“Best” Indications for RBx:

- Nephrotic syndrome in an adult
- Steroid-resistant nephrotic syndrome in a child
- “Unexplained” acute renal failure

- Renal biopsy is most useful to evaluate for the presence of glomerular disease
Nephrotic Syndrome

- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous glomerulopathy

- Mainly diseases which lack cellular proliferation (i.e. not "glomerulonephritis")
Outcomes of FSGS Variants:

**Columbia University**

Glomerular Disease Collaborative Network

**UNC Chapel Hill**

Membranous glomerulopathy

Heymann nephritis model established that deposits in iMN form in situ

Phospholipase A2 Receptor is the target antigen in iMN

Nephritic Syndromes (+/- nephrotic)
- IgA nephropathy
- Acute post-infectious glomerulonephritis
- Membranoproliferative glomerulonephritis & C3 glomerulopathy
- Pauci-immune necrotizing & crescentic glomerulonephritis (ANCA-associated)
- Anti-GBM disease

Nephritic = cellular proliferation & inflammation
IgA nephropathy

Oxford Classification of IgA-N
(Kidn Int 76:534–545; 546–556, 2009)

Table 1: Distribution of pathological variables used in the classification of IgA nephropathy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerular hypercellularity</td>
<td>Mild-moderate</td>
</tr>
<tr>
<td>Hyalinosis</td>
<td>None</td>
</tr>
<tr>
<td>Mesangial proliferation</td>
<td>None</td>
</tr>
<tr>
<td>Tubulointerstitial fibrosis</td>
<td>None</td>
</tr>
</tbody>
</table>

M.E.S.T.

Acute Post-Infectious Glomerulonephritis
5 Criteria for Acute Post-Infectious GN

1. Recent infection
2. Hypocomplementemia
3. LM: Exudative GN (neutrophils*)
4. IF: C3 dominant or co-dominant staining
5. EM: Subepithelial hump-shaped deposits

Membranoproliferative Glomerulonephritis
Dense Deposit Disease (MPGN type 2)


MPGN 1

MPGN 2

MPGN 3

C3

IgG
THREE SUBTYPES OF CRESCENTIC GLOMERULONEPHRITIS

- Immunocomplex
  - A dominant basement membrane
  - Pauciimmune

- IF: Granular deposits
- IF: Linear deposits
- IF: Still see fibrin scaffolding
- IF: No deposits
- Anti-glomerular basement membrane
- Goodpasture's syndrome
- Circulating ANCA which target GBM

Necrotizing & crescentic GN (NCGN)
THREE SUBTYPES OF CRESCENTIC GLOMERULONEPHRITIS

- **Immune Complex**
  - IF: Granular deposits
  - Ag-Ab Complexes, HLA or circulating
  - Lupus, SLE, IgA Nephropathy, Post-infectious GN

- **Anti-Glomerular Basement Membrane**
  - IF: Linear deposits
  - Circulating AB's which target GBM
  - Vasculitis/ANCA

- **Pauciimmune**
  - IF: No deposits
  - No AB's seen in Lung
  - Pauciimmune Syndromes

PAUCI-IMMUNE NCGN

NCGN c/w anti-GBM disease
“Isolated Hematuria”

- IgA nephropathy (mild)
- Thin basement membrane nephropathy
- Hereditary nephritis

- Hematuria dominates the clinical picture

**Thin basement membrane nephropathy**

**Hematuria**

**Hereditary nephritis**

- Alpha chains of type IV collagen
- Chromosome location
  - 1 & 2: 13
  - 3 & 4: 2
  - 5 & 6: X

*α3, α4, α5: expressed in mature kidney (glomeruli, tubules, cochlea, lens capsule)
Acute Kidney Injury (ARF)
- Glomeruli
- Tubules
- Interstitium
- Vessels

AKI – Tubular: ATN

Etiologies of AIN
- Allergic/Drug-induced 70%
- Autoimmune/CV – SLE, Sjogren's, MCTD
- Infectious – mainly mycobacteria & fungal
- Systemic – IgG4 Dx, sarcoidosis, TINU synd
- Collectively 20%
- Idiopathic 10%

70% / 20% / 10% rule
**AKI – Vascular: Atheroembolic disease**

**AKI – Vascular: Thrombotic microangiopathy**

**Etiologies of TMA**
- HUS & TTP
- Malignant HTN
- Scleroderma
- Antiphospholipid syndrome (+/- SLE)
- Pre-eclampsia / eclampsia / HELLP syndrome
- HIV infection
- Disseminated malignancy
- Drug-induced: cyclosporine, tacrolimus, gemcitabine, mitomycin C, anti-VEGF agents, ...

