بنام خدا
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Professor of Nephrology

Shahid Beheshti University of Medical Sciences
Normal kidney
Normal renal vasculature
Proximal tubular transporters

Lumen

- Na⁺
- Sugars
- Na⁺
- Amino acids
- Na⁺
- Phosphate
- Na⁺
- Citrate
- Na⁺
- H⁺

Cell

- K⁺
- Na⁺
- HCO₃⁻
- Na⁺
- K⁺
- Cl⁻
- K⁺
- Cl⁻
- α-ketoglutarate²⁻
- Organic anion

Interstitial fluid
Clinical signs of kidney disease

- Symptoms of associated disease
- Renal colic and pain
- Hematuria
- Foamy urine (possibly proteinuria)
- Volume overload
- Uremic syndrome: CNS, GI, CV, skin
Clinical assessment of extracellular volume

- BP and heart rate
- Skin turgor
- Mucous membrane moisture
- Jugular venous pressure
- Pulmonary crackles
- Third heart sound
- Edema
CKD
Kidney Failure is the Tip of the Iceberg...

<table>
<thead>
<tr>
<th>Stage 5</th>
<th>Kidney Failure/End-stage kidney disease (GFR &lt;15): 400,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 4</td>
<td>GFR 15–29: 300,000</td>
</tr>
<tr>
<td>Stage 3</td>
<td>GFR 30–59: 7,400,000</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Kidney damage &amp; GFR 60–89: 5,700,000</td>
</tr>
<tr>
<td>Stage 1</td>
<td>Kidney damage &amp; GFR &gt;90: 5,600,000</td>
</tr>
</tbody>
</table>

19 million Americans with CKD
8 million Americans with GFR<60

Relationship between serum creatinine and glomerular filtration rate

Serum creatinine (mg/dL)

Inulin clearance (mL/min per 1.73m²)
<table>
<thead>
<tr>
<th>Test</th>
<th>Method</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma creatinine</td>
<td>Random blood sample</td>
<td>Simple</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inaccurate especially with mild renal impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced with low muscle mass</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Raised following cooked meat meal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Affected by some drugs – altered tubule secretion (Fig. 3.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drug influences creatinine assays (Fig. 3.5)</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>24-h urine collection and blood sample</td>
<td>Urine collections unreliable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overestimates glomerular filtration rate (tubular secretion of creatinine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drug influences creatinine assays (Fig. 3.5)</td>
</tr>
<tr>
<td>Estimated creatinine clearance (Cockcroft-Gault formula) (Fig. 3.6a)</td>
<td>Random blood sample</td>
<td>Avoids urine collection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More accurate than plasma creatinine especially with mild renal impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Underestimates in obesity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overestimates on low protein diet</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate (equation from MDRD study) (Fig. 3.6b, Fig. 3.7)</td>
<td>Random blood sample</td>
<td>Avoid urine collection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Better estimation of glomerular filtration rate than creatinine clearance or estimate by Cockcroft-Gault formula</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not tested in persons with extreme low serum albumin concentration</td>
</tr>
<tr>
<td>Plasma clearance</td>
<td>Single i.v. injection and at least two, timed blood samples</td>
<td>Best approximation to true glomerular filtration rate</td>
</tr>
<tr>
<td>isotopic: 51-iodohippurate</td>
<td></td>
<td>Invasive</td>
</tr>
<tr>
<td>51-Cr-EDTA</td>
<td></td>
<td>May use radioisotopes</td>
</tr>
<tr>
<td>99mTc-DTPA</td>
<td></td>
<td>Not often needed in routine clinical care</td>
</tr>
<tr>
<td>non-isotopic: iodohippurate, iohexol</td>
<td></td>
<td>Mandatory in clinical trials investigating progressive renal failure</td>
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</tbody>
</table>
### Cockcroft-Gault formula

