Lab 3, case 1

12-year-old Costa Rican boy is brought into clinic by his parents because of dark brownish-red urine over the last 24 hours. The family has been visiting friends in Indianapolis for two weeks. While touring the Children’s Museum 2 days ago they noticed their son had puffiness around his eyes. The week prior to leaving home, the child had a febrile illness associated with a sore throat but he improved within five days while taking children’s Tylenol. On exam the boy has a blood pressure of 132/92 mmHg as well as periorbital and ankle edema bilaterally. A Monospot test was negative. No known family history of kidney disease.

Questions:
• What would you expect the urinalysis to show?
• What blood tests would you order and what would you expect them to show? Do any of these tests help you to determine if a renal biopsy is necessary?
• Is this an example of nephrotic or nephritic syndrome? Why?
• Which portion of the nephron would you expect to be abnormal?
• What is the expected characteristic pathology associated with this patient?

Urine reagent “dipstick” and microscopy
Dysmorphic red cells  Scanning microscopy showing dysmorphic red cells in a patient with glomerular bleeding. Acanthocytes can be recognized as ring forms with vesicle-shaped protrusions (arrows). Courtesy of Hans Köhler, MD.
H&E (left) and Jones' (right) – hypercellular glomeruli

Hypercellular glomeruli (where?)

Jones’ silver

PAS stain
Anti-IgG

Anti-C3

Positive or negative?
Capillary loop or mesangial?
Granular or linear?
What are these inflammatory cells?

Define the deposits in relationship to the GBM and podocytes
Describe the deposit in this image.

Subepithelial deposits may be seen with Masson's trichrome stain.
Lab 3, case 2

Case 2: A 29-year-old Country-Western singer (67 kg Caucasian female) presents with complaints of facial rash, generalized malaise, pleuritic chest pain, and diffuse joint pain that has gradually worsened over the last week. On exam she has a blood pressure of 160/98 mmHg, a palpable malar rash in a butterfly distribution over her face, and a pleural rub. Negative family history. She smokes unfiltered cigarettes, drinks two 6-packs of Lone Star Pilsner each week, recently lost her boyfriend and her Bluetick Coon dog ran away.

Questions:
1. What is the reason for the edema and hypertension?
2. What is the clinical syndrome? Why?
3. What simple “bedside” (point-of-case) test could you do to support your clinical diagnosis?
4. What blood tests would provide further support for your diagnosis?
5. What would you expect a renal biopsy on this patient to show?
6. Is this an example of: (1) *in situ* immune complex deposition or (2) circulating immune complexes with antigen of endogenous origin (DNA) or (3) circulating immune complex deposition with antigen of exogenous origin?
Urine reagent “dipstick” and microscopy

H&E stain of glomeruli

normal  hypercellular (glomerulonephritis)
mesangial

global endocapillary

segmental endocapillary

extracapillary (crescent)

karyorrhexis

wire loops
anti-IgG labeling of glomerulus
anti-IgG labeling of tubules
anti-IgG of nuclei (like “ANA” but in tissue, not serum)

mesangial (*) and subendothelial (arrows) electron dense deposits

capillary lumen
urinary space
mesangium

mesangial (+) and subendothelial (arrows) electron dense deposits
What is this inclusion?

Lab 3, case 3

55-year-old pharmaceutical representative (102 kg African American man) presents with complaints of increasing shortness of breath over the last week. Yesterday he coughed up blood but reports no fever or chills. He usually smokes a pack of cigarettes a day and one cigar per week but he quit 3 weeks ago. No alcohol. His territory includes Indiana, Michigan, Kentucky and Ohio so he spends many hours sitting in his car. On exam he has a blood pressure of 178/100 mmHg, bilateral crackles on auscultation of the chest and 1+ edema of the lower extremities. The patient has no rashes. CXR reveals bilateral infiltrates and serum creatinine is 8.9 mg/dl. His creatinine was 0.9 mg/dl six months ago when he had a work-related physical exam. PPD at that time was negative. No family history of renal disease.

Questions:
What clinical syndrome does this man have? What are the potential causes for this syndrome?
What simple test could you do in the office to provide support for your clinical diagnosis?
What other clinical and laboratory tests would be helpful in sorting out this problem? What would you expect them to show?
What is the significance of the previous serum creatinine and urinalysis?
Would you do a tissue biopsy on this patient? If so, would you biopsy the lung or the kidney?
If you decide to do a renal biopsy what would you expect it to show?
H. Is this an example of: (1) in situ immune complex deposition or (2) circulating immune complexes with antigen of endogenous origin or (3) circulating immune complex deposition with antigen of exogenous origin?
Urine microscopy

Urine reagent “dipstick” and microscopy
rupture of GBM (small arrows) & fibrin clot = necrotizing glomerulonephritis

mitosis of parietal epithelial cell
Jones' silver H&E multi-nucleated giant cells

glomerulus

Anti-fibrinogen immunofluorescence of glomerulus with crescent
Direct immunofluorescence

Anti-IgG labeling of glomerular capillary loops. Granular or linear staining of GBM?

anti-IgG labeling of glomerular loops, higher resolution
crescent collapsed GBM

EM of glomerulus with crescent

crescent

collapsed GBM

Gross appearance of kidneys at autopsy
Compare chest x-ray to gross appearance of lungs at autopsy

anti-neutrophil cytoplasmic antibody

P-ANCA  C-ANCA

(negative in our patient)