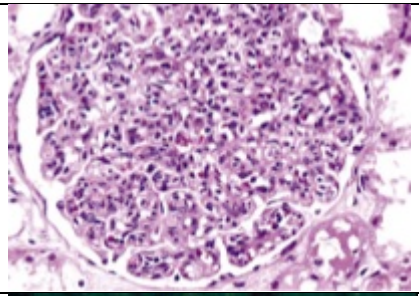
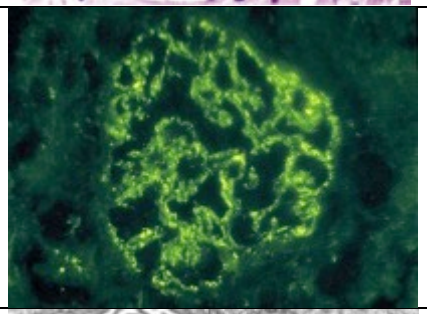
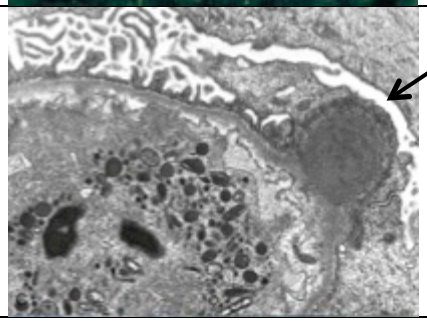
Clinical Manifestations of Renal Disease

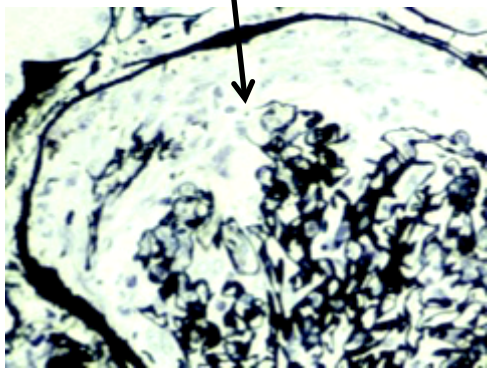
What makes the GBM?	Podocytes = foot processes = visceral epithelial cells (VEC)	
AZOTEMIA	***Elevated BUN & creatinine*** as a result of **decreased GFR** (decreased kidney function); *does not indicate acute or chronic renal failure* **Pre-renal azotemia:** hypoperfusion of the kidneys (i.e. L heart failure) **Post-renal azotemia:** urine flow is obstructed distal to kidney creating back pressure up the nephron (i.e. stones, cancer)	
UREMIA	Complex of signs & symptoms of **CHRONIC renal failure**; indication of significant kidney damage; ***Azotemia + GFR < 20%*** *Pruritis, anorexia, nausea, vomiting, uremic gastroenteritis, sallow (gray) color, anemia, uremic fibrinous pericarditis, peripheral neuropathy*	
NEPHRITIC SYNDROME	**Acute** onset of **hematuria**, **RAPID** ↓GFR, azotemia, oliguria, mild to moderate proteinuria, HTN**, RED CELL CASTS** in the URINE Secondary to glomerular disease; usually characterized by **glomerular inflammation** ***Classic cause of Nephritic Syndrome: POST-STREP GLOMERULONEPHRITIS (APGN)** **Acute Proliferative Glomerulonephritis (APGN):** Post-streptococcal Glomerulonephritis, Post-infectious Glomerulonephritis **Rapidly Progressive Glomerulonephritis (RPGN):** Anti-GBM Disease, Immune-complex mediated, Pauci-immune RPGN	
NEPHROTIC SYNDROME	**MASSIVE PROTEINURIA** (>3.5 g/day), **hypoalbuminemia**, severe **generalized edema**, hyperlipidemia, **LIPIDURIA** Results from abnormalities in the ***glomerular capillary wall*** that leads to increased permeability to plasma proteins ***Classic cause of Nephritic Syndrome: MEMBRANOUS GLOMERULOPATHY**	
	HYPOALBUMINEMIA	Decreased serum albumin secondary to heavy proteinuria that exceeds livers ability to replenish albumin levels Increased renal catabolism of albumin
	GENERALIZED EDEMA	Commonly in **periorbital region** & dependent regions of the body *Secondary to decreased intravascular colloid osmotic pressure* Accentuated by Na^+ & water retention – due to compensatory aldosterone secretion secondary to hypovolemia-enhanced renin secretion
	PROTEINURIA	Principally albumin, but may be further classified as: *Highly selective:* low molecular weight proteins only (i.e. albumin, transferrin) *Poorly selection:* high MW proteins (i.e. IgG) May result in **increased vulnerability to infections** secondary to loss of IgG or **thrombosis** secondary to loss of endogenous anticoagulants (anti-thrombin III) – ***Renal vein thrombosis as a result of Nephrotic Syndrome***
ASYMPTOMATIC HEMATURIA & PROTEINURIA	Secondary to mild glomerular disorders ***Microalbuminuria*** *is the earliest indicator of renal involvement in diabetic patients.*	
ACUTE KIDNEY INJURY	**RAPID** decline in GFR (hours to days), dysregulation of fluid & electrolyte balance (**hyperkalemia**), azotemia, oliguria (<500ml) or anuria (<100ml) Secondary to glomerular, tubular, interstitial, OR vascular disorders of the kidney	
CHRONIC KIDNEY DISEASE	**GFR < 60ml/min for 3 months or greater** Persistent albuminuria; can be clinically silent or present as uremia Most common causes: **diabetes, HTN**	
END-STAGE RENAL DISEASE (ESRD)	**GFR < 5% of normal** Presents as uremia	
RENAL TUBULE DEFECTS	Polyuria, nocturia, & electrolyte disorders	
TUBULOINTERSTITIAL NEPHRITIS	Renal diseases with inflammatory injuries of tubules & interstitium; often insidious in onset & present with azotemia Primary vs. Secondary; Acute vs Chronic;	

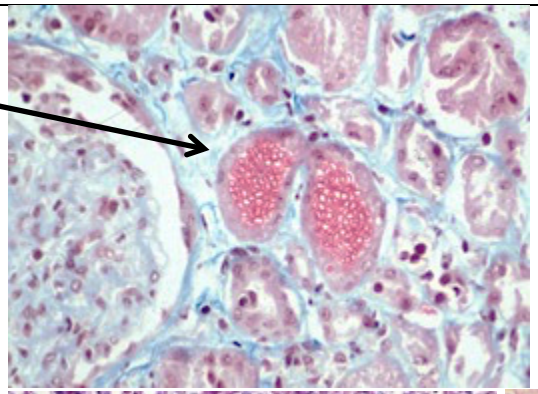
	POST-STREPTOCOCCAL GLOMERULONEPHRITIS: *Nephritic, APGN, Granular* **Children 6-10 years old**
CLINICAL	**NEPHRITIC SYNDROME** w/ malaise, fever, & nausea; **cola-colored urine;** periorbital edema may be present Onset 1-4 weeks after strep infection of pharynx or skin
PATHOGENESIS	**Immune complexes** are formed in the **glomerulus** – *Ag **planted** in subendothelium where Ab attach; IC then elicit inflammatory response via activation of complement; IC dissociates, **migrates** across GBM, & reforms in **sub-visceral epithelium***
LIGHT MICROSCOPY	**ACUTE PROLIFERATIVE GLOMERULONEPHRITIS (APGN)** Enlarged hypercellular glomeruli w/ obliteration of capillary lumens **TUBULAR RBC CASTS*** Interstitial edema & inflammatory infiltrate 
IMMUNO-FLUORESCENCE	**GRANULAR deposits of IgG & C3** in the mesangium & **along the GBM** 
ELECTRON MICROSCOPY	Discrete, amorphous, **ELECTRON-DENSE DEPOSITS** on the **EPITHELIAL SIDE of the GBM** – often have the appearance of **"humps"** *Subendothelial deposits may be seen early in the disease* 

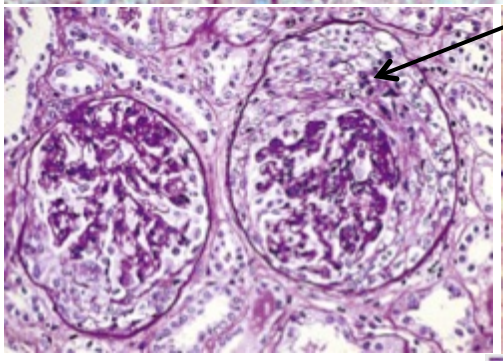
You can also have non-streptococcal acute glomerulonephritis (APGN) from:

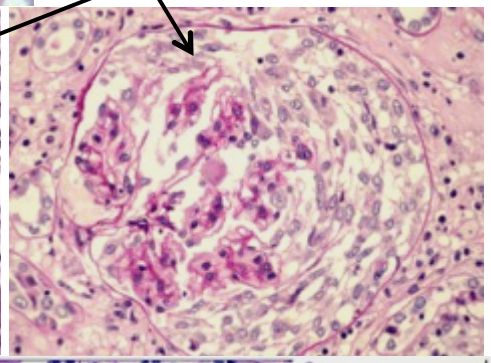
- *Bacterial infections: staphylococcal endocarditis*
- *Viral infections: HepA, HepB, HIV*
- *Parasitic infections: Malaria*

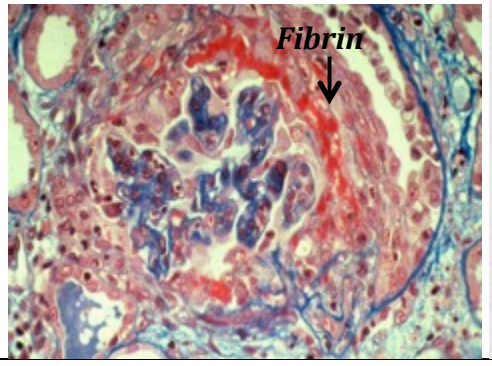
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS: RPGN Types I, II, III)	
CLINICAL	A syndrome characterized by **rapid & progressive loss of renal function** with severe oliguria & **NEPHRITIC** Syndrome: *hematuria, HTN, malaise* **DEATH** from renal failure in weeks to months if no treatment.
LIGHT MICROSCOPY ★	**RED BLOOD CELL CASTS** **FOCAL & SEGMENTAL NECROSIS** Diffuse or focal endothelial & mesangial proliferation **CRESCENTS** – proliferations of **PARIETAL CELLS** **RUPTURE OF THE GBM**

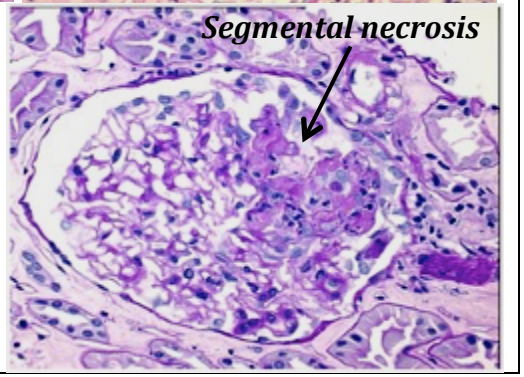


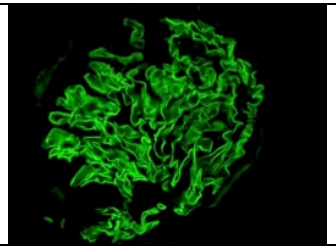


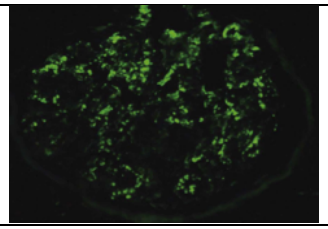








RPGN – TYPE I: Anti-GBM Antibody Males, 20-40 years old		
CLINICAL	Rapid/progressive loss of renal function + **NEPHRITIC SYNDROME** **GOODPASTURE SYNDROME:** Anti-GBM + *pulmonary* involvement **Treatment**: high dose corticosteroids & immunosuppressive drugs	
PATHOGENESIS	Antibody reacts with a peptide within the non-collagenous portion of the α_3 chain of **COLLAGEN TYPE 4** *Unknown trigger for antibody formation (viruses, hydrocarbon solvents, drugs, cancers have been implicated in some cases)*	
LIGHT MICROSCOPY	***See above***	
IMMUNO-FLUORESCENCE	**LINEAR deposits of IgG & C3** in the GBM	

