HARRISON

EDITION 22nd

NEPHROLOGY

Nephrology

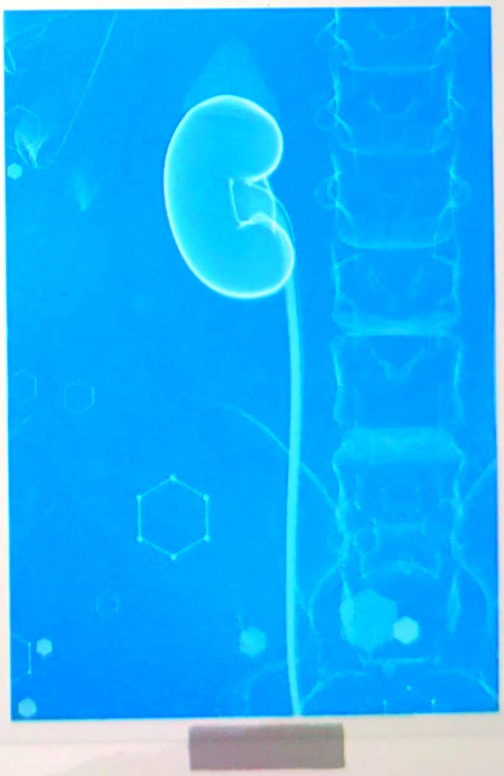
Chapter 319 - Approach To The Patient With Renal Disease Or Urinary Tract Disease	Completed
Chapter - 321 Acute Kidney Injury	Completed
Chapter - 323 Dialysis In The Treatment Of Kidney Failure	Completed
Chapter - 325 Kidney Transplantation	Completed
Chapter - 326 Glomerular Diseases	Completed
Chapter - 328 Tubulointerstitial Diseases Of The Kidney	Completed
Chapter 324 - Interventional Nephrology	Completed
Chapter 330 - Nephrolithiasis	Completed
Chapter 331 - Urinary Tract Obstruction	Completed
CKD	Completed

Chapter - 319 Approach to the Patient with Renal Disease or Urinary Tract Disease

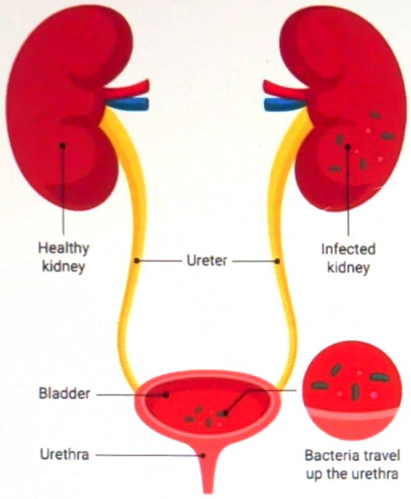
Dr. Manu

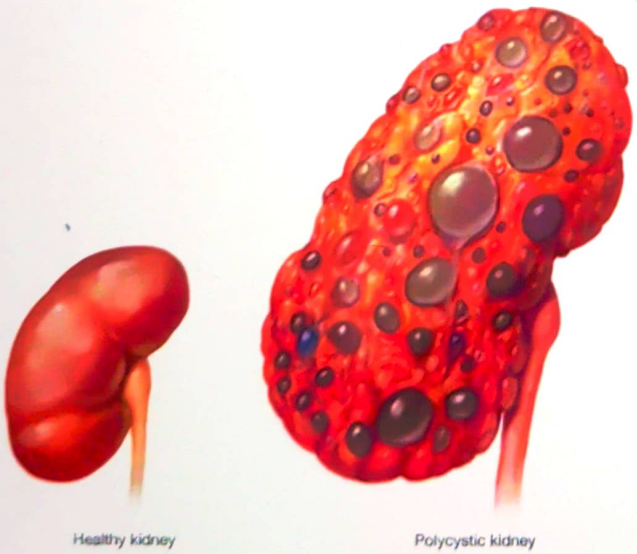
Urinary Tract Overview

- **Upper tract**: Kidneys, renal vasculature, parenchyma, collecting system
- **Lower tract**: Ureters, bladder, urethra
- **Function**: Ultrafiltration → tubular modification → urine excretion
- **Clinical relevance**: Disease can affect any level, often asymptomatic

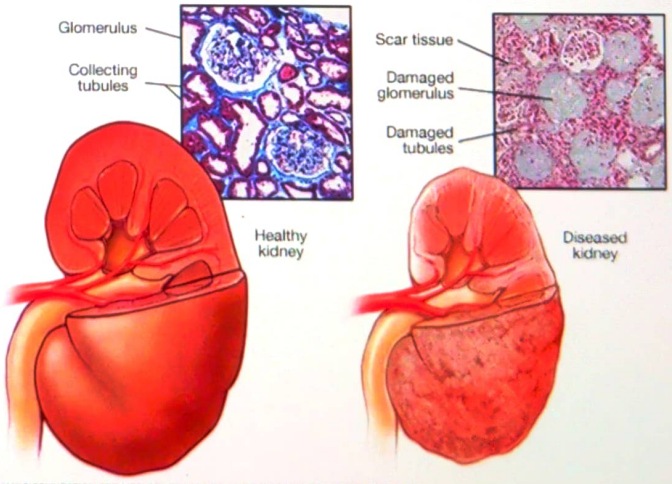


URINARY TRACT INFECTION - UTI





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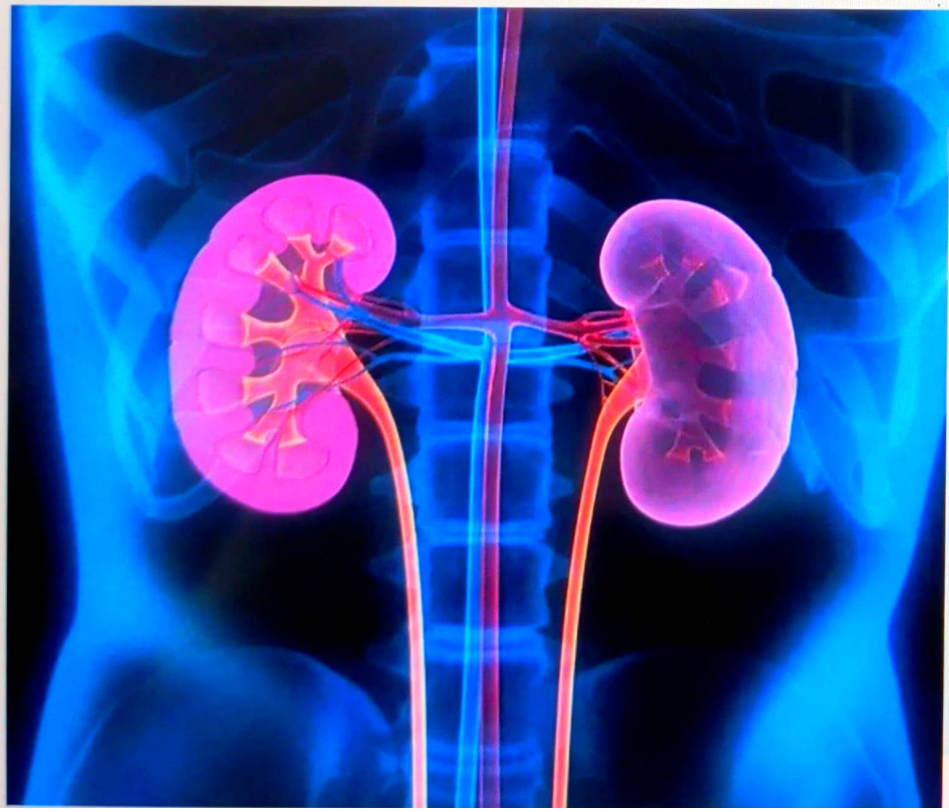


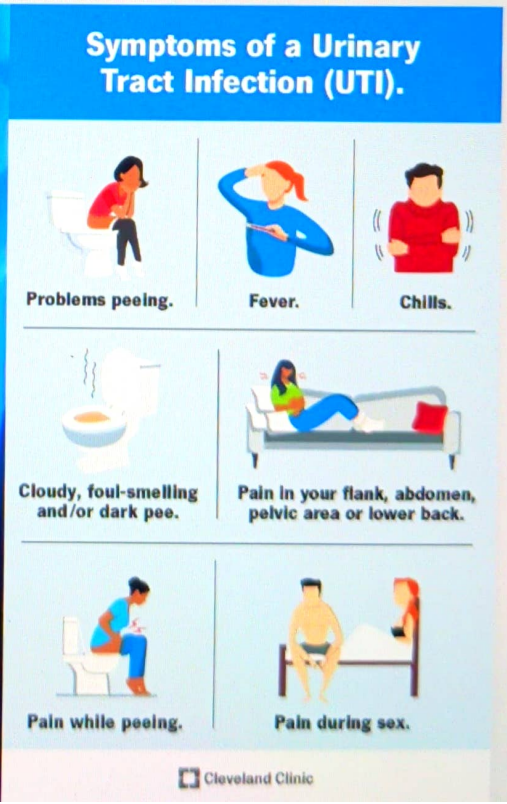
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Initial Patient Evaluation Essentials

- **History**: Fatigue, polyuria, hematuria, incidental imaging findings
- **Risk factors**: Diabetes, lithium use, occupational toxins
- **Systemic screening**: eGFR, microalbuminuria in high-risk patients
- **Avoid random testing**: Use targeted diagnostics based on clinical clues

