Renal Pathology - I
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rēn, rēnēs (Latin) = kidney, nephros, nephroi (Greek) = kidney, nephrology

Outline

• Lectures I – V
  • Glomerular diseases lectures I – III
       • Nephritic syndrome – lecture I - II
       • Nephrotic syndrome, nephrotic + nephritic syndrome – lecture II - III
       • Systemic diseases, vascular diseases – lecture III
  • Tubules and interstitium – lecture IV
  • Cystic diseases and tumors – lecture V

Renal Pathology, lecture I

Goals:

• analyze glomerular diseases associated with
     • nephritic syndrome
     • isolated hematuria
     • rapidly progressive glomerulonephritis

• Robbins Basic Pathology, 10th edition, chapter 14, pp 560-564
• Introduction to glomerular diseases (recorded)
• Urinary tract histology – part II (recorded)
Objectives:
- explain the clinical and laboratory findings associated with postinfectious glomerulonephritis
- describe glomerular pathology in postinfectious glomerulonephritis and how it correlates with pathogenesis and clinical findings
- explain the clinical, laboratory findings and pathology of IgA nephropathy
- explain the clinical, laboratory findings and pathology of hereditary nephritis
- contrast and compare the different types of rapidly progressive glomerulonephritis and the implications for clinical management
- analyze the pathomechanism of anti-glomerular basement membrane glomerulonephritis
- analyze the general pathomechanism of type II rapidly progressive glomerulonephritis and explain how it differs from prototypic glomerular diseases
- analyze the pathomechanism of type III rapidly progressive glomerulonephritis
- compare and contrast rapidly progressive glomerulonephritis type I and type III

New Cases of Kidney Failure by Primary Cause

Glomerular diseases fit into a much bigger category of intrarenal diseases and are actually much less common than diabetes and hypertension. However, their evaluation via biopsy plays a major role in the selection of therapies.

Main clinical syndromes

Nephritic Syndrome
- Proteinuria
- Hematuria

Nephrotic Syndrome
- Proteinuria
- Edema
- Hyperlipidemia
**Nephritic syndrome** = a clinical entity, usually of acute onset:

(i) hematuria (blood in urine) with dysmorphic cells and red blood cell casts in the urine

(ii) some degree of oliguria and azotemia and

(iii) hypertension

**Rapidly progressive renal failure**

**Isolated hematuria**

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To study glomerular diseases caused by immune mechanisms - please check the recorded introduction to glomerular diseases...

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**Nephritic syndrome/isolated hematuria**

**Postinfectious glomerulonephritis**

IgA nephropathy

Hereditary nephritis

Rapidly progressive glomerulonephritis
Acute postinfectious glomerulonephritis (1)

1. Typical clinical presentation:
   children: acute nephritic syndrome (hematuria, edema, hypertension, renal failure)
   adults: acute nephritic syndrome may be less common

2. Epidemiology:
   typically children 6-10 years,
   rarer in adults
   sporadic or epidemic

3. Etiology/pathogenesis:
   - 1-4 weeks after recovery from infection:
     - pharynx group A β-hemolytic streptococcal infection (GABHS, "nephritogenic",
       M protein virulence factor)
     - other infections (certain pneumococcal, staphylococcal, viral)
     - skin (impetigo)
   - glomerulonephritis follows prior infection
   - immune complexes form in the circulation (antigen + IgG antibody)
   - subsequent deposition of circulating immune complexes within glomeruli (because of physico-chemical properties and hemodynamic factors peculiar to the glomerulus) activates complement, which attracts neutrophils, which mediate damage with endocapillary proliferation and structural damage ("swiss cheese") with hematuria (sub-endothelial or proximal zone – see introduction).
   - The antibodies are directed against the infectious agent and have NO specificity for glomerular components
   - immune complexes are also formed in situ leading to formation of big subepithelial deposits "humps" (white arrow) which are unique to postinfectious glomerulonephritis and therefore diagnostically useful
   - it is not clear if immune complexes are formed mostly in the circulation or in situ by binding of antibodies to bacterial antigens "planted" in the glomerular basement membrane

   The classic case of poststreptococcal glomerulonephritis is a prototype of the circulating immune complex glomerulonephritis. However, its exact pathogenesis has not been fully understood.