<table>
<thead>
<tr>
<th>Gender</th>
<th>Formula 1</th>
<th>Formula 2</th>
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</thead>
<tbody>
<tr>
<td>MEN</td>
<td>$C_{cr} = \frac{(140 - \text{age})(\text{weight})}{72 \times P_{cr}(\text{mg/dL})}$</td>
<td>$C_{cr} = \frac{1.23(140 - \text{age})(\text{weight})}{P_{cr}(\text{µmol/L})}$</td>
</tr>
<tr>
<td>WOMEN</td>
<td>$C_{cr} = \frac{(140 - \text{age})(\text{weight})}{85 \times P_{cr}(\text{mg/dL})}$</td>
<td>$C_{cr} = \frac{1.04(140 - \text{age})(\text{weight})}{P_{cr}(\text{µmol/L})}$</td>
</tr>
</tbody>
</table>

If patient is female, multiply the value by 0.762
If patient is Black, multiply the value by 1.18
Cockcroft–Gault formula

\[
\begin{align*}
\text{MEN} & \quad C_{cr} = \frac{(140 - \text{age})(\text{weight})}{72 \times P_{cr}(\text{mg/dL})} \\
\text{WOMEN} & \quad C_{cr} = \frac{(140 - \text{age})(\text{weight})}{85 \times P_{cr}(\text{mg/dL})}
\end{align*}
\]

or

\[
\begin{align*}
\text{MEN} & \quad C_{cr} = \frac{1.23(140 - \text{age})(\text{weight})}{P_{cr}(\mu\text{mol/L})} \\
\text{WOMEN} & \quad C_{cr} = \frac{1.04(140 - \text{age})(\text{weight})}{P_{cr}(\mu\text{mol/L})}
\end{align*}
\]

GFR prediction equation from MDRD study

**Equation from MDRD study**

\[
\text{GFR} = 170 \times P_{cr}(\text{mg/dL})^{-0.999} \times \text{age}^{-0.176} \times \text{SUN}^{-0.170} \times \text{Alb}^{0.318}
\]

If patient is female, multiply the value by 0.762

If patient is Black, multiply the value by 1.18
Toxins retained in uremia:

**Low molecular weights (MW<300 D)**
- Urea
- Creatinine
- Guanidines
- Lipids
- Hippuric acid, indoxyl sulfate, p-cresol
- Oxalate
- Hcy, Po4, H+, Na+, K+, water

**Middle molecules (MW=300-12000 D)**
- PTH
- B2 microglobulin
- AGE

**High molecules (MW >12000 D)**
- Cystatin C
- Clara cell Protein
- Retinol Binding Protein
- Leptin
Anemia

AVF

Hyperlipidemia

Fluid overload

Altered vasopressor/NO

Unidentified toxins

Pericardial diseases

Hypertension

K+

R.F

Cardiovascular Damage

Bioincompatibility

Air emboli & hemolysis

Dialysis

Volume and osmolarity and electrolyte changes
End-stage renal disease

- Diabetic nephrosclerosis
- Hypertensive nephrosclerosis
- Chronic glomerulonephritis
- Chronic interstitial nephritis
- Polycystic kidney disease
Urine analysis
<table>
<thead>
<tr>
<th>Cast</th>
<th>Main clinical Associations</th>
</tr>
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<tbody>
<tr>
<td>Hyaline</td>
<td>Normal subject, Renal disease</td>
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<tr>
<td>Granular</td>
<td>Renal disease</td>
</tr>
<tr>
<td>Waxy</td>
<td>Renal insufficiency, Rapidly progressive, Glomerulonephritis</td>
</tr>
<tr>
<td>Fatty</td>
<td>Marked proteinuria, Nephrotic syndrome</td>
</tr>
<tr>
<td>Erythrocyte</td>
<td>Glomerular bleeding, Proliferative/necrotizing glomerulonephritis</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Glomerular bleeding, Proliferative/necrotizing glomerulonephritis, Hemoglobinuria</td>
</tr>
<tr>
<td>Leukocyte</td>
<td>Acute pyelonephritis, Acute interstitial nephritis, Proliferative glomerulonephritis</td>
</tr>
<tr>
<td>Epithelial</td>
<td>Acute tubular necrosis, Acute interstitial nephritis, Glomerulonephritis</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>Rhabdomyolysis</td>
</tr>
</tbody>
</table>
PROXIMAL TUBULAR CELL
DISTAL TUBULAR CELL
COLLECTING DUCT CELL
INTRACELLULAR LIPIDS
CHOLESTEROL CRYSTAL
LEUKOCYTE CAST
BACTERIAL CAST
YEAST CAST
CALCIUM OXALATE BYHYDRATED (U-pH <5.4-6.7)
CALCIUM PHOSPHATE (U-pH ≥7.0)
TRIPLE PHOSPHATE (U-pH \geq 7.0)
CYSTINE
Uric Acid Crystals
Uric acid Crystals By polarizing microscopy
Qualitative identification of Cystine stone

