NOTES
NEPHRITIC SYNDROME

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Diseases caused by inflammation, damage to glomeruli of kidney; become more permeable, allow red blood cells (RBCs) into urine → hematuria

CAUSES

- *Children/adolescents:* IgA nephropathy, post-streptococcal glomerulonephritis, hemolytic uremic syndrome
- *Adults:* systemic lupus erythematosus, Goodpasture's syndrome, rapidly progressive glomerulonephritis

COMPLICATIONS

- Acute kidney failure

SIGNS & SYMPTOMS

- Damaged, permeable glomeruli → hematuria, proteinuria
- Decreased glomerular filtration rate → edema, hypertension
- Less waste product excreted → uremia

DIAGNOSIS

LAB RESULTS

- Protein/blood, RBC casts in urine
- Decreased glomerular filtration

Kidney biopsy

- Changes under light/electron microscope, immunofluorescence

TREATMENT

MEDICATIONS

- Edema
  - Diuretics (furosemide), medical nutrition therapy
- Blood pressure control
  - Angiotensin converting enzyme inhibitors (ACE) inhibitors

OTHER INTERVENTIONS

- Reduce salt, potassium intake

ACUTE PROLIFERATIVE GLOMERULONEPHRITIS

osms.it/proliferative-glomerulonephritis

PATHOLOGY & CAUSES

- Inflammation of glomeruli, complication of bacterial infection
- AKA poststreptococcal glomerulonephritis
  - Commonly arises several weeks after group A beta-hemolytic streptococcus infection
- Type III hypersensitivity reaction
  - IgG/IgM antibodies bind to bacterial antigens, form immune complexes → complexes travel through bloodstream to glomerulus, deposit in glomerular basement membrane
- Immune complex/complement deposits trigger immune reactions
  - Activate complement system → enzyme cascade → formation of membrane attack complex → damage to podocytes, mesangial cells
  - Recruit inflammatory cells → proteases, oxidants release → basement membrane damage → hematuria, proteinuria → nephritic syndrome

CAUSES

- Group A beta-hemolytic streptococcus infection

RISK FACTORS

- Most commonly in children (who are biologically male)
  - Six weeks after impetigo, 1–2 weeks after throat infection

COMPLICATIONS

- Rapidly progressive glomerulonephritis, renal failure

SIGNS & SYMPTOMS

- *Nephritic syndrome:* hematuria, oliguria, edema, hypertension
- Fever, headache, malaise, anorexia, nausea

DIAGNOSIS

LAB RESULTS

- Protein/blood in urine
- Antibodies against group A streptococcus (e.g. anti-DNase B antibodies, anti-Streptolysin O antibody)
- Decreased complement levels

Renal biopsy

- Light microscopy
  - Mesangial proliferation → hypercellular glomerulus
- Electron microscopy
  - Subepithelial deposits of immune complexes, "humps"
- Immunofluorescence
  - "Starry sky," granular deposition of IgG, complement in basement membrane, mesangium

TREATMENT

- Usually supportive

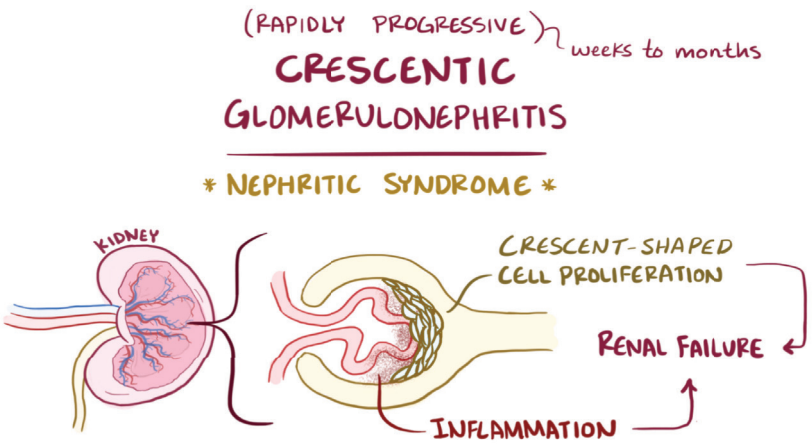

Figure 117.1 The effect of crescentic glomerulonephritis on the nephron.