Pathogenesis of post-infectious glomerulonephritis - review

(explained in the introduction to glomerular diseases [recorded])

1. glomerulonephritis follows prior infection

2. immune complexes form in the circulation (antigen + IgG antibody)

3. subsequent deposition of circulating immune complexes within glomeruli (because of physico-chemical properties and hemodynamic factors peculiar to the glomerulus) activates complement, which attracts neutrophils, which mediate damage with endocapillary proliferation and structural damage ("swiss cheese") with hematuria (sub-endothelial or proximal zone – see introduction).
   - The antibodies are directed against the infectious agent and have NO specificity for glomerular components

4. Immune complexes are also formed in situ leading to formation of big subepithelial deposits “humps” (white arrow) which are unique to postinfectious glomerulonephritis and therefore diagnostically useful

5. It is not clear if immune complexes are formed mostly in the circulation or in situ by binding of antibodies to bacterial antigens “planted” in the glomerular basement membrane.

   The classic case of poststreptococcal glomerulonephritis is a prototype of the circulating immune complex glomerulonephritis. However, its exact pathogenesis has not been fully understood.

Postinfectious glomerulonephritis - Pathology 2

Electron microscopy: "hump"-like deposit (white arrow), diagnostic

Immunofluorescence: glomerulus with immune complex deposits of IgG + Complement (bright green spots)
Acute postinfectious glomerulonephritis (2)

4. Histology/pathology:
   - endocapillary proliferation (hypercellular tuft, capillaries occluded)
   - neutrophilic infiltration
   - immune complex deposits by immunofluorescence & electron microscopy

5. Laboratory tests:
   - tea-color (smoky, coca-cola) urine
   - hematuria, mild proteinuria
   - ASO (anti-streptolysin O, anti-streptococcal antibody) titer ↑↑↑
   - Complement levels ↓↓↓

6. Prognosis:
   - children: total recovery with resolution of pathology in >95%
   - adults: slow progression to chronic glomerulonephritis
   - 15-50% of adults develop end stage kidney disease
   - a small subset of children and adults may develop very severe acute illness with gross hematuria and rapid progressive renal failure (discussed later)

7. Treatment: supportive

Post infectious glomerulonephritis

Typical case

Clinical history:
A 7 y o boy abruptly developed malaise (fatigue), nausea, oliguria and Coca cola-colored (smoky) urine

PMH: 2 weeks prior sore throat

PE: mild edema, mild to moderate hypertension

UA: dysmorphic red blood cells, mild proteinuria (<1 gm/day)

Labs:
- ASO (anti-streptolysin O, anti-streptococcal antibody) titer ↑↑
- Complement levels ↓↓↓

Final clinical diagnosis: post-streptococcal glomerulonephritis

An 8-year-old boy presents with headaches, dizziness, and malaise. He was seen for a severe sore throat 2 weeks ago. Physical examination reveals facial edema. The blood pressure is 180/110 mm Hg. A 24-hour urine collection demonstrates oliguria, and urinalysis shows hematuria. What test(s) may be helpful in the differential diagnosis in this child?

a. ASO (anti-streptolysin O antibody)
b. Complement level
c. both
d. neither
Postinfectious glomerulonephritis is a prototypic disease of proliferative glomerulonephritis

Postinfectious glomerulonephritis = acute (1 shot) immune complex disease, exogenous antigen

SLE – systemic lupus erythematosus = chronic immune complex disease, endogenous antigens

Nephritic syndrome/isolated hematuria

- Postinfectious glomerulonephritis
- IgA nephropathy
- Hereditary nephritis
- Rapidly progressive glomerulonephritis

Review

IgG:
- main immunoglobulin (75%) serum & extravascular spaces

IgA:
- second most common serum immunoglobulin
- major immunoglobulin in secretional/mucosal immunity
- neutralizes microbes in the lumens of the respiratory and gastrointestinal tract
- IgA poor activator of the complement system
- complement involvement is via the alternative complement pathway

In IgA nephropathy immune complexes contain IgA + C3 complement

IgA exists in two isotypes, IgA1 and IgA2. IgA1 predominates in serum (~80%), IgA2 % higher in secretions
IgA nephropathy (aka Berger disease) (1)

1. Typical clinical presentation:
   - recurrent gross & microscopic hematuria
   - episodes of gross hematuria within 1-2 days of a nonspecific upper respiratory tract infection
   - “painless hematuria following infection” = suggestive of IgA nephropathy
   - hematuria for days, recurrence every few months