**“Best” Indications for RBx:**
- **Level 1 = best indications**
  - Nephrotic syndrome in an adult
  - Steroid-resistant nephrotic syndrome in children
  - "Unexplained" acute renal failure

- Renal biopsy is most useful to evaluate for the presence of glomerular disease

**Indications for Renal Biopsy**
- **Level 2 = Very good indications**
  - Need 2 out of 4:
    - Gross or microscopic hematuria
    - Significant proteinuria (i.e. >1 g/day)
    - Renal insufficiency
    - Positive serologies

  - Eval & follow-up of pts with SLE & renal disease
  - Eval of pts with dysproteinemia & renal disease
  - DM or HIV (on HAART) with atypical course

  - Note: These are opinions...
Indications for Renal Biopsy

- **Level 3 = "Good" indications**
  - Need 1 out of 4:
    - Gross or microscopic hematuria
    - Significant proteinuria (i.e. >1 g/day)
    - Renal insufficiency, subacute
    - Positive serologies

- **Level 4 = Weak indications**
  - Probable diagnosis & risk of biopsy exceeds benefit
  - Known diagnosis with no treatment planned
  - Known diagnosis on maximal treatment
  - Slowly progressive CKD

- **Level 5 = Poor indications/Bx not worthwhile**
  - ESRD with small kidneys
  - Acute pyelonephritis
  - Polycystic kidney disease
  - Hepatorenal syndrome

Renal diseases associated with dysproteinemia

- **Major categories**
  - 1. Conditions associated w/light chain casts & crystals
     - Myeloma cast nephropathy
  - 2. Systemic conditions which involve all components of the renal parenchyma
     - Light chain amyloidosis
     - Monoclonal immunoglobulin deposition disease (MIDD; most commonly LCDD)
  - 3. Isolated glomerular diseases, variably associated with dysproteinemia
OR

Light chain amyloidosis
Light chain deposition disease

Lupus Nephritis


<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Minimal mesangial lupus nephritis</td>
</tr>
<tr>
<td>II</td>
<td>Mesangial proliferative lupus nephritis</td>
</tr>
<tr>
<td>III</td>
<td>Focal lupus nephritis*</td>
</tr>
<tr>
<td>IV</td>
<td>Diffuse segmental (IV-S) or global (IV-G) lupus nephritis*</td>
</tr>
<tr>
<td>V</td>
<td>Membranous lupus nephritis*</td>
</tr>
<tr>
<td>VI</td>
<td>Advanced sclerosing lupus nephritis</td>
</tr>
</tbody>
</table>

*Indicates the proportion of glomeruli with active and/or sclerotic lesions.
*Indicates the proportion of glomeruli with fibrinoid necrosis and cellular crescents.
*Class V may occur in combination with class III or IV, in which case both will be diagnosed.

Mesangial proliferative LN (class II)

Segmental endocapillary proliferation

If present in <50% of glomeruli ... Focal LN (class III)
Segmental endocapillary proliferation

If present in >50% of glomeruli ... Diffuse segmental LN (class IV-S)

Global endocapillary proliferation

Diffuse global LN (LN class IV-G)

Membranous LN (LN class V)

Diabetes Mellitus

Nodular Diabetic Glomerulosclerosis
2 more entities...

MPGN c/w cryoglobulinemic GN (HCV +)

Fibrillary glomerulonephritis
Fibril Diameter

<table>
<thead>
<tr>
<th>10 nm</th>
<th>20 nm</th>
<th>30-50 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyloidosis</td>
<td>Fibrillary GN</td>
<td>Immunotactoid GN</td>
</tr>
</tbody>
</table>

Most Common Indications for Renal Biopsy

- Pooled data from 8 large biopsy series
  - #1 = Proteinuria/nephrotic syndrome
  - #2 = ARF / RPGN
  - #3 = Hematuria
  - #4 = “Systemic disease”