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|  | **minimal change disease**   * most common nephrotic syndrome in kids * **Etiology:** podocyte injury; cytokines?; ↓ negative charge of GBM; → loss of neg proteins (albumin); can result from NSAIDs * **immune?** can follow URTI; ↑ #s w/Hodgkin’s   **pathology**   * **LM:** no discernable Δ * **IF:** negative – no immuine complexes present * **EM:** foot process effacement (specialization retracts w/injury)   **prognosis**   * good – responds to steroids |
|  | **focal segmental glomerular sclerosis (fsgs)**   * 2nd among kids; most among AAs; resistant to steroids; progressive → renal failure (years); Tx w/immunosuppressives * **etiology:** ideopathic; circulating factor?; not immune complex or Ab; occurs post-transplant; serum causes lesion in other * **pathology**: scattered glomerular sclerosis; segmental → global; IF negative (except C3 and IgM (big) get stuck); EM foot process effacement * **prognosis:** focally sclerotic gloms → completely sclerosed; → renal failure; steroid resistant   **secondary**   * ↓ # glomeruli; hypertrophy; ↑ glomerular BP & filtration; injures remaining glomureli; vicious cyle → renal failure * **rarely** occurs as a result of a loss of one kidney   **collapsing (lower right-hand image)**   * variant of FSGS; **HIV infection**; IV heroin; ↑ # among Aas; **not** immune complex-mediated – so IF negative |
|  | **membranous glomerulonephritis**   * autoummine disorder:Abs against podocyte cell membrane Ags * **poor prognostic indicators:** ↑ age, ↑ BUN & Cr, ♂, HTN   **etiology**   * 85% idiopathic; infections (malaria, syphilis **Hep B)**; autoimmune (**SLE, RA)**; **paraneoplastic** (lung, colon, melanoma); meds: **gold** (Tx RA), penicillamine   **pathology**   * auto-Abs to podocyte FP Ags; activate C5b-9 MAC; → **subepithelial space**; GBM grows between deposits * **LM** diffuse, unifrom thickening w/spikes & holes * **IF** coarse, regular, granular staining IgG & C3 * **EM** lots of dense deposits over FP injury/effacement   **course**   * may resolve, stasis, progress to RF; Tx primary cause if possible |
|  | **membranoproliferative glomerulonephritis (MPGN)**   * may present nephrotic, nepritic, mixed, asymptomatic… * suspect in Pts w/nephrotic range proteinuria and ↑ #s RBCs in UA or RF w/↑Cr   **clinical**   * kids & young adults: ↓ complement, persistent hematuria, HTN, RF (↑Cr)   **etiology**   * immune-complex deposition; endothelial injury & GBM reduplication * infectious (Hep B&C, IE); immune (SLE, cryoglobinemia); paraneoplastic * **pathology:** IC deposition in **mesangium & subendothelial space** * **LM** mesanfial hypercellularity & tram-tracking * **IF** IgG & C3 in capillary & mesangium * **EM** e--dense deposits; GBM reduplication   **course**   * idiopathic = bad (progressive) * 2° – Tx 1° and reversal may follow |
|  | **post-streptococcal glomerulonephritis**  **acute nephritic syndrome:** hematuria, protenuria, HTN, mild renal insufficiency  **clinical**   * 1-3 wks post throat infection, 3-6 post skin infection * edema, HTN, hematuria, azotemia, mild proteinuria & oliguria * positive for titres of anti-SLO & anti-DNAse B   **pathogenesis**   * circulating ICs or Ags plant in glomerulus → subepithelial deposits   **pathology**   * **LM:** subepithelial humps; inflammatory cells (PMNs & monos) * **IF:** lumpy-bumpy granular peripheral capillary loop deposis (IgG, C3) * **EM:** large, random “humps” or “honkers”   **prognosis**   * children: 95% recover spontaneously, 5% progression (fast or slow) * adults: 60% recover spontaneously, 40% progress to RPGN or RF |