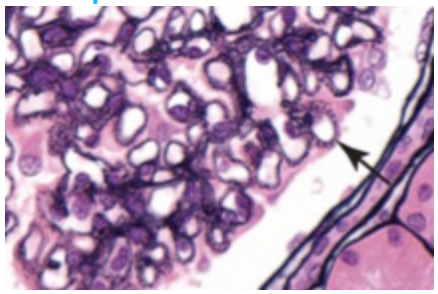
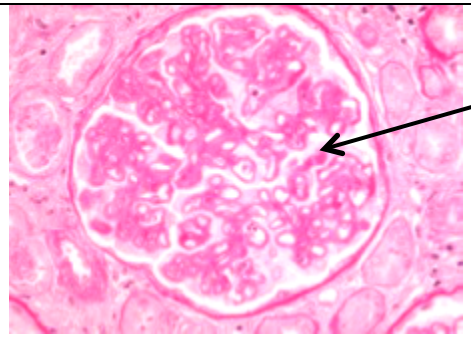
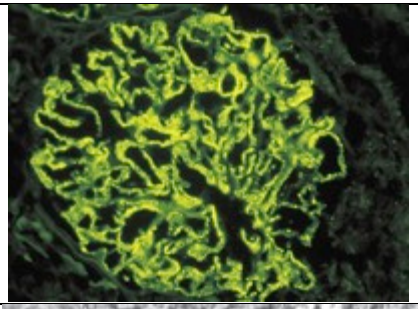
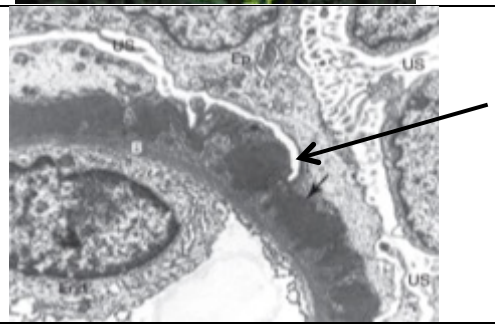
RPGN – TYPE II: Immune Complex Mediated		
CLINICAL	Rapid/progressive loss of renal function + **NEPHRITIC SYNDROME**	
PATHOGENESIS	*Can be a complication of any of the immune complex nephritides – Post-infectious GN, Lupus nephritis, Henoch-Schonlein purpura, IgA nephropathy*	
LIGHT MICROSCOPY	***See above***	
IMMUNO-FLUORESCENCE	**GRANULAR** immune complexes	

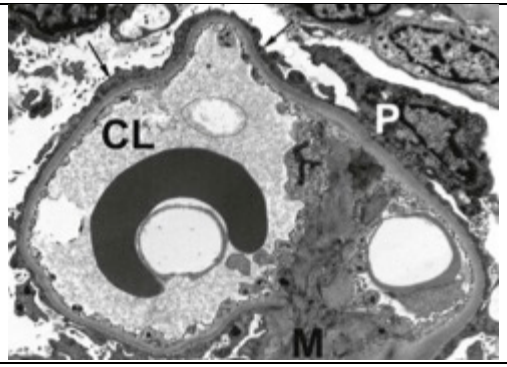
RPGN – TYPE III: Pauci-Immune *Most common RPGN		
CLINICAL	Majority have circulating anti-neutrophil cytoplasmic antibodies (**ANCA**) – **Targets for ANCA:** PR3 (cANCA) & MPO (pANCA) *ANCA-associated, Idiopathic, Wegener's granulomatosis, Microscopic polyangiitis*	
LIGHT MICROSCOPY	***See above***	
IMMUNO-FLUORESCENCE	**LACK** of detectable anti-GBM antibodies or IC in glomeruli	

MEMBRANOUS NEPHROPATHY

***Most common cause of Nephrotic Syndrome in Adults (30%)**

75% of cases are **Primary** (Autoimmune Disorder – linked to **HLA alleles: DQA1**)
Secondary causes: Drugs (penicillamine, captopril), **Malignant tumors** (*Most common with carcinomas of the lung, colon, & melanoma),* SLE, Infections (Chronic Hepatitis B, Hepatis C, Malaria), Autoimmune: thyroiditis

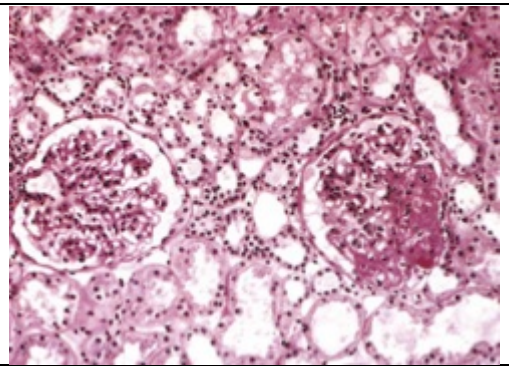
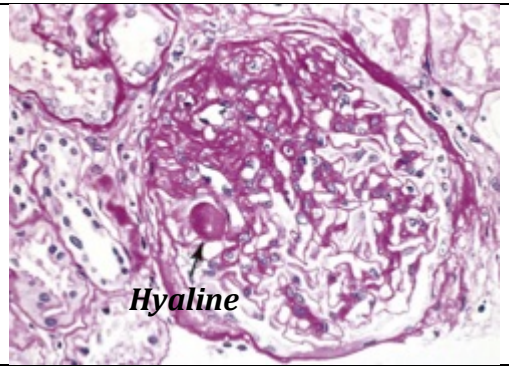
CLINICAL	**NEPHROTIC SYNDROME**: *hematuria & mild HTN* 10% die or progress to **renal failure** in 10 years	
PATHOGENESIS	**Chronic immune complex disease** **Primary MN:** AutoAb to renal antigens; phospholipase A_2 receptor on visceral epithelial cells GBM made leaky by **complement C5b-C9 MAC**, which activates visceral epithelial cells & mesangial cells to liberate proteases & oxidants that injury the capillary wall	
LIGHT MICROSCOPY	**DIFFUSE GLOBAL THICKENING** OF **GLOMERULAR CAPILLARY WALLS** **GBM spike** formation over time  ***Bristles come off BM*** *– visceral epithelial cells start forming BM around the deposits* ****Characteristic of Membranous Nephropathy***	 *IC in membrane causing thick appearance*
IMMUNO-FLUORESCENCE	**GRANULAR** pattern of Ig & complement *along capillary walls*	
ELECTRON MICROSCOPY	**Electron-dense IC deposits** between GBM & visceral epithelial cells (**sub-epithelial – outside the BM**) Foot process effacement of visceral epithelial cells	

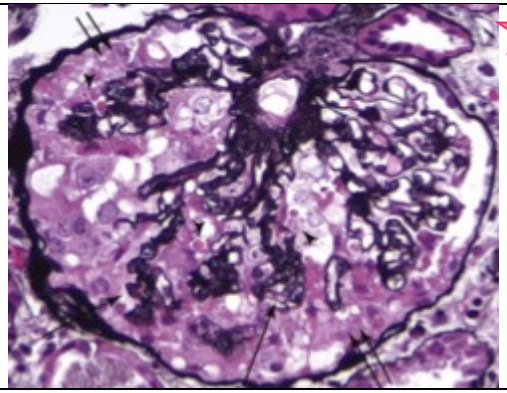
MINIMAL CHANGE DISEASE Most common causes of Nephrotic Syndrome in Children (75%) – Peaks between ages 2 & 6 years old		
CLINICAL	**NEPHROTIC SYNDROME**: highly-selective proteinuria (**hyperalbuminuria**) **NO** HTN or HEMATURIA *Relatively BENIGN disorder – 90% of children have dramatic response to **corticosteroids***	
PATHOGENESIS	Immune dysfunction/inflammatory disorder that leads to synthesis of factors that damage visceral epithelial cells (i.e. **angiopoietin-like-4**) *May follow respiratory infections, certain HLA associations, associated with atopic disorders, increased incidence in patients w/ Hodgkin Lymphoma*	
LIGHT MICROSCOPY	**NORMAL glomeruli**	
IMMUNO-FLUORESCENCE	**NEGATIVE** – no evidence of Ig of complement	
ELECTRON MICROSCOPY	Visceral epithelial cells show **diffuse effacement of foot processes with loss of slit diaphragms** **Foot process broadening is NOT specific to Minimal Change Disease, but it is the ONLY thing that you see in Minimal Change Disease*	

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)

Most common causes of Nephrotic Syndrome in AFRICAN AMERICAN Adults in the US (35%)

1. In association with HIV, heroin addiction, massive obesity
2. Secondary event reflecting **scarring** of prior necrotizing glomerular lesions
3. Maladaptive response to loss of renal tissue (Renal Ablation FSGS): *progressive, unrelenting movement toward ESRD when you lose >50% of GFR*
4. Associated with inherited forms of Nephrotic Syndrome
   - AR FSGS: mutations in podocin gene normally localized in slit diaphragm
   - AD FSGS: mutations in gene encoding α-actinin 4

CLINICAL	Acute or subacute **NEPHROTIC SYNDROME** + HTN & microscopic hematuria + azotemia	
PATHOGENESIS	Acquired or inherited dysfunction of the glomerular filtration barrier May be secondary to abnormal proteins/structures in VEC or to circulating factors (**Renal Transplant Recurrences**)	
LIGHT MICROSCOPY	Focal & Segmental **COLLAPSING** of capillaries & sclerosis Increase in matrix Entrapment of plasma proteins along capillary wall – **HYALINOSIS** Associated tubular atrophy & interstitial fibrosis	 
IMMUNO-FLUORESCENCE	Entrapped **IgM & C3** in sclerotic areas +/- mesangium	
ELECTRON MICROSCOPY	Diffuse effacement of **VEC** foot processes	

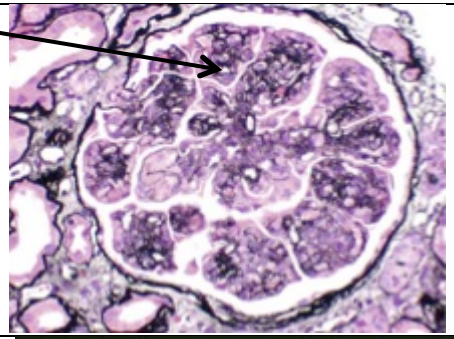
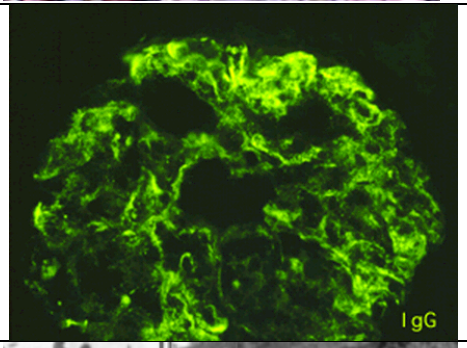
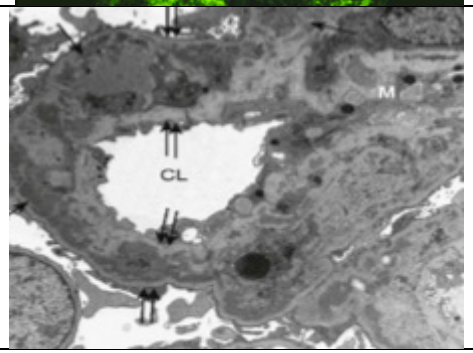
HIV-ASSOCIATED NEPHROPATHY *Most common cause of ESRD in HIV-1 (+) patients; principally affects patients of AFRICAN descent		
CLINICAL	**NEPHROTIC SYNDROME** *Rapidly progresses to ESRD, if untreated* **Treatment:** steroids & ACE inhibitors appear to improve renal function	
PATHOGENESIS		
LIGHT MICROSCOPY	**COLLAPSING GLOMERULOPATHY** – Marked hypertrophy & proliferation of **VECs** – Collapse of entire glomerulus – *A variant of FSGS* **Tubuloreticular inclusions** in endothelial cells – tubular injury & ***microcysts***	 **NOT a crescent because it's not made up of parietal epithelial cells, but it is a proliferation & expansion of the visceral epithelial cells*
IMMUNO-FLUORESCENCE		
ELECTRON MICROSCOPY		

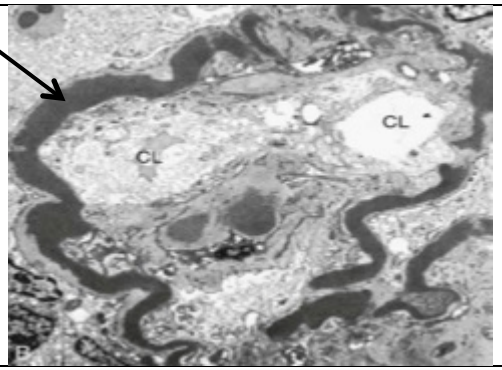
Membranoproliferative Glomeruonephropathy (MPGN): A ***pattern*** of immune-mediated injury representative of many causes.