Sodium Nitroprosside
Cystine Crystals
2,8-HYDROXYADENINE (BF)
2,8-HYDROXYADENINE (POL)
SULPHADIAZINE (POL)
AMOXICILLIN (BF)
INDINAVIR
EGG OF SCHISTOSOMA HAEMATOBIUM (120-150 μm)
"Well, your urine seems to be all right."
Normal glomerulus
Presentation of renal diseases

Glomerulopathies  proteinuria/hematuria
  - Nephrotic syndrome
  - Acute glomerulonephritis
  - Hemolytic uremic syndrome

Tubulointerstitial diseases
Nephrotic syndrome
Negative charges on glomerular capillaries
Loss of negative charges
Minimal change disease

Diffuse effacement of foot processes
PROTEINURIC GLOMERULUS
Nephrotic syndrome

Definition:

Always present
- Proteinuria
- Hypoalbuminemia

Usually present
- Edema
- Hyperlipidemia

Sometimes present
- Hematuria
- Azotemia
- Hypertension
Lipiduria

Maltese cross
Picture of a child with nephrotic syndrome
Peritubular capillaries modulate fluid reabsorption

**Normal**

- Lumen
- Proximal tubule (containing $\text{Na}^+$, $\text{H}_2\text{O}$, $\text{Na}^+$, $\text{K}^+$)
- Interstitial fluid ($\pi_{ic}$ (high))
- Peritubular capillary ($P_{pc}$ (low))

**Reduced peritubular capillary oncotic pressure**

- Lumen
- Proximal tubule (containing $\text{Na}^+$, $\text{H}_2\text{O}$, $\text{Na}^+$, $\text{K}^+$)
- Increased paracellular backflux
- Interstitial fluid (raised pressure)
- Peritubular capillary (less fluid reabsorbed)
Steroid-Resistant Nephrotic Syndrome

Focal segmental glomerulosclerosis (FSGS)
Sequence of events in nephrotic syndrome

**Pathophysiology**
- Glomerular injury
  - Increased permeability of the glomerular basement membrane
    - Albuminuria
      - Decreased serum albumin
        - Decreased plasma oncotic pressure
          - Decreased peripheral capillary return
            - Increased interstitial fluid
  - Heavy proteinuria (foamy urine)
  - Occasional hematuria
- Hypoproteinemia
- Decreased urine sodium
- Decreased renal Na reabsorption
- Peripheral and periorbital edema

**Clinical manifestations**
Distribution of histologic lesions in children and adults

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal change</td>
<td>80%</td>
<td>20%</td>
</tr>
<tr>
<td>Proliferative</td>
<td>15%</td>
<td>25%</td>
</tr>
<tr>
<td>Membranous</td>
<td>&lt;1%</td>
<td>30%</td>
</tr>
<tr>
<td>Focal sclerosis</td>
<td>5%</td>
<td>25%</td>
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</table>
Glomerulonephritis
Mesangial cell architecture
# Mesangial function

<table>
<thead>
<tr>
<th>Function</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>Structural support</td>
<td>Matrix production and remodeling</td>
</tr>
<tr>
<td>Modulation of circulation</td>
<td>MC contraction</td>
</tr>
<tr>
<td>Immune/inflammatory modulation</td>
<td>Cytokine production</td>
</tr>
<tr>
<td>Filtration and clearing</td>
<td>Endocytosis</td>
</tr>
<tr>
<td></td>
<td>Protease secretion</td>
</tr>
</tbody>
</table>
Mesangial proliferative glomerulonephritis
Mesangial deposition of immunoglobulin
Mesangial deposits
Sequence of events in acute glomerulonephritis

**Pathophysiology**
- Glomerular injury
  - Inflammation of glomerular capillary bed
  - Decreased glomerular capillary perfusion
    - Decreased GFR
    - Decreased tubular fluid
      - Decreased urine volume - oliguria
      - Hypertension - CHF, encephalopathy
      - Edema formation
      - Anemia
    - Increased ECF volume
  - Increased Na and water reabsorption
  - Azotemia
    - Increased urine osmolality
    - Decreased urine sodium
- Renal failure

