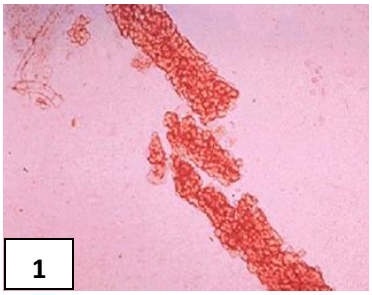
Unit V – Problem 9 – Pathology: Nephritic Syndrome

- **It is a clinical complex usually of an acute onset. It is characterized by the following:**
  - Hematuria and RBC casts in the urine (image-1).
  - Azotemia (e.g. increased BUN: Blood Urea Nitrogen).
  - Oliguria.
  - Hypertension (due to salt retention).
  - Proteinuria (< 3.5 g/day).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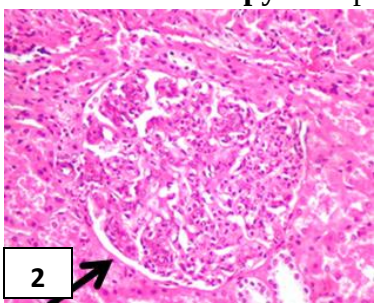
- **Causes of nephritic syndrome:**
  - Acute post-streptococcal glomerulonephritis.
  - Rapidly Progressive (crescentic) Glomerulonephritis (RPGN).
  - Diffuse Proliferative Glomerulonephritis (DPGN).
  - IgA nephropathy (Berger disease).
  - Alport syndrome.
- **Acute post-streptococcal glomerulonephritis:**
  - **Pathogenesis**: most frequently seen in children. Occurs two weeks after group A beta hemolytic streptococci infection of the pharynx or skin:
    - ✓ When there is infection with group A streptococci → antibodies will be formed against streptococci antigens → resulting in the formation of immune complexes → which will get deposited in glomeruli → activating complement system → and leading to mesangial and endothelial cell proliferation + attraction of neutrophils and monocytes.
  - **It is a type-III hypersensitivity reaction which resolves spontaneously.**
  - **Clinical features:**
    - ✓ Peripheral and periorbital edema.
    - ✓ Dark urine (cola-colored).
    - ✓ Hypertension.
  - **Investigations:**
    - ✓ RBC casts in the urine.
    - ✓ Decreased serum complement.
    - ✓ Increased serum ASO levels.
  - **Light microscopy**: glomeruli enlarged and hypercellular (image-2)
  - **Immunofluorescence**: "starry sky" franular appearance (lumpy bumpy) due to IgG, IgM and C3 deposition along GBM and mesangium (image-3)
  - **Electron microscopy**: subepithelial immune complex (IC) humps (image-4)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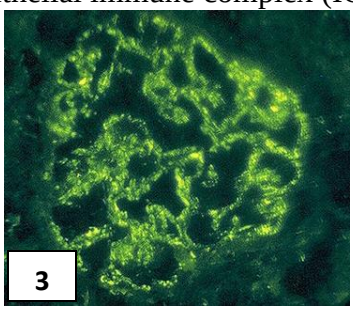
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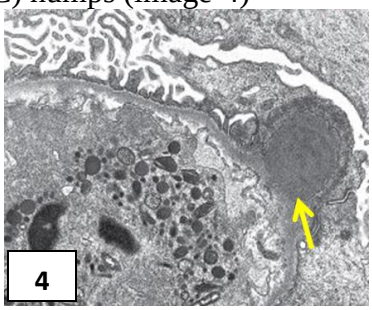
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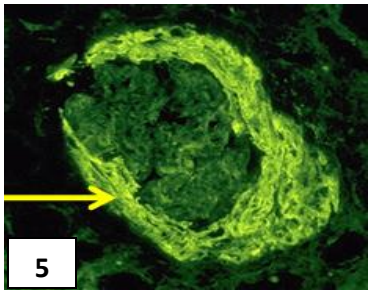
- **Rapidly Progressive (crescentic) Glomerulonephritis (RPGN):**
  - **Definition**: it is a clinical syndrome characterized by rapidly progressive form of nephritic syndrome with acute renal failure and histologically characterized by glomerular crescents.
  - **Crescent formation (image-5) :** severe glomerular injury will result in breakdown of glomerular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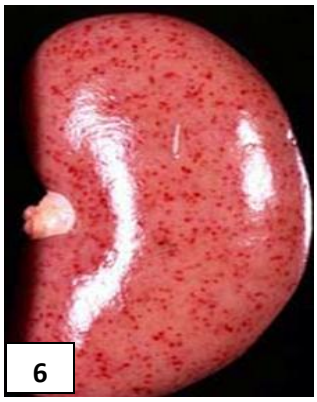
basement membrane → leading to exudation of plasma proteins and fibrin into Bowman's space → this will enhance parietal cell proliferation and the formation of crescents.

