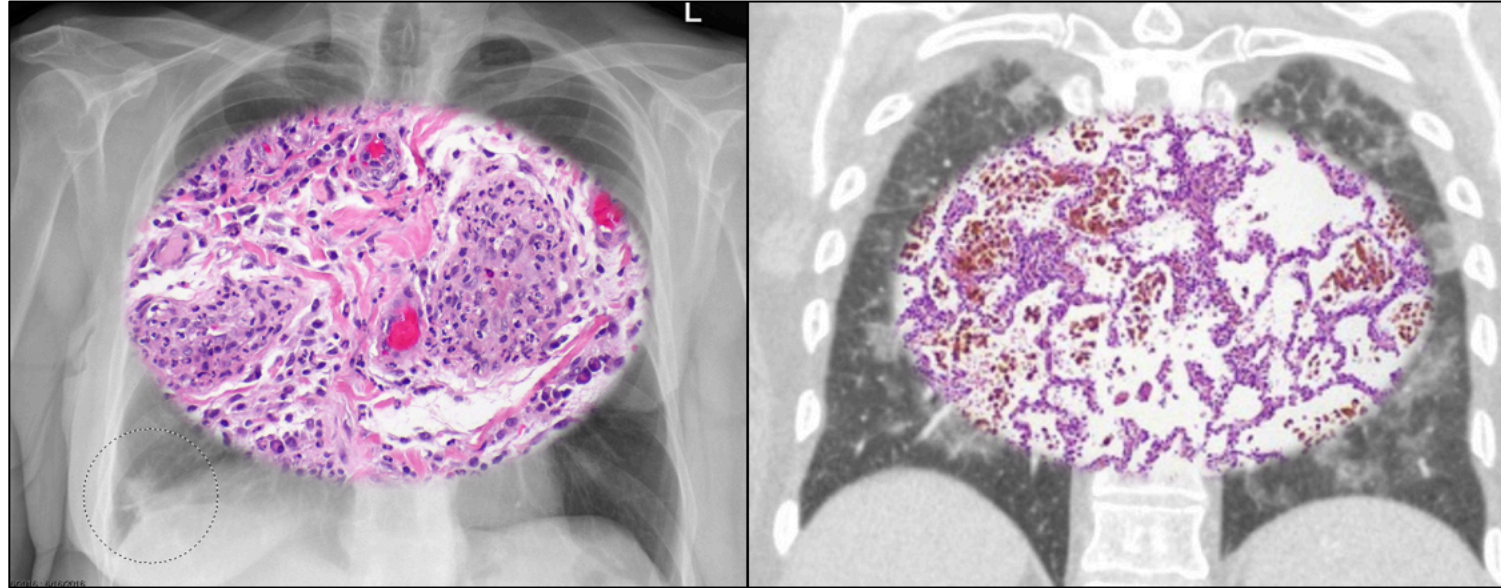
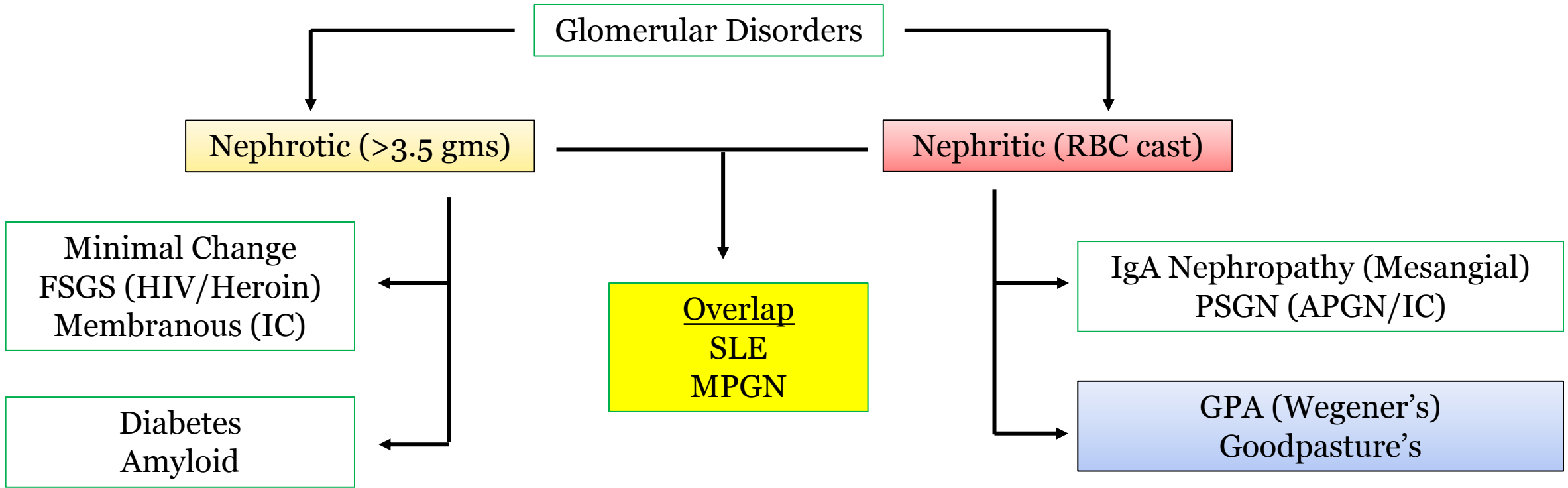


Part 3b. Nephritic Syndromes **GPA* (Wegener's) and Goodpasture (Anti-GBM)**
for USMLE Step One



* *Granulomatosis with polyangiitis*

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the Language of the Nephritic Syndromes

AKI/Elevated Cr

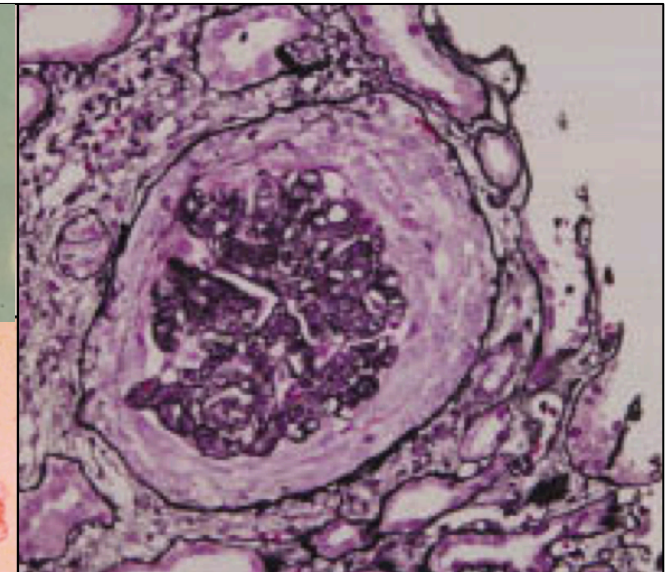
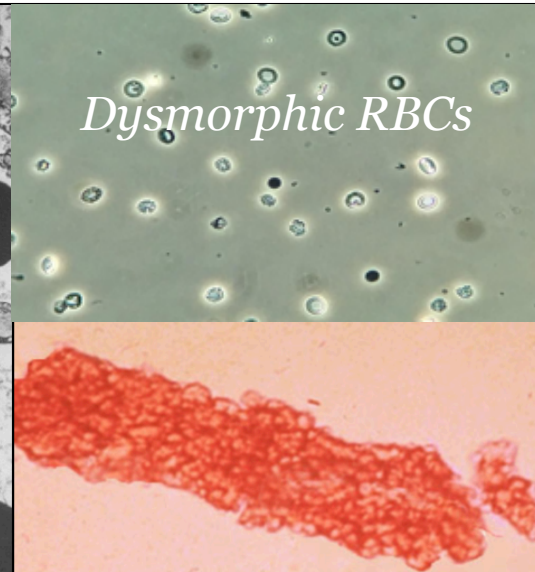
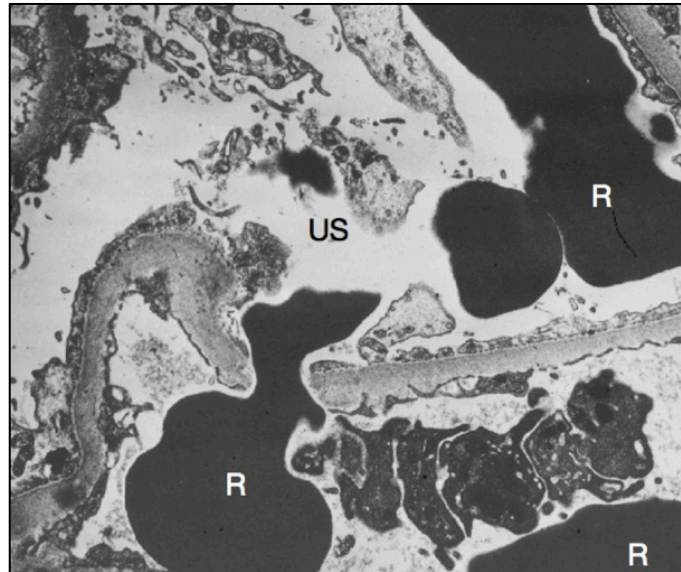
RBC Casts

RPGN/Crescents

Proteinuria, mild

Renal Injury:
Elevated Creatinine
HTN
Edema, mild (↓ GFR)

Clinico-Pathology
RPGN*
Crescents



The Players:

IgA Nephropathy
PSGN

GPA (Wegener's)
Goodpasture's (anti-GBM)

