Case 1

A 72-year old white female with a 20-year history of well-treated hypertension was referred for further evaluation of impaired kidney function. She was feeling well until 3 months ago when easy fatigability was noted and severe anemia (hemoglobin of 8.4gm/dL) and a serum creatinine of 2.4 mg/dL were discovered. A renal ultrasound was said to be "normal." She received 2 units of packed RBC, and a colonoscopy revealed multiple polyps which were removed and proved to be benign. A week later, she noticed some blood in the stool, and received another blood transfusion. The serum creatinine was now 4.2 mg/dL. Urinalysis showed 20-50 rbc/hpf and 1+ protein. Repeat colonoscopy showed a post-polypectomy ulcer with a large visible vessel protrusion for which she underwent in hospital photo-coagulation. Kidney failure was believed to be of pre-renal origin secondary to GI bleeding superimposed on chronic kidney disease (CKD) due to long-standing hypertension. She was sent home with a serum creatinine of 3.9 mg/dL. Two weeks later, the serum creatinine rose further to 4.6 mg/dL. She was referred for further evaluation. Physical examination is unremarkable except for edema 1+ bilaterally.

Laboratory Evaluation:

Hemoglobin 10.6 g/dL, leukocytes 5.4 x 10^9/L, platelets 120,000 x 10^9/L;
Sedimentation rate: 65 mm/h; Creatinine: 5.3 mg/dL, BUN 75 mg/dl, Endogenous Creatinine Clearance (CrCl) 16 ml/min; Urinalysis: 20-30 rbc/hpf (<25% dysmorphic), protein 1.8 g/24h; C3 109 mg/dl (nl 70-175mg/dL), C4 17 mg/dl (nl 14-40mg/dL); Rheumatoid factor: 81 IU/ml (nl 0-39 IU/ml), ANA: 1.2 (<1.0); pANCA +; MPO-ANCA 62.9 EU/ml (nl <5 EU/ml). A renal biopsy is performed (see Figures 1 a, b). Ten glomeruli were identified, none of which were normal, with one or two being globally sclerosed. All glomeruli show segmental capillary loop consolidation, with matrix replacement and tuft-capsular adhesions. Silver stains show segmental fragmentation of peripheral capillary loop basement membranes. No immune complex type deposits were found. Viable regions of glomeruli show focal endocapillary proliferation, with leukocyte accumulation and localized fibrin deposition. Silver stains show segmental fragmentation of Bowman's capsule surrounding several glomeruli. Focal interstitial fibrosis with associated tubular atrophy, involved over two-thirds of the biopsy area. Tubules contained red blood cells and red cell casts. The final diagnosis was of a focal segmental proliferative and necrotizing glomerulonephritis, pauci-immune type III.

Question 1: Which ONE of the following therapies would you NOW recommend?

