

Clinical Features.

- This disorder usually presents either with the
 1. Insidious onset of the nephrotic syndrome or
 2. Non nephrotic proteinuria in 15% of patients,
 3. Hematuria and mild hypertension are present in 15% to 35% of cases.

Note: The proteinuria is nonselective

- The course of the disease is variable but generally indolent.
- Usually does not respond well to corticosteroid therapy.
- Complete or partial remissions may occur in up to 40% of patients, even in some patients without therapy. but proteinuria persists in more than 60% of patients

- Spontaneous remissions and a relatively benign outcome occur more commonly
 - a. In women and
 - b. In those with proteinuria in the nonnephrotic range.

- a. only about 10% die or progress to renal failure within 10 years,
- b. and no more than 40% eventually develop severe chronic kidney disease or end-stage renal disease

Note: The disease recurs in up to 40% of patients who undergo transplantation for end-stage renal disease.

2.Minimal change disease

- Is a relatively benign disorder
- Is the most frequent cause of nephrotic syndrome in children
- The peak incidence is between 2-6 years
- Sometimes it follows respiratory infection or prophylactic immunization

- Several features of the disease suggest immunologic basis
 1. The clinical association with respiratory tract infection
 2. The response to corticosteroids or immunosuppressive therapy
 3. The increased incidence in patients with Hodgkin disease

Pathogenesis

- The current hypothesis that minimal change disease involves some immune dysfunction that results in elaboration of factors that damage the visceral epithelial cells and cause proteinuria

morphology

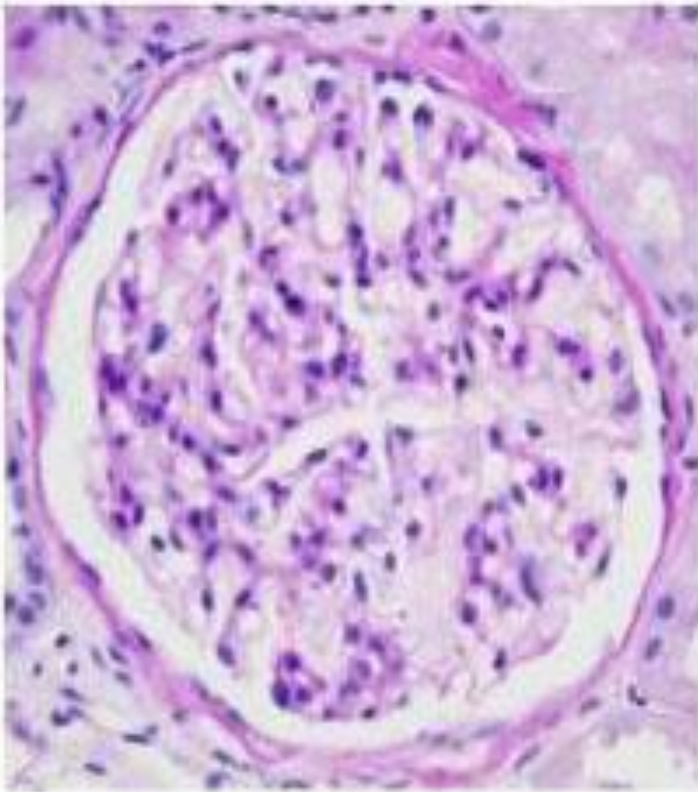
Light microscopy

- Normal
- The proximal tubular cells contain lipid (previous name lipoid nephrosis)