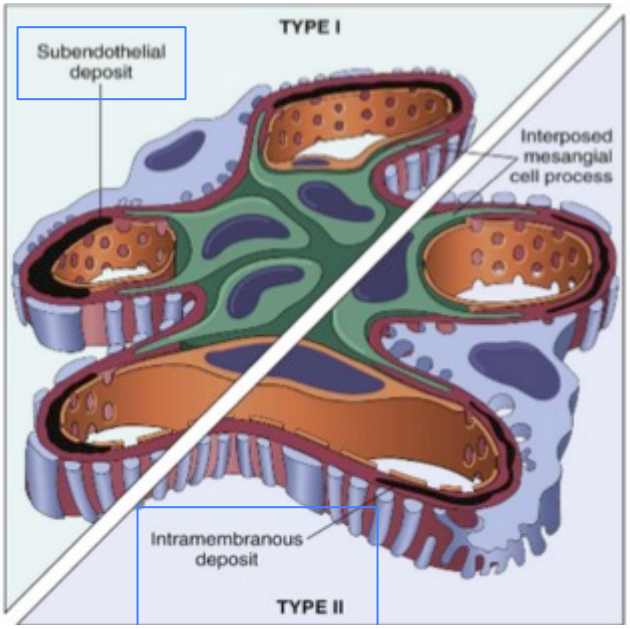
Primary/Idiopathic: no other systemic disease

Secondary MPGN: *vast majority type 1*

- Chronic Immune Complex Disorders: SLE, HepB, HepC, endocarditis, infected ventriculoatrial shunts (*often follows infection*)
- α_1-antitrypsin deficiency
- **CANCER**, particularly lymphoid tumors, i.e. Chronic Lymphocytic Lymphoma

PRIMARY MEMBRANOPROLIFERATIVE GLOMERULONEPHROPATHY (MPGN) I Adolescents & Young Adults		
CLINICAL	**NEPHROTIC SYNDROME** + hematuria ***Poor response to therapy/Poor prognosis – Most (50%) develop CHRONIC RENAL FAILURE/ESRD within 10 years***	
PATHOGENESIS	Deposition of ICs, **IgG & C3**	
LIGHT MICROSCOPY	Glomeruli are large & **hypercellular** with a **LOBULAR APPEARANCE** Cellularity is principally **mesangial cell proliferation** w/ some endothelial proliferation – *no open capillary lumens* Infiltrating leukocytes	
IMMUNO-FLUORESCENCE	**GRANULAR** pattern of IgG & C3 *Large masses in the inner regions – **mesangium***	
ELECTRON MICROSCOPY	**Sub-endothelial electron dense deposits (ICs)** **GBM is thickened w/ DOUBLE CONTOUR or 'TRAM TRACK'**	

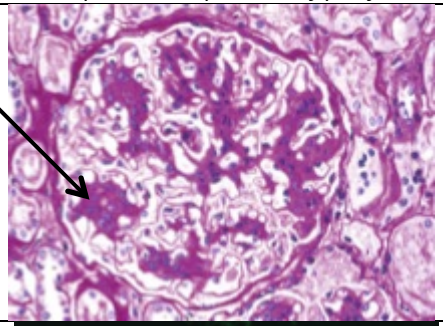
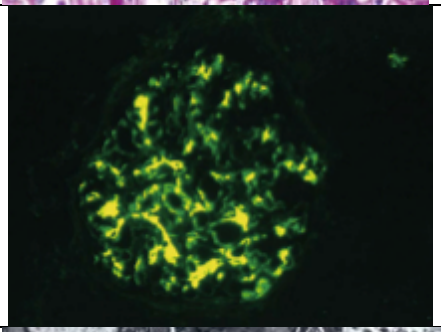
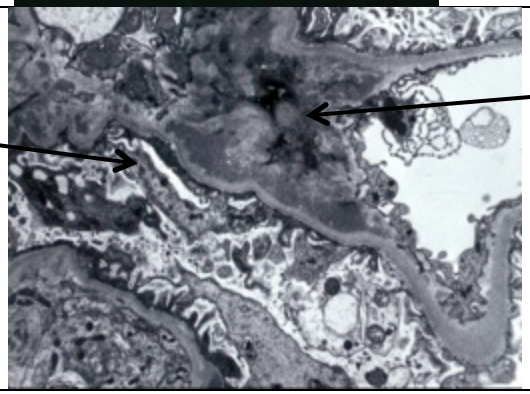
MEMBRANOPROLIFERATIVE GLOMERULONEPHROPATHY II: Dense Deposit Disease Children & Young Adults		
CLINICAL	**NEPHROTIC SYNDROME** and/or Nephritic Syndrome ***Very poor prognosis – Most (50%) progress to ESRD***	
PATHOGENESIS	Results from excessive activation of alternative complement pathway 70% of patients have **C3 Nephritic Factor** – AutoAb that binds **alternative pathway C3 convertase** & prevents its inactivation *(Some patients have decreased liver C3 synthesis – they have low complement levels in their blood)*	
LIGHT MICROSCOPY	**MPGN pattern or just mesangial proliferation**	
IMMUNO-FLUORESCENCE	Irregular **GRANULAR OR LINEAR** GBM staining for C3 NO IgG! MESANGIAL C3	
ELECTRON MICROSCOPY	**Ribbon-like** homogenous electron dense material in GBM	

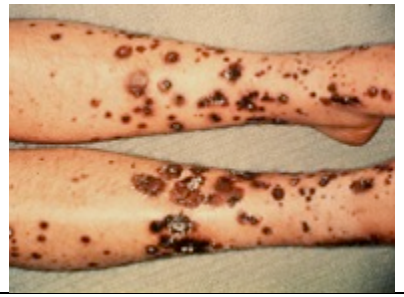


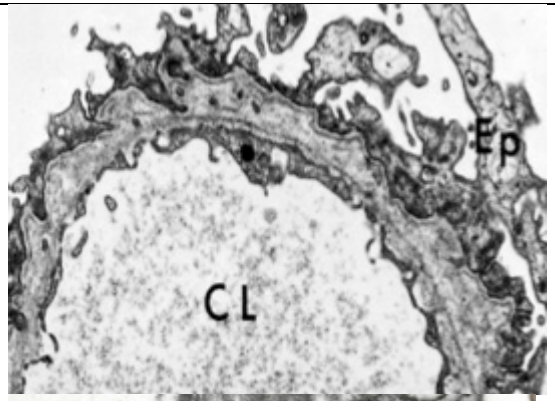
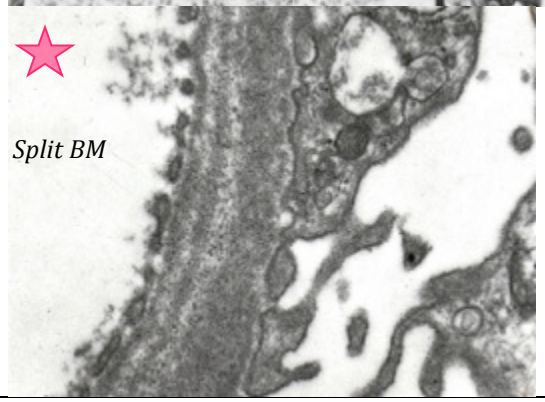
IgA GLOMERULOPATHY

Young Adults & Older Children

***Most common form of glomerulonephritis worldwide**

CLINICAL	Presents as gross **hematuria** ***after URT infection*** (mostly microscopic hematuria) *Hematuria declines after several days, then returns every few months!* ***Most patients have normal renal function for decades – slow progression to chronic renal failure in 15-40% of cases, but most patients do well!*** (5-10% of patients present with Acute Nephritic Syndrome & some with RPGN)
PATHOGENESIS	1. Increase in **plasma polymeric IgA** – *Synthesis increased in response to respiratory (&GI) infections* 2. **Aberrant glycosylation of polymeric IgA**, which forms immune complexes – *Deposition of pre-formed ICs or formation of ICs in mesangium*
LIGHT MICROSCOPY	**Mesangial proliferation** with **increased mesangial matrix** & **cellularity** 
IMMUNO-FLUORESCENCE	Mesangial deposition of **IgA & C3**  ***Classic mesangial proliferation pattern**
ELECTRON MICROSCOPY	**Electron dense deposits** in the mesangium *Foot process broadening also apparent (not as important)* 

HENOCH-SCHONLEIN PURPURA: *In the same family as IgA Nephropathy* **Childhood Syndrome**		
CLINICAL	Child present with purpuric skin lesions, abdominal pain & intestinal bleeding, & arthralgia *Patients normally have an underlying vasculitis (hence, purpuric skin lesions)* **1/3 of patients present with Renal Disease –** *hematuria, Nephritic OR Nephrotic Syndromes* *May represent a* ***spectrum of IgA Glomerulopathy –*** *often follows URI* 	
PATHOGENESIS		
LIGHT MICROSCOPY	Ranges from mild mesangial proliferation to CRESCENTIC GLOMERULONEPHRITIS (RPGN = poor prognosis)	
IMMUNO-FLUORESCENCE	Mesangial deposition of **IgA & C3**	
ELECTRON MICROSCOPY		

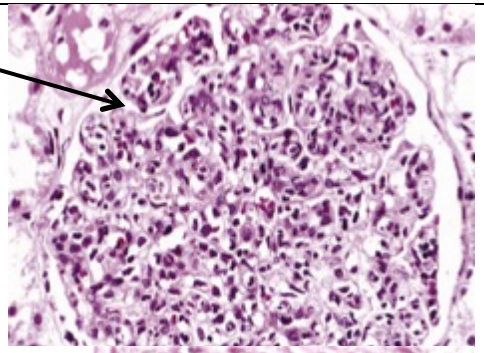
HEREDITARY NEPHRITIS/GLOMERULOPATHY: Alport Disease 5-20 years old (MALES – XLINKED)		
CLINICAL	***CLASSIC TRIAD: Hematuria, Nerve Deafness, Eye Disorders** (Lens dislocation, cataract formation, corneal dystrophy) 90% of affected **MALES** progress to **ESRD** before 40 years old! *Affected females present with only hematuria*	
PATHOGENESIS	Mutations in genes encoding **collagen IV** subunits – results in defective assembly of type IV collagen with secondary dysfunction of GBM	
LIGHT MICROSCOPY	Unremarkable, but **FSGS** *as disease progresses*	
IMMUNO-FLUORESCENCE	NEGATIVE	
ELECTRON MICROSCOPY	Alternating thickening & thinning of the GBM with splitting & lamination – **"basket weave" appearance**	 

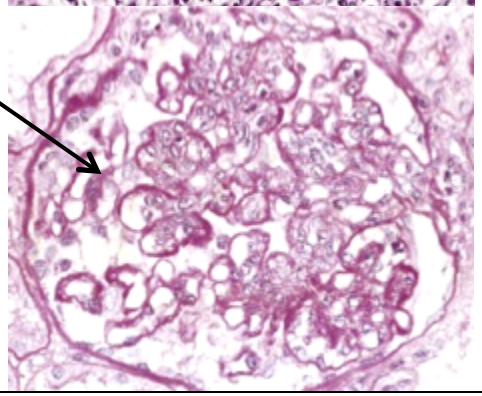
HEREDITARY NEPHRITIS/GLOMERULOPATHY: **Thin Basement Membrane Disease** (Benign Familial Hematuria)		
CLINICAL	Asymptomatic hematuria discovered by **routine** UA w/ variable mild to moderate proteinuria **NORMAL RENAL FUNCTION & Excellent prognosis**	
PATHOGENESIS	Mutations in genes encoding α_3 or α_4 chains of **type IV collagen** *Autosomal inheritance – homozygotes may resemble Alport syndrome*	
LIGHT MICROSCOPY	Unremarkable	
IMMUNO-FLUORESCENCE	Unremarkable	
ELECTRON MICROSCOPY	**Abnormally THIN GBM** (150-225nm vs. normal 300-400nm)	

LUPUS NEPHRITIS (6 classifications)

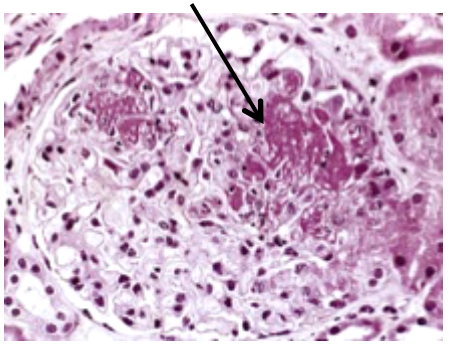
Diffuse Lupus Nephritis: *Most common & severe form of Lupus Nephritis

CLINICAL	Hematuria, proteinuria, & HTN Mild to severe **ACUTE renal failure**
PATHOGENESIS	All glomerular lesions are a result of **immune complex deposition**
LIGHT MICROSCOPY	Endothelial & mesangial cell **proliferation** Leukocytes **(inflammation)** Capillary **THROMBI & NECROSIS** **WIRE-LOOP LESIONS:** eosinophilic thickening of capillary walls
IMMUNO-FLUORESCENCE	IgG, IgA, IgM, & complement in mesangium, capillary walls, sub-endothelial, & sub-epithlial
ELECTRON MICROSCOPY	**Electron dense deposits** that may be continuous in mesangium, capillary walls, **sub-endothelial**, & sub-epithelial **No other disease have deposits in all three*

