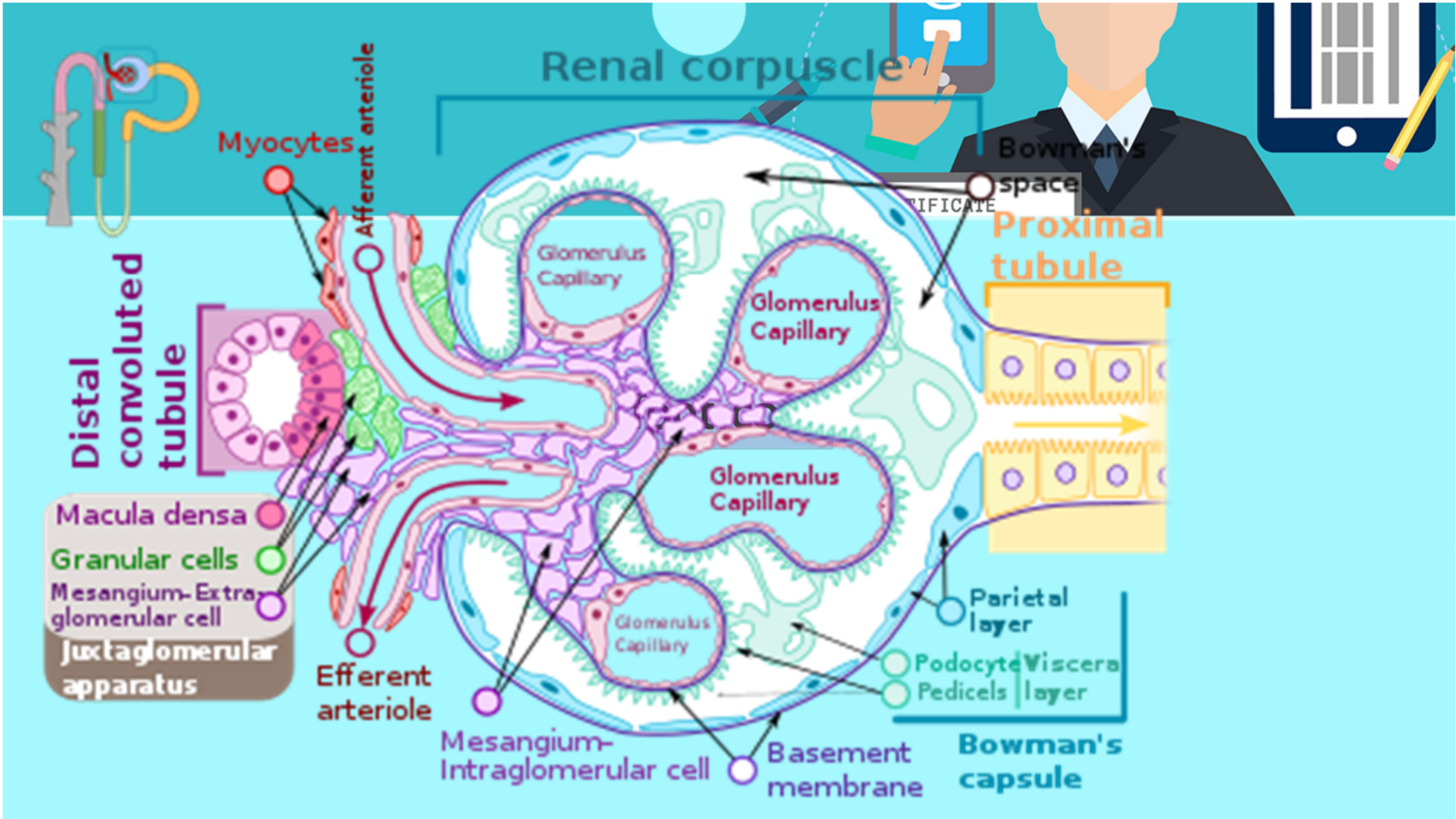


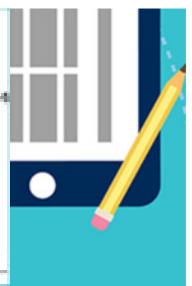
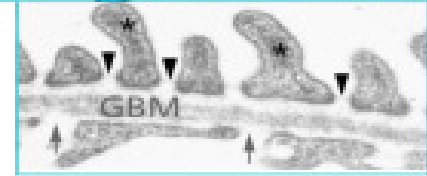