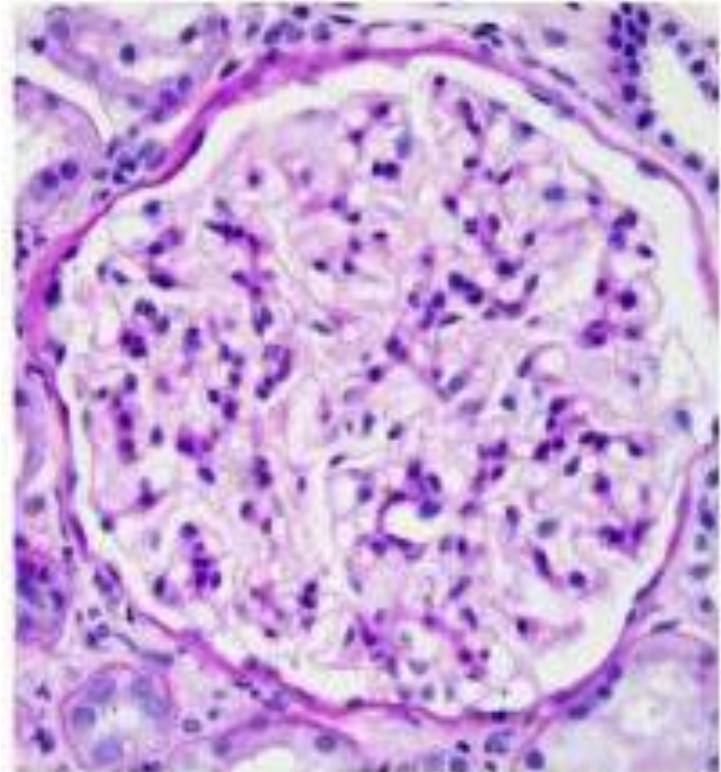
Immunofluorescence:

- No deposition of Ig or complements

Normal glomerulus



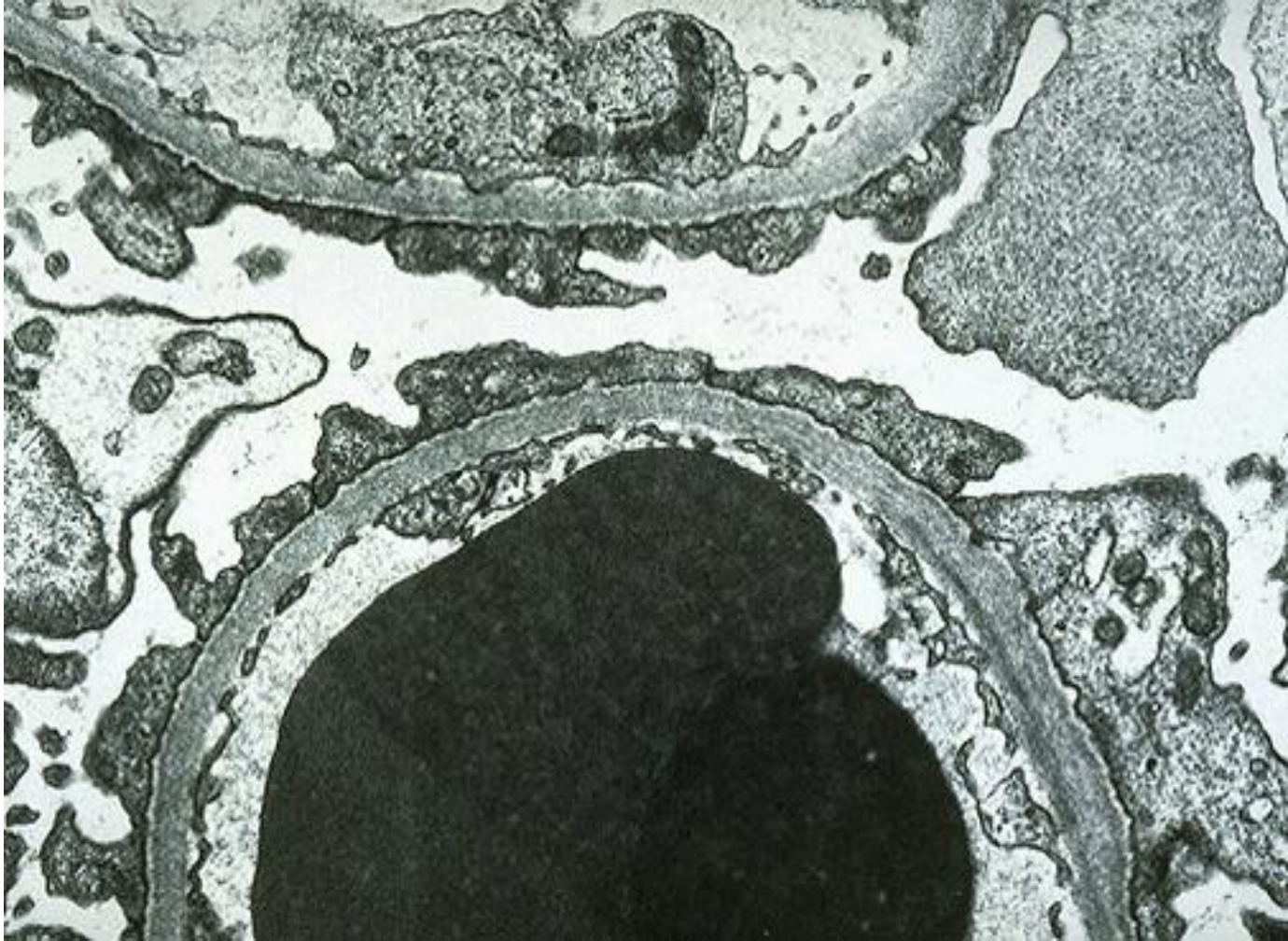
Minimal change disease



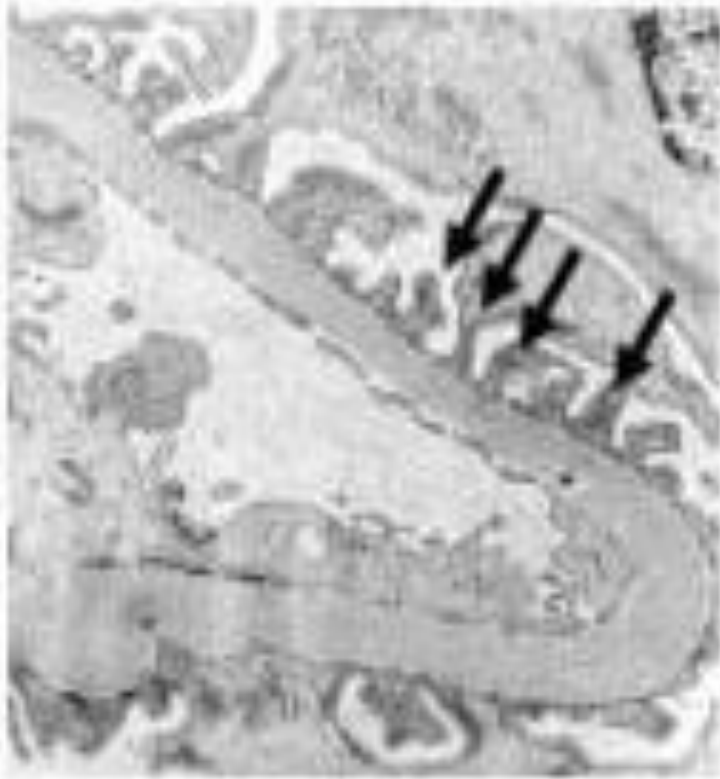
Electron microscope:

- The principal lesion is in the visceral epithelial cells that shows uniform and diffuse effacement of foot processes and being reduced to a rim of cytoplasm without intervening slit diaphragm
- **No dense deposits**

Minimal change disease



Normal glomerulus



Minimal change disease



Note

- Foot process effacement is also present in other proteinuric states (e.g., membranous glomerulopathy, diabetic nephropathy)
- It is when the effacement is associated with normal glomeruli by light microscopy, the diagnosis can be made
- The visceral epithelial changes is completely reversible with corticosteroid therapy

Clinical Features.

- Despite massive proteinuria, renal function remains good,
- No hypertension or hematuria.
- The proteinuria usually is highly selective, most of the protein being albumin.
- **A characteristic feature is its usually dramatic response to corticosteroid therapy.**

- Most children (>90%) with minimal-change disease respond rapidly to this treatment.
- However, proteinuria may recur, and some patients may become steroid-dependent or resistant.

- Nevertheless, the long-term prognosis for patients is excellent, and even steroid-dependent disease usually resolves when children reach puberty.
- Although adults are slower to respond, their long-term prognosis is also excellent.

3. Focal segmental glomerulosclerosis

- Is the most common cause of nephrotic syndrome in adults in the USA
- It is sometimes considered to be a primary disorder of podocytes, like minimal change disease.