Nephritic: What They Share in Common

GPA

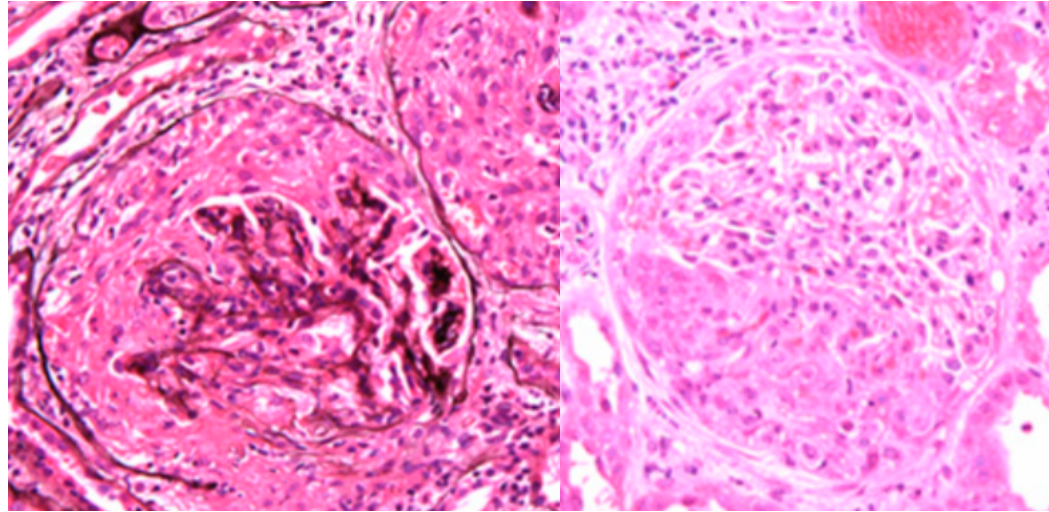
Goodpasture's

Vasculitis: Small Vessels
Prototypic Pulmonary-Renal Syndromes
Characteristic Serologies
RPGN/Crescents (AKI)

Nephritic: What They Share in Common

GPA

Goodpasture's



RPGN/Crescentic GN = ↑ **BUN/Cr**

Pathologic Description: proliferation of *parietal cells* with migration of *monocytes/macrophage* into urinary (Bowman's) space. The crescents obliterate the US and compress the glomerular tuft.

Fibrin strands can be seen between the cellular layers of the crescents.

Nephritic: How They Differ

GPA

Goodpasture's

Identifiers

Pathogenesis

Pathology

Presentation

Diagnostics

Pulmonary-Renal syndrome, classified as small vessel vasculitides, causing RPGN/crescentic GN

Nephritic: How They Differ

GPA

Goodpasture's

Identifiers

Pulmonary-Renal Syndrome (Nephritic/RPGN)

Upper respiratory tract

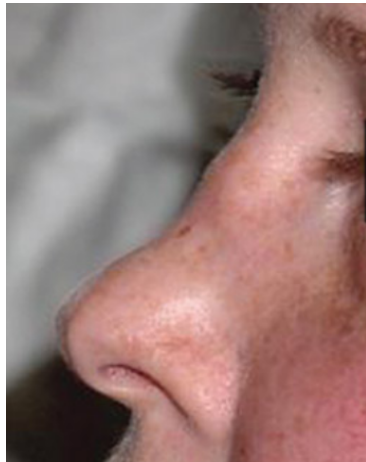
Rhinosinusitis

(nasal crusting/ulcers)

Reticulonodular infiltrates

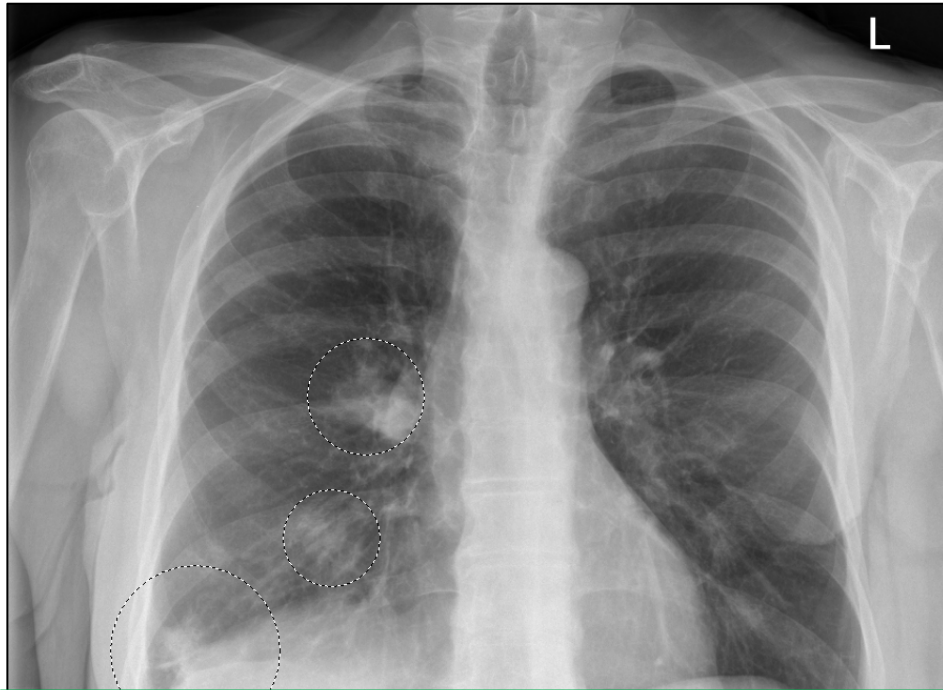
Pulmonary Hemorrhage

Hemoptysis, SOB



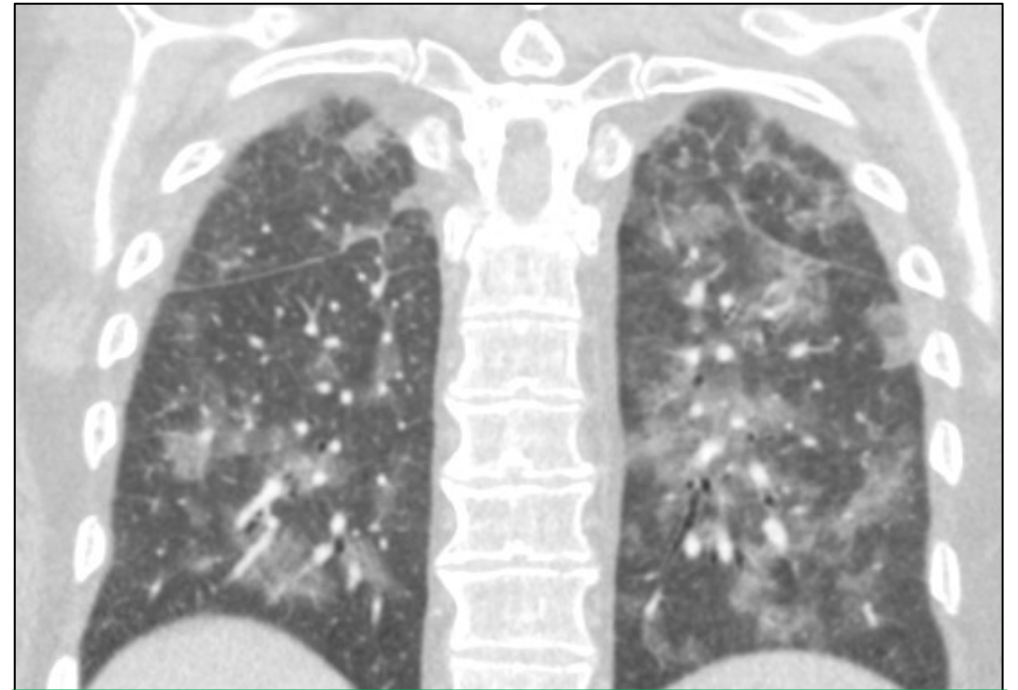
Saddle nose deformity

GPA



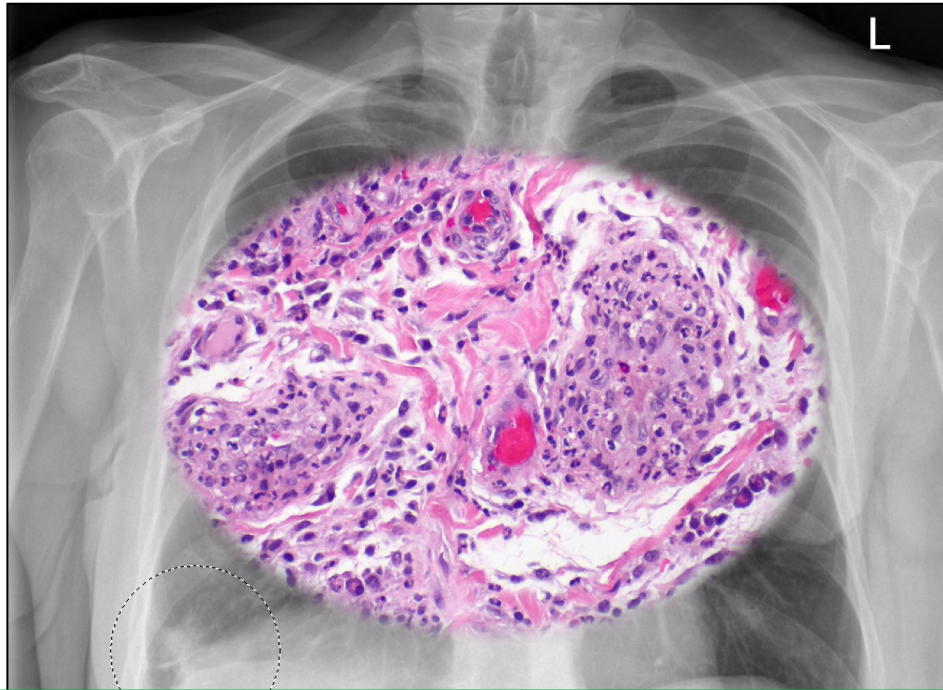
Reticulo-**nodular** infiltrates
Cavitation (necrotizing granulomas)