|  | **lupus nephritis**  auto-immune, immune-complex mediated disease  nephrotic syndrome, acute nephritic syndrome, asymptomatic h/p, or frank ARF  **pathogenesis**   * IC deposition throughout kidney; complement→ WBCs→ inflammation;   **proliferative change**   * mesangial proliferation: hypercellularity & ↑ matrix * endocapillary: subendothelial deposits of inflammation; damage to GBMs; margination, necrosis, & rupture * pathology * IF: “full house effect” – IgG, IgA, IgM, C3… * EM: subendothelial IC deposition; “fingerprint” substructure   **membranous change:** parallel to MPGN; Abs vs. podocyte Ags  **prognosis**   * better predicted by chronic changes rather than active lesions   **treatment**   * steroids & cytotoxic agents (cytoxan) |
|  | **IgA nephropathy (Berger’s Disease)**  asymptomatic hematuria/proteinuria  clinical factors   * affects: children & young adults; indigenous populations * often anctecedent URTI or GI; Hx of intermittent macroscopic hematuria * may present as frank nephritic syndrome; (rarely) RPGN   **etiology**   * unknown trapping of IgA throughout mesangium   **pathology**   * **LM:** mesangial hypercellularity & ↑ matrix * **IF:** IgA & C3 (alternative path!); may also find IgG & IgM * **EM:** immune-type e--dense mesangial deposits, hypercellularity, ↑ matrix   **prognosis**   * bening or progress to CRF (10%-50%) |
|  | **alports disease**   * hereditary defect in Type IV collage – GBM, cochlea, eye   **presentation**   * hematuria, ↑F hearing loss, ocular defects   **pathogenesis**   * absence of α-5 (XLR), α-3,4 (AR/AD) isoform → disturbance of production   **pathology**   * **LM** nonspecific * **IF** negative – non-immune * **EM** “basket weave” characteristic lamellation of GBM   **outcomes**   * ♂ w/XLR, both sexes with AR/AD → ESD at varying rates   **treatment**   * transplant; rarely Type IV collagen of new kidney recognized as “not self”   note: **Thin Basement Membrane disease** is similar, with Δ error in Type IV collagen |
|  | **crescentic glomerulonephritis**  histopathologic hallmark of RPGN  **Type I: Anti-GBM**   * Abs to GBM; w/pulmonary – Goodpasture; mostly ideopathic * may follow hydrocarbon solvent exposure, Influenze A2, malaria, Hodgkins * **LM:** crescents; **IM:** linear fluorescence of GBMs for IgG; **EM:** no deposits * prognosis good, if caught early   **Type II: Immune-Complex**   * etiology: IC-mediated diseases (SLE, post-strep, MPGN, IgA nephropathy) * biopsy to ID and Tx   **Type III: Pauci-Immune**   * defined by lack of findings of ICs or anti-GBM Abs * >90% *p* or *c*-*ANCA* positive * idiopathic or systemic vasculitis (Wegener’s or Microscopic polyangiitis) |
| Figure26  tubularnecrosis Figure33 | **acute tubular necrosis**  most common cause of ARF   * **Ischemic:** patchy; due to sepsis, burns, surgery, or hemorrhage * **Tubulo-toxic:** uniform; due to, e.g., aminoglycosides, dyes, rhabdomyolysis   **1° mechanism**   * injury → ↓synthetic f’ns → ↓ phosphate stores (↑E) → lysosomal destruction   **pathology**   * **mild:** loss of brush border (1st slide), vacuolization (2nd slide), swelling cells * **severe:** necrotic cells slough off into lumen (3rd slide), leaving BM naked * **regeneration:** flat epithelia (4th), mitotic figures, reactive nuclei w/↑ nucleoli   **other harmful mechanisms in ATN**   * vasoconstriction * necrotic cells in casts obstructing tubules, ↑ pressure, ↓ filtration * backleal of filtered urine into kidney vasculature & interstitium   **prognosis:** often reversible if support is maintained (dialysis) |
| acute_pyelo | **acute pyelonephritis**   * **most common cause:** ascending UTI (*e. coli*); ♂ < 1 – ♀ – 50 < ♂ * also fungi (*candida albicans*) and CMV (transplant)   **pathology**   * **gross:** pinpoint or largere pustules, may meld; streaks of yellow pus * **micro:** intense *streaky* neutrophilic interstitial & tubular infiltrate   **complications**   * pyonephrosis: kidney → bag of pus * perinephric abscess: infection spreds into perinephric soft tissue * **necrotizing papillitis:** requires: infection, obstruction, compromised blood flow; appears as coagulatoin necrosis w/sharp, inflamed edges |