2. Epidemiology:
   - IgA nephropathy = most common glomerular disease worldwide
   - children and young adults

3. Etiology/pathogenesis:
   - abnormally glycosylated IgA1 (galactose-deficient IgA1) is thought to play a central role
   - mucosal infection leads to production of IgA & formation of IgA containing immune complexes which deposit in the mesangium
   - activation of the complement via alternative pathway (C3 in the absence of C1q)
   - abnormalities in clearance of IgA (due to decreased hepatobiliary clearance, secondary IgA nephropathy)
   - genetic or acquired abnormality of immune regulation (celiac disease)

The multihit pathogenesis model of IgA nephropathy

Hit 1 = increased production of galactose-deficient IgA1
   (after respiratory/gastrointestinal exposure to viruses, bacteria, food products)

Hit 2 = formation of autoantibodies that recognize galactose-deficient IgA1

Hit 3 = subsequent formation of pathogenic immune complexes

Hit 4 = deposition of immune complexes in the mesangium, activation of mesangial cells, induction of glomerular injury, complement activation via alternative pathway

IgA nephropathy - genetic contributions

- geographic and racial differences in IgA nephropathy prevalence have long been recognized
- until recently it was postulated that these differences were due to differences in disease diagnosis (e.g., due to diverse local biopsy practices) rather than biology
- it is now clear that a substantial portion of disease risk is conferred genetically
- a series of genomewide association studies have identified at least 7 susceptibility loci for IgA nephropathy
- the genetic loci identified thus far comprise genes associated with innate, adaptive immunity & the complement system
- the complement locus involves genes encoding proteins which regulate the alternative complement pathway

ECM, extracellular matrix

Kiryluk K et al, Kidney International 2015
IgA nephropathy (2)

4. Histology/pathology:
- mesangial proliferation of variable intensity
- IgA-containing immune complexes in the mesangium = diagnostic
- electron dense deposits by electron microscopy

IgA nephropathy (3)

5. Laboratory tests:
- hematuria, mild proteinuria
- complement levels are replenished by the liver and usually not decreased

6. Prognosis: variable, dependent on glomerular pathology
- many relatively indolent/prolonged, ultimately renal failure
- rare patients with clinical course of rapidly progressive glomerulonephritis (discussed later)
- systemic IgA vasculitis in children – Henoch-Schönlein purpura (HSP) – excellent prognosis

7. Treatment:
- supportive
- other?

IgA nephropathy – typical case

- 32 yo male initially presented 4 months ago with gross hematuria after a respiratory tract infection
- Hematuria lasted for several days and then subsided
- Now he is presenting with gross hematuria again...
- UA: hematuria, trace protein
- Scr (serum creatinine): 1.5 MG/DL [n=0.7-1.5]
- Clinical diagnosis: recurrent hematuria
- ASO – N, Complement – N
- How this case differs from a case of postinfectious glomerulonephritis?
IgA nephropathy with extra-renal symptoms (systemic IgA) = Henoch-Schönlein purpura (HSP):

- Chapter 10, page 393, Fig. 10.22
- Prior lecture: small vessel immune complex vasculitis
- mainly children, 3-8 yo
- kidney, skin, gastrointestinal, joints
- hematuria, purpuric skin lesions, abdominal pain & gastrointestinal bleeding, arthralgia
- small vessel IgA vasculitis in affected sites

Nephritic syndrome/isolated hematuria

- Postinfectious glomerulonephritis
- IgA nephropathy
- Hereditary nephritis
- Rapidly progressive glomerulonephritis

Hereditary nephritis

- a group of hereditary glomerular diseases
- mutations leading to error in synthesis of collagen type IV, which is the major component of the glomerular basement membrane, cochlea, lens
- Alport syndrome - best studied
- Inheritance most commonly X-linked
- triad:
  (i) nephritis, isolated hematuria without infection
  (ii) nerve deafness
  (iii) various eye disorders, early cataracts
Hereditary nephritis (1)

1. Typical clinical presentation: triad
   - isolated hematuria
   - hearing and
   - ocular abnormalities

2. Epidemiology:
   - age 5-20 years at presentation
   - 20-50 years with overt renal failure

3. Etiology/pathogenesis:
   - X-linked inheritance most commonly
   - (+) family history
   Male patients – full spectrum
   Females – carriers, rare with disease (X-chromosome inactivation)