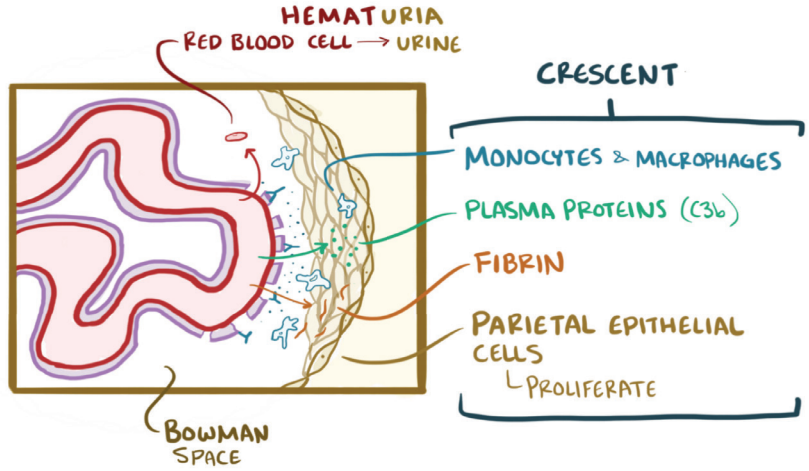

Figure 117.2 The constituent parts of the crescent seen in crescentic glomerulonephritis.

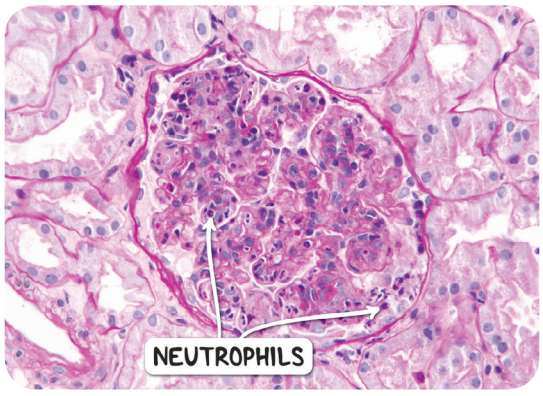

Figure 117.3 Histological appearance of the glomerulus in post-infective glomerulonephritis. The glomerulus is expanded and compressed due to infiltration of neutrophils and other inflammatory cells.

GOODPASTURE'S SYNDROME

osms.it/goodpasture-syndrome

PATHOLOGY & CAUSES

- AKA anti-GBM antibody disease; damage of basement membrane in lungs, kidneys; mostly composed of Type IV collagen
- Damaged by Type II hypersensitivity reaction
  - IgG antibodies (rarely IgM/IgA) bind to alpha 3 folded chain → activate complement system → damage collagen fibers of basement membrane

RISK FACTORS

- Bimodal distribution with peak incidence age 20–30 (biologically male), 60–70 (biologically female)
- *Genetic:* predisposition for genes that code for HLA-DR15 (immune molecule; identifies, binds to foreign molecules)
- *Environmental:* infection, smoking, oxidative stress, hydrocarbon-based solvents

COMPLICATIONS

- Chronic renal failure; require dialysis/kidney transplant; hemoptysis

SIGNS & SYMPTOMS

- Pulmonary manifestations usually occur before renal ones; minority (20–40%) with only renal manifestations
  - Damaged lung alveoli → cough, hemoptysis, dyspnea
  - Kidney filtration problems (e.g. hematuria, proteinuria) → nephritic syndrome

DIAGNOSIS

LAB RESULTS

Renal biopsy

- Light microscopy
  - Crescentic glomerulonephritis
- Electron microscopy
  - Diffuse thickening of glomerular basement membrane
- Immunofluorescence
  - Linear deposition along basement membrane

TREATMENT

MEDICATIONS

- Corticosteroids, cyclophosphamide, plasmapheresis to filter plasma/fluid of blood (reduces risk of chronic renal failure)

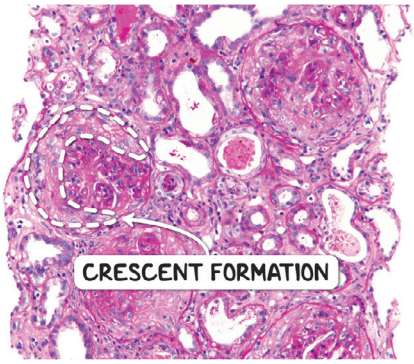

Figure 117.4 Histological appearance of the kidney in a case of crescentic glomerulonephritis caused by Goodpasture's syndrome.glomerulonephritis on the nephron.