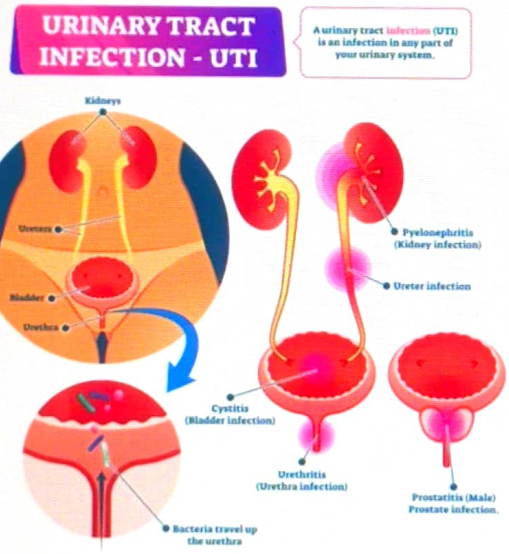


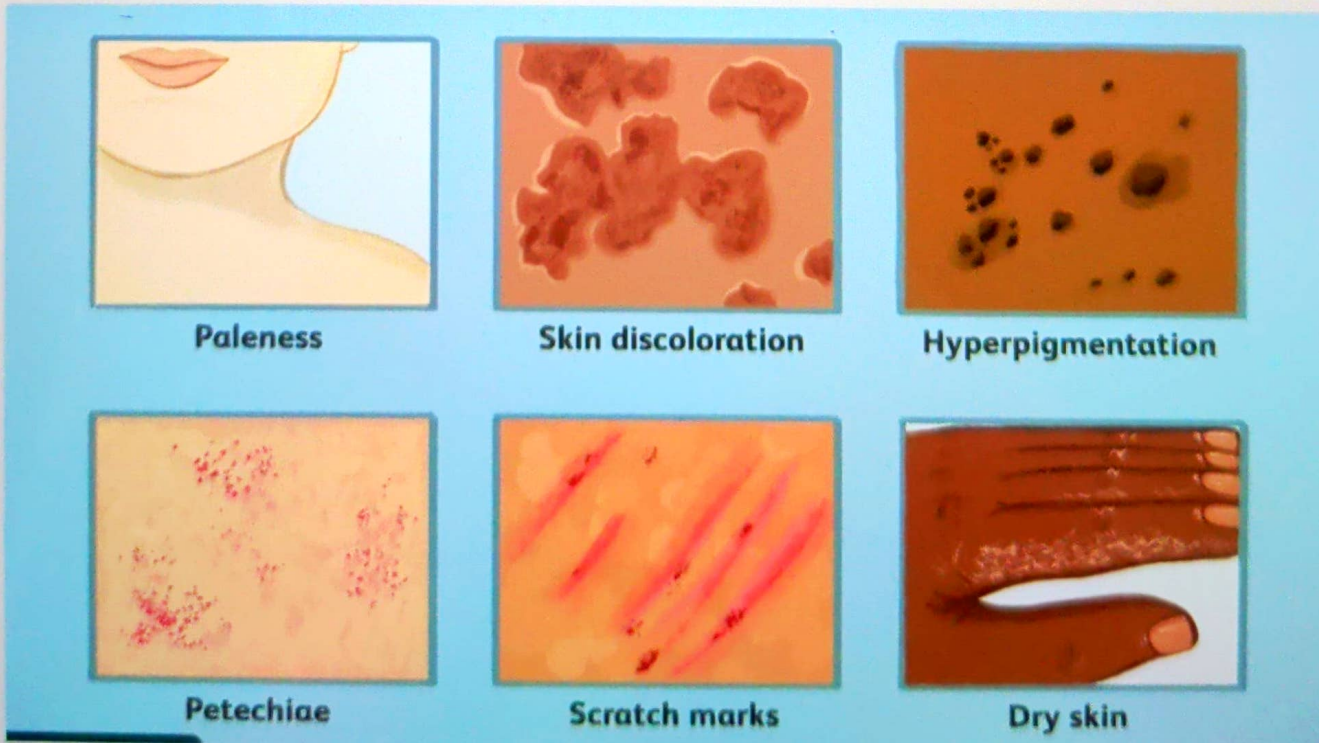




Diagnostic Approach

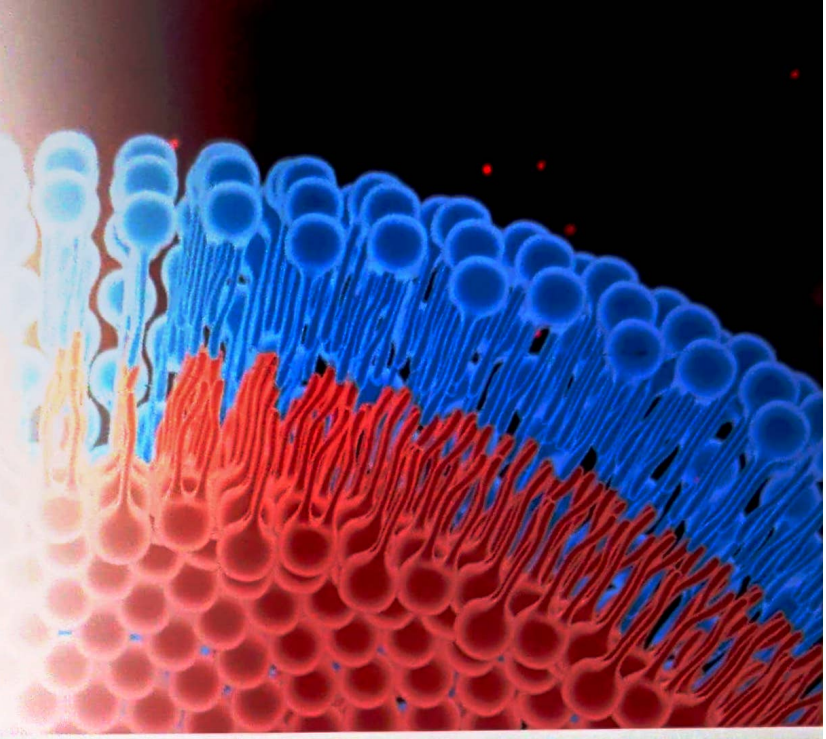
- **Urinalysis**: Proteinuria, casts, dysmorphic RBCs
- **Lab markers**: BUN/Cr ratio, electrolytes, PTH, complement levels
- **Imaging**: Ultrasound for hydronephrosis, CT/MRI for masses
- **Functional tests**: FENa, urine osmolality, U/P ratios

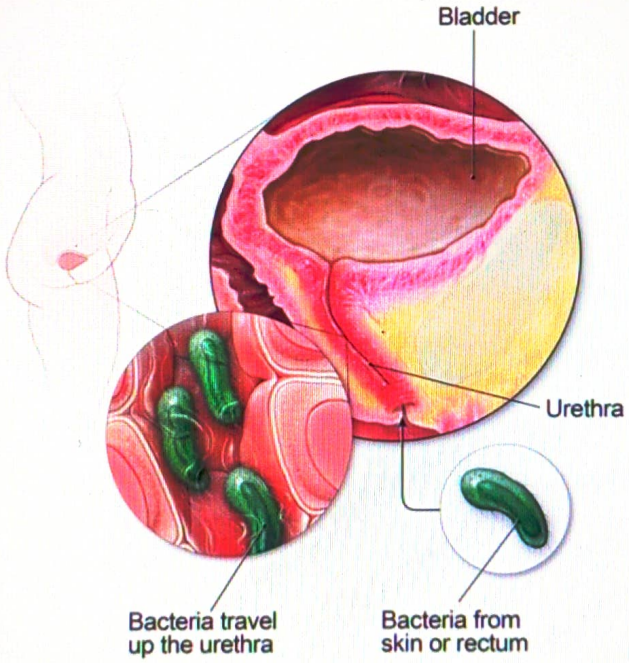


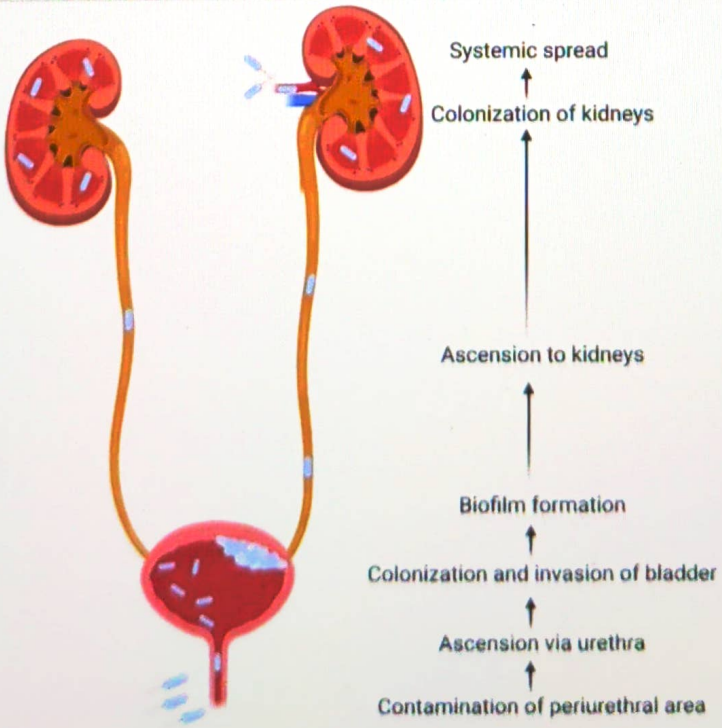


Role of Complement Cascade

- **Pathways**: Classical, alternative, lectin-binding
- **Key proteins**: C3, C5, membrane attack complex (MAC)
- **Diseases**: TTP, atypical HUS, lupus nephritis
- **Therapeutic targets**: C3/C5 convertase inhibitors