Hereditary nephritis - pathology:
- paraffin sections: normal, non-diagnostic
- immunofluorescence: negative
- electron microscopy diagnostic: lamina densa splitting & lamination, "basket weave"

4. Histology/pathology:
   - normal in paraffin sections
   - NO immune complexes
   - electron microscopy diagnostic

5. Laboratory tests:
   - hematuria
   - genetic testing

6. Prognosis: overt renal failure between 20-50 years of age

7. Treatment: supportive, transplantation, counseling, family testing
   Molecular genetic testing of the type IV collagen gene is available on a clinical basis (detection of mutation >60%). Prenatal testing is available for X-linked Alport syndrome.
Hereditary nephritis – typical case:

A 20 year old male was found to have hematuria via pre-employment testing
- scr (serum creatinine): 2.5 MG/DL [n=0.7-1.5]

Family history:
- Several members of his family, mostly males, with chronic renal failure by age 50 years
- Affected individuals with hearing problems, various eye disorders, including lens dislocation.

### Nephritic syndrome/hematuria

<table>
<thead>
<tr>
<th>Disease</th>
<th>Presentation</th>
<th>Epidemiology</th>
<th>Etiology/Pathogenesis</th>
<th>Pathology</th>
<th>C-Complements</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-infectious</td>
<td>Acute nephritic syndrome</td>
<td>Children</td>
<td>Infection</td>
<td>Endocapillary proliferation, PMNs “humps”</td>
<td>ASO↑ C↓</td>
<td>Good</td>
</tr>
<tr>
<td>IgA recurrent hematuria</td>
<td>Young adults</td>
<td>IgA</td>
<td>Mesangial proliferation (IgA immune stain diagnostic)</td>
<td>N</td>
<td>Slow progression</td>
<td></td>
</tr>
<tr>
<td>Hereditary isolated hematuria</td>
<td>Children</td>
<td>Mutation</td>
<td>Lamina densa splitting (electron microscopy diagnostic)</td>
<td>N</td>
<td>Slow progression</td>
<td></td>
</tr>
</tbody>
</table>

A 32-year-old man complains of recurrent hematuria since his youth. The hematuria typically occurs following upper respiratory tract infections. Vital signs are normal. Urinalysis shows hematuria and mild proteinuria. Laboratory studies disclose normal levels of BUN and creatinine. Which of the following is the most likely diagnosis?

- (A) Alport syndrome
- (B) IgA nephropathy
- (C) Hereditary nephritis
- (D) Pneumonia
- (E) Postinfectious glomerulonephritis
A 20 year old male was found to have hematuria via pre-employment testing. Also his scr (serum creatinine) was elevated at 2.5 MG/DL [n=0.7-1.5]. He has been otherwise healthy. Several members of his family, mostly males, were diagnosed with chronic renal failure by age 50 years. Which best applies to this patient:

a. recommend repeated testing at age of 50
b. eye testing may be needed, no hearing testing needed
c. only hearing testing needed
d. he has IgA nephropathy
e. eye and hearing testing may be needed

Nephritic syndrome/isolated hematuria

- Postinfectious glomerulonephritis
- IgA nephropathy
- Hereditary nephritis
- Rapidly progressive glomerulonephritis

Rapidly progressive glomerulonephritis (RPGN)

- clinical syndrome:
  - rapidly progressive loss of renal function
  - nephritic syndrome, gross hematuria
  - histology = crescents
  - DIVERSE PATHOGENESIS
Glomerular crescent = "glomerular stopper" - stops bleeding but compresses tuft, ↓ filtration → rapidly progressing renal failure

Crescents form in response to hematuria
- hematuria is a consequence of severe glomerular basement membrane injury (necrosis, breaks)
- leakage of blood (fibrin) into the Bowman space leads to proliferation of parietal epithelial cells
- crescent: blood, fibrin, macrophages, parietal epithelial cells

Rapidly progressive glomerulonephritis (RPGN)
pathogenesis variable:
- anti-glomerular basement membrane antibody (RPGN type I)
- a subset of circulating immune complex glomerulonephritis (RPGN type II)
- "pauci-immune"/ANCA associated (RPGN type III)

Rapidly progressive glomerulonephritis type I:
- anti-glomerular basement membrane antibody disease