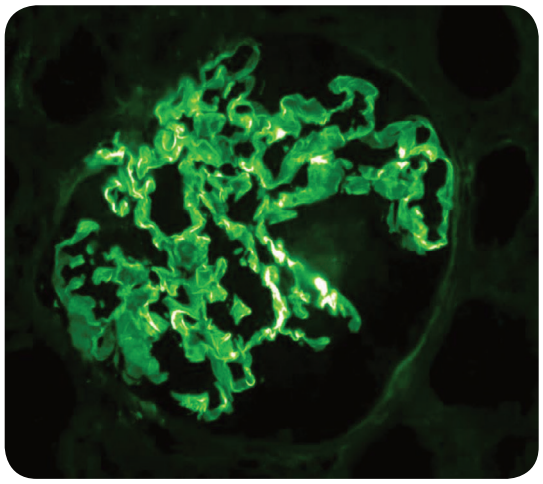

Figure 117.5 Immunofluorescence with positive signal for antibodies to IgG. In addition the IgG deposition is linear. These features are consistent with Goodpasture's syndrome.

HEMOLYTIC-UREMIC SYNDROME

osms.it/hemolytic-uremic-syndrome

PATHOLOGY & CAUSES

- Small blood clots in tiny blood vessels, mostly in kidneys → RBCs break down, kidney function decreases → urea levels in blood increase
- Triggered by bloody diarrhea
  - Diarrhea-positive/D+ hemolytic uremic syndrome (HUS/typical HUS)

Atypical hemolytic uremic syndrome

- D-hemolytic uremic syndrome
  - No preceding diarrhea
- Damage to endothelial cell lining of glomerular capillaries from infections not related to diarrhea, medication, autoimmune causes
- Infants, children
  - *Streptococcus pneumoniae* presents as pneumonia/meningitis
- Familial forms
  - Genetically increased tendency for endothelial cell damage

CAUSES

- *Escherichia coli* (*E. coli*) from contaminated food/drink
  - Enterohemorrhagic E. coli (EHEC, serotype O157:H7); may be caused by other strains
  - *E. coli* attaches to intestinal wall → secretes Shiga-like toxin → absorbed by intestinal blood vessels → attaches to immune cells → toxins from white blood cells (WBCs) bind to endothelial cells of glomerular capillaries → inhibition of protein synthesis → apoptosis → many tiny blood clots form in kidneys

RISK FACTORS

- Children < five years old, people 75+ years old, genetic predisposition to endothelial cell damage

SIGNS & SYMPTOMS

- Bloody diarrhea
- Weakness, fatigue, lethargy, jaundice due to red blood cell destruction
- Fever, blood clots: affect brain blood supply → visual disturbances, altered mental status, seizures, stroke → death

DIAGNOSIS

LAB RESULTS

- Requires thrombocytopenia, microangiopathic hemolytic anemia (MAHA), acute renal failure
- Proteinuria, hematuria
- Schistocytes/helmet cells
- D+ hemolytic uremic syndrome
  - Shiga toxin (ELISA), gene encoding Shiga toxin (PCR)
- Differential diagnosis
  - *Thrombotic thrombocytopenic purpura (TTP) hemolytic uremic syndrome:* measure ADAMTS13 activity in plasma
  - *Disseminated intravascular coagulation (DIC):* DIC panel (e.g. pTT, INR, d-dimer, fibrinogen)

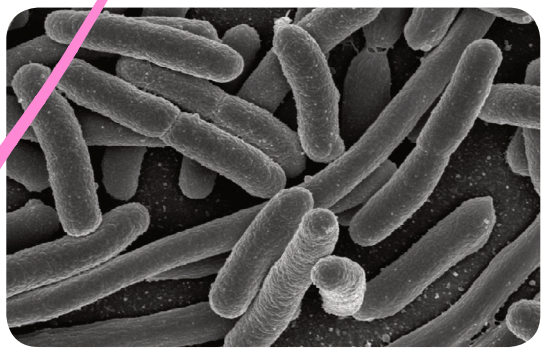

Figure 117.6 90% of hemolytic-uremic syndrome cases are a result of a prior infection with Shiga toxin producing *E. coli*.