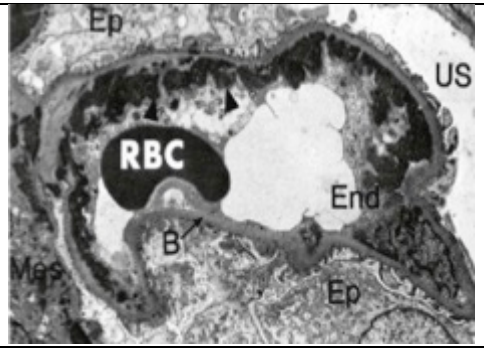


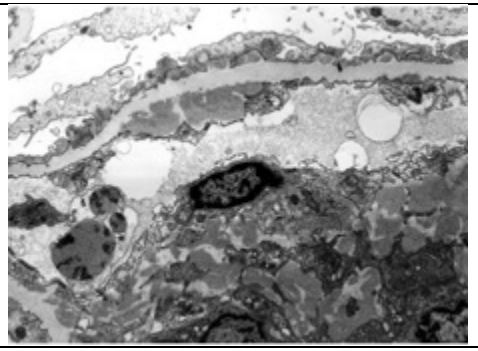


Necrosis



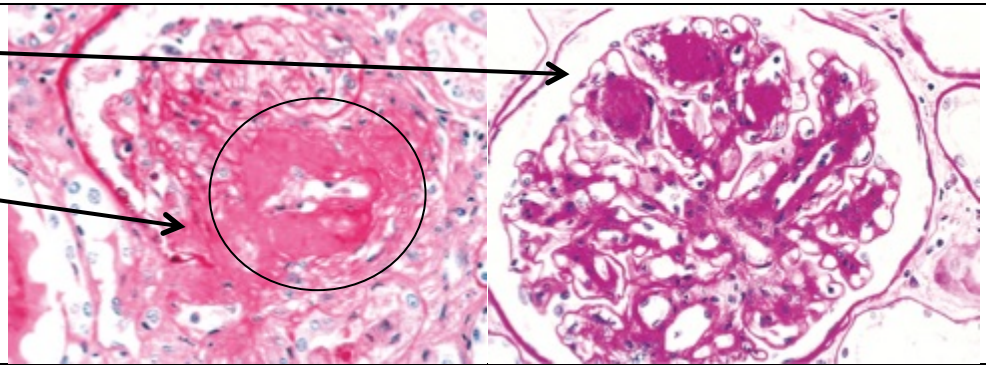
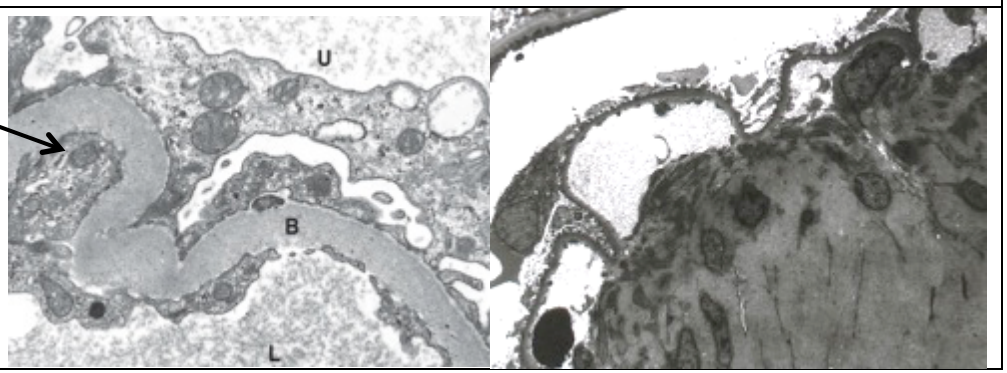
**Note: deposits here are underneath the ENDOthelium, as compared to under the EPIthelium in Membranous*

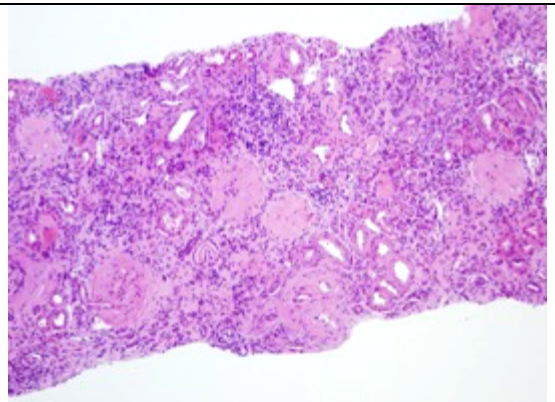
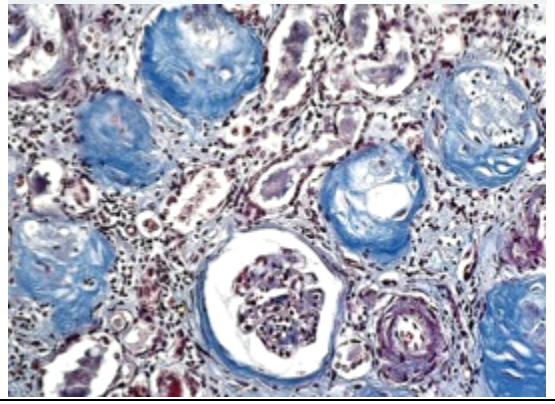




DIABETIC NEPHROPATHY

***Leading cause of Chronic Renal Failure in the US**

CLINICAL	**Microalbuminuria** is the first clinical manifestation of renal disease →30mg/day & less than 300 mg/day *Without treatment, almost all Type I DM & 30% of Type II DM will develop overt nephropathy & macroalbuminuria in 10-15 years* **40% diabetics develop ESRD** – *More frequent in Type I DM; in type II, ESRD occurs more commonly in Native Americans, Hispanics, & African Americans*	
PATHOGENESIS		
LIGHT MICROSCOPY ★	Homogenous, diffuse thickening of GBMs (NO DEPOSITS) **NODULAR GLOMERULOSCLEROSIS (KIMMELSTIEL-WILSON LESION) –** *spherical nodules of expanded mesangial matrix* **HYALINOSIS** of afferent & efferent arterioles	
IMMUNO-FLUORESCENCE	NEGATIVE – no immunoglobulins	
ELECTRON MICROSCOPY	**Homogenous, diffuse thickening of GBMs (NO DEPOSITS)** **Can rupture of the GBM** = *hematuria* *(image on the R predisposed to rupturing)* Foot process broadening (*not as important*)	

CHRONIC GLOMERULONEPHRITIS *End-stage glomerular disease resulting from PRIOR glomerular injury (i.e. PSGN, RPGN) in patients with/without a prior history of glomerular disease*		
CLINICAL	Develops **insidiously** – *can occur years later & patient may be unaware* Presents with **NON-SPECIFIC SIGNS & SYMPTOMS** – anorexia, anemia, weakness, vomiting (UREMIA) + most patients HYPERTENSIVE *Slowly progresses to **Chronic Renal Insufficiency** or **Death by Uremia***	
GROSS	Small kidneys with granular surfaces Thin cortex	
LIGHT MICROSCOPY	***OBLITERATION of glomeruli (scarred)** by collagen, trapped plasma proteins, increased mesangial matrix, & basement membrane-like material Arterial & arteriolar **sclerosis** Tubular atrophy & sclerosis Interstitial fibrosis with mononuclear cell infiltration (**chronic inflammation**)	 
IMMUNO-FLUORESCENCE		
ELECTRON MICROSCOPY		

ACUTE TUBULAR INJURY/NECROSIS

***Most common cause of ACUTE RENAL FAILURE/INJURY in HOSPITALIZED patients (50%)**

CLINICAL

ACUTE Renal Failure; Patients present with signs of uremia (azotemia, etc.) & HTN

Stage 1: Initiation Phase – *36 hours, injury phase, slight ↓UO & ↑BUN*

Stage 2: Maintenance Phase – *sustained ↓UO of 40-400 ml/day (oliguria), Na^+ & H_2O overload, ↑↑BUN,* ***hyperkalemia****, metabolic acidosis, uremia*

Stage 3: Recovery Phase – *↑UO up to 3L/day, hypokalemia*

*Recovery related to magnitude/duration of Acute Tubular Injury; 95% recovery in pts who get supportive care & don't succumb to precipitating cause

PATHOGENESIS

1. Tubular injury

- Tubular epithelial cells (TECs) sensitive to ischemia & have increase increased vulnerability to toxins
- Results in ↑Na^+ delivery is Distal Tubules that incites ***vasoconstriction***. Ischemic TEC releases ***cytokines*** that recruit leukocytes that participate in further damage cells. Detachment of injured TEC with ***obstruction of tubules*** – increased intraluminal pressure with back-pressure ***↓in GFR***

2. Persistent severe disturbances in blood flow

LIGHT MICROSCOPY

Loss of proximal TEC brush borders (ischemic injury) – *earliest indicatory of injury*

Tubular epithelial necrosis along nephron

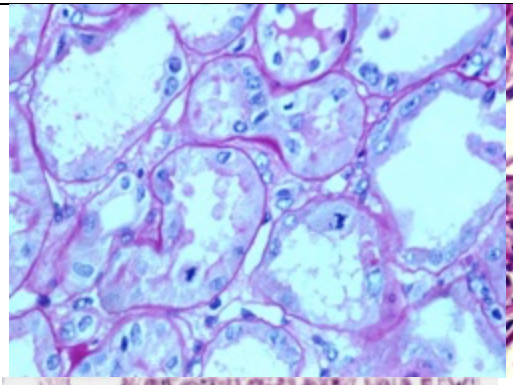
- **ISCHEMIC injury**: **patchy** necrosis
- **TOXIC injury**: **continuous** necrosis

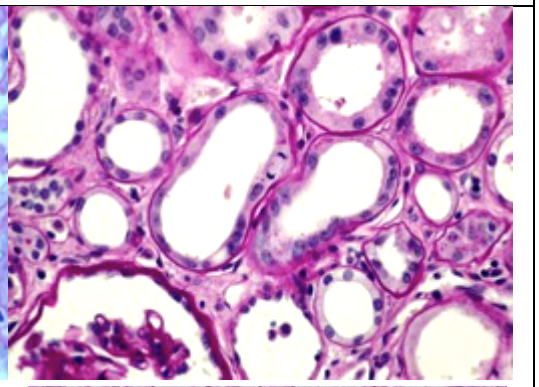
Rupture of tubular basement membrane, *sometimes*

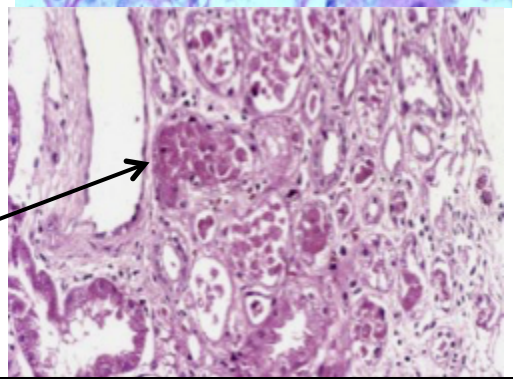
Occlusion of tubular lumens by epithelial cell casts

Regenerative changes denoted by **TEC mitoses**

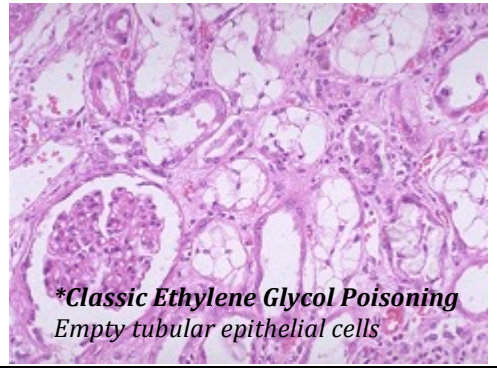
Interstitial edema







Sloughed epithelial cells – this will obstruct & cause back pressure on the glomerulus



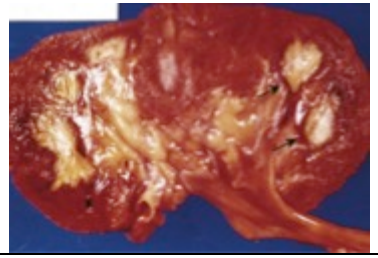
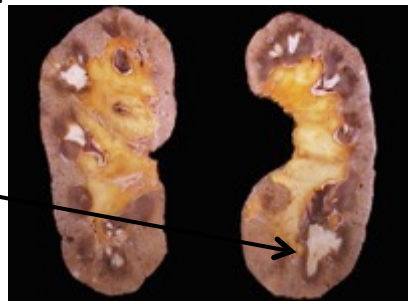
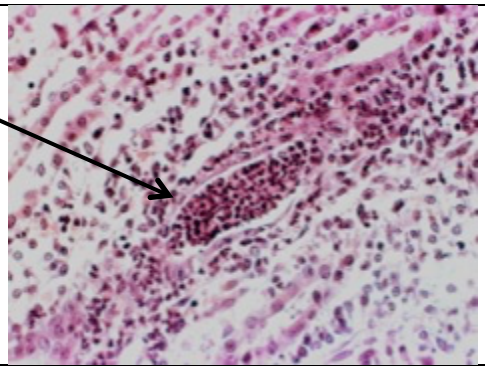
****Classic Ethylene Glycol Poisoning***
Empty tubular epithelial cells

