There are no conflicts of interest.
Goals and Objectives

Goals
- Provide introduction to evaluation of kidney biopsy
- Review microscopic anatomy of the human nephron
- Compare and contrast normal microscopic anatomy to that seen in diseased states

Objectives
- Student should be able to recognize normal microscopic anatomy
- Students should be able to identify deviations from normal
Overview

- Review normal histology of the kidney
- Case presentations and interactive questions
- Clinical summary
- Review of key points
Components of the Pathologist’s Evaluation of a Kidney Biopsy

Four modalities

– Laboratory and clinical data
– Light microscopy
– Immunofluorescent microscopy
– Electron microscopy
Starting Point

Laboratory and Clinical Data
Clinical History

- Presenting symptoms
- Known systemic diseases
- Family history
- Medication history
Clinical Lab Values

Blood
- Renal function tests
- Electrolytes

Urinalysis
- pH
- Osmolality
- Glucose
- Protein
- Cells
The Biopsy
Light Microscopy

- Histology: determine whether findings are normal or abnormal

- Determine which compartment(s) affected
  - Glomeruli
  - Tubules
  - Interstitium
  - Blood vessels
Normal Glomerulus

In practice, renal corpuscle = glomerulus
Glomerulus

- Determine if components of glomerulus are normal or abnormal
- **Mesangium**
  - Evaluate overall cellularity
  - Mesangial cells should be centered near the hilum and not overlapping
- **Capillary walls**
  - Should be thin
Mesangial cells

Capillary walls

Mesangial cells
Tubules, Blood Vessels, and Interstitium
Immunofluorescent Microscopy

- Kidney stained with antibodies against immunoglobulins and complement components; antibodies are linked with a fluorescent dye

- If positive for a given antigen, the glomeruli will light up when using a fluorescent microscope
Immunofluorescent Microscopy

- Evaluate whether positive or negative
- Types of the deposits that are positive
  - Immunoglobulin (IgG, IgA, IgM)
  - Complement (C3, C1q)
- Character of deposits
  - Granular
  - Linear
- Location of deposits
  - Glomerular capillary wall (periphery of glomerulus)
  - Mesangium (central part of glomerulus)
Linear deposits
Granular deposits
Electron Microscopy

- Evaluate whether ultrastructural components are normal or abnormal
- Podocyte foot processes
  - Normal or effaced/flattened
- Mesangium
  - Cellularity
  - Electron-dense deposits
- Basement membrane of capillary walls
  - Structure (normal or thickened)
  - Electron-dense deposits
Case I

Renal Biopsy:
10-year-old male
History

- 10 year-old male presents with trouble putting on shoes
- Physical examination: ankle edema
- Laboratory testing: proteinuria and mild renal insufficiency (elevated serum creatinine)
- A renal biopsy is performed
Light Microscopy

[Images of normal and patient tissue samples]
The light microscopic appearance of the glomeruli in the biopsy tissue is:

1. Normal
2. Frankly abnormal
3. Slightly abnormal
4. I can't tell--I didn't complete the renal section
Immunofluorescent Microscopy

- Negative for immunofluorescent staining
  - No immunoglobulin staining
  - No complement staining
Electron Microscopy

Normal

Patient
Electron microscopy was performed. Given your knowledge of the normal renal ultrastructure, your evaluation shows which of the following?

1. Normal ultrastructure, as compared to the normal control
2. Ultrastructural abnormalities of the visceral epithelial cells
3. Ultrastructural abnormalities of the mesangium
4. There are red blood cells in the urinary space
Given your physiologic knowledge of the role of visceral epithelial cells and glomerular filtration, you expect which of the following laboratory findings?

1. Normal urinalysis
2. Blood in the urine
3. Glucose in the urine
4. Protein in the urine
Case Summary

- Diagnosis: **Minimal change disease**
- Symptoms
- Biopsy results
- Pathophysiology
- Therapy
- Outcome
Case II

Renal biopsy:
30-year-old woman
30-year-old female complains of change in urine color. You elicit a history of prior sore throat.