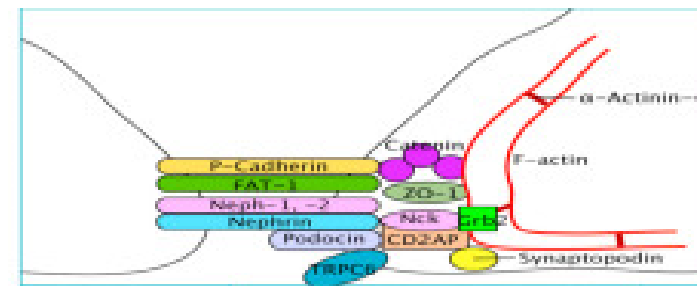
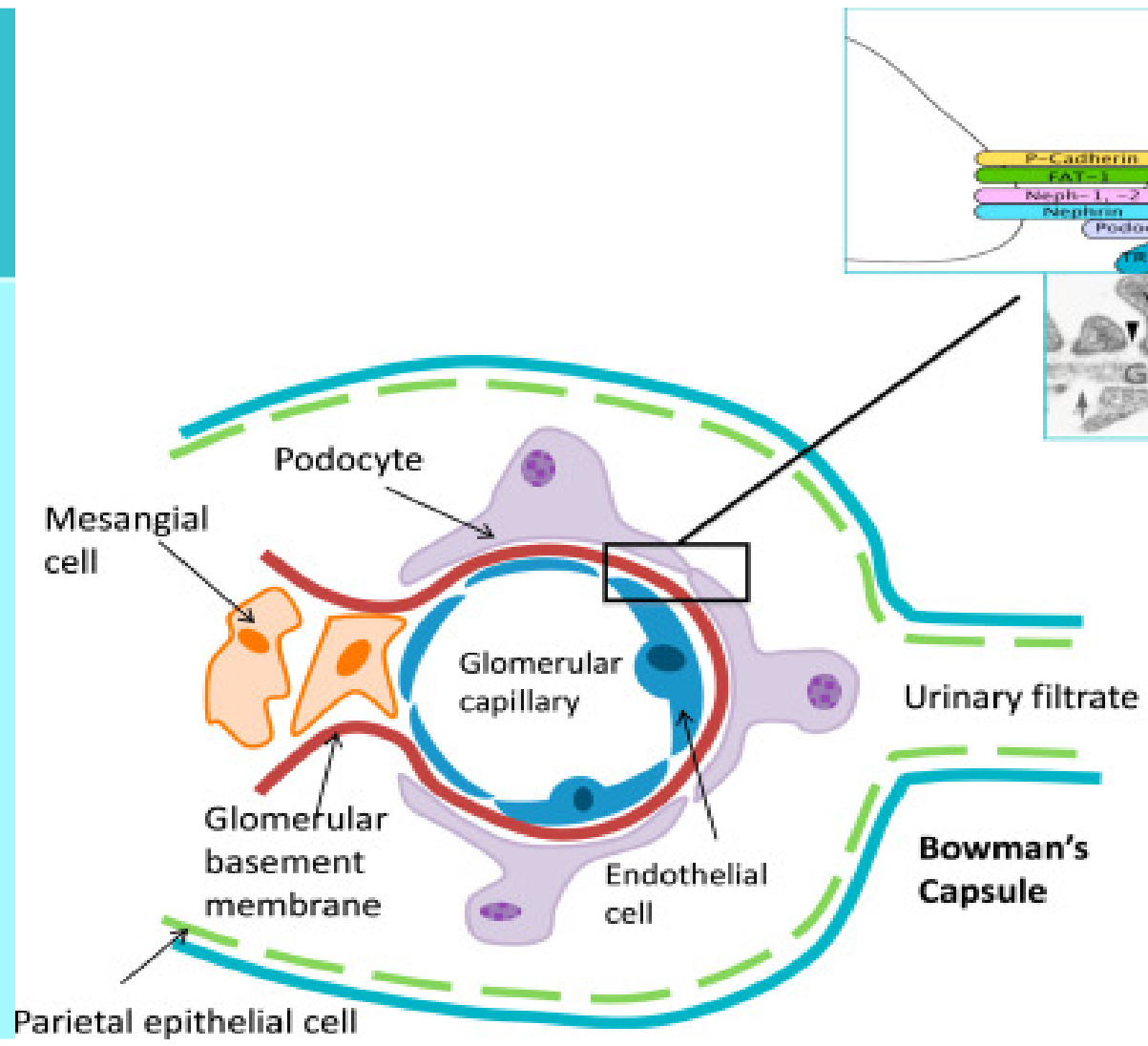
# Capillary Wall Structure