Classification and Types

1. As a primary disease (idiopathic focal segmental glomerulosclerosis)
 - Accounts for 10% and 35% of cases of nephrotic syndrome in children and adults, respectively.
2. In association with r known conditions, such as
 - a. HIV infection (HIV-associated nephropathy),
 - b. heroin addiction (heroin nephropathy),

3. As a component of the adaptive response to loss of renal tissue (renal ablation)
4. Inherited focal segmental glomerulosclerosis

1. The first gene to be identified, is *NPHS1*, on ch 19 and encodes the protein *nephrin*.
 - Nephrin is a key component of the slit diaphragm the structure that controls glomerular permeability.
 - Several mutations of the *NPHS* gene have been identified that give rise to *congenital nephrotic syndrome*

2. Autosomal recessive FSGS

- Results from mutations in the *NPHS2* gene, on ch 1 and encodes *podocin*.
- Podocin has also been localized to the slit diaphragm..
- Mutations in *NPHS2* result in a syndrome of steroid-resistant nephrotic syndrome of childhood onset

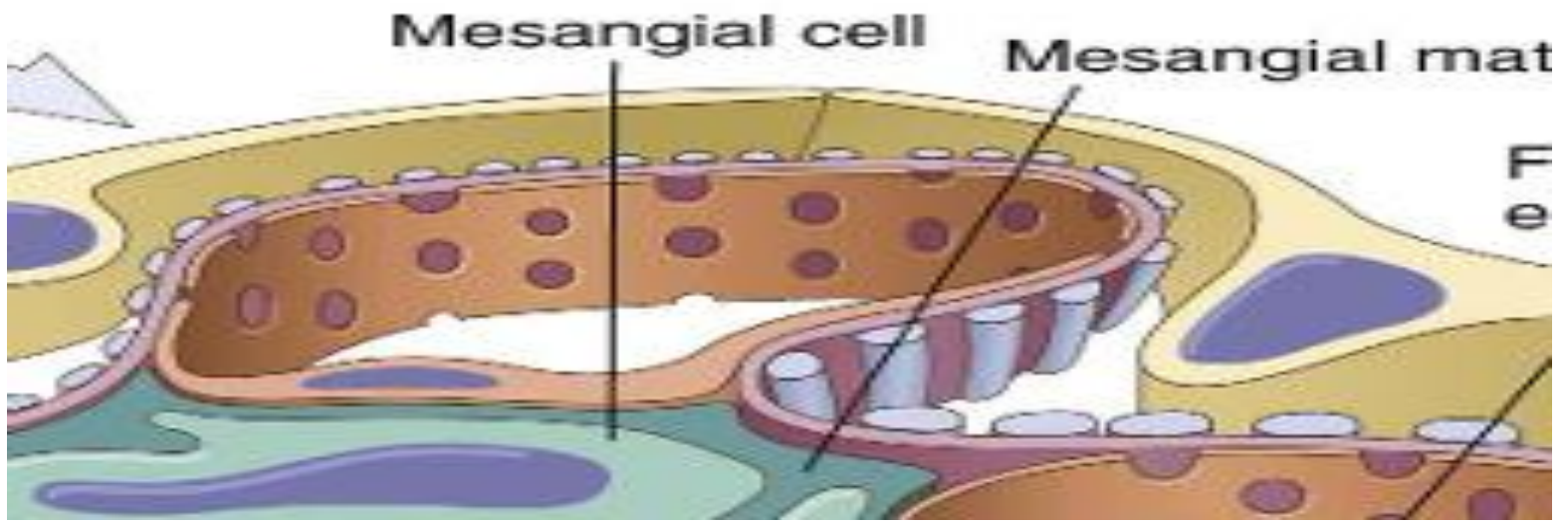
3. Autosomal dominant FSGS

- Caused by mutations in the gene encoding the podocyte actin-binding protein α -actinin 4,
- The disease can be insidious in onset but has a high rate of progression to renal insufficiency.

Pathogenesis.

- The characteristic degeneration and focal disruption of visceral epithelial cells with effacement of foot processes resemble the diffuse epithelial cell change typical of minimal-change disease and other podocytopathies.

- ***It is this epithelial damage that is the hallmark of FSGS.***
- Multiple different mechanisms can cause such epithelial damage, including
 - a. circulating factors and
 - b. genetically determined defects affecting components of the slit diaphragm complex.



- The hyalinosis and sclerosis stem from entrapment of plasma proteins in extremely hyperpermeable foci and increased ECM deposition

- The recurrence of proteinuria after transplantation, sometimes within 24 hours, with subsequent progression to overt lesions of FSGS, suggests that an unknown circulating factor is the cause of the epithelial damage in some patients.

