

RENAL SYSTEM - 2

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DISEASES OF THE GLOMERULI

IMMUNOLOGICAL


- Antibodies reacting with glomerular antigens
 - Anti GBM antibodies (Goodpasture's syndrome)
- Circulating immune complexes (Post streptococcal)

VASCULAR

- Hypertension
- Diabetes

FOREIGN MATERIAL

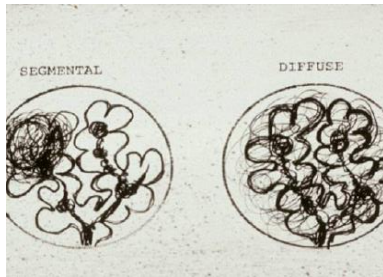

- Amyloidosis: Renal involvement occur almost always in systemic amyloidosis.



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Glomerular response to damage


- Histological changes**
 - Hypercellularity
 - BM thickening
 - Hyalinization and sclerosis
 - diffuse
 - segmental

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INFLAMMATION OF GLOMERULI (GLOMERULONEPHRITIS)

- It may be of few glomeruli (**focal** or multifocal), or involve all the glomeruli (**generalized**)
- The term diffuse glomerulonephritis is used to indicate involvement of the entire glomerulus in contrast to segmental involvement.
- In most cases of glomerulonephritis, there are secondary changes involving **tubules** and the **interstitium** and sometimes **blood vessels**.
- In absence of secondary lesions, term **glomerulitis** is preferred.

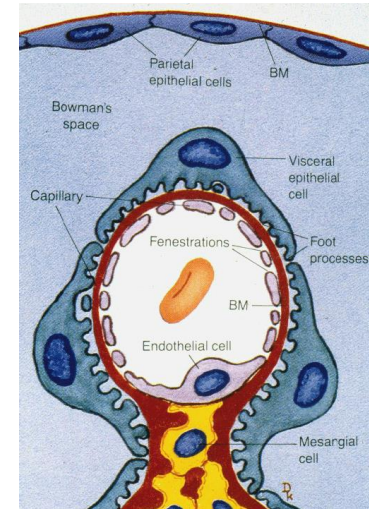


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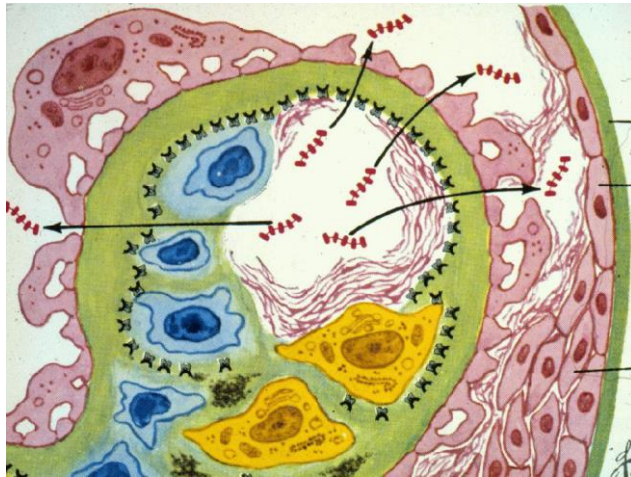
- Glomerulitis is virtually always accompanied by secondary changes which in turn cause renal failure.
 - Haematuria, proteinuria, oliguria, and **azotaemia**
 - **Proteinuria**, occurs in the absence of urinary tract inflammation,
 - caused by increased permeability of glomerular membranes
 - Most of the filtered protein is **albumin** and this results in hypo-albuminaemia.
 - Eventually, this will lead to the "**nephrotic syndrome**" characterized by
 - Hypo-albuminaemia,
 - generalized oedema, and
 - hypercholesterolemia.



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Acute Proliferative Glomerulonephritis

- is a clinical syndrome with characteristic inflammatory lesions involving glomeruli that has been reported in children and animals.
- In humans, it is an immunologically mediated disease associated with certain specific strains of **streptococci**
- The incubation period is 2 week (time required to produce sufficient antibodies).

Grossly

- The kidneys appear enlarged and pale with **petechial haemorrhages** outline the glomeruli.



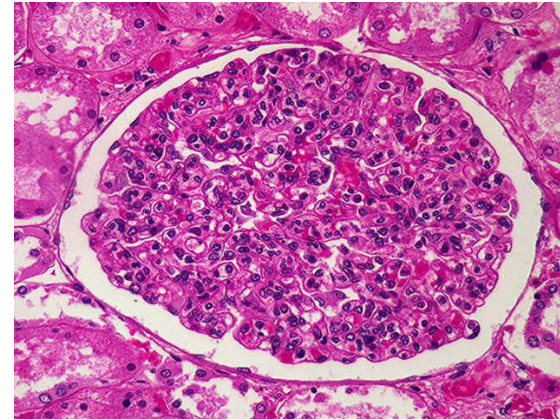
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Histologically

- There is enlargement of the glomerular tufts with increased numbers of endothelial cells filling the Bowman's spaces.
- In early stages, **neutrophils** appear in glomeruli but as the disease progresses, there is proliferation of epithelial cells in the visceral layer of the Bowman's capsule and **adhesions** often develop between the **parietal and visceral layers**.
- These eventually form the epithelial "**crests**" seen in the subacute and chronic forms.
- Thrombosis and necrosis of glomerular capillaries may occur with subsequent haemorrhage into the renal corpuscle.