**Clinical manifestations**
- RBC casts
- Hematuria
- Proteinuria
- Anemia
RBC cast is the typical feature in urine
Immunologic mechanisms of glomerular injury

- Antibodies against fixed glomerular antigens
  - Planted antigens
  - Autoantigens
- Circulating antigen-antibody complexes
  - Antigens unrelated to the kidney
  - Autoantigens unrelated to the kidney
- T cell cytokine mediated
Anti-basement membrane antibodies
Anti-GBM crescentic glomerulonephritis
Linear deposition of anti-GBM antibodies
Circulating complexes

- “Single shot” serum sickness
- Chronic serum sickness
- Titered immune complex formation
Immune complex nephritis
Acute proliferative glomerulonephritis
Immune complex deposits
Subendothelial deposits
Membranous glomerulonephritis
Membranous pattern of immunoglobulin deposition
Subepithelial deposits deposits
Mediators of glomerular injury

- Complement
- Antibody mediated cellular cytotoxicity
- Activation of coagulation
- Apoptotic signals
- T cell cytokines
Antibody deposition

Immune complexes

Complement activation

C5b-9

C5a

Neutrophils

Platelets

Macrophages

Mesangial cells

Epithelial

Endothelial

Mesangial

Proteinuria

Oxidants

Cytokines

Proteases

Growth factors

Eicosanoids

Nitric oxide

Others

Proteinuria, decreased GFR, inflammation.
Criteria for diagnosis of acute post-streptococcal glomerulonephritis

1. **Latent interval- time from infection to symptoms**
   1. Not less than 5 days and not more than 28 days
   2. Usually 10-21 days.

2. **Documentation of preceding streptococcal infection**
   a) Culture of throat or skin
   b) Serologic changes in strep titers

3. **Evidence of immunologic involvement**
   a) Appropriate complement profile or low serum C₃

4. **Clinical course characteristic of post-streptococcal GN**
   a) Lack of nephrotic syndrome at onset
   b) Oliguria followed by a diuresis in 10-30 days
   c) Edema formation and hypertension proportional to decrease in renal function
   d) Return of C₃ to normal levels in 6-12 weeks
Non-streptococcal GN

Primary renal disease
- Primary hematuria
- Hypocomplementemtic nephritis
- Chronic (non-specific) GN
- Rapidly progressive GN
- Hereditary nephritis

Systemic disease with renal involvement
- Anaphylactoid nephritis
- Lupus nephritis
- Hemolytic uremic syndrome
- Hypersensitivity angiitis
- Polyarteritis

Focal or mild proliferative GN
Mesangiocapillary GN
Focal or diffuse irreversible GN
Severe proliferative GN with crescents
Chronic non-specific changes
Focal or diffuse proliferative lesion
Focal or diffuse proliferative lesion
Membranous lesion
Microthrombi in capillary loops
Focal areas of necrosis
Perivascular infiltrate
Renal diseases associated with a low C₃

- Post-infectious glomerulonephritis
  - Post-streptococcal GN
  - SBE
  - Shunt nephritis

- SLE nephritis
  - Diffuse proliferative type

- Mesangial capillary nephritis
  - A.K.A. membranoproliferative GN
  - Partial lipodystrophy syndrome
THROMBOTIC MICROANGIOPATHY
Hemolytic uremic syndrome

**Definition**
- Microangiopathic hemolytic anemia
- Thrombocytopenia
- Azotemia

**Frequently associated findings**
- Abdominal pain
- Bloody diarrhea
- Oliguria
- Hypertension
Mechanisms of Vascular Injury

- Endothelial Activation
  - Stretch / Shear Forces
  - Inflammation
  - Immune Response

- Activation of Coagulation
  - Platelets
  - Tissue Factor
  - Factor X

- Smooth Muscle Activation
  - Contraction
  - Ischemia
  - Hyalnosis

- Autocrine regulation
  - Renin - Angiotensin
  - Cytokines, Growth Factors
Sequence of events in hemolytic uremic syndrome