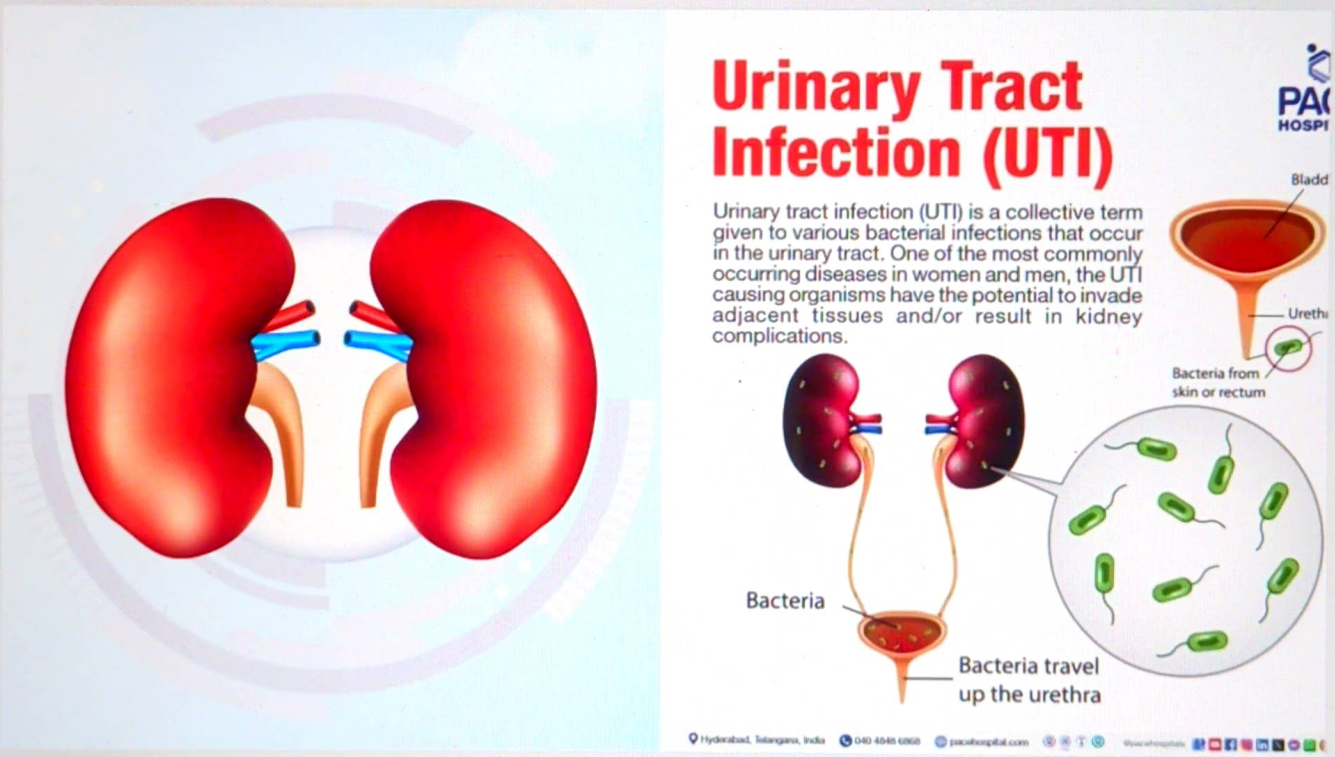


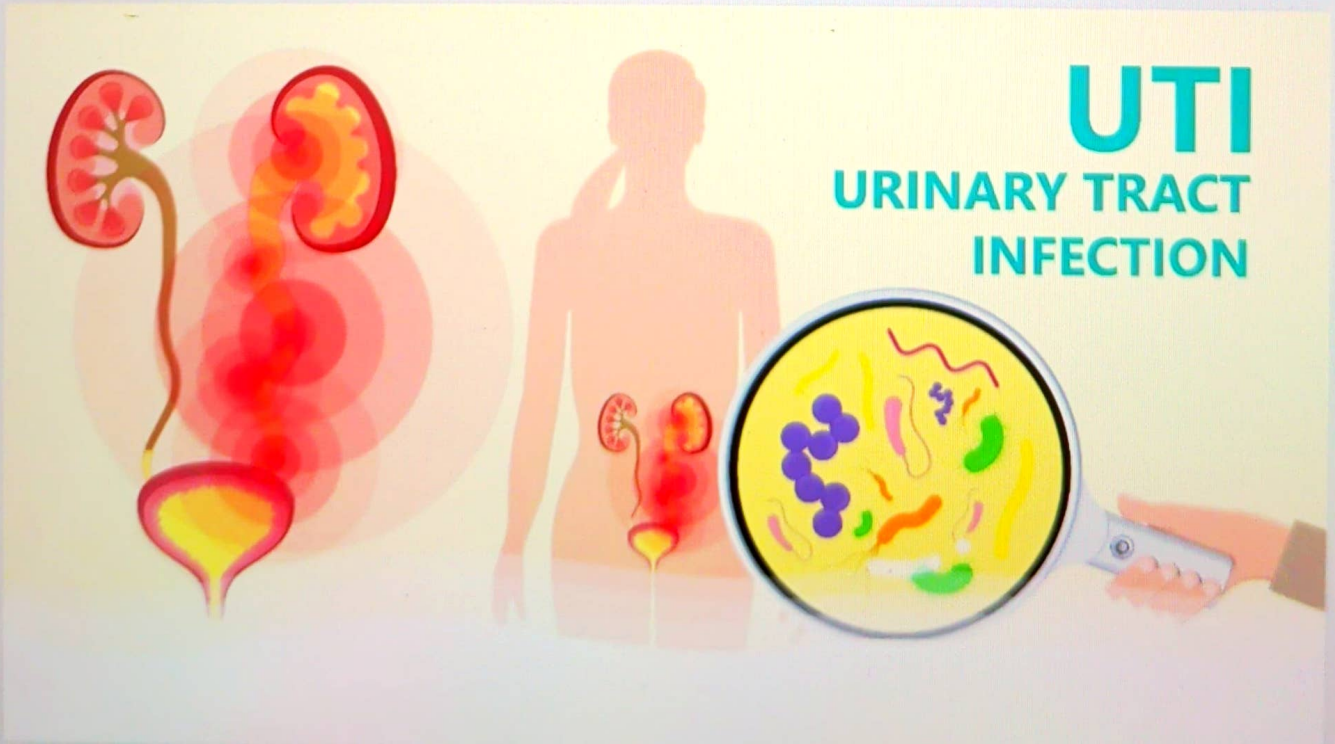




Acute Kidney Injury (AKI) Classification

Type	Causes	Urine Output	Key Features
Prerenal	Shock, dehydration, heart failure	Oliguria	High BUN/Cr, low FENa
Renal	ATN, AIN, GN	Variable	Casts, hematuria
Postrenal	Obstruction, stones, tumors	Anuria/polyuria	Hydronephrosis on imaging

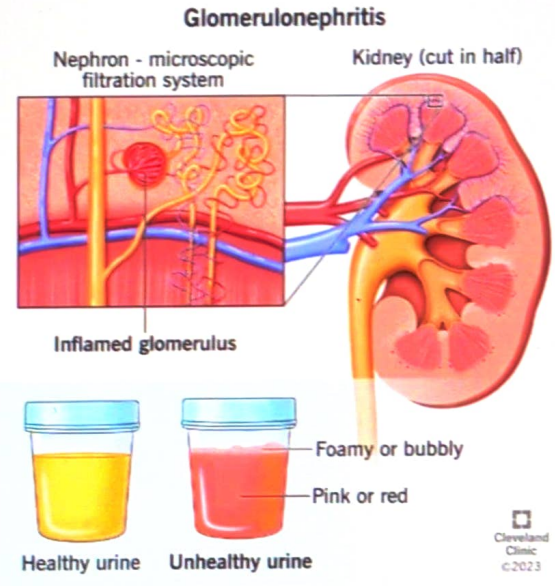




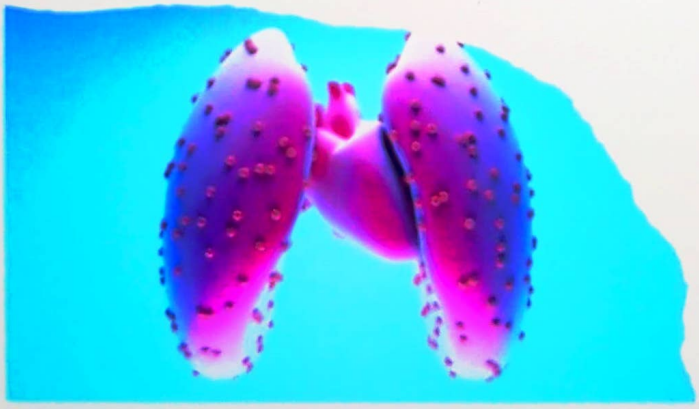
Introduction to Nephritic Syndromes

- **Definition**: Inflammatory conditions affecting kidney structures
- **Causes**: Infections, autoimmune diseases, medications, toxins
- **Symptoms**: Flank pain, costovertebral tenderness, edema
- **Classification**: Based on site (glomerular, interstitial, vascular) and time course (acute, subacute, chronic)

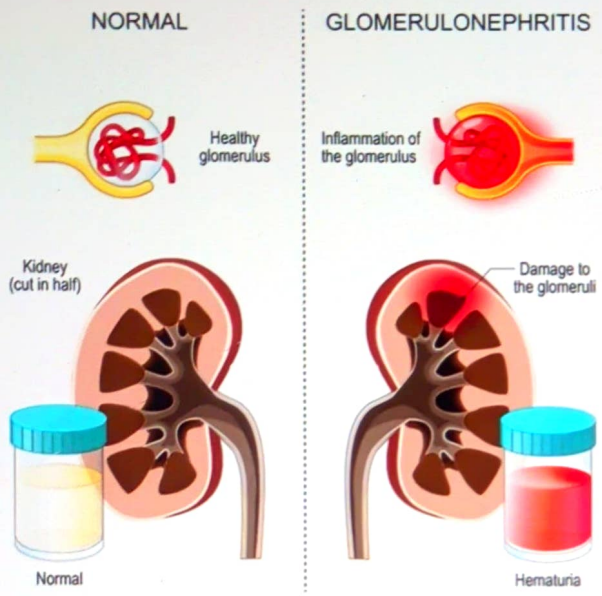




Glomerulonephritis (GN)