Morphology

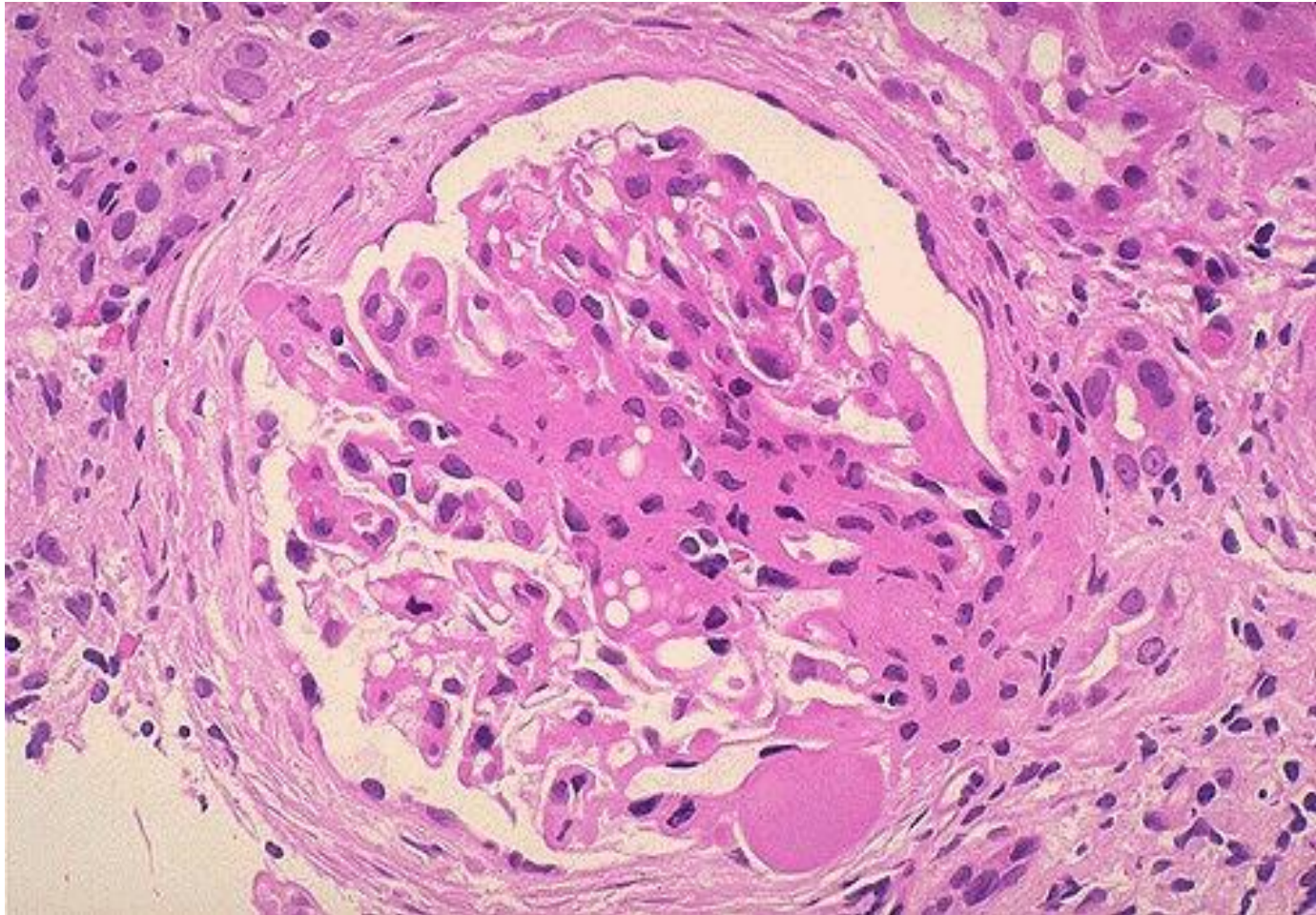
Light microscopy:

1. It is focal (few glomeruli) and segmental (part of the glomerulus) lesion
2. May involve only minority of the glomeruli especially juxtamedullary glomeruli

Note: And may be missed if the biopsy doesn't contain sufficient number of glomeruli

- In the sclerotic segment, there is:
 1. Collapse of the capillary loops
 2. Increase in the mesangial matrix
 3. Segmental deposition of plasma proteins along the capillary walls with hyalinosis which may be so pronounced to obliterate the capillary lumina

FSGS



FSGS-Tricchrome stain