TREATMENT

MEDICATIONS

Typical, D+ hemolytic uremic syndrome

- Shiga-like toxin clears in days to weeks, antibiotics not recommended as dead bacteria potentially release more toxins

Atypical hemolytic uremic syndrome

- Identify underlying cause

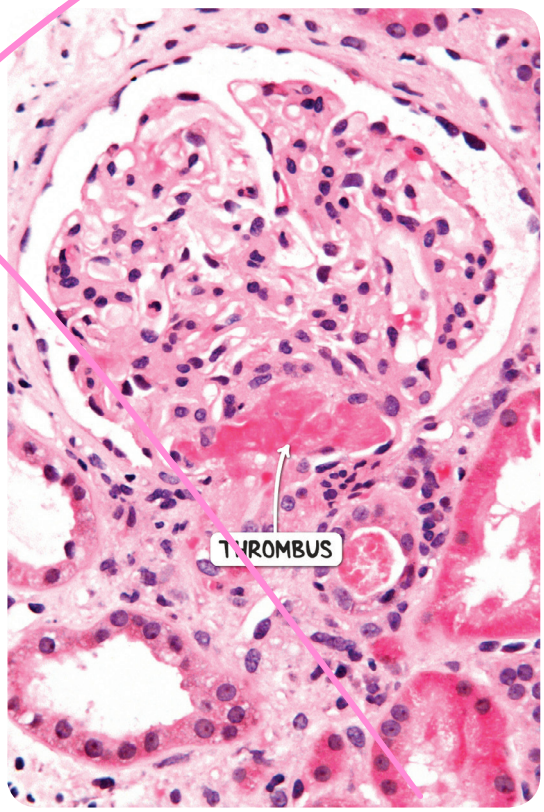

Figure 117.7 Histological appearance of acute thrombotic microangiopathy which is the pathological mechanism of renal failure in hemolytic uremic syndrome. Endothelial damage caused thrombus formation in small capillaries.

IgA NEPHROPATHY

osms.it/IgA-nephropathy

PATHOLOGY & CAUSES

- AKA Berger's disease; abnormal IgA forms, deposits in kidneys → kidney damage
- Abnormal post-translational modification of IgA → development of IgA immune complexes preferentially deposited in mesangium → alternative complement pathway activated → cytokines released → macrophages migrate to kidney → glomerular injury → RBCs leak into urine
- Associated with gastrointestinal (GI)/respiratory tract infections

RISK FACTORS

- Most common nephropathy worldwide; usually presents in childhood
- Highest prevalence in people of East Asian/European ancestry
- Family history of chronic nephritis, alcohol consumption, recurrent infections

COMPLICATIONS

- Nephrotic syndrome, chronic kidney disease

SIGNS & SYMPTOMS

- Episodic hematuria
  - Sometimes accompanying upper respiratory tract infections
- Asymptomatic microscopic hematuria
  - With subnephrotic proteinuria
- Classic nephrotic syndrome/kidney injury (minority)

DIAGNOSIS

LAB RESULTS

- RBCs, RBC casts

Renal biopsy

- Light microscopy
  - Mesangial proliferation, immune complexes deposited in mesangium
- Electron microscopy
  - Immune complexes deposited in mesangium
- Immunofluorescence
  - Mesangial IgA deposits, +/- IgA, +/- IgM

TREATMENT

MEDICATIONS

- Corticosteroids
  - Prevent immune system making defective IgA1, anti-glycan IgG

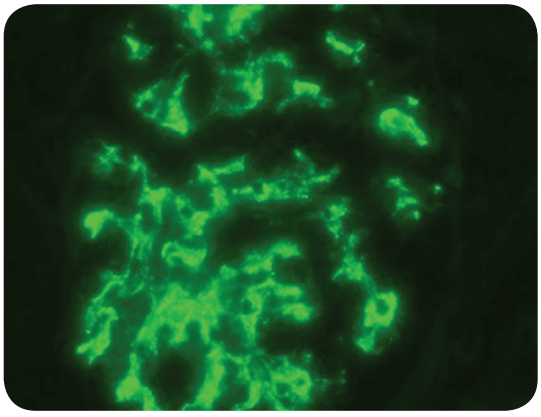

Figure 117.8 Immunofluorescence with positive signal for antibodies to IgA immunoglobulin. The pattern of deposition in the glomerulus is granular.

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

osms.it/progressive-glomerulo

PATHOLOGY & CAUSES

- Inflammation of kidney's glomeruli → crescent-shaped proliferation of cells in Bowman's capsule → renal failure within weeks/months
- Inflammation damages glomerular basement membrane → inflammatory mediators, complement proteins, fibrin, monocytes macrophages pass into Bowman's space → expansion of parietal layer of cells into thick, crescent-moon shape → may undergo sclerosis/scarring