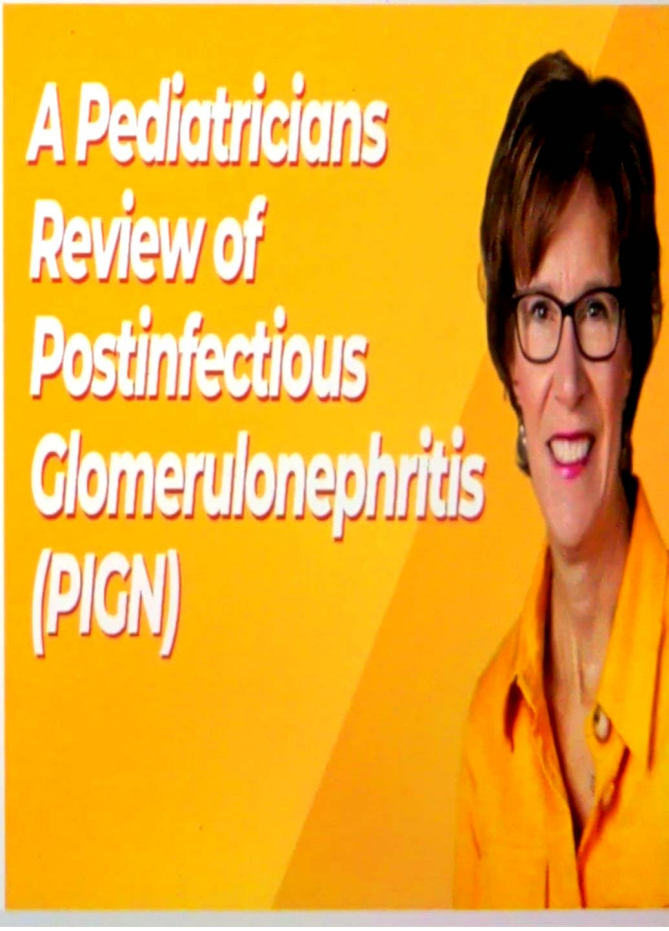


- **Features**: Hypertension, edema, oliguria, abnormal urinalysis
- **Urine findings**: Hematuria, proteinuria, dysmorphic RBCs, casts
- **Disease course**: Acute (e.g. PIGN), subacute, or chronic progression
- **Diagnosis**: History, physical exam, spun urinary sediment

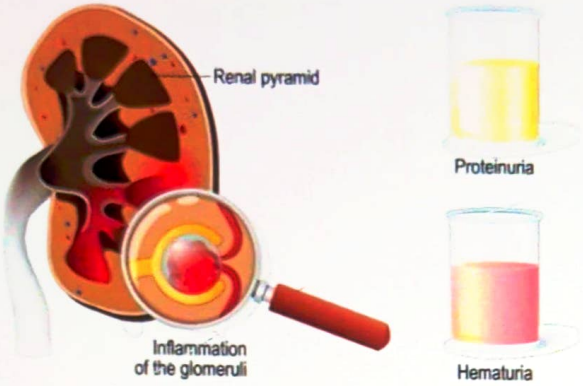


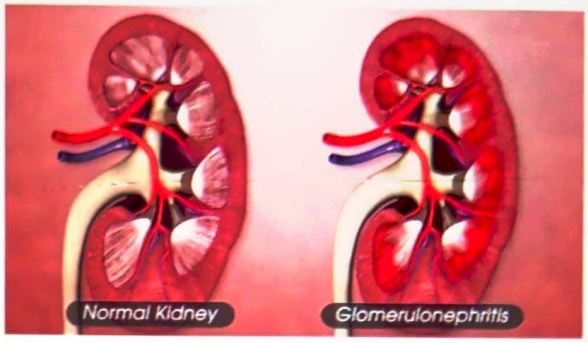
Postinfectious GN (PIGN)

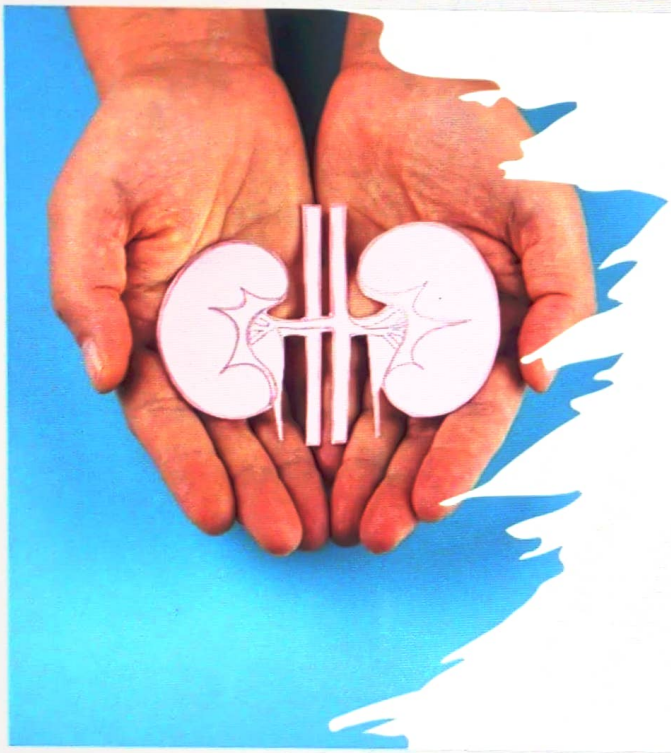
- **Cause**: Immune complexes post-streptococcal infection
- **Complement**: Low serum C3 due to activation cascade
- **Urine findings**: Active sediment, oliguria, proteinuria
- **Histology**: Subepithelial "humps," bloodless capillaries



GLOMERULONEPHRITIS

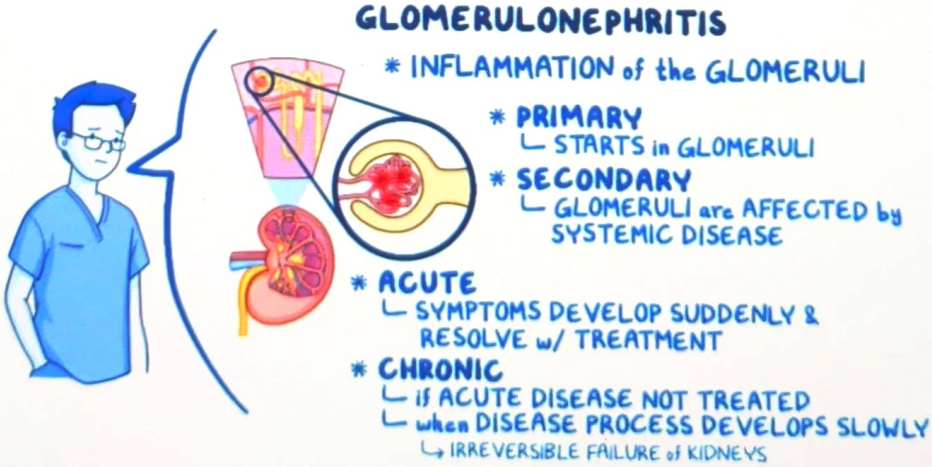




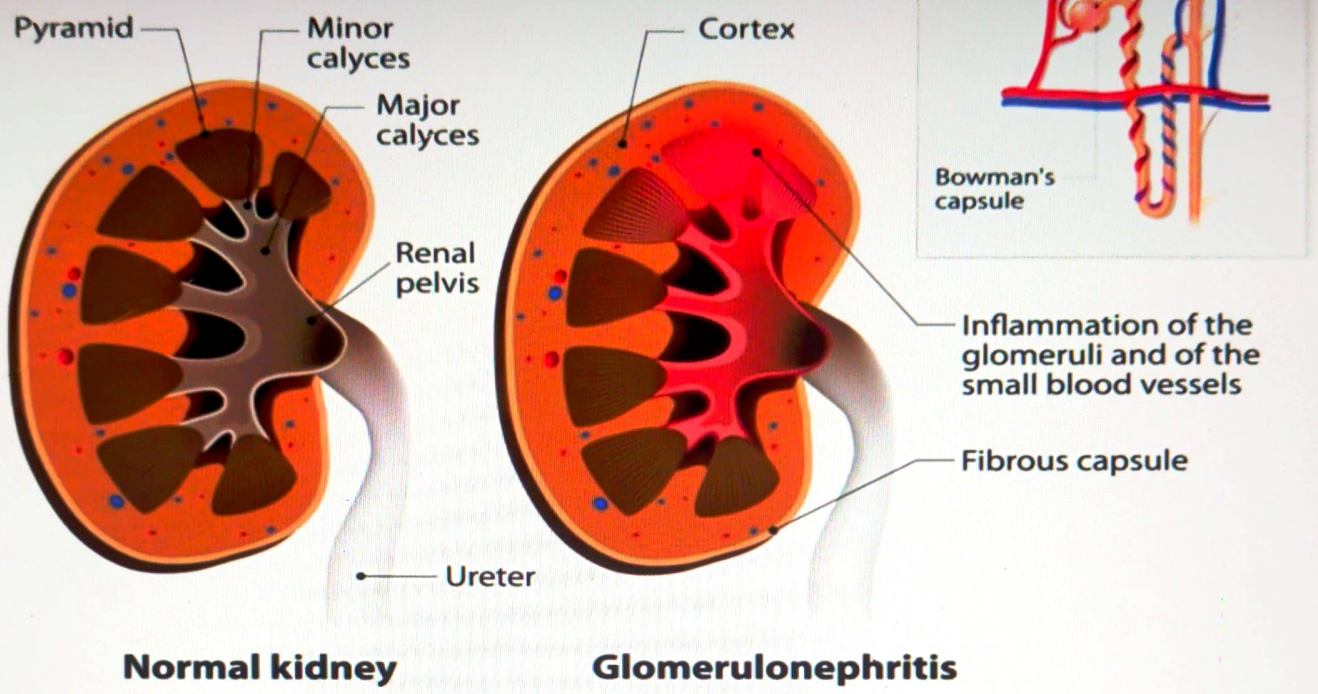


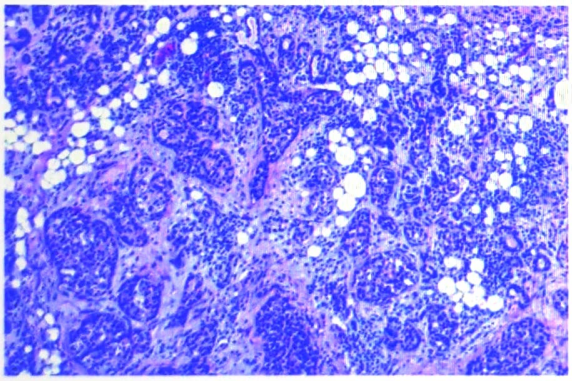
IgA Nephropathy (IgAN)