1. Typical presentation:
   - gross hematuria
   - drop in urinary output (acute renal failure)
   - hemoptysis
2. Epidemiology:
   - young MEN
3. Etiology/pathogenesis:
   - anti-glomerular basement membrane antibodies
   - exposure: viruses, smoking, solvents (paints, dyes), drugs
   - genetic predisposition to autoimmunity
crescents + linear stain for IgG (antibody)
Antibody is directed against the glomerular components
Antibody deposited along the entire length of the glomerular basement membrane which is rapidly destroyed, multiple areas of necrosis
"sieve effect" - many holes, GROSS hematuria
[explained in the introduction to glomerular diseases (recorded)]

Rapidly progressive glomerulonephritis type I: pathology
- anti-glomerular basement membrane antibody disease

Rapidly progressive glomerulonephritis type I: continued
- anti-glomerular basement membrane antibody disease

4. pathology:
   • crescents
   • linear stain for IgG by immunofluorescence, not seen by electron microscopy
   • in glomeruli/pulmonary alveoli

5. Laboratory tests:
   • anti-glomerular basement membrane antibodies in serum levels may be low in rapid binding on the kidney

6. Prognosis:
   • renal failure
   • pulmonary failure

7. Treatment:
   • plasmapheresis, (removal of pathogenic antibodies from the circulation)

Goodpasture Disease/Syndrome: anti glomerular basement membrane antibody cross-reactivity with pulmonary alveolar basement membrane

linear IgG deposits along glomerular and alveolar basement membranes
Antigen: non-collagenous protein (NC1); normally encrypted and does not elicit antibody response
Clinically pulmonary-renal syndrome:
rapidly progressive glomerulonephritis with hematuria + pulmonary hemorrhage (hemoptysis)
Rapidly progressive glomerulonephritis type I: typical presentation

Young male
- hemoptysis
- blood in urine, gross
- drop in urinary output

History:
smoker
working in a car garage during summer
other industrial exposure

UA: abundant red blood cells with casts
sCr elevated to 5.0 MG/DL [n=0.7-1.5]
Chest X-ray bilateral pulmonary opacities...

Rapidly progressive glomerulonephritis type II:
- severe immune complex

1. Typical clinical presentation:
   - gross hematuria
   - drop in urinary output (acute renal failure)

2. Epidemiology:
   - rare -1% of postinfectious,
     small subset of IgA,
     systemic lupus erythematosus (SLE)
   - older children, young adults (10-40 years old)

3. Etiology/pathogenesis:
   - severe immune complex formation with necrosis and
     breaks in glomerular basement membrane

Thus, except for the severity and the presence crescents, the other diagnostic pathology remains the same as in the corresponding forms of glomerulonephritis not complicated by crescents (the prototype):
- granular deposits containing immune complexes of IgG + Complement
- in postinfectious glomerulonephritis and lupus nephritis
- IgA + Complement immune complexes in IgA nephropathy
Rapidly progressive glomerulonephritis type II
- severe immune complex

4. Pathology:
   crescents
   immune complexes (IgG+C3; IgA+C3)
   electron dense deposits by electron microscopy

5. Laboratory tests: depending on etiology
   postinfectious, IgA nephropathy,
   diffuse proliferative lupus

6. Prognosis:
   chronic renal failure

7. Treatment:
   immunosuppression

Rapidly progressive glomerulonephritis type III:
- "pauci-immune"/ANCA-associated

1. Typical clinical presentation:
   • drop in urinary output (acute renal failure)
   • gross hematuria
   • frequent (75%) extrarenal manifestations: hemoptysis*, shortness of breath

2. Epidemiology:
   • older patients

3. Etiology/pathogenesis:
   • antineutrophil cytoplasmic autoantibodies (ANCA)

   • heterogeneous group of autoantibodies
   • formation induced by drug, cross reactive microbial antigen, other…
   • react with neutrophil antigens causing premature degranulation/activation; release of lytic enzymes, leading to vascular damage
   • present in serum
   • do not form circulating immune complexes
   • ANCA = antibody-mediated disease (type II hypersensitivity)
   • direct cause of pauci-immune crescentic glomerulonephritis/systemic small vessel vasculitis
   • highly sensitive diagnostic marker of pauci-immune glomerulonephritis/systemic vasculitis

ANCA - review
(chapter 5, p.130, tables 5-4, chapter 10, page 384; lecture on vasculitis)
Glomerulus = "bundle of small vessels"