Goodpasture's



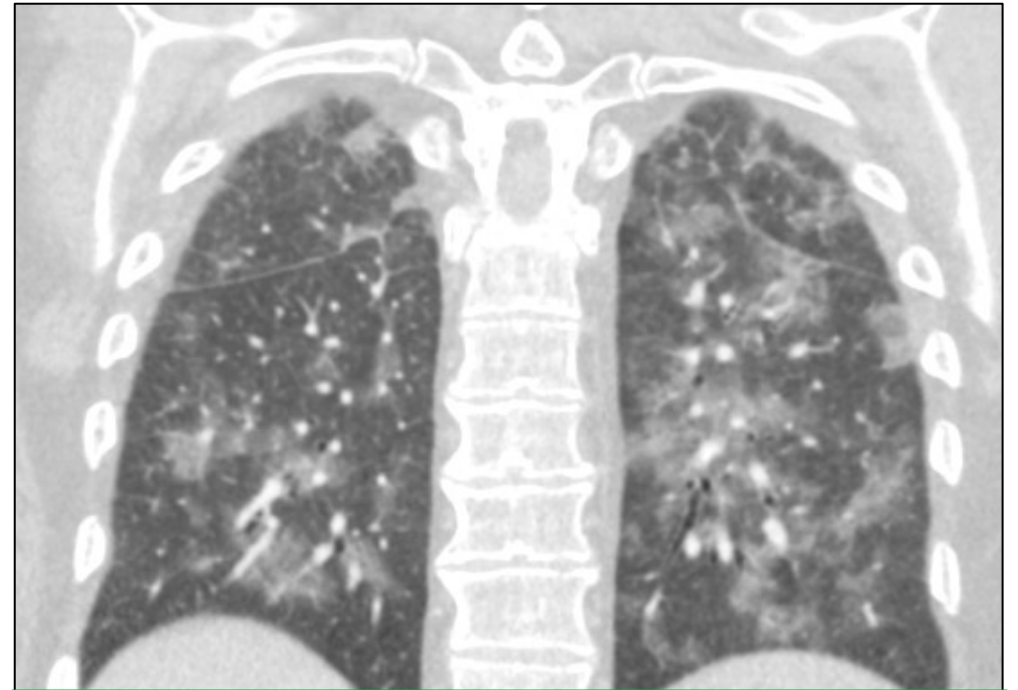
Fluffy and diffuse infiltrates from
alveolar hemorrhage

GPA



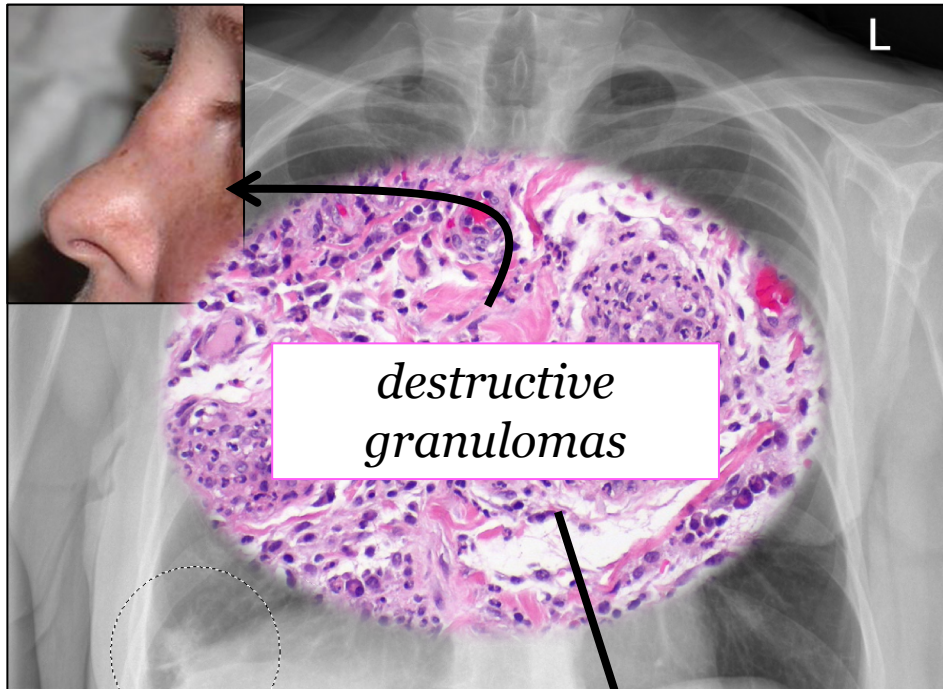
Granulomas may coalesce to form nodular densities (→ cavitate)

Goodpasture's



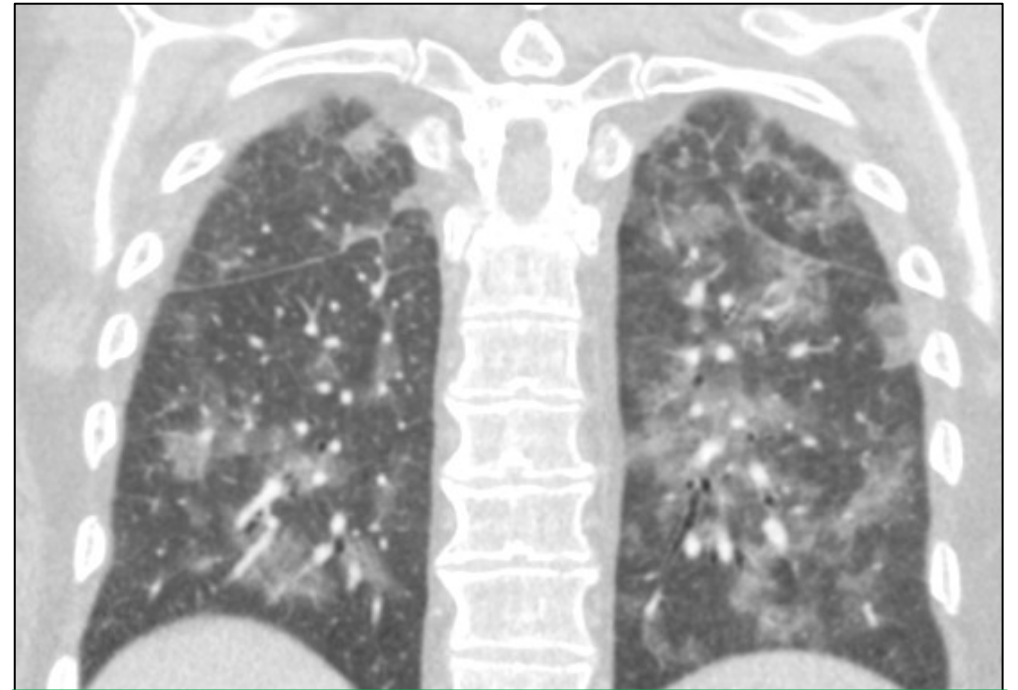
Focal necrosis of the alveolar walls associated with intra-alveolar hemorrhage

GPA



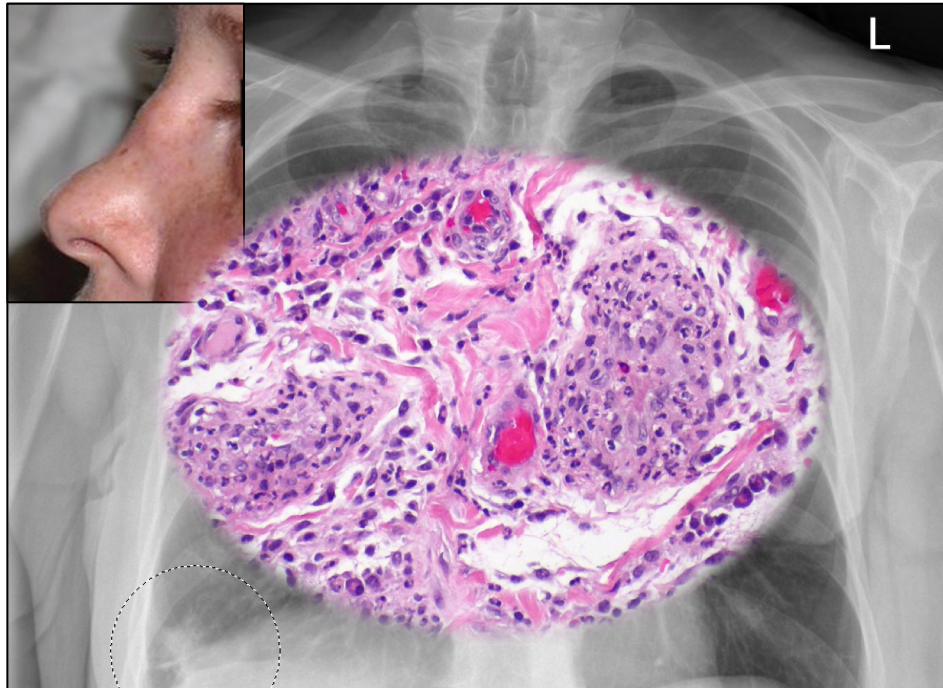
Granulomas may coalesce to form nodular densities (→ **cavitate**)

Goodpasture's



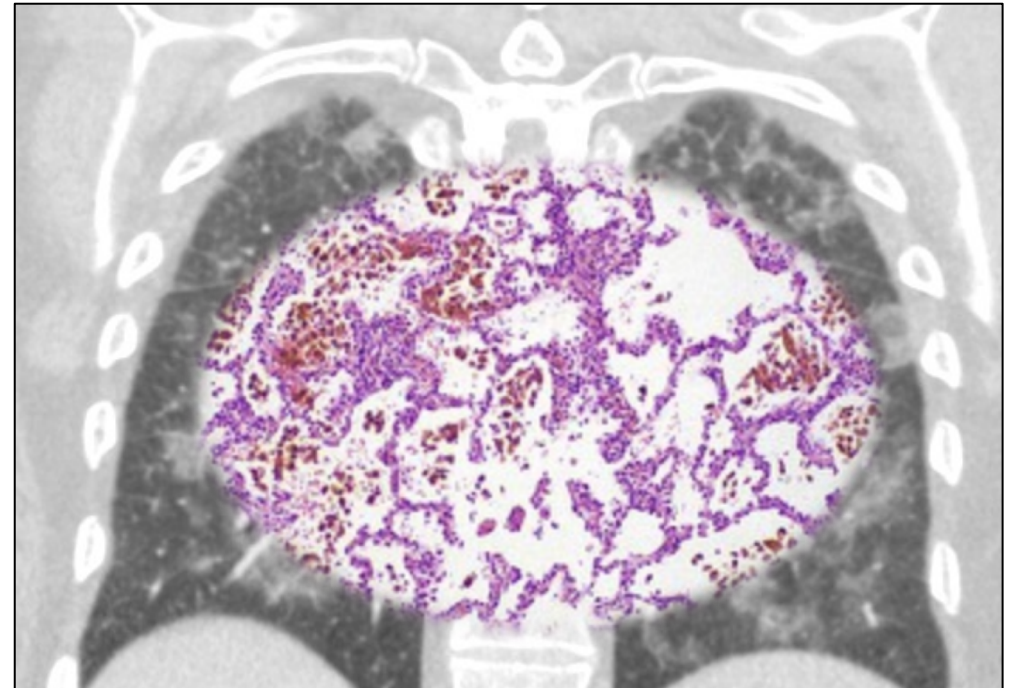
Focal necrosis of the alveolar walls associated with intra-alveolar hemorrhage