- **Cause**: Mesangial deposition of galactose-deficient IgA-1
- **Presentation**: Synpharyngitic hematuria, proteinuria
- **Treatment**: ACE inhibitors, corticosteroids, complement blockers
- **Advances**: Biopsy-guided therapy, FDA-approved dual receptor antagonists



GLOMERULONEPHRITIS



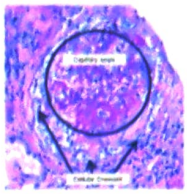


Overview of RPGN

- **Definition**: A nephritic syndrome with rapid loss of kidney function over days to weeks
- **Pathology**: Formation of cellular crescents compressing glomerular capillaries
- **Progression**: Leads to glomerulosclerosis if >50% glomeruli affected
- **Clinical urgency**: Requires prompt diagnosis and treatment to prevent irreversible damage

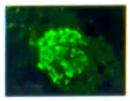
Rapidly Progressive Glomerulonephritis (RPGN)

- Loss of kidney function over a short period of time
- Urinalysis with evidence of glomerular disease (hematuria, proteinuria)
- Crescent formation (extra-capillary proliferation in Bowman's space)



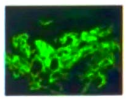
Immune-Complex Mediated

- Presence of immune deposits in glomeruli
- Ex: IgA nephropathy, lupus nephritis, cryoglobulinemia, post-infectious GN



Anti-Glomerular Basement Membrane (GBM)

- Typically circulating autoAb against type IV collagen (α3 chain)
- Linear, ribbon-like GBM staining on IF
- No EM deposits

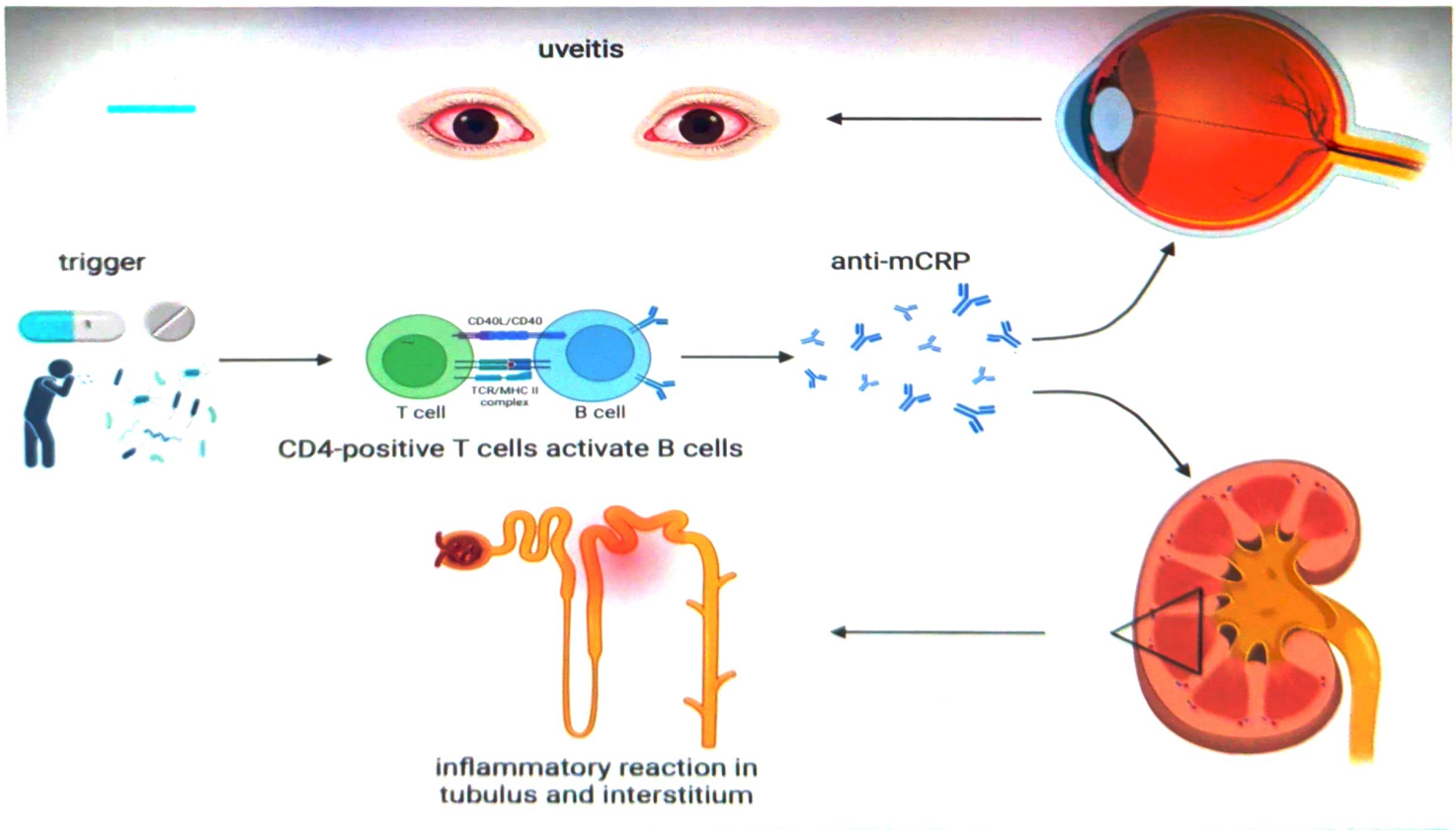


Pauci-Immune

- Minimal immune deposits, negative IF
- Majority anti-neutrophil cytoplasmic antibody (ANCA) +
- c-ANCA: anti-proteinase 3 (CPR) → cytoplasmic neutrophilic staining
- p-ANCA: anti-myeloperioxidase (MPO) → perinuclear cytoplasmic staining

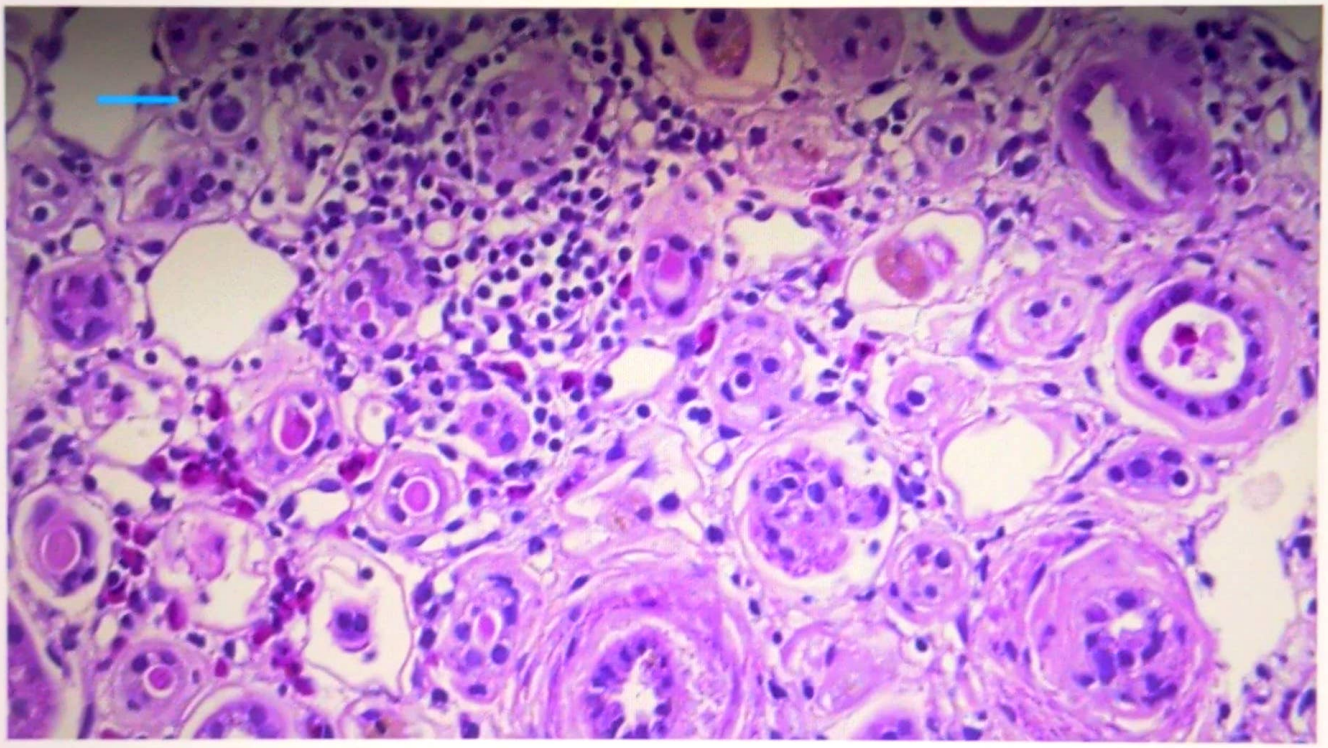


NephSim
www.nephsim.com



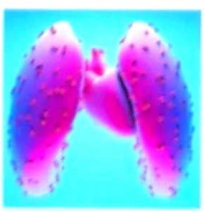
Causes and Diagnostic Clues

- **Immune-mediated**: ANCA-associated vasculitis, anti-GBM disease, immune complex GN
- **Pulmonary-renal syndromes**: Hemoptysis, sinusitis, nasal congestion
- **Key tests**: ANCA, anti-GBM antibodies, renal biopsy
- **Differential clues**: Low complement in immune complex GN; normal in IgA vasculitis