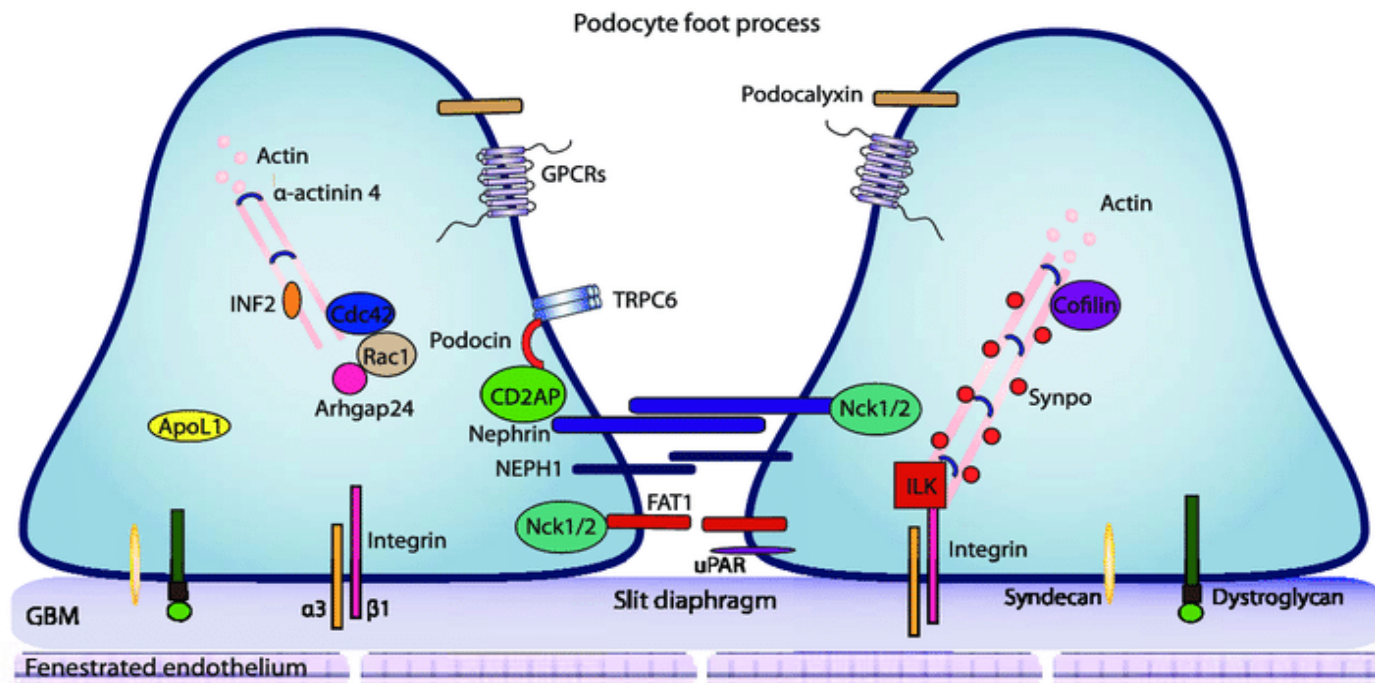


- **Endothelial Cell**
- **Basement Membrane**
- **Epithelial Cell (Podocyte)**









Slit diaphragm	Cytoskeleton	GBM attachment	Other
FAT1	Arhgap 24	Dystroglycan	ILK
Nephrin	Rac1	Syndecan	TRPC6
NEPH1	Cdc42	Integrin	GPCRs
CD2AP	INF2		uPAR
Nck1/2	Cofilin		Podocalyxin
Podocin	α-actinin 4		ApoL1
	Synaptopodin		

# Investigations



## Baseline

- 1) Urinalysis and urine microscopy
- 2) Urine albumin or protein:creatinine ratio
- 3) 24-h timed collection of urine for protein quantification
- 4) Serum electrolytes, albumin, total protein, renal function, and cholesterol

## Additional

- 1) Serum complement C3 and C4
- 2) Serum immunoglobulins
- 3) Antistreptolysin titres
- 4) Anti-DNAse B antibodies
- 5) Antinuclear antigen antibodies
- 6) Anti-double-stranded DNA antibodies
- 7) Anti-neutrophil cytoplasmic antibodies

# Treatment Protocols



- **Prednisolone**
- **Cyclophosphamide**
  - Oral
  - Monthly pulses
- **Cyclosporine**
- **Tacrolimus**
- **Mycophenolic acid**
- **Rituximab**