IMMUNO-FLUORESCENCE

ELECTRON MICROSCOPY

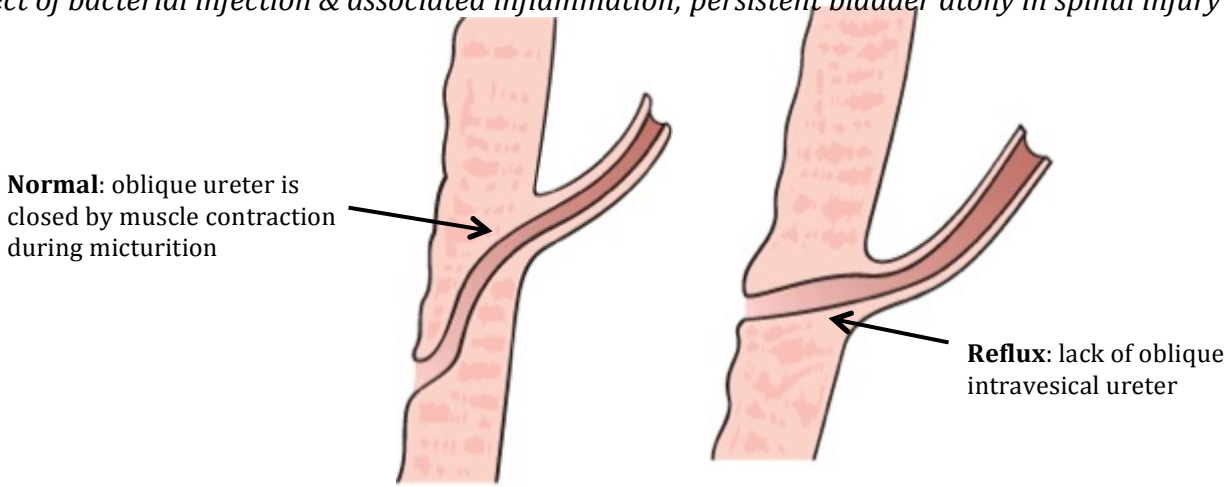
ACUTE PYELONEPHRITIS: Primary Tubulointerstitial Nephritis (TIN)

***Pyelonephritis: Most common cause of Acute Kidney Injury**

CLINICAL	**SUDDEN ONSET** of pain at the **costovertebral angle** Present with *fever & malaise, often bladder & urethral irritation – dysuria, frequency, urgency*; ***leukocyte casts in urine*** **BENIGN** course with antibiotics (*May lead to septicemia if unrelieved urinary tract obstruction, diabetes, or immunodeficiency*)
PATHOGENESIS	**ASCENDING bacterial infection is the most common cause of Clinical Pyelonephritis** – *gram-neg bacilli (E. coli > Proteus > Klebsiella & Enterobacter)* 1. **Colonization of distal urethra** 2. **Urethra to bladder:** *urethral trauma secondary to instrumentation (catheter); in absence of instrumentation,* ***UTIs more common in females*** 3. **Mechanisms of bacterial movement from bladder to kidneys:** – UT obstruction & stasis of urine (*i.e. BPH*) – **Vesicoureteral reflux*** – **Intrarenal reflux***  *Infarcted papillae* 
COMPLICATIONS	– **PAPILLARY NECROSIS:** tips of pyramids; *occurs in* ***Acute Pyelonephritis, Diabetes, Sickle Cell Disease, & Analgesic Nephropathy**** – **PYONEPHROSIS:** renal pelvis, calyces, & ureter filled with pus – **PERINEPHRIC ABSCESS:** results from direct extension
LIGHT MICROSCOPY	**PATCHY interstitial suppurative inflammation** – abscesses may be present (& seen grossly) **INTRATUBULAR AGGREGATES OF NEUTROPHILS*** Neutrophilic tubulitis Tubular necrosis **DOES NOT AFFECT GLOMERULI* 

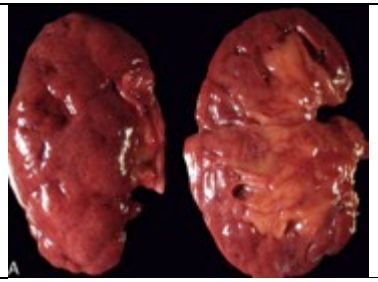
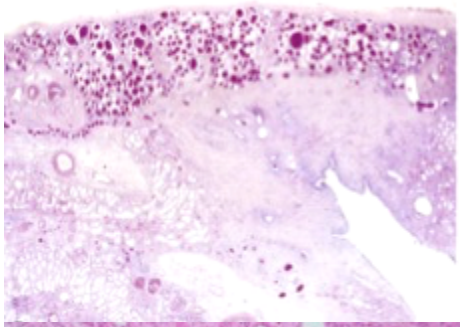
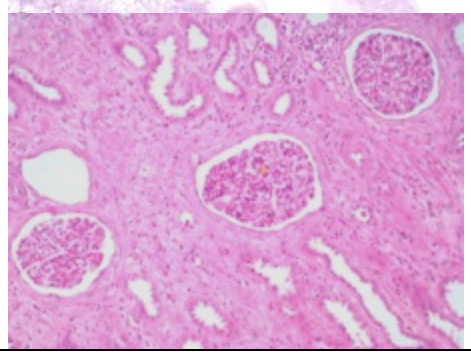
Vesicoureteral Reflux

- Incompetence of vesicoureteral valve allows bacteria to ascend the ureter into the renal pelvis
- *Secondary to congenital absence or shortening of intravesical portion of ureter*
- *Acquired: effect of bacterial infection & associated inflammation; persistent bladder atony in spinal injury*



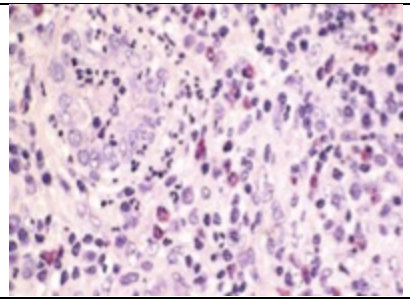
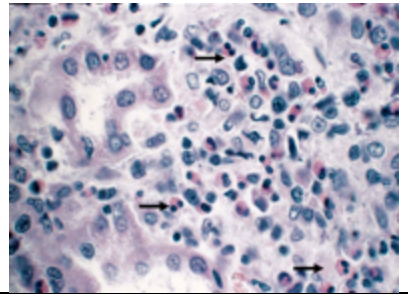
Intrarenal Reflux

- Infected urine propelled into renal parenchyma
  - Through open ducts in renal papillae
  - **Most common in the upper & lower poles of the kidney –** *papillae have flattened or concave tips rather than pointed*

CHRONIC PYELONEPHRITIS: Primary Tubulointerstitial Nephritis (TIN) ***Pyelonephritis: Most common cause of Acute Kidney Injury**		
CLINICAL	Chronic tubulointerstitial **inflammation & scarring** of the calyces & renal pelvis resulting from recurrent episodes of Acute Pyelonephritis May have silent onset or present as **Acute Recurrent Pyelonephritis** *Gradual onset of renal insufficiency & HTN* Subset of patients develop secondary ***focal segmental glomerulosclerosis*** with significant proteinuria up to Nephrotic levels – *Ablative Nephropathy* Reflux Nephropathy & Chronic Obstructive Pyelonephritis	
GROSS	**Irregularly scarred**; *if bilateral, scarring is not symmetrical* Scars overlie flattened papillae & dilated/deformed calcyces Primarily in upper & lower poles (where the concave papillae are)	
LIGHT MICROSCOPY	**Atropic or dilated tubules** Dilated tubules have flattened epithelium & filled with **hyaline-like casts** similar to thyroid colloid – ***thyroidization*** Chronic interstitial inflammation **Interstitial fibrosis** *Glomeruli may be normal or may show fibrous obliteration or periglomerular fibrosis* Fibrointimal hyperplasia of intrarenal arteries **4 structures affected: glomerulus, **tubules, interstitium**, vessels*	 

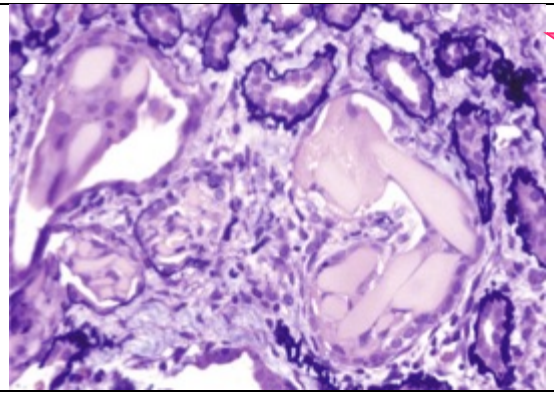
Tubulointerstitial Nephritis

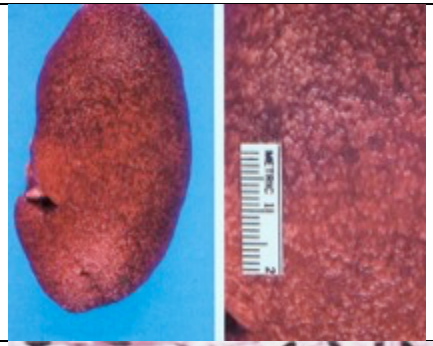
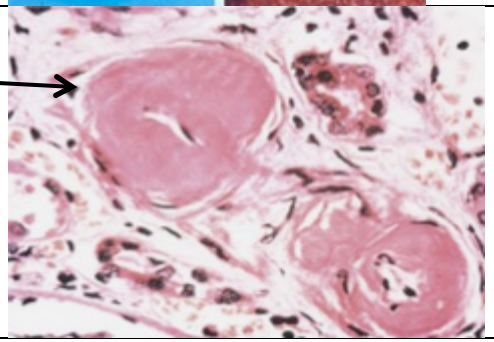
- Second most common cause of Acute Kidney Injury
- Most common cause is drug-induced → triggering of an acute hypersensitivity reaction

ACUTE DRUG-INDUCED INTERSTITIAL NEPHRITIS (AKA Allergic Interstitial Nephritis)			
CLINICAL	Begins 15 days post-drug exposure *Fever, eosinophilia, rash, renal abnormalities – hematuria, mild proteinuria, leukocyturia w/ eosinophils, +* ***AZOTEMIA*** **Treatment:** most patients respond to removal of drug		
PATHOGENESIS	**Most frequent with ANTIBIOTICS (methicillin, ampicillin, rifampin), thiazide diuretics, NSAIDS, & miscellaneous drugs (cimetidine)**		
LIGHT MICROSCOPY	**Interstitial edema** Interstitial mononuclear cells Lots of **eosinophils** commonly in interstitium Tubulitis Acute Tubular Necrosis		

NSAID ASSOCIATED NEPHROPATHY		
CLINICAL	Complications secondary to NSAIDs ability to inhibit cyclooxygenase-dependent prostaglandin synthesis (COX-2), which are expressed in the kidney **Syndromes**: – *Acute kidney injury (azotemia)* – *Acute hypersensitivity interstitial nephritis (AKA allergic interstitial nephritis)* – *Acute interstitial nephritis & Minimal-change disease* – *Membranous nephropathy (cancers: lung, colon, melanoma)*	
PATHOGENESIS		
LIGHT MICROSCOPY		

ACUTE URIC ACID NEPHROPATHY		
CLINICAL	Preciptation of **uric acid crystals** in the renal tubules, particularly **collecting ducts** – Leads to **obstruction of nephrons & acute renal failure**	
PATHOGENESIS	***Associated with chemotherapy of leukemias & lymphomas – Tumor Lysis Syndrome***	
LIGHT MICROSCOPY	Needle-like crystals	

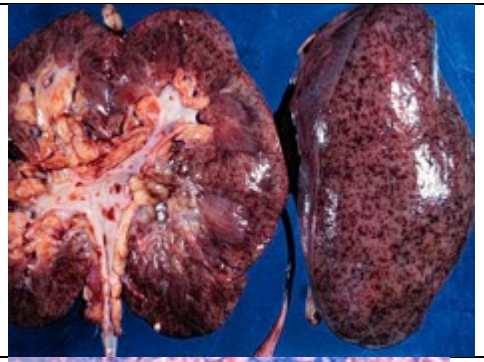
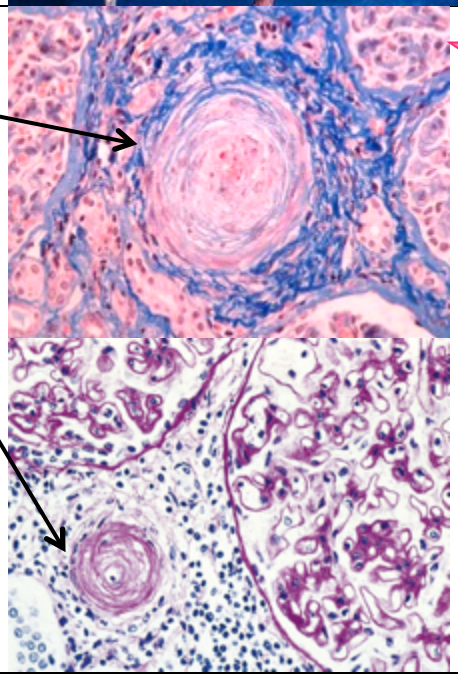
LIGHT-CHAIN CAST NEPHROPATHY/MYELOMA KIDNEY ★		
CLINICAL	***Renal insufficiency*** develops in 50% of patients with **MULTIPLE MYELOMA** & related lymphoplasmacytic neoplasms Most commonly presents as **Chronic Kidney Disease** that has developed insidiously **over months to years**	
PATHOGENESIS	**BENCE-JONES PROTEINURIA** *(monoclonal light chains in urine)* **& LIGHT-CHAIN CAST NEPHROPATHY** – Light chains are toxic to tubular epithelial cells – Form casts that obstruct tubular lumens & create an inflammatory reaction – *Can cause acute tubular injury* **AMYLOIDOSIS of AL type** **Light-chain deposition disease (glomerulopathy)**	
LIGHT MICROSCOPY	**'Fractured' casts surrounded by GIANT CELLS** **If you see this, you would immediately think the patient has malignancy*	 ★