|  | **acute tubulo-interstitial nephritis (atin)**   * inflammation of interstitium → tubules   **etiology/antecedents**   * Hx of hypersensitivity, ICs in TBMs, anti-TBM Abs, T-cell mediated damage * most commonly, rxn to a drug (β-lactam, sulfonaminde, NSAIDS, diuretic) * systemic infections (group A strep, diphtheria, toxoplasmosis, legionnaire’s)   **microscopic pathology**   * tubules seperated by edema * inflammatory infiltrate (lymphocytes, monocytes, ***eosinophils***, PMNs)   **clinical presentation**   * hypersensitivity: fever, hematuria, eosinophilia, pyuria, skin rash, mild proteinuria, eosinophiluria |
|  | **diabetis mellitus – diffuse and nodular glomerulosclerosis**   * renal disease 2° to Db is ↑ cause of ESRD in US; > ½ dialysis pts * clinical features: proteinuria; microalbuminemia; frank nephrotic syndrome; ↓GFR along with other complications of Db (retinopathy)   **pathogenesis**   * 1° lesion: excess ECM throughout the kidney (many GFs, esp. TGF-β)   **biopsy conditions:** renal disease w/in 10 yrs of Db; ↓ retinopathy; unexplained hematuria or unusually accelerated renal impairment  **pathology**   * **gross:** enlarged, esp. Type 1 Db; evidence of arteriosclerosis/arteriolosclerosis * **LM:** progressive, uniform ↑ in GBM thickness & corresponding ↑ in ECMatrix * ½ pts: ↑ mesangial matrix → frank hypocellular nodules (Kimmelstiel-Wilson) * **IF:** linear deposition of IgG (sticky) * **EM:** uniform thickening of GBMs, podocyte foot process efffacement * **pink/hyaline deposits:** fibrin cap, capsular droplet * **tubules & interstitial** thickening of TBMs & tubular atrophy * **vasculature:** ↑ deposition of ECM in both afferent & efferent arterioles |
|  | **amyloidosis**   * deposition of protein → proteinuria, nephrotic syndrome, & renal insufficiency * β-pleated sheet: stains w/Congo Red; polarized-light “apple-green” refringence   **forms of amyloid**   * AL: 1° amyloidosis – most common; often from multiple myeloma * AA: 2° amyloidosis – serum AA (acute phase reactant) from chronic inflammatory conditions (RA, TB, osteomyelitis)   **Pathology**   * glomerulus: mesangial expansion & nodule formation * vasculature: lumen diminution of arteries & arterioles * LM: amorphous pink or hyaline material * EM: masses of thin, nonbranching fibrils * IF: reagents of κ, λ light chains, or SAA protein |
|  | **renal cell carcinoma**  clear cell carcinoma   * most common kidney tumor of adults   **gross presentation**   * solid, cystic, bright yellow, with some necrosis/hemorrhage   **microscopic presentation**   * clear cells (lipids & glycogen) in small nests and sinusoidal arrangement   **typical clinical presentation**   * associated w/von Hippel-Lindau; ♂ > ♀ (2:1); smoking; obese ♀   **important predictors of behavior**   * **stage:** local → perinephric fat → renal vein → surrounding structures * **grade:** nuclear appearance (differentiation) |
|  | **wilm’s tumor**  most common tumor of childhood  **histological features:**  blastemal, epithelial, and mesenchymal |
|  | **transitional cell carcinoma (tcc)**  **(aka) urothelial carcinoma**  **(mostly papillary)**  **classification**   * papilloma; PUNLMP; low-grade papillary ca; high-grade papillary ca;   **biological implications of classification**   * ↑ risk of recurrence & progression   **histological description**   * fronds consisting of fibrovascular cores surrounded by uroepithelium   **important predictors of behavior**   * ↑ size; ↑ #; ↑ grade; dysplasia of “uninvolved” mucosa * progress: carcinoma in situ → invasive; 20% |
|  | **adenocarcinoma of the prostate**   * most common tumor of the prostate in adults   **histologic presentation**   * fairly uniform proliferation of small, round glands   **presumed precursor lesion**   * prostatic intraepithelial neoplasia (PIN) within ducts   **important predictors of tumor behavior**   * Gleason score: sum of 2 scores measuring tumor architecture * absolute predictor of 5-year survival |