GPA



Granulomas may coalesce to form nodular densities (→ cavitate)

Goodpasture's



Focal necrosis of the alveolar walls
associated with intra-alveolar hemorrhage

alpha-3 chain of Type IV collagen

Nephritic: How They Differ

GPA

Goodpasture's

Identifiers

Pulmonary-Renal Syndrome (Nephritic/RPGN)

Upper respiratory tract

Rhinosinusitis

(nasal crusting/ulcers)

Reticulonodular infiltrates

Pulmonary Hemorrhage

SOB, hemoptysis



Saddle nose deformity

Nephritic: How They Differ

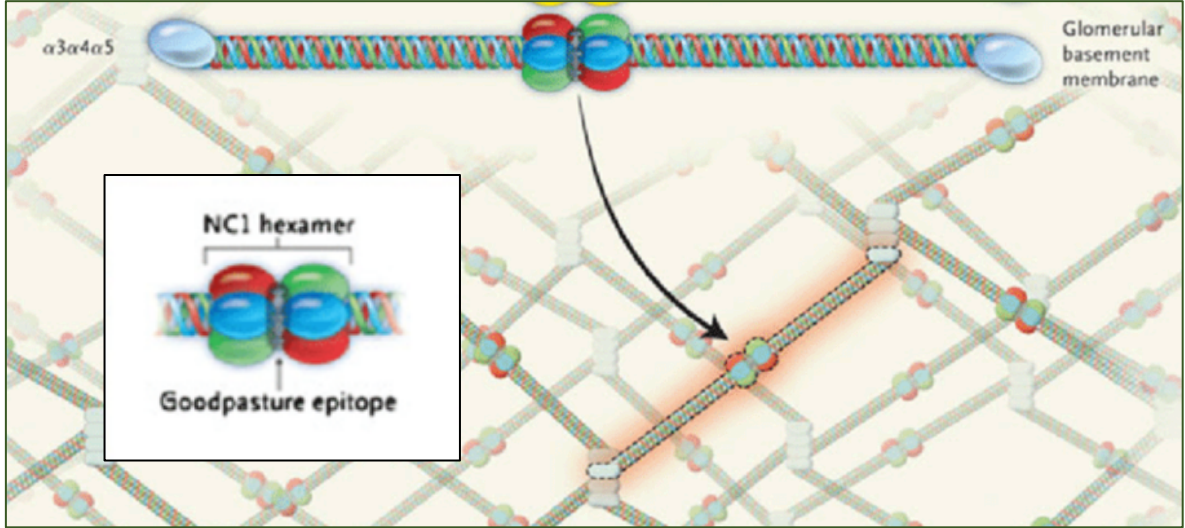
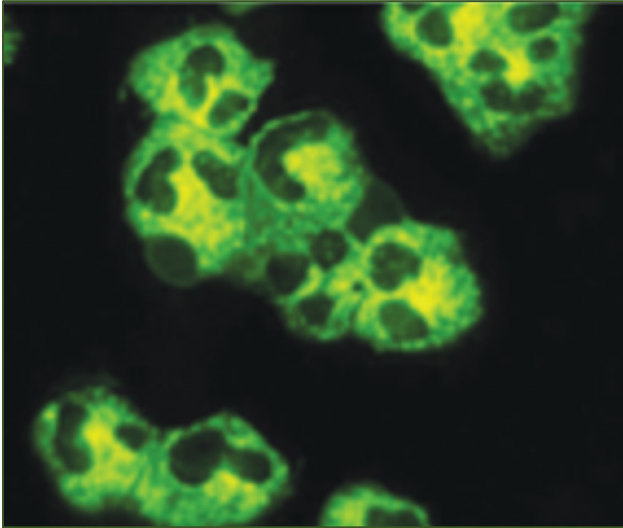
GPA

Goodpasture's

Pathogenesis

c-ANCA autoantibody

anti-GBM antibody



Cytoplasmic PR3
(proteinase-3)
PR3-ANCA

*NC1 - non-collagenous domain
Type II Hypersensitivity (*fixed tissue antigen*)
Target: α -3 chain, Type IV Collagen (BM)
Location: **Alveoli, GBM**

Nephritic: How They Differ

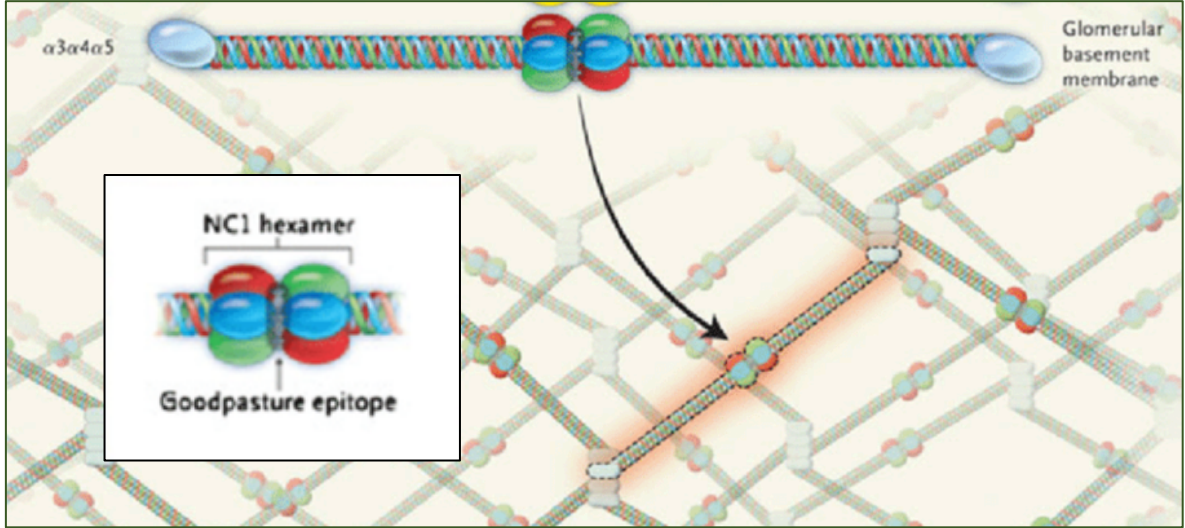
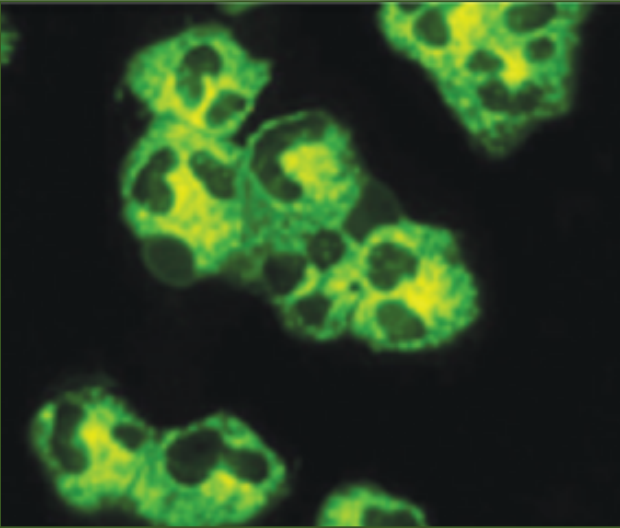
GPA

Goodpasture's

Pathogenesis

c-ANCA autoantibody

anti-GBM antibody



Cytoplasmic PR3
(*proteinase-3*)
PR3-ANCA

*NC1 - non-collagenous domain

Type II Hypersensitivity (*fixed tissue antigen*)
Target: α -3 chain, Type IV Collagen (BM)
Location: Alveoli, GBM, (**Skin, Lens, Cochlea**)

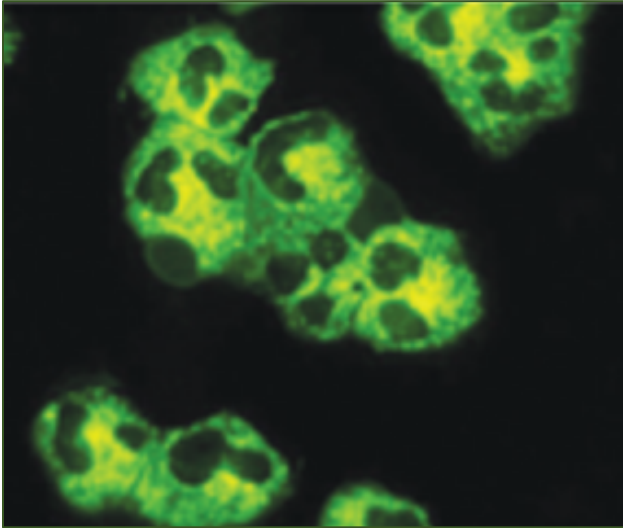
Nephritic: How They Differ

GPA

Pathogenesis

c-ANCA autoantibody

Mutation



Normal



Alport's

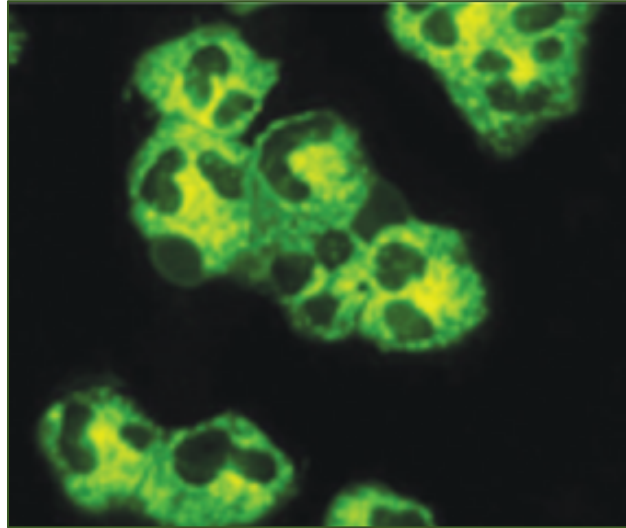
Cytoplasmic PR3
(proteinase-3)
PR3-ANCA

Alport's Syndrome ('Hereditary Nephritis')
Target: α -3, 4, 5 chain, Type IV Collagen (BM)
Location: Alveoli, **GBM**, (Skin, **Lens**, **Cochlea**)