- **Grossly**: Kidney is enlarged, pale with petechial hemorrhages (flea bitten kidney: image-6).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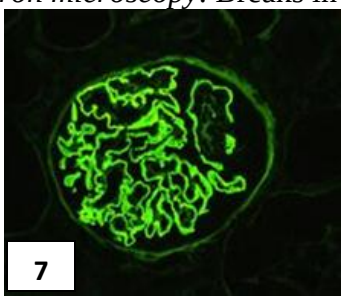
- **This condition is classified to three types:**
  - ✓ Type-I (Anti-GBM Antibody Crescentic Glomerulonephritis: 10%):
    - ❖ Idiopathic and Goodpasture's syndrome (type-II hypersensitivity reaction; antibodies to GBM and alveolar basement membrane resulting in linear immunofluorescence).
    - ❖ *Immunofluorescence*: linear ribbon-like deposits of IgG & C3 on GBM (image-7).
    - ❖ *Electron microscopy*: Breaks in GBM (image-8).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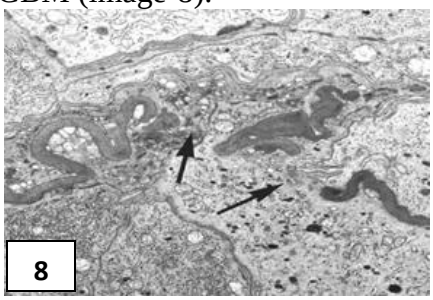
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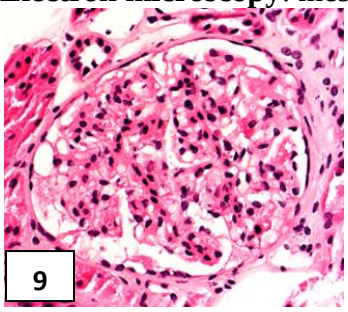
  - ✓ Type-II (Immune Complex Mediated Crescentic Glomerulonephritis: 45%):
    - ❖ Idiopathic, post-infectious, SLE or IgA nephropathy.
    - ❖ *Immunofluorescence*: granular "lumpy bumpy" pattern of IgG and complement along basement membrane and/or mesangium.
    - ❖ *Electron microscopy*: rupture in GBM and discrete deposits.
  - ✓ Type-III (Pauci-Immune Crescentic Glomerulonephritis: 45%):
    - ❖ Idiopathic or vasculitis.
    - ❖ Almost all patient have ANCA (Anti-Neutrophil Cytoplasmic Antibodies).
    - ❖ *Immunofluorescence*: negative for IgG or complement.
    - ❖ *Electron microscopy*: supture in GBM with no deposits.

- **IgA nephropathy (Berger disease):**
  - One of the most common glomerular diseases.
  - **Pathogenesis**: increased IgA synthesis secondary to mucosal infection with decreased IgA clearance → resulting in circulating IgA immune complexes and IgA → which will bind to mesangial cells and activate alternate complement pathway → glomerular injury.
  - **Light microscopy**: mesangial proliferation (image-9).
  - **Immunofluorescence**:IgA-based immune complex deposits in mesangium(image-10)
  - **Electron microscopy**: mesangial immune complex deposits (image-11).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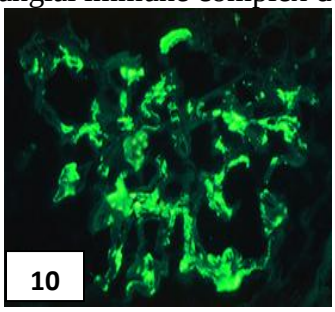
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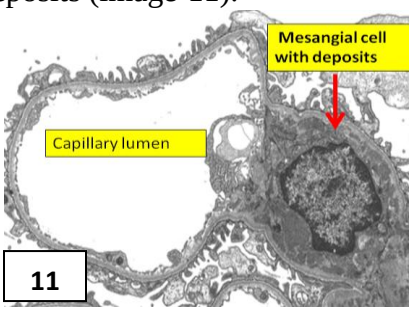

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  - Often presents/flares with URI or acute gastroenteritis. There is episodic hematuria with RBC casts.

- **Membranoproliferative glomerulonephritis was discussed in problem 8.**
- **Alport syndrome:**
  - Mutation in type IV collagen resulting in thinning and splitting of the glomerular basement membrane.
  - Most commonly X-linked.
  - **Characterized by the following:**
    - ✓ Glomerulonephritis.
    - ✓ Deafness.
    - ✓ Eye problems (less common).