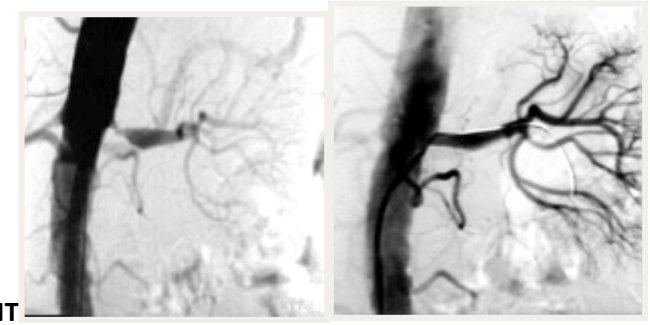
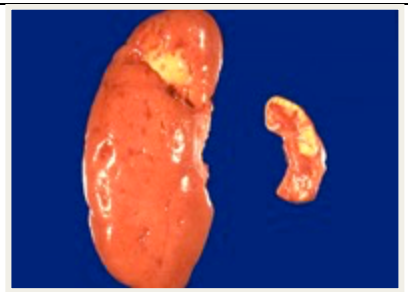
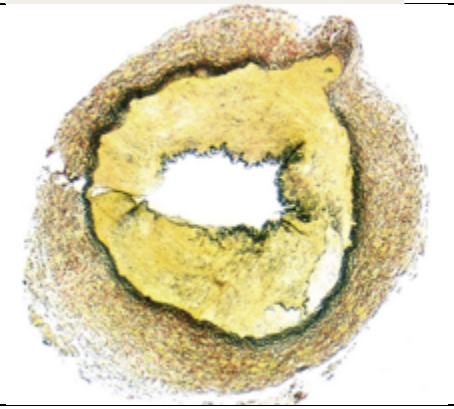
NEPHROSCLEROSIS Strongly associated with **HYPERTENSION**, which is both a cause & a consequence		
CLINICAL	***Sclerosis of renal arterioles & small arteries*** Uncomplicated nephrosclerosis does NOT cause renal insufficiency	
PATHOGENESIS		
COMPLICATIONS	**Patients at increased risk of renal failure: AFRICANS w/ HTN, Elevated BP, Diabetes**	
GROSS PATHOLOGY	Normal to moderate **reduction in size** Fine, evenly-distributed **granularity** of surface Thinning of cortex **"FOOTBALL KIDNEY"**	
LIGHT MICROSCOPY	Thickening & hyalinization of walls of arterioles & small arteries – **hyaline arteriolosclerosis*** **Microscopic subcapsular scars with sclerotic glomeruli** & tubular dropout alternating with normal parenchyma **Fibroelastic hyperplasia** of interlobular & arcuate arteries: medial hypertrophy, replication of internal elastic lamina, intimal myofibroplasia	

MALIGNANT NEPHROSCLEROSIS

1-5% of all individuals with HTN

Primary Form: Younger, Men, Africans

CLINICAL ★	*Renal vascular disorder associated with **malignant hypertension*** **SBP > 200 mmHg + DBP > 120mmHg, papilledema, retinal hemorrhages, encephalopathy w/ convulsions, RENAL FAILURE (+ proteinuria, hematuria)** **EARLY SYMPTOMS:** headaches, nausea, vomiting, visual impairments (i.e. scotomas)
PATHOGENESIS	Initiating event causes **injury to endothelium of renal vessels** *(increased permeability to fibrinogen, platelet deposition)* Release of platelet mitogenic factors (**PDGF**) w/ **hyperplasia of intimal smooth muscle cells** Activation of **RAAS** with **marked intrarenal vasoconstriction** – **THIS IS AN ACUTE VASCULAR DISEASE!**
COMPLICATIONS	Important to treat! 75% survival rate 5years later. Without treatment, 50% mortality in 3 months
GROSS	**Petechial hemorrhages** on cortical surface **"FLEA-BITTEN APPEARANCE"** 
LIGHT MICROSCOPY	**Fibrinoid necrosis** of arterioles – ***glomerular thrombosis, necrosis*** **Concentric intimal proliferation "ONION SKINNING"** of interlobular arteries & arterioles – ***intraluminal thrombosis***  ★

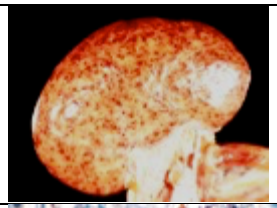
RENAL ARTERY STENOSIS **MALES;** *increased incidence with age and in* ***DIABETES***		
CLINICAL	***Patient with severe HTN who is unresponsive to medications, then you begin to look at secondary causes.*** Most cases secondary to **narrowing of renal artery by ATHEROSCLEROTIC PLAQUES** Some causes due to **FIBROMUSCULAR DYSPLASIA of renal artery** with secondary diffuse ischemic atrophy of kidney parenchyma (**YOUNG FEMALE**) **Treatment: STENT PLACEMENT**  **PRE-STENT** **POST-STENT**	
PATHOGENESIS	Narrowing of renal artery causes stimulation of **renin secretion** by low pressure response of JG apparatus → angiotensin II **(vasoconstriction)**	
COMPLICATIONS		
GROSS	**Scarred (R)**	
LIGHT MICROSCOPY	**FIBROMUSCULAR DYSLASIA**	

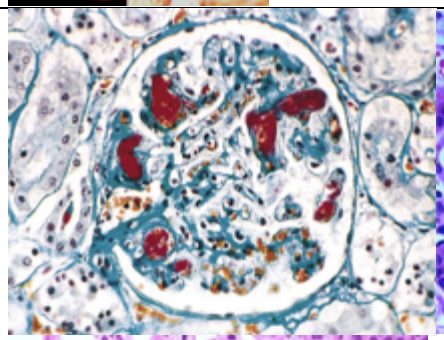
THROMBOTIC MICROANGIOPATHY

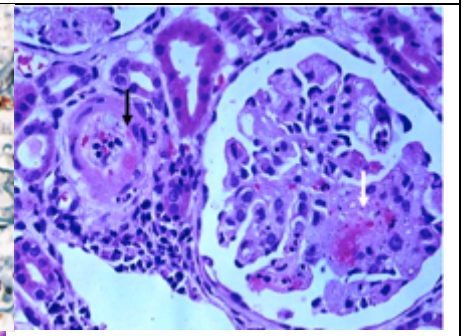
TYPICAL HEMOLYTIC UREMIC SYNDROME (HUS): Epidemic, Classic, Diarrhea-Positive HUS

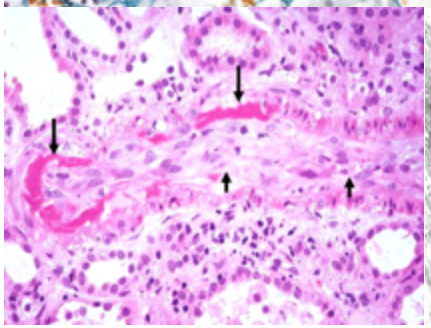
Children & Older Adults

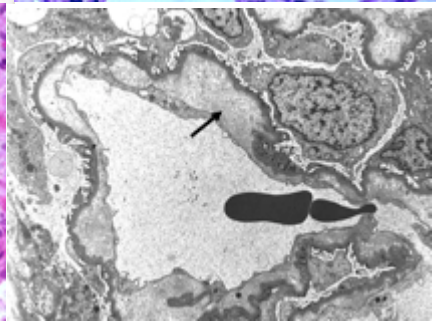
CLINICAL	***Influenza-like or diarrheal prodrome*** ***SUDDEN ONSET*** *of bleeding manifestations (hematemesis, melena), severe oliguria, hematuria, Microangiopathic Hemolytic Anemia, thrombocytopenia, neurologic s/s in a subset, HTN in most* **Treatment: DIALYSIS –** *Most patients recover clinical function*
PATHOGENESIS	Most cases follow **intestinal infection with specific strains of *E. coli* (0157:H7)**, which produces *Shigella dysenteriae-like toxins* **Toxin may:** Activate endothelium, which activates platelets & induces vasoconstriction; Directly activate platelets; Bind Factor H & cause hyperactivation of complement
COMPLICATIONS	7% develop chronic renal disease 15-25 years POST-HUS
GROSS	**Patchy or diffuse CORTICAL NECROSIS** **SUBCAPSULAR PETECHIAE**
LIGHT MICROSCOPY	Glomerular capillaries: – thrombi, particularly platelets – **endothelial swelling** w/ **subendothelial expansion** containing deposits of **fibrin** & **cell debris** **Fibrinoid necrosis** + **occlusive thrombi** in interlobular artery/arterioles – *CHRONIC CASES: increased layering **"ONION SKINNING"*** Acute & chronic ischemic damage to renal parenchyma



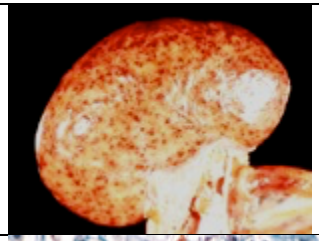
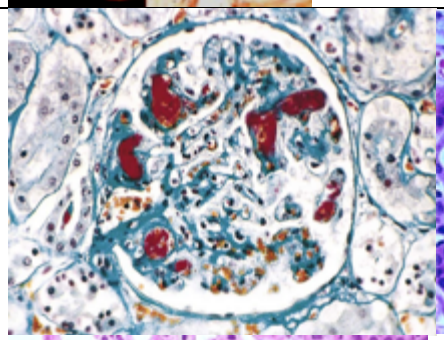
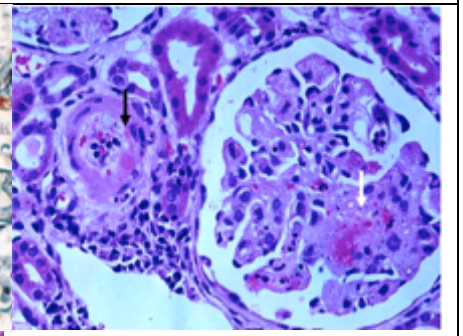
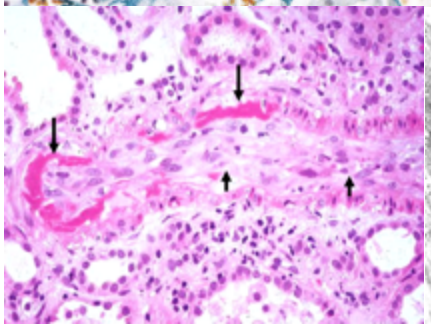
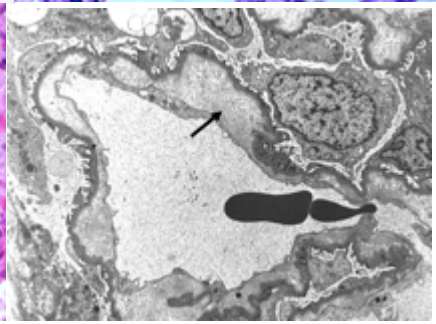








EM: **Very characteristic*

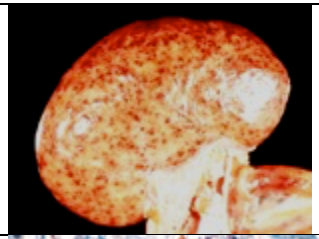
THROMBOTIC MICROANGIOPATHY: ATYPICAL HUS Adults		
CLINICAL		
PATHOGENESIS	Inherited mutations of **abnormal complement regulatory proteins** Acquired causes of endothelial injury (antiphospholipid antibodies, scleroderma, HTN, complications of pregnancy or oral contraceptives)	
COMPLICATIONS		
GROSS	**Patchy or diffuse CORTICAL NECROSIS** **SUBCAPSULAR PETECHIAE**	 *Necrosis – too subtle*
LIGHT MICROSCOPY	Glomerular capillaries: – thrombi, particularly platelets – **endothelial swelling** w/ **subendothelial expansion** containing deposits of **fibrin** & **cell debris** **Fibrinoid necrosis** + **occlusive thrombi** in interlobular artery/arterioles – *CHRONIC CASES: increased layering **"ONION SKINNING"*** Acute & chronic ischemic damage to renal parenchyma	    **EM**: **Very characteristic*