GPA

'Pathogenesis'

c-ANCA autoantibody

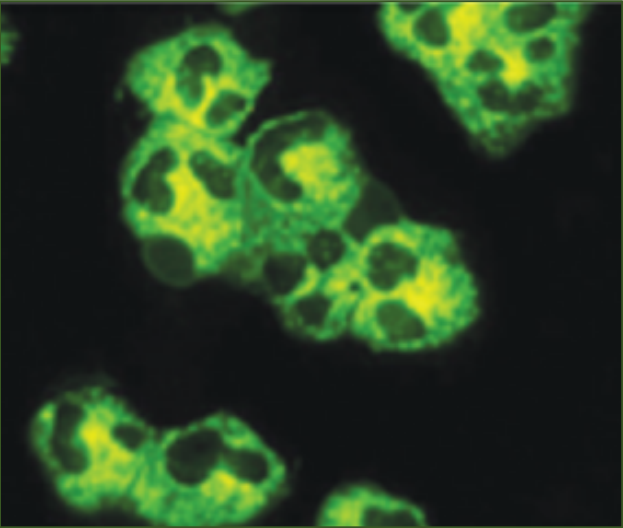


Cytoplasmic PR3
(proteinase-3)
PR3-ANCA

GPA

'Pathogenesis'

c-ANCA autoantibody



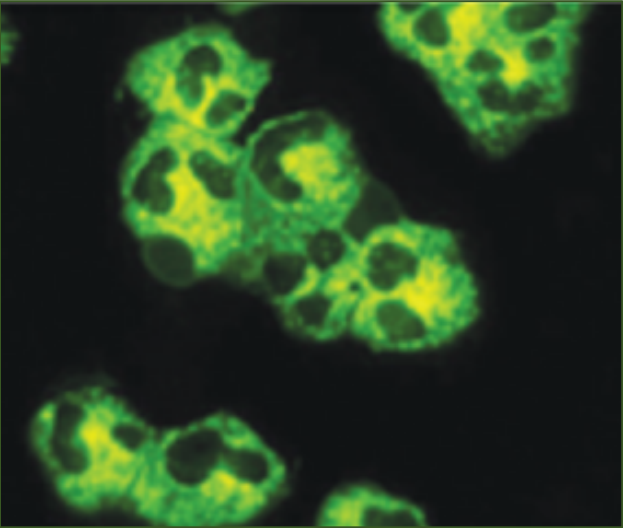
Neutrophil: *anti-neutrophil cytoplasmic antibody*

Cytoplasmic PR3
(*proteinase-3*)
PR3-ANCA

GPA

'Pathogenesis'

c-ANCA autoantibody



Neutrophil

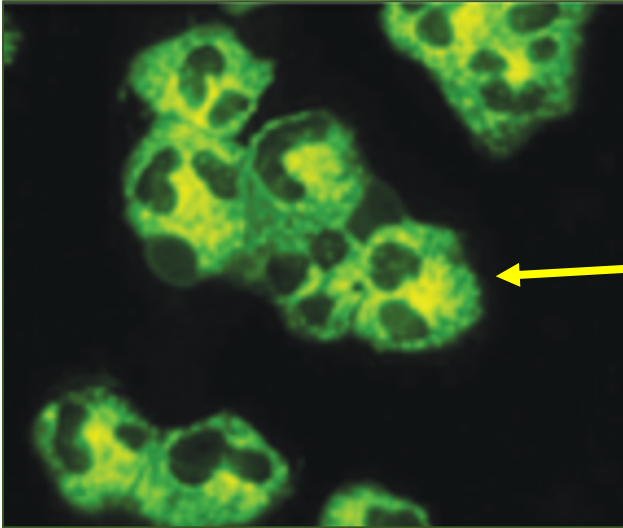
Antigenic target: **Proteinase-3** (*azurophilic granules*)

Cytoplasmic **PR3**
(*proteinase-3*)
PR3-ANCA

GPA

'Pathogenesis'

c-ANCA autoantibody



Neutrophil

Proteinase-3 (*azurophilic granules*)

'C' - **cytoplasmic** staining on IF

Cytoplasmic PR3
(*proteinase-3*)
PR3-ANCA

Nephritic: How They Differ

GPA

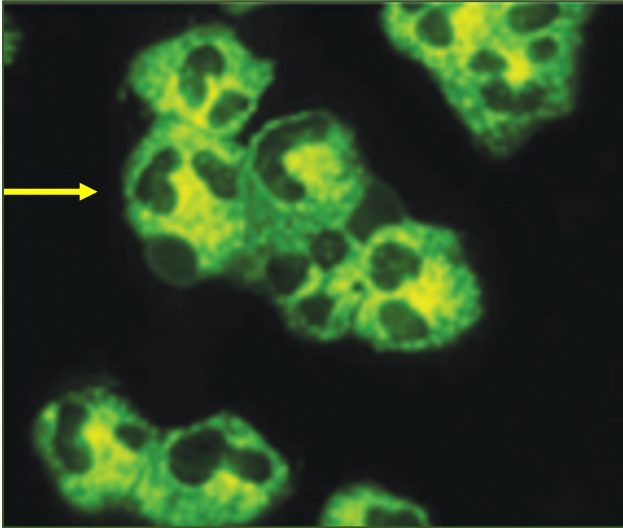
Vasculitis

'Pathogenesis'

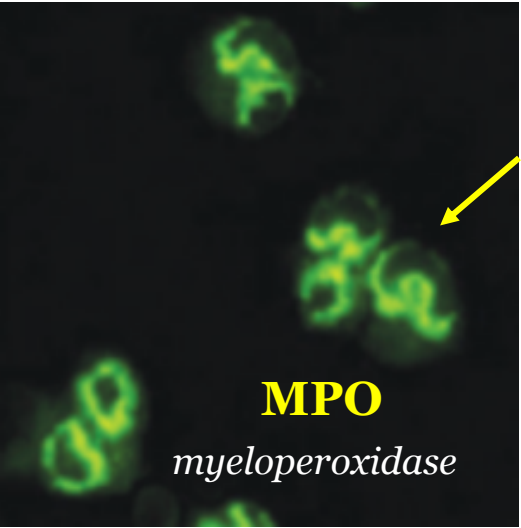
c-ANCA autoantibody

p-ANCA autoantibody

cytoplasmic



perinuclear



Cytoplasmic PR3
(*proteinase-3*)
PR3-ANCA

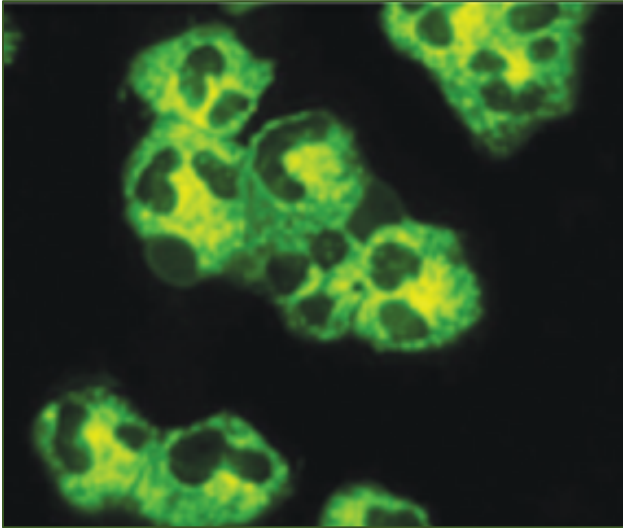
Microscopic polyangiitis
Churg-Strauss (EGPA)
MPO-ANCA

Nephritic: How They Differ

GPA

'Pathogenesis'

c-ANCA autoantibody



Neutrophil

Proteinase-3 (*azurophilic granules*)