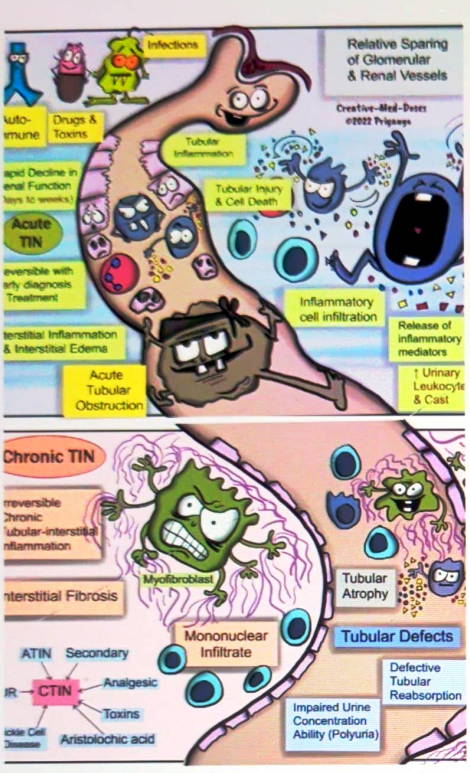
ANCA & Anti-GBM Diseases

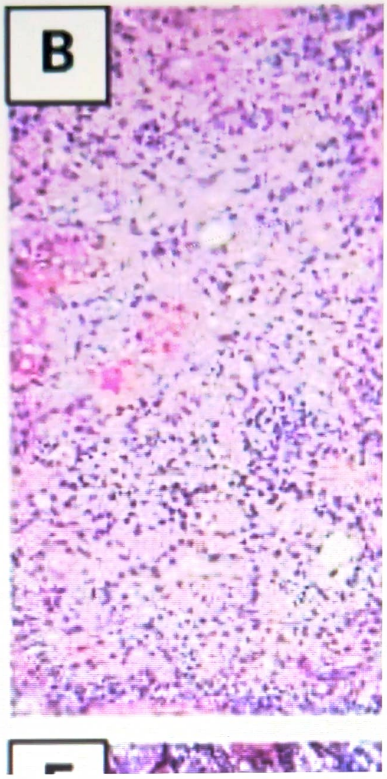


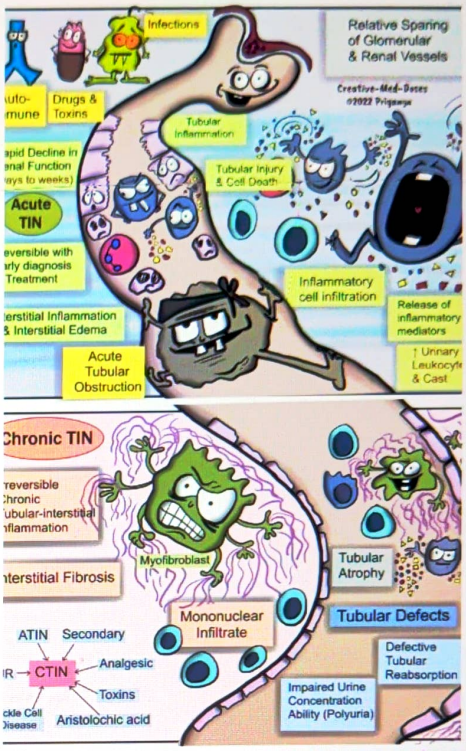


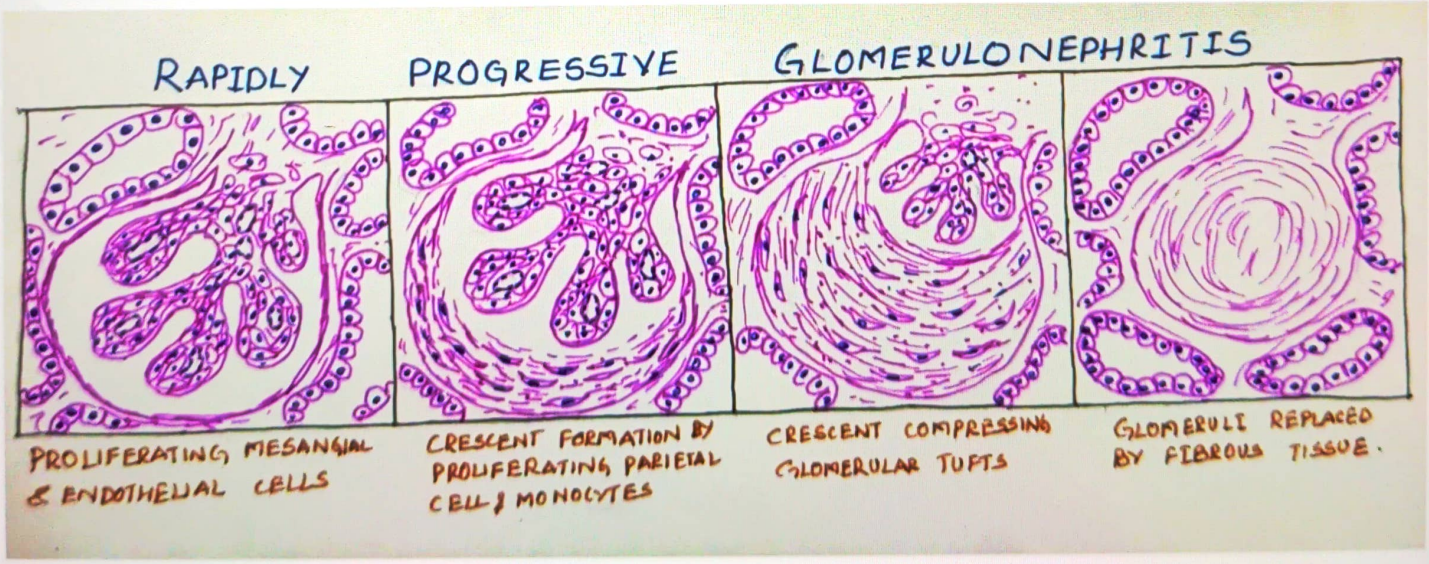


- **ANCA-positive**: Granulomatosis with polyangiitis, microscopic polyangiitis
- **Anti-GBM**: Goodpasture's disease—renal and pulmonary hemorrhage
- **Overlap**: Some cases show both antibodies; treated similarly
- **Treatment**: Plasmapheresis, corticosteroids, cyclophosphamide or rituximab

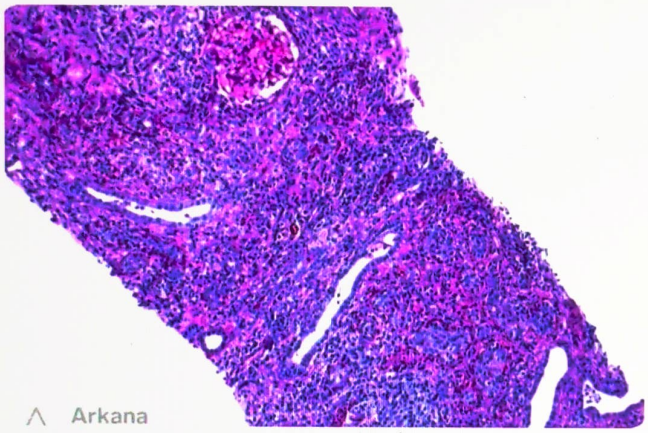

Infections
Relative Sparing of Glomerular & Renal Vessels
Drugs & Toxins
Tubular Inflammation
Tubular Injury & Cell Death
Acute TIN
Inflammatory cell infiltration
Release of inflammatory mediators
Acute Tubular Obstruction
Chronic TIN
Myofibroblast
Tubular Atrophy
Mononuclear Infiltrate
Tubular Defects
Defective Tubular Reabsorption
Impaired Urine Concentration Ability (Polyuria)
ATIN
Secondary
CTIN
Analgesic
Toxins
Aristolochic acid


B

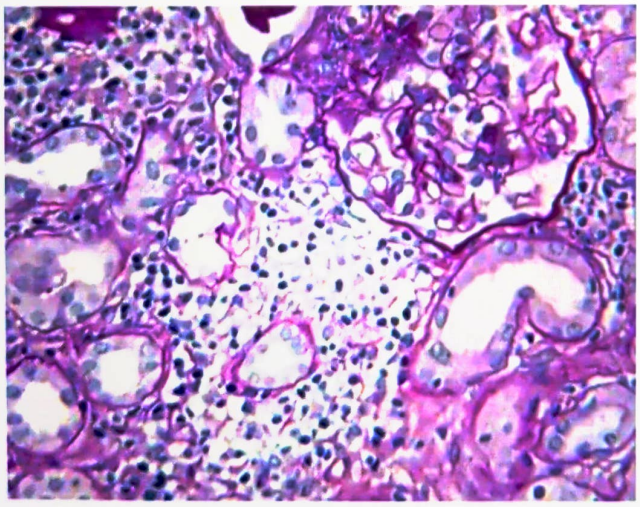

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Chronic TIN
Myofibroblast
Tubular Atrophy
Mononuclear Infiltrate
Tubular Defects
Defective Tubular Reabsorption
Impaired Urine Concentration Ability (Polyuria)
Secondary
CTIN
Analgesic
Toxins
Aristolochic acid


RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS
PROLIFERATING MESANGIAL & ENDOTHELIAL CELLS
CRESCENT FORMATION BY PROLIFERATING PARIETAL CELLS & MONOCYTES
CRESCENT COMPRESSING GLOMERULAR TUFTS
GLOMERULI REPLACED BY FIBROUS TISSUE.