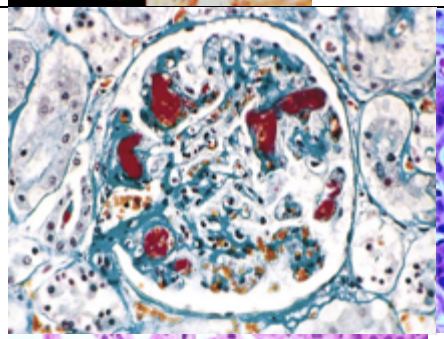
THROMBOTIC MICROANGIOPATHY

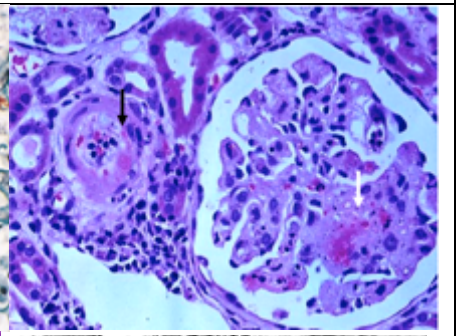
THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

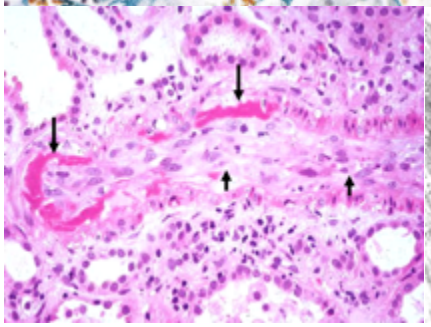
Young Adults < 40 years old

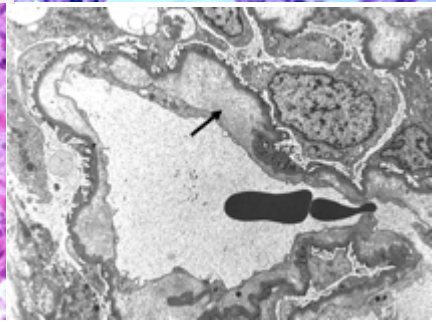
CLINICAL	**CLASSIC PENTAD:** fever, **NEUROLOGICAL SYMPTOMS***, Microangiopathic Hemolytic Anemia, thrombocytopenia, Renal failure **Treatment:** plasma exchange to remove autoantibodies
PATHOGENESIS	Deficiency in **ADAMTS13:** *plasma proteinase that cleaves vWF multimers into smaller sizes* – Most secondary to autoantibodies (FEMALES > MALES) – Some associated with inherited deficiency
COMPLICATIONS	
GROSS	**Patchy or diffuse CORTICAL NECROSIS** **SUBCAPSULAR PETECHIAE**
LIGHT MICROSCOPY	Glomerular capillaries: – thrombi, particularly platelets – **endothelial swelling** w/ **subendothelial expansion** containing deposits of **fibrin** & **cell debris** **Fibrinoid necrosis** + **occlusive thrombi** in interlobular artery/arterioles – *CHRONIC CASES: increased layering **"ONION SKINNING"*** Acute & chronic ischemic damage to renal parenchyma



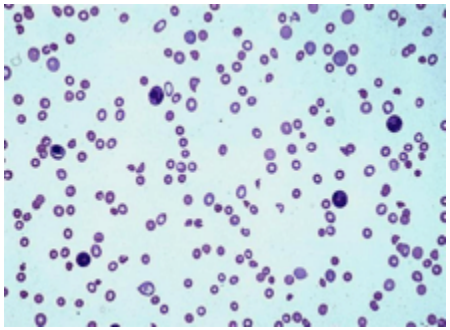




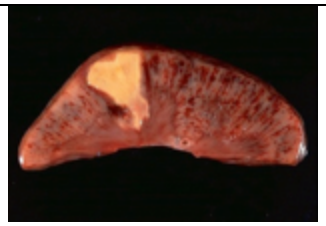


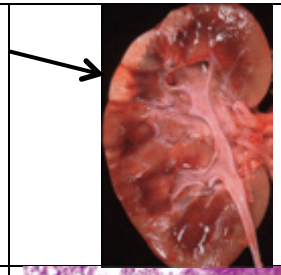
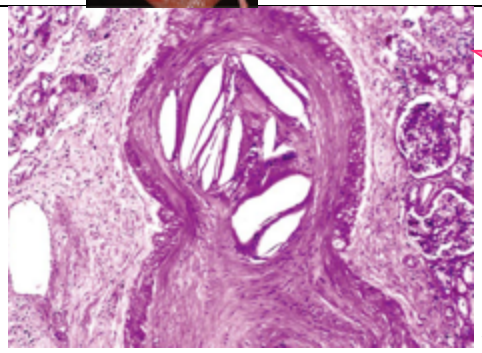


EM: **Very characteristic*

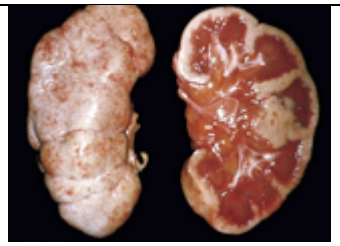


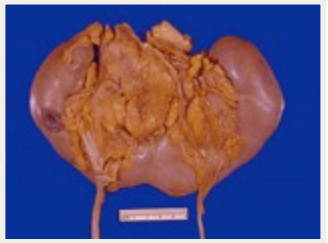
SHISTOCYTES – sheared RBCs

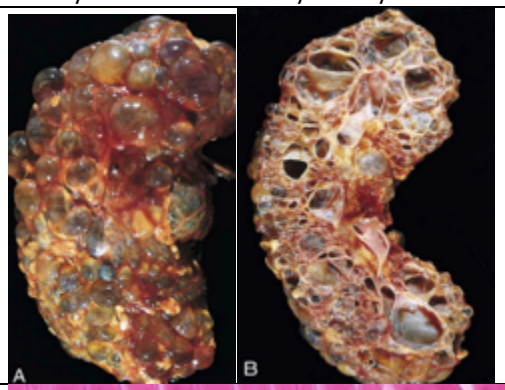
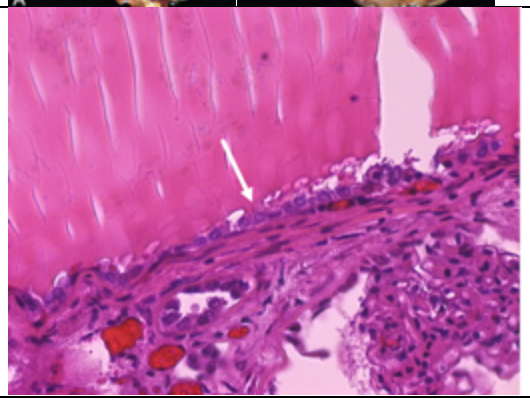
RENAL INFARCTION		
CLINICAL	*Kidneys are a common site for infarcts given the limited collaterals & large blood flow (25% CO)* Majority of renal infarcts are **CLINICALLY SILENT**, but on occasion will present with *pain at CVA & hematuria*	
PATHOGENESIS	Majority of renal infarcts are secondary to **EMBOLI** **Most common source of emboli: L atrial & L ventrical mural thrombi post-MI**	
COMPLICATIONS		
GROSS	24 hours – sharply demarcated, **wedge-shaped, pale-yellow** ★	 *What other lesion could look like this really quick? Papillary necrosis*
LIGHT MICROSCOPY	**COAGULATIVE NECROSIS**	

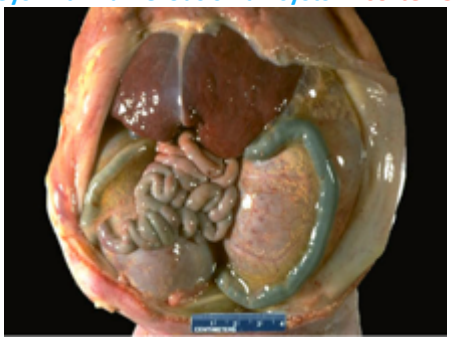
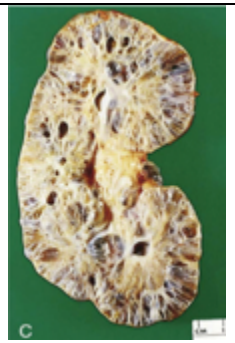
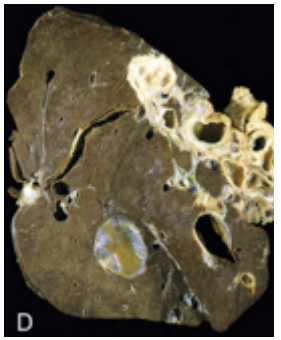
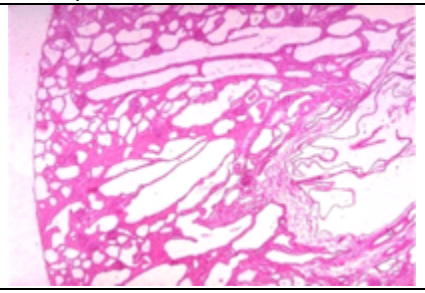
ATHEROEMBOLIC RENAL DISEASE (AKA Cholesterol Embolus) **Older Adults**		
CLINICAL	Embolization of **ARTHEROSCLEROTIC PLAQUE** FRAGMENTS often ***follows a vascular procedure*** Presents with **acute renal failure**	
GROSS		
LIGHT MICROSCOPY	Infarcts of variable size Emboli with **CHOLESTEROL CLEFTS**	 ★ **Classic picture*

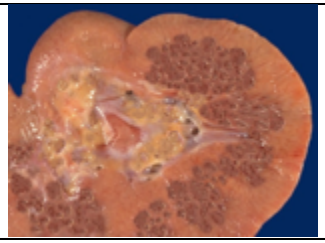
SICKLE CELL NEPHROPATHY		
CLINICAL	Hematuria, decreased ability to concentrate urine (hyposthenuria), proteinuria	
PATHOGENESIS	Nephropathy may occur in those with homozygous or heterozygous form	
LIGHT MICROSCOPY	Sickle cells in capillaries **PAPILLARY NECROSIS**, focal	

DIFFUSE CORTICAL NECROSIS		
CLINICAL	Uncommon condition with **SUDDEN anuria** & uremic death arising most frequently after: – Obstetric emergency (i.e. abruption placentae) – Septic shock – Extensive surgery	
GROSS	**PALE, ischemic necrosis in CORTEX & columns of Bertin** **Essentially, the entire cortex dies*	 ★ **Classic picture*
LIGHT MICROSCOPY	Glomerular & arteriolar **thrombi** with associated acute ischemic infarction & **COAGULATIVE NECROSIS** of **parenchyma**	

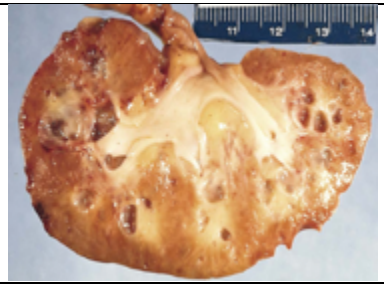
HORSESHOE KIDNEY: Congenital Anomaly		
CLINICAL	Usually incidental finding on radiograph	
PATHOGENESIS	Nephropathy may occur in those with homozygous or heterozygous form	
GROSS	Fusion at the lower poles	

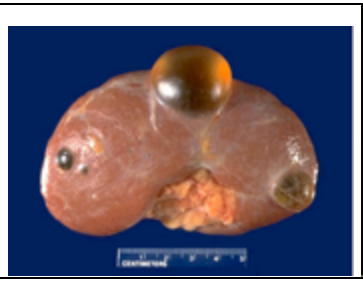
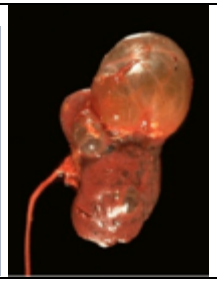
ADULT POLYCYSTIC KIDNEY DISEASE (AKA Autosomal Dominant Polycystic Kidney Disase) Older Adults Accelerates in Blacks, Males, & in presence of HYPERTENSION		
CLINICAL	Fairly common disease; many patients are **ASYMPTOMATIC** until presentation of **RENAL INSUFFICIENCY** Some may initially present as *hematuria or hemorrhage + pain* due to sudden marked increase in cyst size; *blood clots may cause renal colic*	
PATHOGENESIS	Mutations in **PKD1** & PDK2 genes, resulting in abnormal **polycystin 1 & 2**, which causes abnormality of **cilia-centrosome complex** in TECs END RESULT → **CYST FORMATION**	
COMPLICATIONS	***Generally ends in ESRD!*** A subset of these patients die from **SUBARACHNOID HEMORRHAGES** secondary to intracranial berry aneurysms	
GROSS	**Bilaterally enlarged – MASSIVE** **Mass of cysts**	
LIGHT MICROSCOPY	**Cysts lined by epithelial cells** If lucky, you'll see normal nephrons between cysts	