**Pathophysiology**
- Glomerular injury
  - Endothelial damage in arterioles and capillary loops
  - Platelet consumption and utilization
    - Formation of fibrin strands
      - Intravascular thrombosis
    - Decreased glomerular capillary perfusion
      - Decreased GFR
        - Increased Na and water reabsorption
        - Decreased urine formation
          - Renal failure

**Clinical manifestations**
- Thrombocytopenia
- Microangiopathic hemolytic anemia
- Hematuria and proteinuria
- Decreased urine osmolality
- Azotemia
- Decreased urine sodium
- Oligo-anuria
Typical features of microangiopathic hemolytic anemia
Tubulo-interstitial disorders
Interstitial nephritis
Mechanisms of tubulointerstitial injury

- Infectious agents
- Toxins
- Immunologic responses
- Obstruction
- Ischemia
Comparison of the clinical presentation of glomerular vs tubular disorders

<table>
<thead>
<tr>
<th></th>
<th>Glomerular</th>
<th>Tubular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>&gt; 1.0 gm/day</td>
<td>&lt; 1.0 gm/day</td>
</tr>
<tr>
<td>Urine sediment</td>
<td>Active many RBC &amp; WBC casts</td>
<td>Inactive few cells</td>
</tr>
<tr>
<td>Urine Na FENa</td>
<td>Low (&lt;1%)</td>
<td>High (&gt;2%)</td>
</tr>
<tr>
<td>Urine osm</td>
<td>High (&gt;500 mosm/L)</td>
<td>Low (&lt;300 mosm/L)</td>
</tr>
<tr>
<td>Acid excretion</td>
<td>Large anion gap</td>
<td>Hyperchloremic acidosis</td>
</tr>
<tr>
<td>Oliguria</td>
<td>Common</td>
<td>Unusual</td>
</tr>
<tr>
<td>Edema</td>
<td>Common</td>
<td>Unusual</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Common</td>
<td>Unusual</td>
</tr>
</tbody>
</table>
Chronic glomerulosclerosis
Glomerular Lesions of Systemic Diseases
Nonimmunologic causes of increased glomerular permeability

- Diabetic nephropathy
- Amyloid
Pathology of diabetic nephropathy

- Thickening of GBM
- Nodular mesangial sclerosis
  - Kimmelsteil-Wilson lesion
- Mesangial widening with an increase in matrix
  - Vm/Vg
- Arteriolar hyalinization
- Linear fluorescence
- Glomerular hypertrophy
Diabetic nephropathy

K-W nodules

Normal
Diabetic nephropathy

Diffuse linear deposition of IgG and albumin
Diabetic nephropathy

Diffusely thickened GBM

Nodular sclerosis
Natural history of diabetic nephropathy

- **Stage 1- Time of initial diagnosis**
  - Increased GFR
  - Increased kidney size
- **Stage II- The first decade (years 1-10)**
  - Early structural changes (GBM, mesangium)
- **Stage III- Microalbuminuria**
- **Stage IV- Onset of clinical disease (years 10-20)**
  - Proteinuria
  - Hypertension
  - Declining GFR
- **Stage V- End-stage renal disease**
Potential mechanisms

- Hyperfiltration
- Hypertension
- Aldose-reductase
  - Excess glucose polyol
  - Increased sorbitol/ decreased myoinositol
- Toxicity of high glucose
- Non-enzymatic glycation
  - Advanced glycation end products
Amyloidosis
Crescentic glomerulonephritis

<table>
<thead>
<tr>
<th>Light microscopy</th>
<th>IF microscopy</th>
<th>Possible pathogenesis</th>
<th>Association</th>
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</thead>
<tbody>
<tr>
<td>Crescents/ necrosis</td>
<td>Linear IgG Fibrinogen</td>
<td>Anti-GBM antibodies</td>
<td>Pulmonary hemorrhage</td>
</tr>
<tr>
<td>Crescents/ proliferation</td>
<td>Granular IgG Complement Fibrinogen</td>
<td>Immune complexes</td>
<td>Bacterial infections</td>
</tr>
<tr>
<td>Crescents/ necrosis</td>
<td>Negative Fibrinogen (?)</td>
<td>ANCA</td>
<td>Systemic Symptoms</td>
</tr>
</tbody>
</table>
Anti-neutrophil cytoplasmic antibodies