Immune Complex RPGN



- **Examples**: Lupus nephritis, cryoglobulinemia, IgA vasculitis
- **Complement levels**: Low C3 in lupus and cryoglobulinemia; normal in IgA vasculitis
- **Extra-renal signs**: Purpura, arthralgia, GI bleeding
- **Biopsy findings**: Mesangial IgA deposits, subendothelial immune complexes



(Tubulo-) Interstitial Nephritis

Inflammatory cells infiltrate the interstitium:
- Impair tubular functioning, reduced GFR.



Etiologies:

Allergic drug reactions:	NSAIDs, Beta-lactams, Diuretics, Proton Pump Inhibitors, Anti-cancer drugs, etc.
Infections:	Legionella, CMV, Streptococcus, etc.
Other disorders:	Sarcoidosis, SLE.
Signs/Symptoms:	Rash, fever, eosinophilia.
Diagnosis:	Urine: Sterile pyuria, Eosinophiluria, WBC casts, Proteinuria. Biopsy: Histopath.
Treatment:	Remove drug/treat infection.
Histopath:	Interstitial edema with WBC infiltration. Poss. granulomas. Can become chronic with fibrosis, scarring, and atrophy.





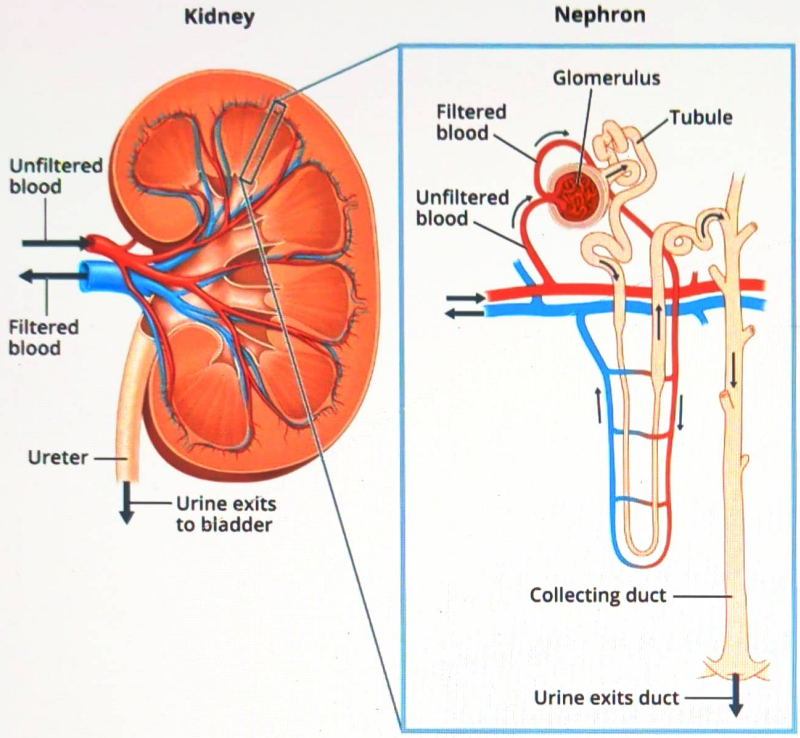


Understanding Proteinuria

- **Definition**: Excess protein in urine; may be glomerular, tubular, or overflow
- **Microalbuminuria**: Early marker in diabetes (30–300 mg/day)
- **Detection**: Dipstick detects only acidic proteins; light chains require immunoelectrophoresis
- **Clinical signs**: Foamy urine, edema, often asymptomatic early