Physical examination: pitting edema

Laboratory testing: hematuria and moderate renal insufficiency (elevated serum creatinine)

A renal biopsy is performed
Light microscopy

[Images of normal and patient tissue samples]
How does the microscopic appearance of the patient’s glomerulus (right) differ from the normal control (left)?

1. There is no difference, they appear similar
2. The glomerulus is too cellular
3. There is marked hemorrhage
4. There is diffuse necrosis of the glomerulus
Immunofluorescent studies (IgG)
This photomicrograph demonstrates immunofluorescent microscopy on a glomerulus reacted with antisera to IgG. You would characterize the results as...

1. Negative
2. Positive with a smooth, linear pattern
3. Positive with a granular pattern
4. The results are not evaluable
Electron Microscopy

Normal

Patient
The slide on the right represents electron microscopy of the patient’s glomerulus. From your evaluation of the glomerular basement membranes, you conclude...

1. There is no deviation from the normal ultrastructure
2. That the patient’s basement membrane has structural breaks in its continuity.
3. That the tissue is poorly preserved.
4. There are electron dense deposits along the outside of the basement membranes.
Case Summary

Diagnosis: Poststreptococcal glomerulonephritis

Symptoms

Biopsy results

Pathophysiology

Therapy

Outcome
Case III

Renal biopsy:
24-year-old male
Clinical History

- 24-year-old male presents with gross hematuria
- Physical examination: within normal limits
- Laboratory testing: numerous red blood cells found in urine (hematuria)
- A renal biopsy is performed
Light Microscopy
How does the patient’s glomerular histology (right) differ from the normal glomerulus (left)?

1. There is mild increase in mesangial cells and matrix
2. There is total occlusion of the capillary lumens
3. There is a marked inflammatory infiltrate
4. The glomerulus shows a marked increase in the number of visceral epithelial cells (podocytes)
Immunofluorescent studies (IgA)
This photomicrograph demonstrates a direct immunofluorescent microscopy on a glomerulus reacted with antisera to IgA. You would characterize the results as…

1. Negative
2. Positive with granular mesangial distribution
3. Positive with linear capillary wall distribution
4. The results are not evaluable
Electron Microscopy

Normal

Patient
The slide on the right represents the electron microscopic appearance of the patient’s glomerulus. From your evaluation, you would draw which of the following conclusions:

1. There is no deviation from the normal ultrastructure
2. The patient’s basement membranes contain coarsely granular electron dense deposits
3. The glomerular basement membranes show duplication into multiple layers
4. The mesangium contains finely granular electron-dense deposits
Case Summary

- Diagnosis: **IgA nephropathy**
- Symptoms
- Biopsy results
- Pathophysiology
- Therapy
- Outcome
Case IV

Renal Biopsy

60-year-old male
Clinical History

- 60-year-old male presents with polydipsia and polyuria
- Physical examination: BMI of 38
- Laboratory testing: glucosuria and proteinuria
- A renal biopsy is performed
Light Microscopy

Normal

Patient
How does the histologic appearance of the biopsy (right slide) differ from that seen in the normal kidney (left slide)?

1. The biopsy is identical to the normal control
2. There is thickening of the glomerular capillary loops
3. There is epithelial cell (podocyte) proliferation
4. There is acute inflammation
Immunofluorescent Microscopy

- Negative results
- Non-specific albumin deposition along glomerular capillary walls
Electron Microscopy

Normal

Patient
Electron microscopy was performed on the biopsy material. The most prominent ultrastructural feature in the glomerulus on the right is:

1. Thickened glomerular capillary basement membranes
2. The presence of electron-dense deposits
3. The presence of viral particles
4. Marked epithelial cell proliferation
Case Summary

- Diagnosis: **Diabetic renal disease**
- Symptoms
- Biopsy results
- Pathophysiology
- Therapy
- Outcome
Take Home Messages

- 4 modalities to the evaluation of the renal biopsy
- Examine all kidney compartments
- Recognize normal microscopic anatomy
- Recognize normal ultrastructure
- Key to being a successful microscopist
  - Internalize a broad knowledge base of what is normal to rapidly recognize what is abnormal
Thank you for your participation.