CHILDHOOD POLYCYSTIC KIDNEY DISEASE (AKA Autosomal Recessive Polycystic Kidney Disease)		
CLINICAL	Most common in perinatal & neonatal forms – *present at birth w/ poor prognosis*	
PATHOGENESIS	Mutation in **PKHD1 gene**, encoding fibrocystin, affecting **cilia-centrosome complex in TECs**	
COMPLICATIONS		
GROSS	**Enlarged kidneys with numerous small cysts in cortex & medulla** 	  *Cysts are visible on cross-section*
LIGHT MICROSCOPY	Cysts lined by cuboidal cells & have a **long axis perpendicular** to the surface, representing **collecting duct origin**	

MEDULLARY SPONGE KIDNEY Adults		
CLINICAL	**Discovered RADIOGRAPHICALLY**—abnormal kidney radiolucency **NORMAL RENAL FUNCTION**	
GROSS	Multiple cystic dilations of **collecting ducts in MEDULLA**	

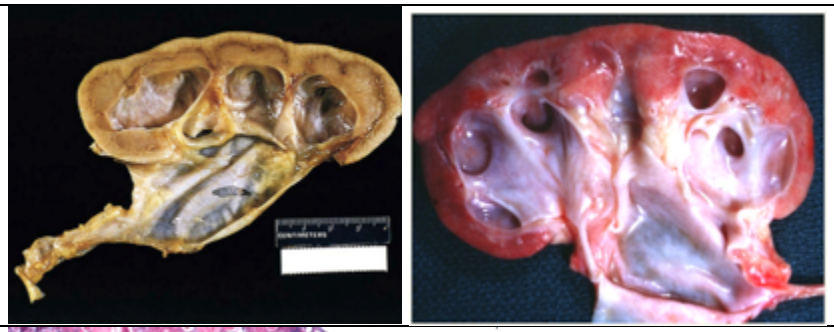
Nephronophthisis: progressive renal disorders characterized by variable number of cysts in the medulla
- **Most common congenital/genital cause of ESRD in children & young adults**
- May result from mutations in different genes (**MCKD1 & MCKD2**)

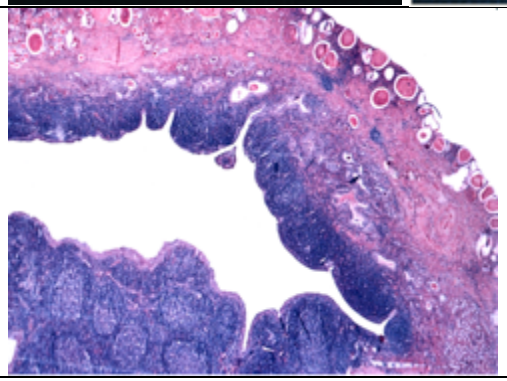
FAMILIAL JUVENILE NEPHRONOPHTHISIS ***Most common nephronopthisis**		
CLINICAL	Children present with polyuria & polydipsia due to abnormal concentrating ability	
PATHOGENESIS	Over 16 genes may be mutated that lead to dysfunctional ciliopathies of TECs	
COMPLICATIONS		
GROSS	SMALL kidneys Cysts – **particularly at the CORTICOMEDULLARY JUNCTION**	
LIGHT MICROSCOPY	Cysts lined by flattened or cuboidal epithelium Surrounded by **inflammatory cells + fibrous tissue** Tubular atrophy & interstitial fibrosis *Biopsy may show only **Chronic Tubulointerstitial Nephritis***	

SIMPLE CYSTS		
CLINICAL	**BENIGN** cysts commonly found **post-mortem** Hemorrhage may cause distension & pain ***Calcification of hemorrhage may lead to bizarre radiographic shadows***	
PATHOGENESIS		
GROSS	Single or multiple in **CORTEX** Smooth inner contours – *differential from cancer*	 

URINARY TRACT OBSTRUCTION

CLINICAL	**ACUTE OBSTRUCTION** – *pain*, attributed to distention of the collecting system or renal capsule; early symptoms secondary to underlying cause of the hydronephrosis (calculi with renal colic, prostatic enlargement with bladder symptoms) **CHRONIC PARTIAL OBSTRUCTION** – *inability to concentrate urine with polyuria & nocturia, distal tubular acidosis, renal salt wasting, renal calculi, chronic tubulointerstitial nephritis, HTN* **COMPLETE BILATERAL OBSTRUCTION** – *oliguria or anuria, incompatible with survival unless obstruction relieved*
PATHOGENESIS	**Unilateral hydronephrosis** – obstruction at or above the ureters; may be clinically silent as unaffected kidney maintains renal function **Bilateral hydronephrosis** – obstruction below the ureters
COMPLICATIONS	
GROSS	Kidney is enlarged ACUTE OBSTRUCTION – Mild dilation of **pelvis & calyces** – Possible atrophy of renal parenchyma CHRONIC OBSTRUCTION – Progressive dilation with subsequent **HYDRONEPHROSIS** – Severe **permanent renal atrophy** with blunting of pyramids – Marked expansion of **calyces & pelvis**
LIGHT MICROSCOPY	ACUTE OBSTRUCTION: interstitial mononuclear cell infiltrate CHRONIC OBSTRUCTION: interstitial fibrosis, tubular atrophy **Germinal Centers, Thyroidization** *Begins to occur after about ~3 weeks*



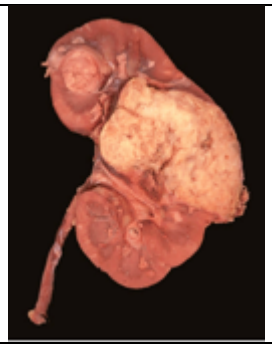


UROLITHIASIS/NEPHROLITHIASIS

Males>Females; 20-30 years

CLINICAL	Rock-like stones found anywhere in the urinary system; Asymptomatic, severe renal colic (intense intermittent pain), hematuria, acute or chronic obstruction **Treatment Nephrolitiasis:** Prevention (drink fluids, dietary changes), Extracorporeal shock wave lithotripsy – Dietary changes: ↓calcium supplements, ↓oxalate-rich foods (spinach, kale)
PATHOGENESIS	**CALCIUM STONES (MOST ALL KIDNEY STONES) – calcium oxalate stones*** – *Most patients present with **hypercalciuria without hypercalcemia**: hyperabsorption of calcium from intestine, intrinsic impairment in renal tubular reabsorption of calcium, idiopathic fasting hyercalciruia with normal parathyroid function* – *20% are associated with uric acid secretion* **STRUVITE/MAGNESIUM AMMONIUM PHOSPHATE STONES** – Most often follow **INFECTION** by **urea-splitting bacteria** – **STAGHORN CALCULUS** URIC ACID STONES – Hyperuricemia CYSTINE STONES
COMPLICATIONS	**Recurrent pyelonephritis** – stones are like a sponge for bacteria
GROSS	 *Chronic pyelo* *Renal atrophy*

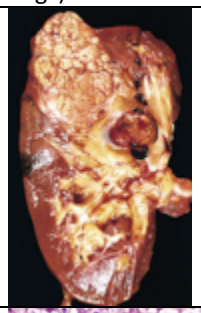
RENAL PAPILLARY ADENOMA		
CLINICAL	**BENIGN** neoplasm arising from tubular epithelium often found incidentally at autopsy	
PATHOGENESIS		
COMPLICATIONS	Potentially malignant when >3 cm	
GROSS	**Yellow-gray well-circumscribed noduels**	
LIGHT MICROSCOPY	**Papillary**	

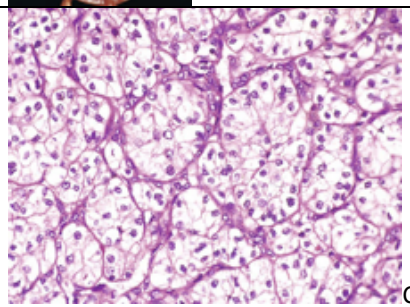
ANGIOMYOLIPOMA		
CLINICAL	**BENIGN** neoplasm composed with blood vessels, smooth muscle, & fat; commonly found in patients with **tuberous sclerosis** May undergo hemorrhage	
PATHOGENESIS		
GROSS	**VERY RARE**	

RENAL CELL CARCINOMA

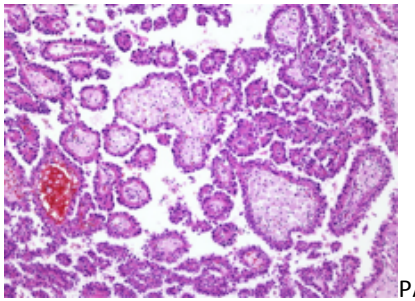
50-60 years old; MALES>FEMALE

CLINICAL	**MALIGNANT** neoplasm of the kidney with **CLASSIC TRIAD:** *costovertebral pain, palpable mass, & hematuria** (most common sign); **ONE OF THE GREAT MIMICS IN MEDICINE** – May be associated with ***polycythemia***, HTN, hepatic dysfunction, feminization or masculinization, Cushing (common paraneoplastic syndromes) ***CLEAR CELL CARCINOMA:** most associated with deletions in 3p *(short arm)* & VHL (TSG) – Solitary unilateral lesions most commonly involving the **poles of the kidney** ***PAPILLARY CARCINOMA:** NOT associated with 3p deletions, but with TRISOMIES 7 & 17 or LOSS OF Y
PATHOGENESIS	**TOBACCO use is the most significant risk factor** (*cigarette users double the incidence)* Other RFs: obesity, HTN, unopposed estrogen therapy, **asbestos exposure, petroleum products, heavy metals**, ESRD *Majority are sporadic (only ~4% associated with familial cancers – Von Hippel-Lindau & Hereditary Leiomyomatosis)*
COMPLICATIONS	**Propensity for invasion of the renal vein** *(remember the tumor going into the R atrium from Cardio Path last semester...)* 25% of patients at time of diagnosis have evidence of metastases (>50% lungs)
GROSS	CLEAR CELL CARCINOMA – **Yellow-gray spherical masses that have clear borders** – **HEMORRRHAGE & NECROSIS COMMON** PAPILLARY CARCINOMA – Multifocal & bilateral – Hemorrhage & cystic
LIGHT MICROSCOPY	CLEAR CELL CARCINOMA – Rounded or polygonal cells with **clear cytoplasm** – Delicate branching vasculature PAPILLARY CARCINOMA – Cuboidal or low columnar cells arranged in papillary formations – **Psammoma bodies**

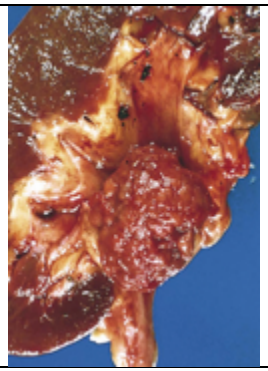




CLEAR CELL



PAPILLARY

UROTHELIAL CARCINOMA OF RENAL PELVIS Smokers		
CLINICAL	**MALIGNANT** neoplasm of the kidney originating in urothelium of renal pelvis (*similar to bladder carcinomas*) Present with marked hematuria or with signs & symptoms of acute obstruction	
PATHOGENESIS		
COMPLICATIONS		
GROSS		
LIGHT MICROSCOPY		

RECAP

Deposits outside of GBM – subepithelial (3)	PSGN, Membranous Nephropathy, Lupus Nephritis
Deposits in the GBM – membranous (1)	MPGN II – Dense Deposit Disease (*ribbon*)
Deposits beneath endothelium – subendothelial (3)	Lupus Nephritis, MPGN I, Thrombotic Thrombocytopenic Purpura (TTP)
Deposits in mesangium (3)	IgA Nephropathy, Henoch-Schonlein Purpura, Lupus Nephritis
Thickened glomerular capillary walls (4)	Membranous Nephropathy, MPGN I & II, Lupus Nephritis (*wire loops*)
Scarred glomeruli (1)	Chronic Glomerulonephritis (*blue glomeruli in image*)
Fibrin (2)	Thrombotic Microangiopathies: HUS, TTP
Disease of the visceral epithelial cells (3)	**HIV Nephropathy** – *hypertrophy & proliferation,* FSGS & Minimal Change – *effacement*
Lesions of parietal epithelial cells (1)	CRESCENTS = RPGN
GRANULAR pattern on IF (4)	PSGN, RPGN II – Immune Complex Mediated, Membranous, MPGN I
LINEAR pattern on IF (1)	RPGN I – Anti-GBM
Thyroidization (2)	Chronic Pyelonephritis, Chronic Urinary Tract Obstruction
NEPHRITIC Syndrome (2)	APGN (PSGN), RPGN
NEPHROTIC Syndrome (6)	Membranous (#1 adults), Minimal Change (#1 children), FSGS (#1 African American), HIV-Associated Nephropathy, MPGN I & II
Associated with CANCERS (4)	Membranous – *associated with carcinomas of lung & colon, melanoma* MPGN Acute Uric Acid Nephropathy – *chemotherapy for leukemia & lymphoma* Light Chain Cast Nephropathy – *Multiple Myeloma*