'C' - **cytoplasmic** staining on IF

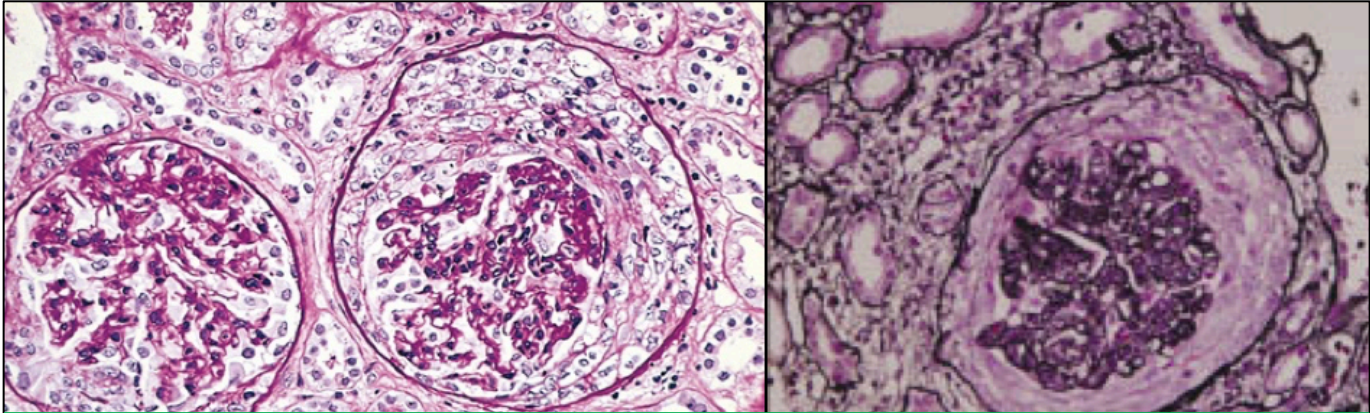
PR3-ANCA: ELISA titre

Cytoplasmic PR3
(*proteinase-3*)
PR3-ANCA

Nephritic: How They Differ

GPA

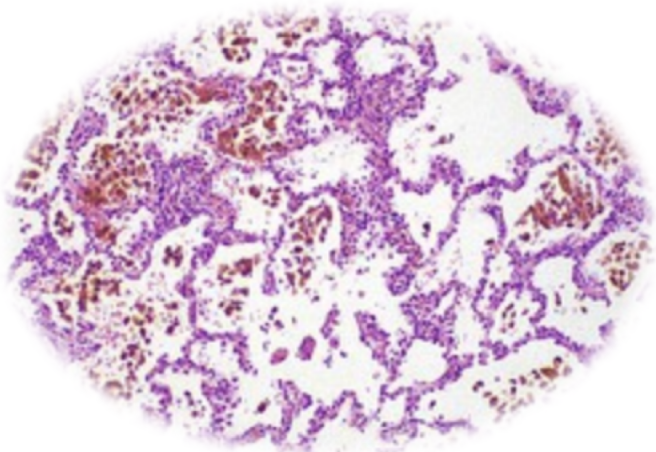
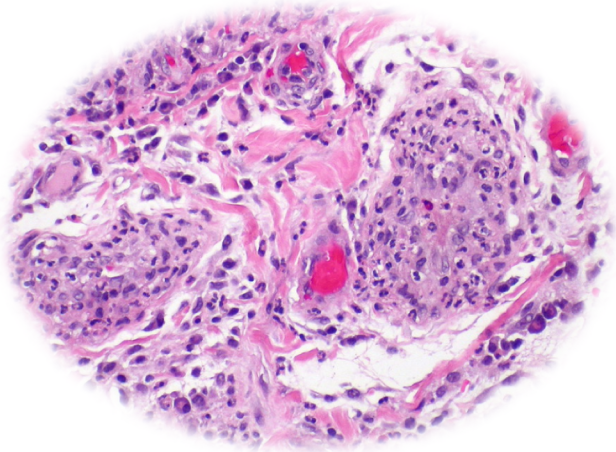
Goodpasture's



Necrotizing/Crescentic Glomerulonephritis (RPGN)

Pathology, Renal

Pathology, Pulm



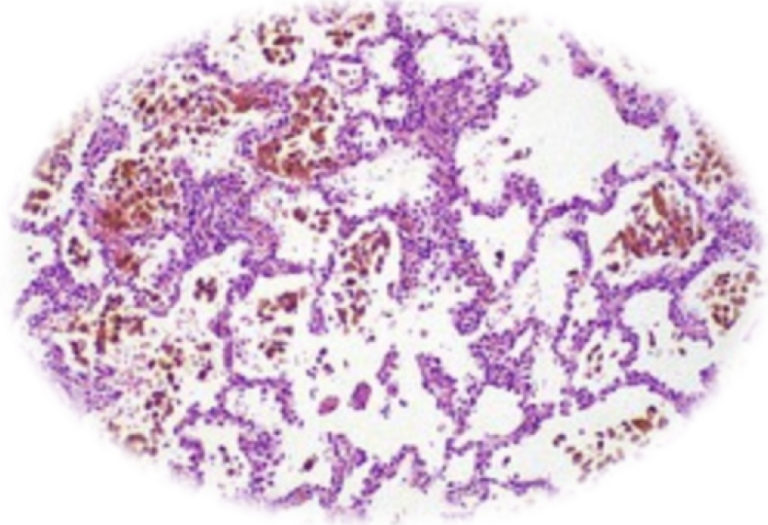
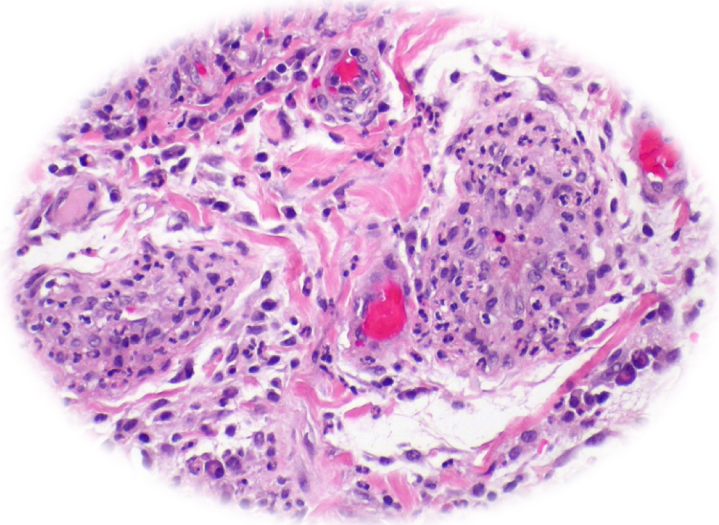
Nephritic: How They Differ

Granulomatosis with Polyangiitis

Goodpasture's

*Respiratory tract with Granuloma
Necrotizing vasculitis (small vessel)*

*Focal necrosis of the alveolar walls
associated with intra-alveolar hemorrhage*



Pathology, Pulm

Hemosiderin-laden macrophages

Granulomatosis with Polyangiitis

Organ	Clinical manifestation
Generic	General malaise, myalgia, arthralgia, anorexia, weight loss and pyrexia
Skin	Leucocytoclastic vasculitis, digital infarcts, purpura, cutaneous ulcers and gangrene
Oral cavity	Oral ulcers, oral granulomatous lesions, gingival hyperplasia with strawberry-like aspect, swallow
Eye	Episcleritis, scleritis, conjunctivitis, keratitis, uveitis, retinal vasculitis, retinal arterial or venous thrombosis, retinal exudates, retinal haemorrhages, blurred vision, blindness, proptosis and orbital granulomatous masses, epiphora
Nose and paranasal sinus	Persistent-recurrent nasal discharges, blood-stained nasal discharge, epistaxis, crusting, mucosal ulceration, nasal bridge collapse, nasal granulomatous lesions, paranasal and sinus inflammation, regional tenderness
Ear	Sensorineural hearing loss and conductive hearing loss
Upper airway	Subglottic or tracheal stenosis
Lower airway	Cough, breathlessness, stridor, wheeze, small air way obstruction, pulmonary nodules, cavitating lung lesions, pleuritis, pleural effusions, pulmonary infiltrates, pulmonary haemorrhage, alveolar capillaritis and respiratory failure
Cardiovascular	Small vessel vasculitis, occlusive vascular disease, pericarditis, pericardial effusions, cardiomyopathy, valvular heart disease, ischaemic heart disease, heart failure
Gastrointestinal	Acute abdomen secondary to peritonitis or bowel ischaemia which may be secondary to mesenteric vasculitis
Kidney	Diffuse pauci-immune crescentic necrotising glomerulonephritis, haematuria, proteinuria, cellular casts on urine cytology, renal impairment manifested as acute kidney injury, chronic kidney disease or end-stage renal failure
Central and peripheral nervous system	Headache, meningitis, seizures, cerebrovascular accidents, spinal cord lesions, cranial nerve palsies, sensory or motor peripheral neuropathy, mononeuritis multiplex, sensorineural hearing loss, cerebral mass lesions
Musculoskeletal	Inflammatory arthritis, erosive or deforming, arthralgia, myalgia, arthralgia

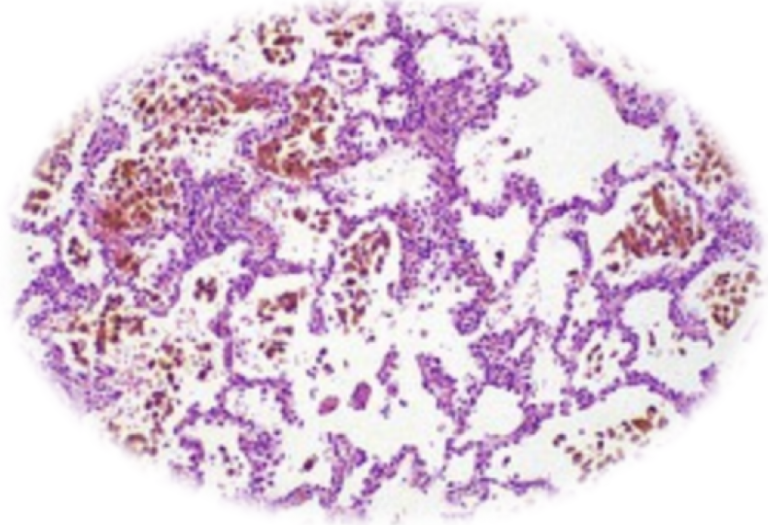
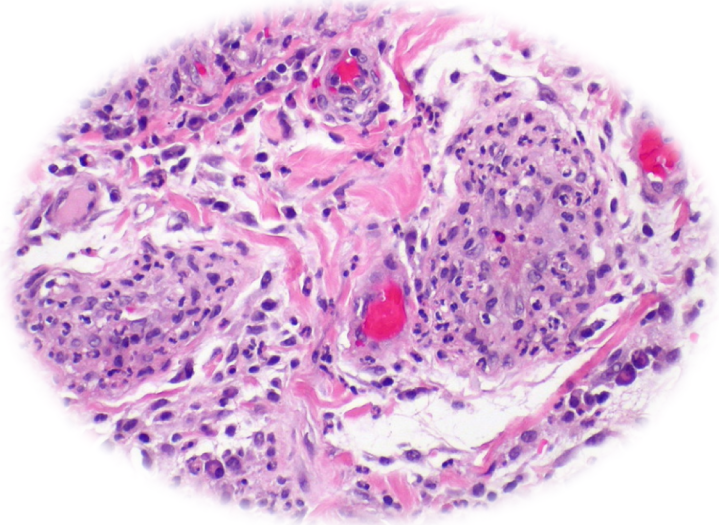
Nephritic: How They Differ