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This enlarged glomerulus is hypercellular due to proliferating mesangial cells, and inflammatory cells (both neutrophils and monocytes). Endothelial swelling is also present, which together with the leukocytes occlude the capillary lumen.



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Membranous Glomerulonephritis

- involves an immunologic process in which **immunoglobulins** or **antigen-antibody complexes** are deposited in the glomerular basement membrane.
- In Situ Immune Complex Formation
- Circulating Immune Complex Deposition
- Elicits Immune/Inflammatory Reaction
 - Fixed Antigens (Intrinsic)
 - Anti-GBM Nephritis
 - Planted Antigens
 - Endogenous e.g. DNA (SLE)
 - Exogenous e.g. DRUGS
- Hyper-gammaglobulinaemia is frequently reported in such cases.



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Grossly

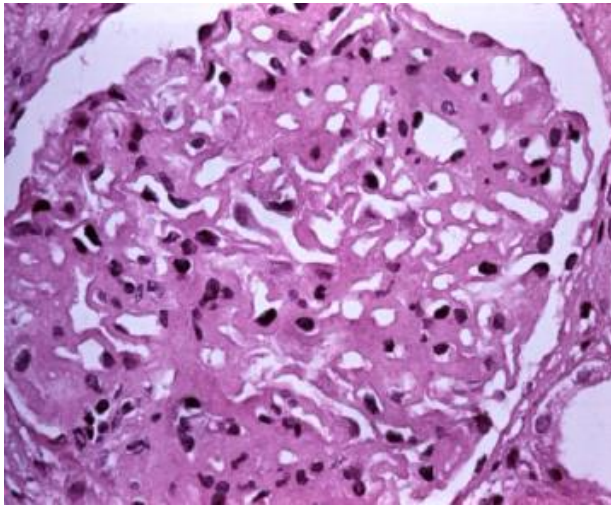
- Affected kidneys appear **enlarged and pale** due primarily to fatty change in renal tubular epithelial cells and oedema of the interstitium
- In the latter stages of the disease, the kidney may become **shrunken and fibrotic**

Histologically

- There is thickening, splitting, and reduplication of the glomerular basement membrane
- Loss of the **foot processes** of the podocytes (epithelial cells of the visceral layer of the Bowman's capsule)
- Swelling and fatty change of glomerular epithelial cells



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Membrano-proliferative Glomerulonephritis

- It is characterized by alterations in the basement membranes as well as proliferation of **mesangial** and **parietal** epithelial cells of the Bowman's capsule.
- Several forms of membrano-proliferative glomerulonephritis have been reported in human including types I, II, and III
- The pathogenesis of the three types seems variable.
- **Type I** MPGN is usually characterized by immune complex deposition in glomeruli.
- **Type II** is usually associated with a deficiency of C3
 - This may be an inherited or an acquired problem
 - In the case of the acquired form, it may be autoimmune in nature.
- **Type III** is rare and has not been reported in animals.



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- An autosomal recessive inherited version of MPGN **has been reported in a breed of sheep.**
- This genetic defect is characterized by a deficiency of C3 **and affected lambs begin to develop glomerular lesions in utero.**
- Clinically, **affected lambs seem normal at birth but die at about 3 months of age due to renal failure.**

Grossly

- the kidneys tend to be enlarged and their cortices are pale.
- Small red spots, representing enlarged glomeruli, are visible throughout the cortices of affected kidneys.



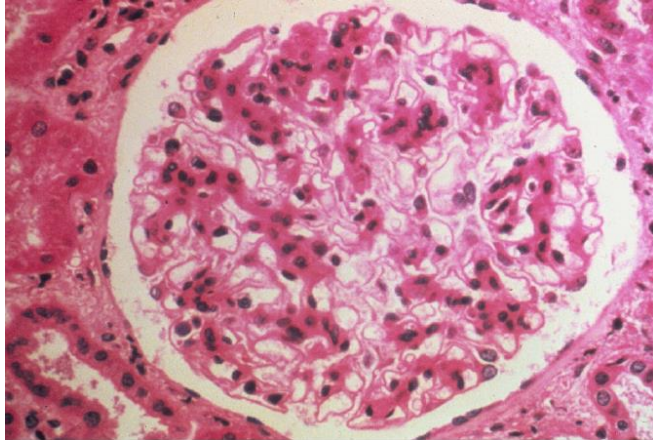
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Histologically

- The glomeruli appears enlarged and hypercellular with most of the increase in cellularity due to proliferation of mesangial cells.
- In addition, there is uneven thickening of the glomerular capillary basement membranes with peripheral portions of the glomerulus more severely affected.
- Membranoproliferative glomerulonephritis tends to be nonstop and it usually progress to chronic renal failure.