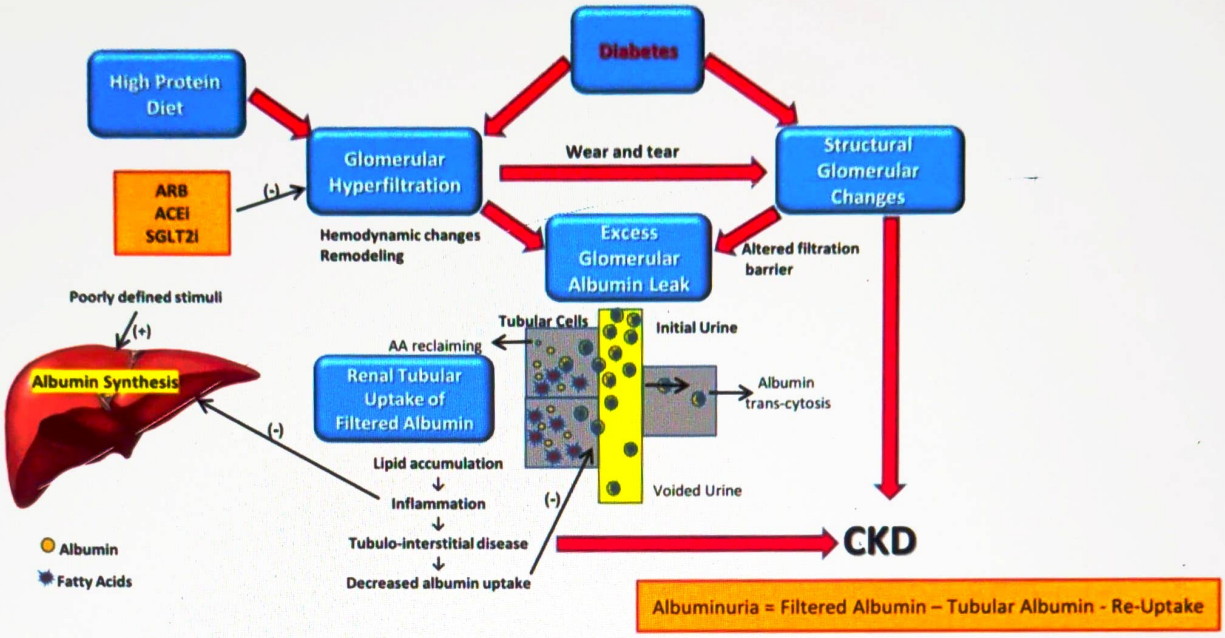
Causes of Proteinuric States

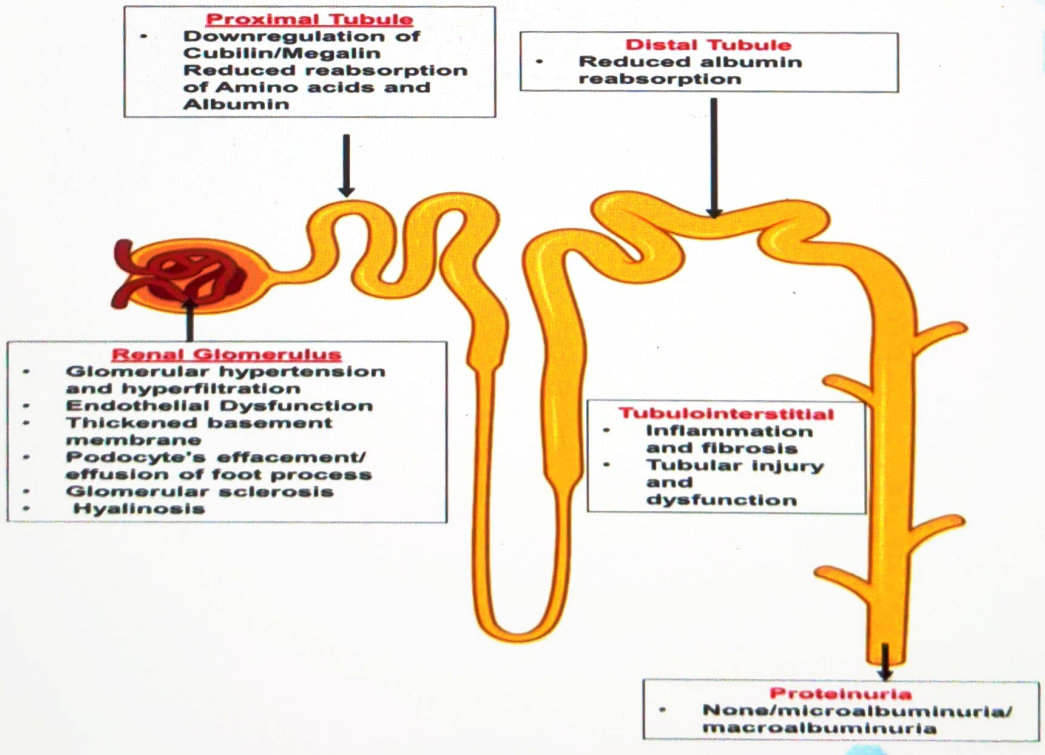


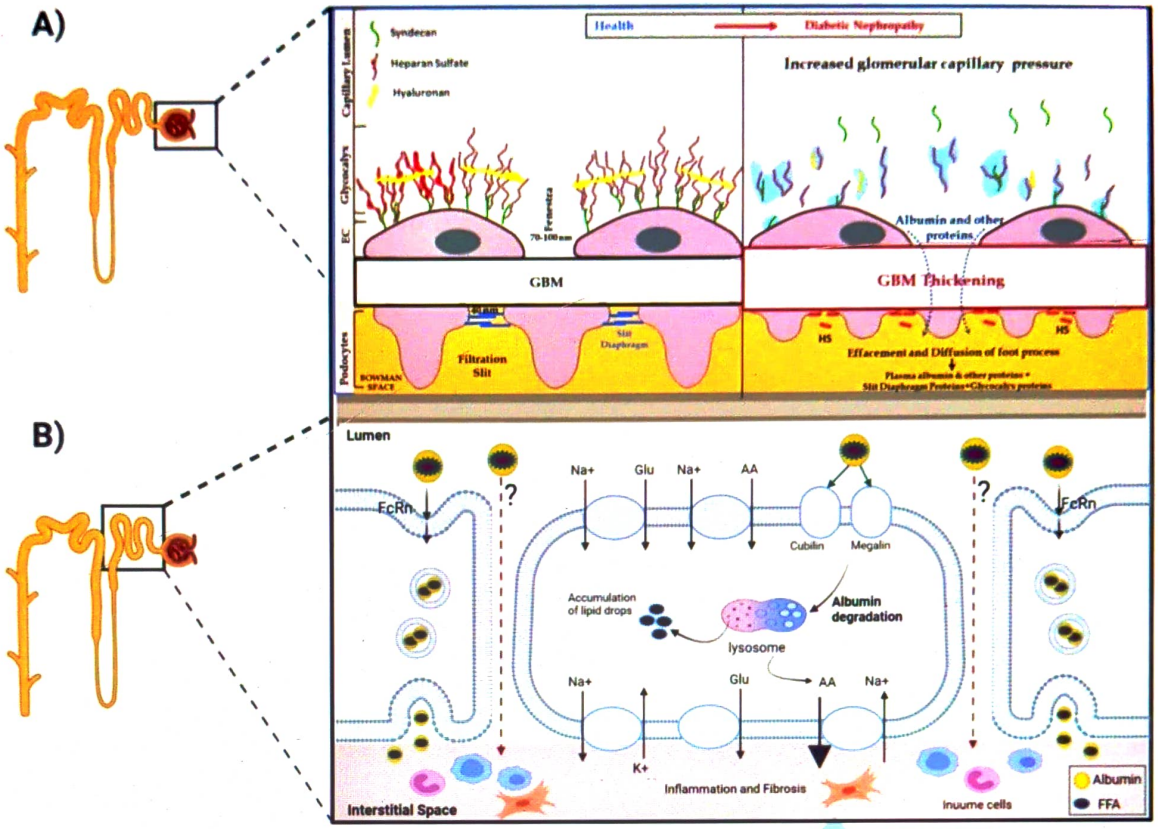


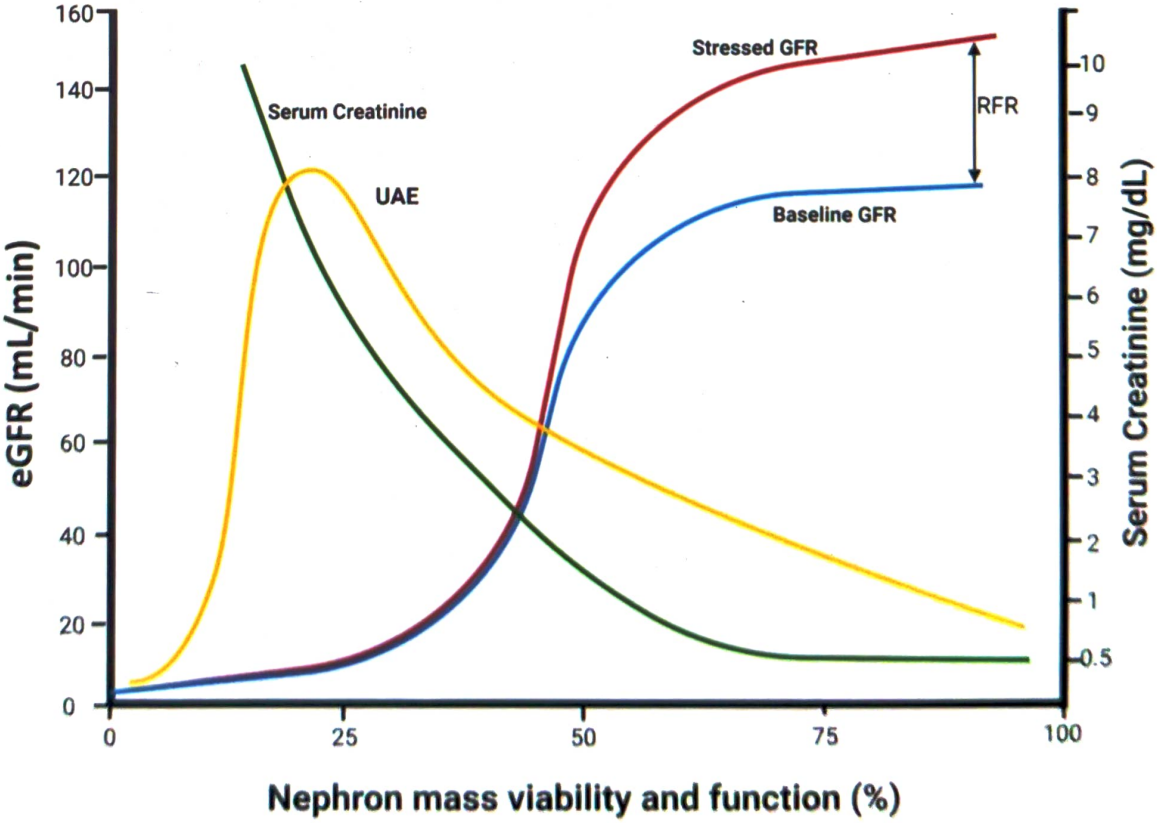


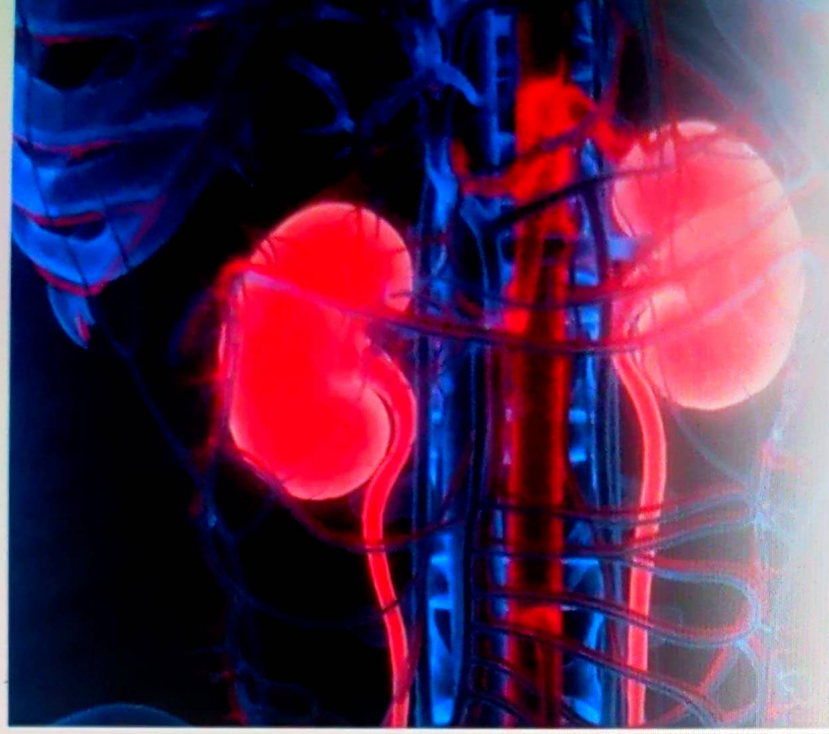
- **Diabetes mellitus**: Microvascular damage leads to glomerular proteinuria
- **APOL1 gene variants**: Risk in African ancestry, triggered by inflammation
- **Overflow proteinuria**: Seen in multiple myeloma (light chains cross glomerular barrier)
- **Other risks**: Hepatitis C, obesity, hypertension, partial nephrectomy


Diabetes
High Protein Diet
Glomerular Hyperfiltration
Wear and tear
Structural Glomerular Changes
ARB
ACEi
SGLT2i
(-)
Hemodynamic changes
Remodeling
Excess Glomerular Albumin Leak
Altered filtration barrier
Poorly defined stimuli
(+)
Albumin Synthesis
Tubular Cells
Initial Urine
AA reclaiming
Renal Tubular Uptake of Filtered Albumin
Albumin trans-cytosis
(-)
Lipid accumulation
Inflammation
Tubulo-interstitial disease
Decreased albumin uptake
Voided Urine
(-)
CKD
Albumin
Fatty Acids
Albuminuria = Filtered Albumin – Tubular Albumin - Re-Uptake


Proximal Tubule
Downregulation of Cubilin/Megalin
Reduced reabsorption of Amino acids and Albumin
Distal Tubule
Reduced albumin reabsorption
Renal Glomerulus
Glomerular hypertension and hyperfiltration
Endothelial Dysfunction
Thickened basement membrane
Podocyte's effacement/ effusion of foot process
Glomerular sclerosis
Hyalinosis
Tubulointerstitial
Inflammation and fibrosis
Tubular injury and dysfunction
Proteinuria
None/microalbuminuria/ macroalbuminuria


A)
B)
Health
Diabetic Nephropathy
Syndecan
Heparan Sulfate
Hyaluronan
Capillary Lumen
Glycocalyx
EC
Podocytes
Increased glomerular capillary pressure
Albumin and other proteins
GBM
GBM Thickening
Filtration Slit
Slit Diaphragm
Effacement and Diffusion of foot process
Lumen
FcRn
Na+
Glu
AA
Cubilin
Megalin
Accumulation of lipid drops
Albumin degradation
lysosome
K+
Inflammation and Fibrosis
Interstitial Space
Albumin
FFA


Stressed GFR
RFR
Serum Creatinine
UAE
Baseline GFR
eGFR (mL/min)
Serum Creatinine (mg/dL)
Nephron mass viability and function (%)
0
20
40
60
80
100
120
140
160
0.5
1
2
3
4
5
6
7
8
9
10
0
25
50
75
100



Nephrotic Syndrome Features

- **Core triad**: Edema, hypoalbuminemia (<3.5 g/dL), proteinuria >3.5 g/day
- **Lipid abnormalities**: High LDL, low HDL, lipiduria with Maltese crosses
- **Edema patterns**: Periorbital, scrotal, vocal cord swelling, bullae formation
- **Unique signs**: Muehrcke's lines on nails, hoarseness from edema