Granulomatosis with Polyangiitis

Goodpasture's

*Respiratory tract with Granuloma
Necrotizing vasculitis (small vessel)*

*Focal necrosis of the alveolar walls
associated with intra-alveolar hemorrhage*



Pathology, Pulm

Hemosiderin-laden macrophages

Nephritic: How They Differ

GPA

Goodpasture's

Presentation

Upper Respiratory Tract*

Pulmonary Hemorrhage

Lower Respiratory Tract

Hemoptysis, SOB

Renal

Organ	Clinical manifestation
Generic	General malaise, myalgia, arthralgia, anorexia, weight loss and pyrexia
Skin	Leucocytoclastic vasculitis, digital infarcts, purpura, cutaneous ulcers and gangrene
Oral cavity	Oral ulcers, oral granulomatous lesions, gingival hyperplasia with strawberry-like aspect, swallow
Eye	Episcleritis, scleritis, conjunctivitis, keratitis, uveitis, retinal vasculitis, retinal arterial or venous thrombosis, retinal exudates, retinal haemorrhages, blurred vision, blindness, proptosis and orbital granulomatous masses, epiphora
Nose and paranasal sinus	Persistent-recurrent nasal discharges, blood-stained nasal discharge, epistaxis, crusting, mucosal ulceration, nasal bridge collapse, nasal granulomatous lesions, paranasal and sinus inflammation, regional tenderness
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Central and peripheral nervous system	Headache, meningitis, seizures, cerebrovascular accidents, spinal cord lesions, cranial nerve palsies, sensory or motor peripheral neuropathy, mononeuritis multiplex, sensorineural hearing loss, cerebral mass lesions
Musculoskeletal	Inflammatory arthritis, erosive or deforming, arthralgia, myalgia, arthralgia

Nephritic: How They Differ

GPA

Goodpasture's

Presentation

Upper Respiratory Tract*

Lower Respiratory Tract

Renal

Anti-GBM (*renal only*)

Organ	Clinical manifestation
Generic	General malaise, myalgia, arthralgia, anorexia, weight loss and pyrexia
Skin	Leucocytoclastic vasculitis, digital infarcts, purpura, cutaneous ulcers and gangrene
Oral cavity	Oral ulcers, oral granulomatous lesions, gingival hyperplasia with strawberry-like aspect, swallow
Eye	Episcleritis, scleritis, conjunctivitis, keratitis, uveitis, retinal vasculitis, retinal arterial or venous thrombosis, retinal exudates, retinal haemorrhages, blurred vision, blindness, proptosis and orbital granulomatous masses, epiphora
Nose and paranasal sinus	Persistent-recurrent nasal discharges, blood-stained nasal discharge, epistaxis, crusting, mucosal ulceration, nasal bridge collapse, nasal granulomatous lesions, paranasal and sinus inflammation, regional tenderness
Ear	Sensorineural hearing loss and conductive hearing loss
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Cardiovascular	Small vessel vasculitis, occlusive vascular disease, pericarditis, pericardial effusions, cardiomyopathy, valvular heart disease, ischaemic heart disease, heart failure
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Central and peripheral nervous system	Headache, meningitis, seizures, cerebrovascular accidents, spinal cord lesions, cranial nerve palsies, sensory or motor peripheral neuropathy, mononeuritis multiplex, sensorineural hearing loss, cerebral mass lesions
Musculoskeletal	Inflammatory arthritis, erosive or deforming, arthralgia, myalgia, arthralgia

GPA

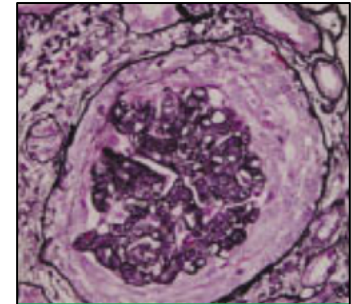
Goodpasture's

Diagnostics

BUN/Cr, Urinalysis with hematuria (RBC casts/dysmorphic RBCs)

	Ref Range & Units	
NA	135 - 145 mmol/L	140
K	3.5 - 5.3 mmol/L	4.6
Cl	97 - 110 mmol/L	109
CO2	24 - 32 mmol/L	20 ▼
Anion Gap	5 - 15	11
Glucose	70 - 99 mg/dL	125 ▲
BUN	7 - 23 mg/dL	89 ▲
Creatinine	0.50 - 1.20 mg/dL	6.55 ▲

RPGN



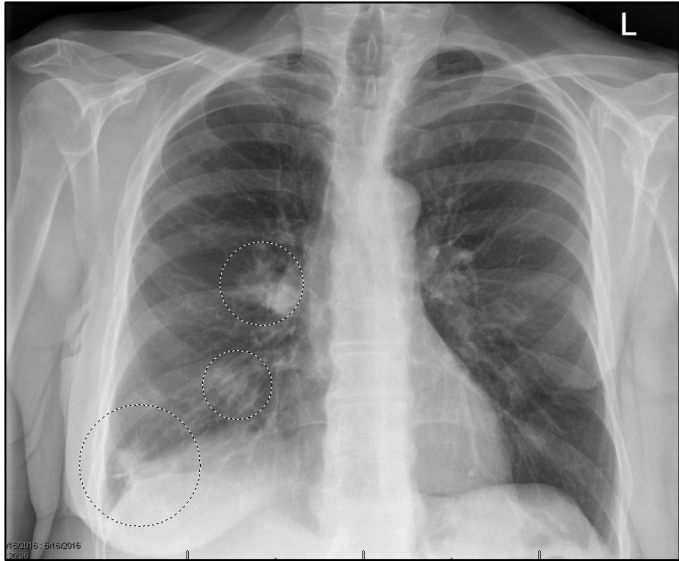
Nephritic: How They Differ

GPA

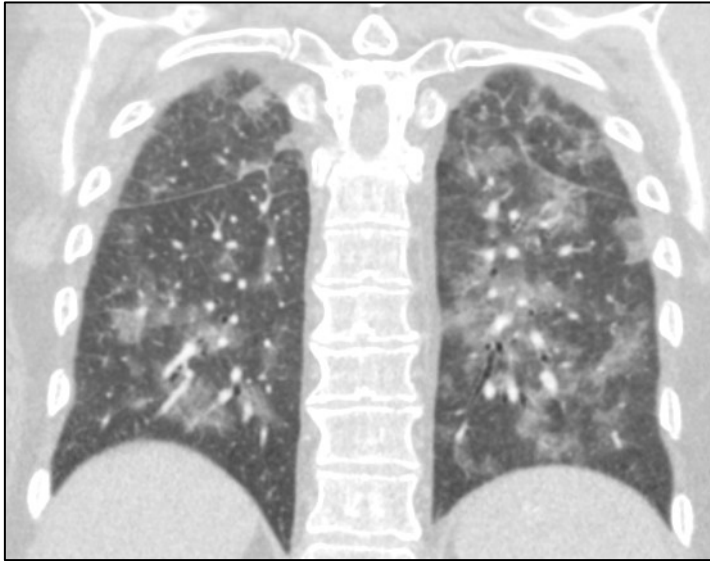
Goodpasture's

Diagnosics

BUN/Cr, Urinalysis with hematuria (RBC casts/dysmorphic RBCs)



Reticulo-Nodular densities
can cavitate



Pulmonary hemorrhage
(*'fluffy infiltrates'*)

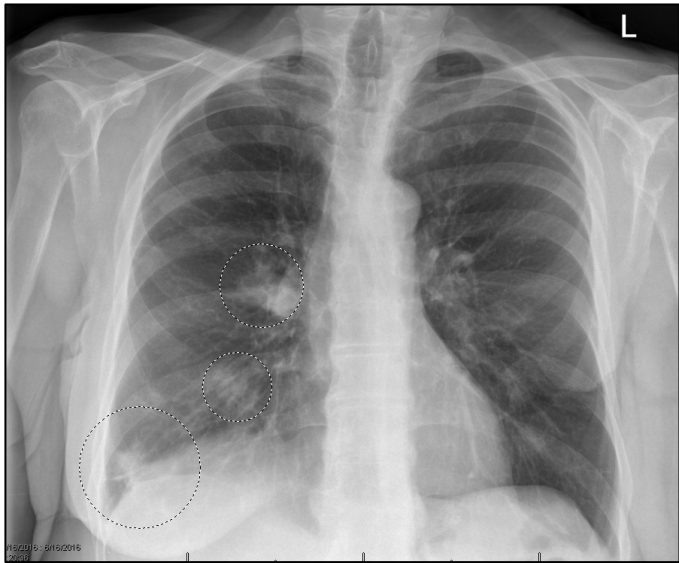
Nephritic: How They Differ

GPA

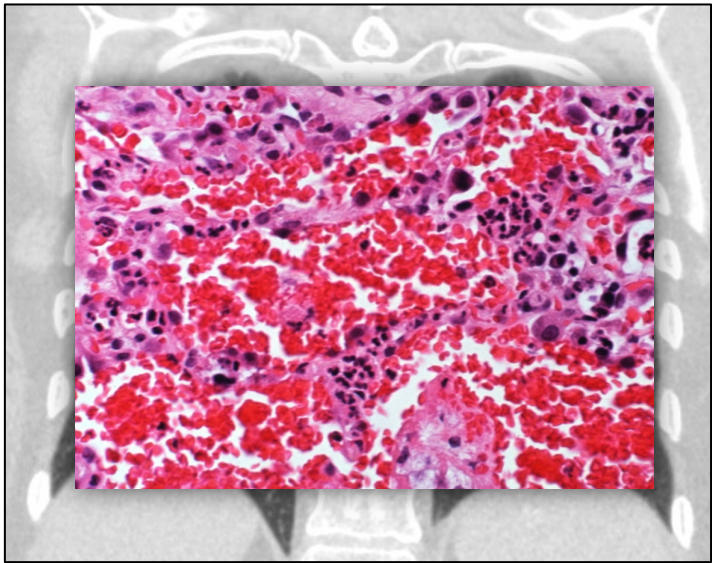
Goodpasture's

Diagnostics

BUN/Cr, Urinalysis with hematuria (RBC casts/dysmorphic RBCs)