TYPES

Primary

- Idiopathic

Secondary

- *Type I:* anti-GBM antibodies
  - Goodpasture syndrome
- *Type II:* immune complexes
  - Poststreptococcal glomerulonephritis, systemic lupus erythematosus, IgA nephropathy, Henoch-Schonlein purpura
- *Type III:* anti-neutrophilic cytoplasmic antibodies (ANCA)
  - *Cytoplasmic ANCA (C-ANCA):* Wegener's granulomatosis
  - *Perinuclear ANCA (P-ANCA):* microscopic polyangiitis, Churg-Strauss syndrome

COMPLICATIONS

- *If untreated:* rapid progression to acute renal failure

SIGNS & SYMPTOMS

- Nephritic syndrome
  - Hematuria, oliguria, edema, hypertension

DIAGNOSIS

LAB RESULTS

Kidney biopsy

- *Light microscopy:* crescent-shaped glomeruli

Immunofluorescence

- *Type I:* linear, antibodies bind to collagen of glomerular basement membrane
- *Type II:* granular, immune complex deposition in subendothelium
- *Type III:* negative (pauci-immune)
  - Type III associated with ANCAs in blood

TREATMENT

MEDICATIONS

- Pulse methylprednisolone, then prednisone/cyclophosphamide/rituximab/plasmapheresis

OTHER INTERVENTIONS

- If renal failure irreversible
  - Dialysis/kidney transplant

TYPES OF GLOMERULONEPHRITIS PART 1

	CLINICAL PRESENTATION	URINALYSIS	MICROSCOPY	TREATMENT
DIABETIC NEPHROPATHY	Mostly no symptoms	Microalbuminuria (30–300 mg/day), macroalbuminuria (> 300 mg/day)	Light microscopy: GBM thickening, nodular glomerulosclerosis (kimmelstiel-wilson bodies)	ACE inhibitors
FOCAL SEGMENTAL GLOMERULOSCLEROSIS	Nephrotic syndrome	Proteinuria	Light microscopy: focal, segmental sclerosis, hyalinosis Electron microscope: effacement of podocyte foot processes Immunofluorescence: nonspecific focal deposits of IgM, C3	Diuretics ACE inhibitors Prednisone
GOODPASTURE'S SYNDROME	Nephritic syndrome	Hematuria, proteinuria	Light microscopy: crescent-shaped glomeruli Electron microscopy: diffuse thickening of GBM Immunofluorescence: linear deposition along GBM	Prednisone, cyclophosphamide, plasmapheresis
HEMOLYTIC-UREMIC SYNDROME	Nephritic syndrome	Hematuria, proteinuria	N/A	Typical: clears in days to weeks Atypical: treat underlying cause
IgA NEPHROPATHY	Nephritic syndrome	Hematuria	Light microscopy: mesangial proliferation Electron microscopy: deposits in mesangium Immunofluorescence: mesangial IgA deposits	Prednisone
LUPUS NEPHRITIS	Both nephrotic and nephritic syndrome	Proteinuria, -/+ hematuria	Dependant upon class	Prednisone, mycophenolate, cyclophosphamide

TYPES OF GLOMERULONEPHRITIS PART 2

	CLINICAL PRESENTATION	URINALYSIS	MICROSCOPY	TREATMENT
MEMBRANO-PROLIFERATIVE GLOMERULONEPHRITIS	Nephrotic syndrome	Proteinuria, -/+ hematuria	Type I: subendothelial deposits; thickening of basement membrane (tram-tracks) Type II: deposits along basement membrane Type III: subepithelial deposits	Prednisone → varying effectiveness
MEMBRANOUS GLOMERULONEPHRITIS	Nephrotic syndrome	Proteinuria	Light microscopy: diffuse thickening of GBM Electron microscopy: "spike and dome" appearance; effacement of podocytes Immunofluorescence: granular deposits along GBM	Diuretics ACE inhibitors High risk of renal failure: prednisone/rituximab
MINIMAL CHANGE DISEASE	Nephrotic syndrome	Proteinuria	Light microscopy: normal Electron microscopy: effacement of foot processes Immunofluorescence: negative	Prednisone
POSTREPTOCOCCAL GLOMERULONEPHRITIS (ACUTE PROLIFERATIVE GLOMERULONEPHRITIS)	Nephritic syndrome	Hematuria, proteinuria	Light microscopy: mesangial proliferation Electron microscopy: subepithelial deposits (humps) Immunofluorescence: deposits within GBM, mesangium (starry sky)	Supportive
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS	Nephritic syndrome	Hematuria	Light microscopy: crescent-shaped glomeruli Immunofluorescence: Type I: linear Type II: granular Type III: negative	Pulse methylprednisolone, along with prednisone, cyclophosphamide, rituximab, plasmapheresis