• heterogeneous group of autoantibodies
• formation induced by drug, cross reactive microbial antigen, other…
• react with neutrophil antigens causing premature degranulation/activation; release of lytic enzymes, leading to vascular damage
• present in serum
• do not form circulating immune complexes
• ANCA = antibody-mediated disease (type II hypersensitivity)
• direct cause of pauci-immune crescentic glomerulonephritis/systemic small vessel vasculitis
• highly sensitive diagnostic marker of pauci-immune glomerulonephritis/systemic vasculitis
Kidney:
- crescents (in response to glomerular capillaries vasculitis)
- immunofluorescence: ~ negative ("pauci immune")
- electron microscopy: ~ negative ("pauci immune")

Rapidly progressive glomerulonephritis type III
- "pauci-immune"/ANCA-associated, continued….

Can be limited to kidneys but 75% of patients have manifestations of systemic small vessel vasculitis at time of initial presentation (see also lecture on vasculitis):

- Granulomatosis with polyangiitis [GPA]
- Eosinophilic granulomatosis with polyangiitis [EGPA]
- Microscopic polyangiitis [MPA]

With systemic involvement

Granulomatosis with polyangiitis [GPA]
(aka pulmonary angiitis and granulomatosis, Wegener granulomatosis)
Vasculitis with necrosis and granuloma-like pathology with "geographic necrosis" c-ANCA aka PR3-ANCA, Robbins p. 388; lecture on vasculitis

Ear/nose/throat
Lung
Kidney

Clinical: nasopharynx/sinusitis involvement is NOT seen in Goodpasture disease
Rapidly progressive glomerulonephritis type III
- "pauci-immune"/ANCA-associated

4. Pathology:
   • Crescents
   • NO immune complex deposits
   • NO antiglomerular basement membrane autoantibodies
   • Look for extrarenal manifestations…

5. Laboratory tests:
   • ANCA: antineutrophil cytoplasmic autoantibodies

6. Prognosis:
   • renal failure
   • pulmonary

7. Treatment:
   • immunosuppression

Rapidly progressive glomerulonephritis type III
- typical case:

• A 75 yo female developed malaise, cough with blood tinged sputum
• PMH: recurrent “sinusitis”
• PE: palpable purpura
• UA: RBCs, protein <1GM
• serum creatinine 3.5MG/DL [n=0.7-1.5]
• Lungs: bilateral opacities
• Clinical diagnosis? – pulmonary-renal syndrome
• What test would be useful?

Rapidly progressive glomerulonephritis - RPGN- summary

RPGN = clinical entity: nephritic syndrome + renal failure
pathogenesis: diverse and treatment dependent on pathogenesis
kidney biopsy needed for establishing pathogenesis & treatment
Pathology: all with crescents but differences in immunofluorescence/electron microscopy

<table>
<thead>
<tr>
<th>RPGN type</th>
<th>Linear antibody</th>
<th>Immunofluorescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Autoantibody against collagen in glomerular and alveolar basement membrane</td>
<td>Goodpasture syndrome/disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hematuria + hemoptysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Classically young adult male</td>
</tr>
<tr>
<td>Type II</td>
<td>Gravelly immune complex deposition</td>
<td>Post-streptococcal in rare patients</td>
</tr>
<tr>
<td></td>
<td>IgG, IgA, C3, C4</td>
<td>IgG in new patients, severe lupus nephritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Young adults/elder children</td>
</tr>
<tr>
<td>Type III</td>
<td>Linear &quot;pauci-immune&quot;</td>
<td>GPA- granulomatosis with polyangiitis</td>
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<tr>
<td></td>
<td>ANCA/PR3-ANCA, p-ANCA/MPO-ANCA</td>
<td>GPA- granulomatosis with polyangiitis</td>
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<tr>
<td></td>
<td></td>
<td>Microscopic polyangiitis</td>
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<tr>
<td></td>
<td></td>
<td>Classically older patients</td>
</tr>
</tbody>
</table>
A kidney biopsy is needed to establish pathogenesis and hence treatment.