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Chronic Glomerulonephritis

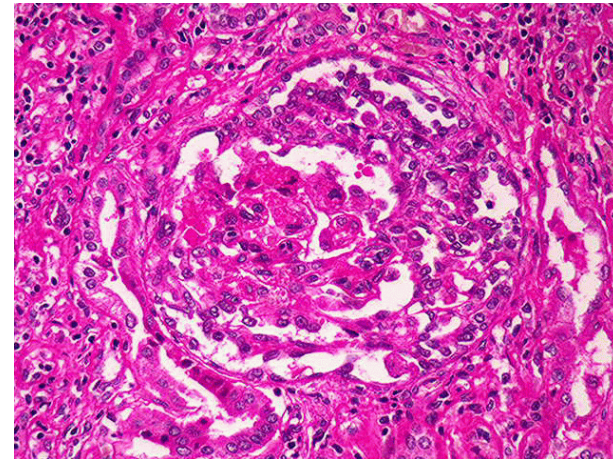
- It is best considered as end-stage finding for the various forms of glomerulonephritis.
- In most cases, chronic glomerulonephritis is preceded by an acute or subacute proliferative or membranous glomerular problem.

Grossly

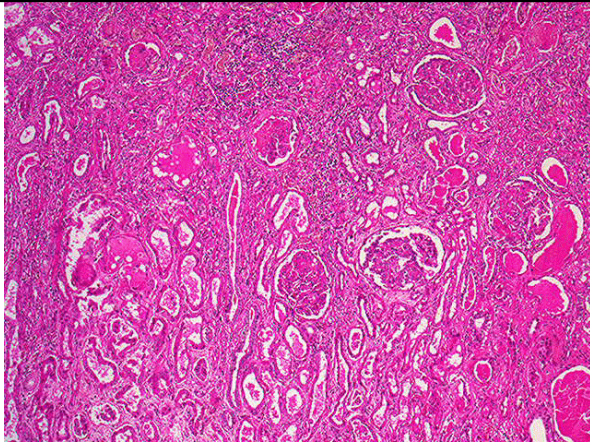
- Affected kidneys appear **smaller** than normal and have a rough or **pitted contour**.
- They are usually firm and they tend to be difficult to incise.
- The cut surface tends to be coarse, granular, and/or cystic.

Histologically

- The glomeruli appears enlarged and hypercellular with most of the **increased cellularity** due to proliferation of **mesangial** and **endothelial** cells.
- Many of the glomerular capillary lumens are occluded and the visceral layer of the Bowman's capsule is adhered to the parietal layer.
- In advanced stages, glomeruli are often obliterated and replaced by **hyaline** connective tissue.
- Decreased blood flow through glomeruli results in decreased perfusion of the tubules and leads to **tubular nephrosis** and **interstitial fibrosis**.
- Crescent formation may be evident in many renal corpuscles causing collapse of the glomeruli.



Glomeruli may still show evidence of the primary disease: for example, there may be crescents



End-stage of glomerular disease. Glomeruli are totally replaced by hyaline connective tissue. There is atrophy of the tubules, which appear shrunken and are surrounded by a thickened basement membrane. There is also fibrosis of the interstitium with arterio- and arteriosclerosis.



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Glomerulosclerosis

- Refers to a condition in which glomeruli become firm or hardened.
- Glomerulosclerosis is most frequently found in association with **diabetes mellitus** and the mechanism for its development is uncertain.
- There are two basic forms of glomerulosclerosis which are **diffuse** glomerulosclerosis and **nodular** glomerulosclerosis.
- **Nodular** glomerulosclerosis is also known as intercapillary glomerulosclerosis.
- Glomerulosclerosis is usually accompanied by secondary tubular and interstitial changes and therefore renal failure often develops.



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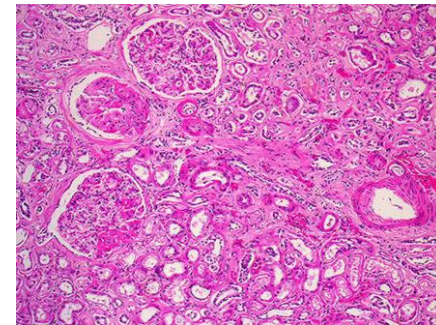
- The clinical features are similar to those of glomerulonephritis; accompanied by those of DM
- There is considerable variation in the gross appearance of affected kidneys depending largely on the duration of the problem and the extent of the secondary changes.
- Severely affected kidneys are smaller than normal and usually have an irregular or nodular contour.
- They tend to be pale and firm and the cut surface tends to be mottled.



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Histologically,

- There is diffuse (diffuse glomerulosclerosis) **thickening of the glomerular capillary membranes or segmental (nodular glomerulosclerosis) thickening of glomerular capillary basement membranes.**



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Nephrotic Syndrome

- The nephrotic syndrome results from excessive glomerular **permeability** to plasma proteins, mainly albumin.
- It occurs in most glomerular diseases including glomerulonephritis, glomerulo-sclerosis, and amyloidosis.
- Clinically, there is
 - proteinuria (principally albuminuria),
 - hypoproteinemia (principally hypoalbuminemia),
 - generalized edema,
 - hyperlipemia, and
 - lipiduria.