**C-ANCA - antiproteinase 3**
- 90% sensitivity for extended Wegener’s granulomatosis
  - Granulomatous respiratory lesion
  - Systemic vasculitis
  - Necrotizing glomerulonephritis
- 75% sensitivity for limited Wegener’s granulomatosis
  - With or without renal involvement
- Potential false positives
  - Amebiasis
  - Propylthiouracil induced vasculitis
- Titer varies with activity

**P-ANCA**
- Variety of antigens
  - Myeloperoxidase
  - Elastase
  - Cathepsin G
  - Lysozyme
  - Lactoferrin
  - B-glucuronidase
  - Enolase
- Broader reactivity
  - MPA, NCGN, C-S, 10-20% PAN, 20% KAW, IgA, ANCA in HSP
- Other diseases
  - Inflammatory bowel disease
  - Autoimmune liver disease
  - Sepsis
  - Neoplasia
cANCA  pANCA
Pauci Immune Glomerulonephritis
RPGN- crescents

Fibrin deposition (immunofluorescence)
## WHO Classification of Lupus Neprhitis, Revised

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Minimal mesangial lupus glomerulonephritis - mesangial deposits</td>
</tr>
<tr>
<td>II</td>
<td>Mesangial proliferative LGN - with immune deposits</td>
</tr>
<tr>
<td>III</td>
<td>Focal LGN (less than 50% of glomeruli) subendothelial deposits,</td>
</tr>
<tr>
<td></td>
<td>Class III (A) Purely active focal proliferative LGN</td>
</tr>
<tr>
<td></td>
<td>Class III (A/C) Active and chronic lesions focal LGN:</td>
</tr>
<tr>
<td></td>
<td>Class III (C) Chronic inactive sclerotic focal LGN</td>
</tr>
<tr>
<td>IV</td>
<td>Diffuse segmental (IV-S) or global (IV-G) LGN - SE deposits,</td>
</tr>
<tr>
<td></td>
<td>Class IV (A) Active lesions: diffuse proliferative LGN</td>
</tr>
<tr>
<td></td>
<td>Class IV (A/C) Active and chronic lesions: proliferative and sclerotic LGN</td>
</tr>
<tr>
<td></td>
<td>Class IV (C) Inactive with glomerular scars: diffuse sclerotic LGN</td>
</tr>
<tr>
<td>V</td>
<td>Membranous LGN - subepithelial immune deposits</td>
</tr>
<tr>
<td>VI</td>
<td>Advanced sclerotic LGN</td>
</tr>
</tbody>
</table>
Lupus nephritis WHO Class I
Lupus nephritis WHO Class II
Hereditary diseases
Polycystic kidney disease
Severe neonatal form of ARPKD:

- intrauterine renal failure,
- oligohydramnios,
- Potter sequence,
- pulmonary hypoplasia leading to respiratory insufficiency and perinatal demise
Alport: Molecular Genetics

- 1 in 50,000 live births
- X-linked form is most common (no father-son transmission, females are carriers)
  - responsible gene is COL4α5
- X-linked form associated with esophageal leiomyomatosis
  - contiguous gene syndrome involving COL4α5 and COL4α6
- autosomal recessive form linked to chromosome 2
  - mutations in COL4α3 and COL4α4
Renal Transplantation
Technique of pancreas-kidney transplant with systemic drainage. The pancreas is placed in the right iliac fossa. The donor portal vein is anastomosed to the recipient iliac vein, resulting in systemic drainage of pancreatic veins.
Acute Renal Allograft Rejection

Antibody-mediated

Cell-mediated

C4d

CD3

Courtesy from S. Florquin
Eosinophils in Acute Renal Allograft Rejection

Courtesy from S. Florquin.
Mechanisms of Effects of CsA and Prednisone on Lipids

Exogenous Pathway

bile acid + cholesterol

INTESTINE

CM → Capillary

Lipoprotein Lipase

CM rem → Capillary

Endogenous Pathway

LDL

1. CSA

LIVER

HMGCoA reductase

cholesterol

2. Prednisone

VLDL → Capillary

Lipoprotein Lipase

EXTRAHEPATIC TISSUE

LDL → HDL
BK Virus Nephropathy
DECOY CELLS BY PHASE CONTRAST
Thank you