Crescentic glomerulonephritis type versus age at diagnosis

<table>
<thead>
<tr>
<th>Type</th>
<th>10–19</th>
<th>20–39</th>
<th>40–64</th>
<th>&gt;65</th>
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<tbody>
<tr>
<td>I - anti-glomerular basement membrane</td>
<td>12%</td>
<td>15%</td>
<td>24%</td>
<td>1%</td>
</tr>
<tr>
<td>II - circulating immune complex</td>
<td>64%</td>
<td>52%</td>
<td>30%</td>
<td>8%</td>
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<tr>
<td>III - ANCA</td>
<td>44%</td>
<td>35%</td>
<td>28%</td>
<td>69%</td>
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Lecture I - summary

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Disease</th>
<th>Pathogenesis</th>
<th>Lecture</th>
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<tbody>
<tr>
<td>Acute nephritic syndrome</td>
<td>Post-infectious IgA, IgG, hereditary</td>
<td>IgG immune complex circulating</td>
<td>I</td>
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<tr>
<td>Severe nephritic syndrome aka rapidly</td>
<td>Progressive glomerulonephritis Type I</td>
<td>Anti-glomerular basement membrane antibodies</td>
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<tr>
<td></td>
<td>Type II</td>
<td></td>
<td>Anti-glomerular basement membrane antibodies</td>
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<tr>
<td></td>
<td>Type III</td>
<td></td>
<td>Anti-glomerular basement membrane antibodies</td>
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<tr>
<td>Nephrotic</td>
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<td>Anti-glomerular basement membrane antibodies</td>
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<tr>
<td>Nephrotic + hematuria</td>
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<td>Anti-glomerular basement membrane antibodies</td>
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<td>Systemic diseases</td>
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<td>Anti-glomerular basement membrane antibodies</td>
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</tr>
<tr>
<td>Blood vessels</td>
<td></td>
<td>Anti-glomerular basement membrane antibodies</td>
<td></td>
</tr>
</tbody>
</table>
A 35-year-old man with a history of smoking presents with hematuria and bloody sputum. Over the next 2 days, he develops oliguria and renal failure, after which he is placed on dialysis. A renal biopsy is stained with antihuman IgG, and the results are shown. Which of the following best described the pattern of direct immunofluorescence observed on this photomicrograph?

- (A) Discontinuous and mesangial
- (B) Finely granular along the perimesangial reflections
- (C) Linear along the glomerular basement membrane
- (D) Mesangial
- (E) Peripheral granular humps

A 68-year-old man complains of nasal obstruction, bloody nose, cough and bloody sputum. A chest x-ray displays cavitated lesions and multiple nodules within both lung fields. Urinalysis reveals 3+ hematuria and red blood cells casts. Laboratory studies show anemia and elevated serum levels of C-ANCA (antineutrophil cytoplasmic antibody). Peripheral eosinophils are not increased. A renal biopsy exhibits focal glomerular necrosis with crescents. What is the appropriate diagnosis?

- (A) eosinophilic granulomatosis with polyangiitis
- (B) Goodpasture syndrome
- (C) Hypersensitivity vasculitis
- (D) postinfectious glomerulonephritis
- (E) granulomatosis with polyangiitis

A 30-year-old man with a history of smoking suddenly develops oliguria, hematuria and hemoptysis. Serologic studies reveal antibodies to the glomerular basement membrane. Which of the following pathologic changes is visible by light microscopy in this biopsy specimen?

- (A) Crescents in the urinary space
- (B) Leukocytic infiltrates in the glomeruli
- (C) Mesangial cell proliferation
- (D) Thickening of the glomerular basement membrane
- (E) Thrombi in glomerular capillaries
A 16-year-old boy comes to the physician with a 1-year history of intermittent, painless hematuria without dysuria on increased frequency of micturition. He says he has also had several respiratory infections and adds that the hematuria increased within several days of the infections. Which of the following is most likely?

- (A) Increased antistreptolysin O titer
- (B) mutation in basement membrane protein gene
- (C) IgA mesangial deposits
- (D) Proteinuria exceeding 3.5 gm/24 h
- (E) subepithelial humps deposits

VOCABULARY

Glomerular diseases usually have the "glomerulo" prefix – see postinfectious glomerulonephritis etc.

Glomerulonephritis is used preferentially in reference to glomerular diseases with inflammatory/proliferative response.

Glomerular pathologies without inflammatory response may be referred to as "nephropathy" or "glomerulopathy", see membranous nephropathy (glomerulopathy).

Nephrosis is meant to indicate a non-inflammatory nephropathy that is associated with nephrotic syndrome.

"nephritis" can also be attached to connect to with other kidney diseases, such as "pyelonephritis"