Reticulo-Nodular densities
can cavitate



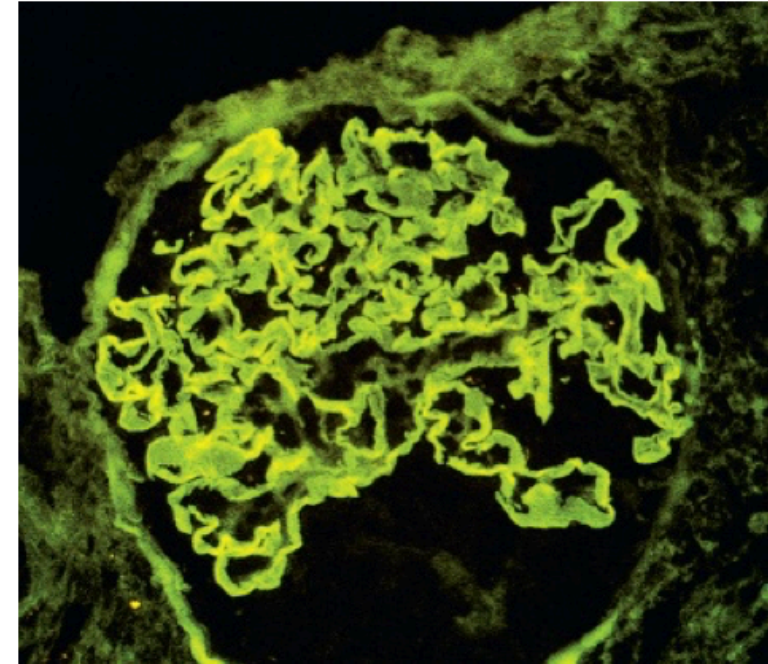
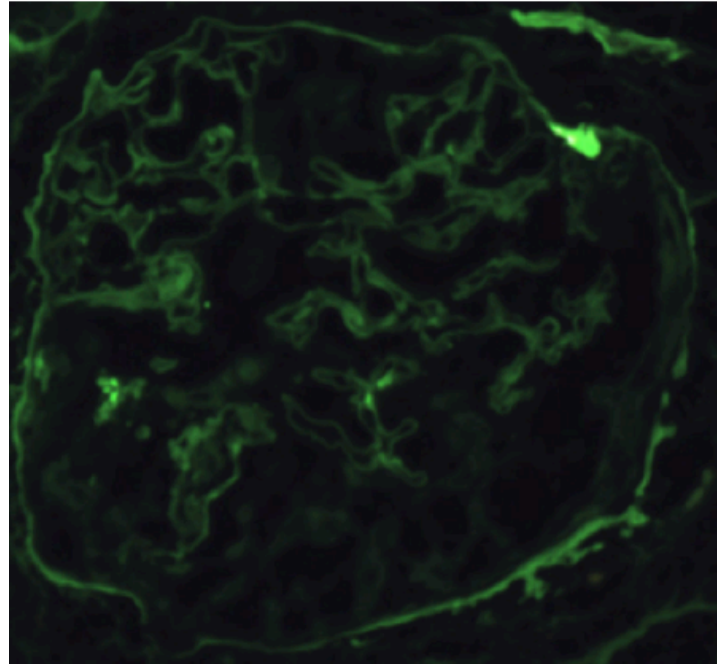
Pulmonary hemorrhage
(*fluffy infiltrates*)
↑ **DLCO**

Nephritic: How They Differ

GPA

Goodpasture's

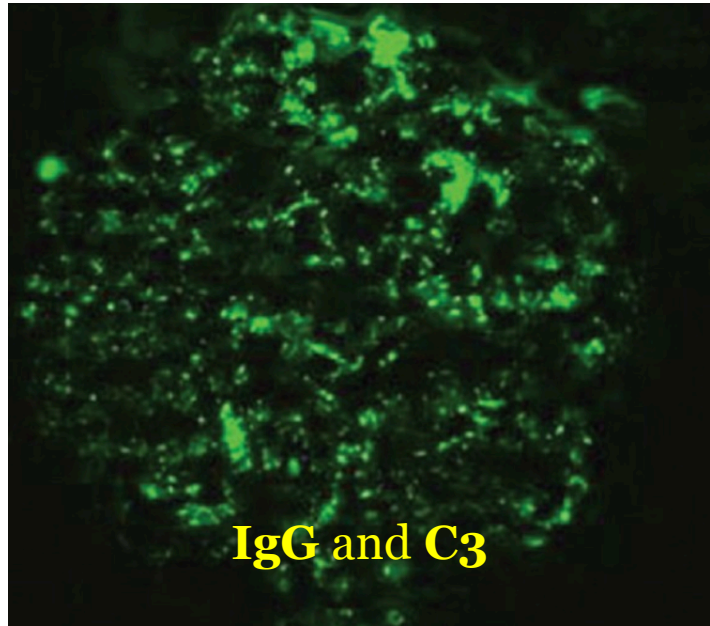
Diagnostics IF



Pauci-immune
No immune complex deposition

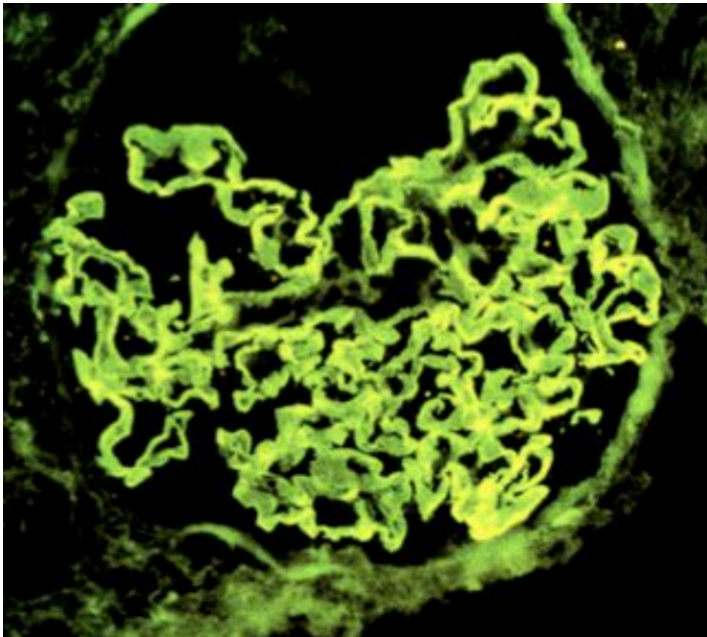
Linear/Ribbon Pattern
 α -3 chain, Type IV collagen

Diagnosics IF



Focal Pattern (*Granular*)
Immune Complex Deposition

Goodpasture's



Linear/Ribbon Pattern
 α -3 chain, Type IV collagen

Nephritic: How They Differ

GPA

Goodpasture's

Identifiers

Pulmonary-Renal Syndrome

Pathogenesis

PR3-ANCA

Anti-GBM

Pathology

Granuloma,
Necrotizing vasculitis

Focal necrosis of alveolar
wall with hemorrhage

Presentation

Upper Respiratory Tract

Hemoptysis

Diagnostics

IF: pauci-immune, (-) IC

IF: linear/ribbon-like

Glomerular Disorders

Nephrotic (>3.5 gms)

Nephritic (RBC cast)

Minimal Change
FSGS (HIV/Heroin)
Membranous (IC)

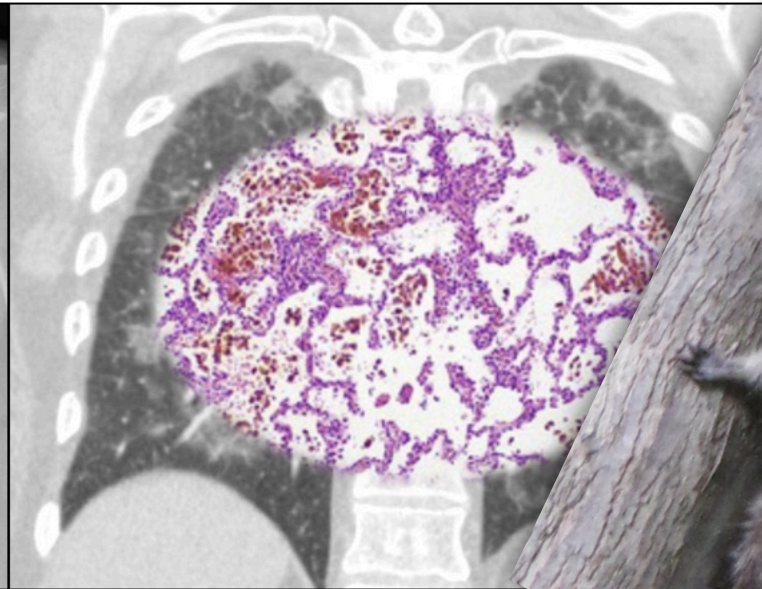
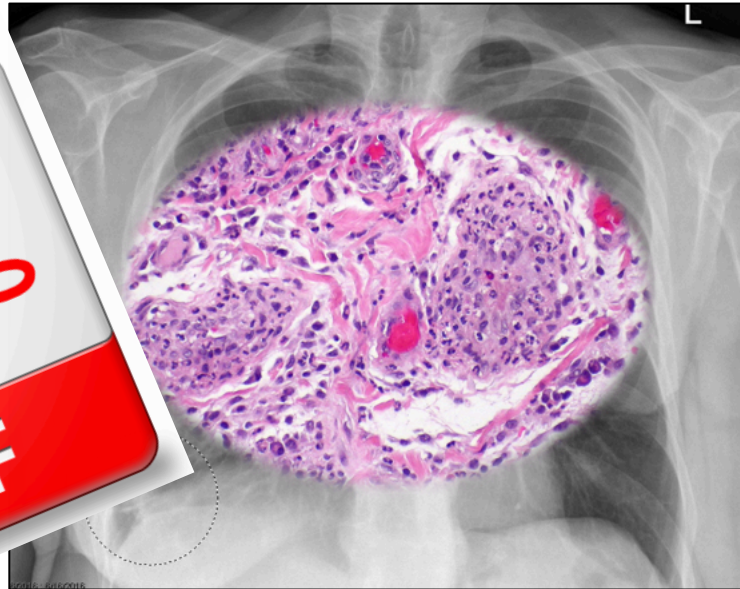
Diabetes
Amyloid

Overlap
SLE
MPGN

IgA Nephropathy (Mesangial)
PSGN (APGN/IC)

GPA (Wegener's)
Goodpasture's

Part 3b. Nephritic Syndromes **GPA* (Wegener's) and Goodpasture (Anti-GBM)**
for USMLE Step One



** Granulomatosis with polyangiitis*

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