    A. Angiotensin converting enzyme inhibitors + low protein diet
    B. High dose corticosteroids + oral or IV cyclophosphamide
    C. High dose corticosteroids + mycophenolic mofetil
    D. High dose corticosteroids + oral or IV cyclophosphamide + plasmapheresis
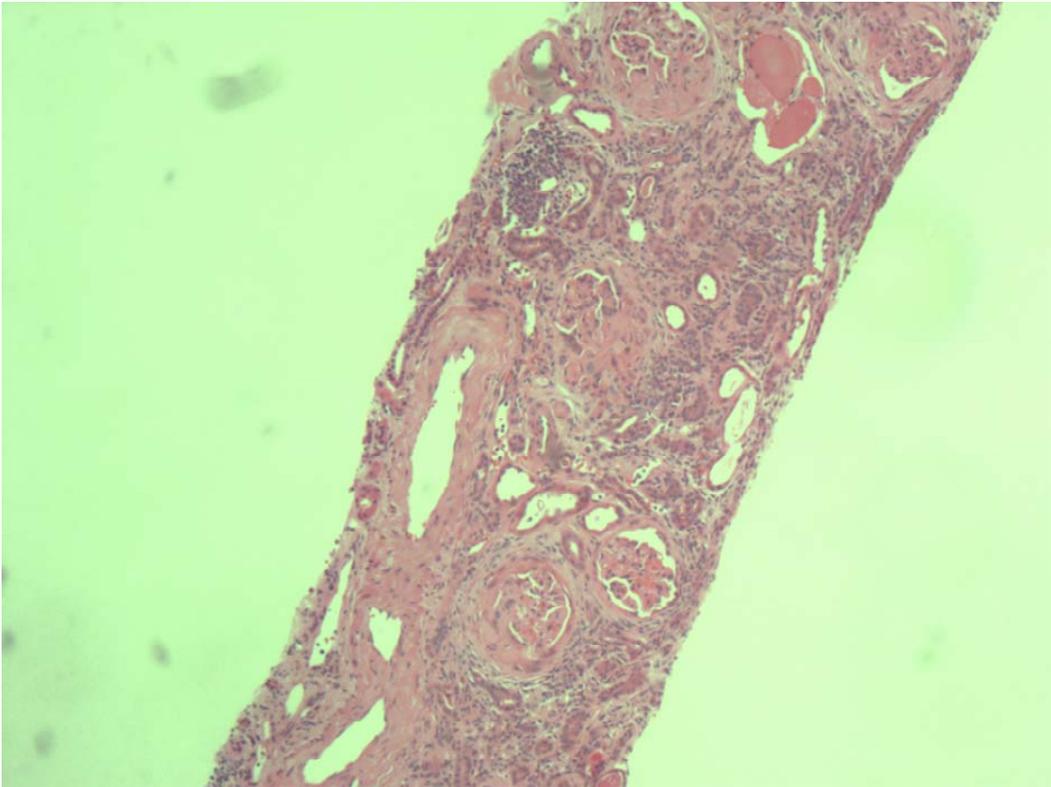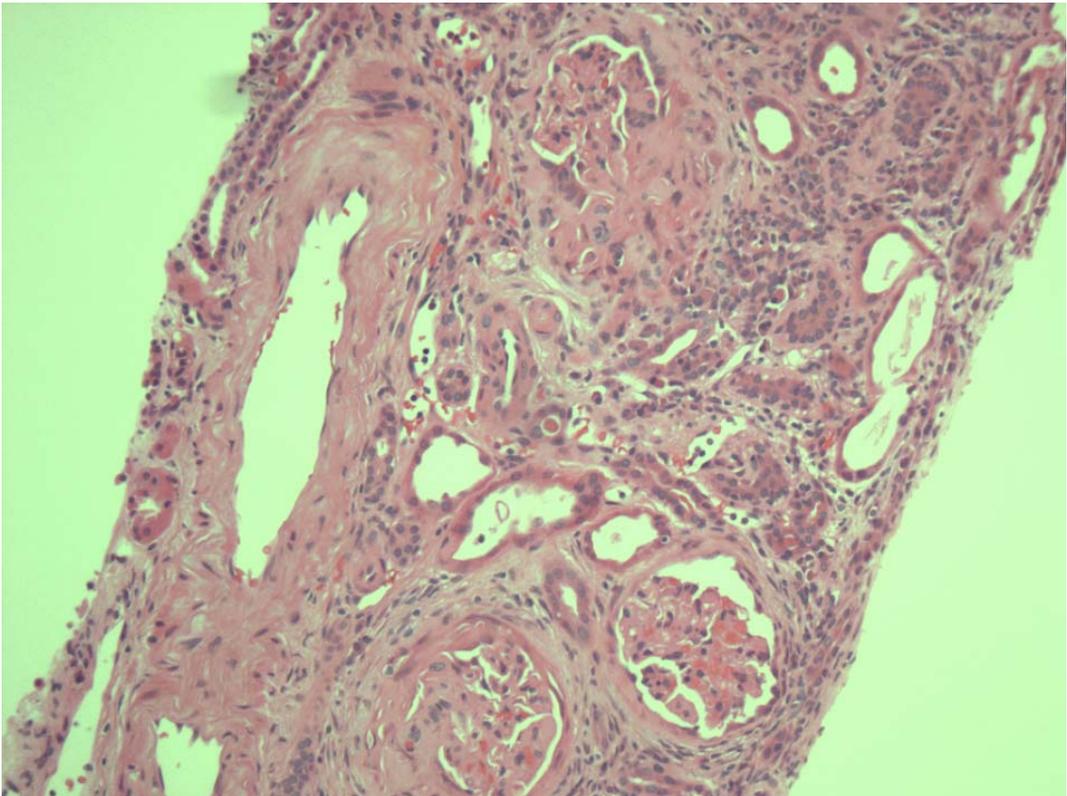   E. High dose corticosteroids + Rituximab

Figure 1a

Figure 1b

Case 2

A 73-year old man was referred for evaluation of edema with tea-colored and foamy urine starting in November 2009. He had no prior history of hypertension, but in October 2009 his systolic blood pressure (BP) was found to be in 160 mmHg and continued to increase to 213mmHg in January 2010. During an evaluation for hypertension, a serum creatinine of 2.1mg/dL was noted; increased from a baseline of 1.0 - 1.2 mg/dL the previous year. Urinalysis showed >50 rbc/hpf; >25% dysmorphic. Urinary protein excretion was 1.7 g/day. Fluorescent anti-nuclear antibody was 1:40, C4 was 15mg/dL (normal) and C3 was 52mg/dL (low). Renal ulstraound showed a right kidney 10.9 cm and a left kidney 12.4 cm in length with no masses, renal artery stenosis, or hydronephrosis. BP was controlled with a beta-blocker, and a kidney biopsy was performed. Light, immunofluorescence and electron microscopy are shown in Figures 2 a, b, c, d.

Question 2: Based on these clinical and pathological findings, which ONE of the following would be the MOST useful diagnostic tests?

> A. Serum free light chain assay
> B. Hepatitis B and C serology
> C. Complement regulation evaluation (Factor H, I, Membrane co-factor)
> D. Muscle-biopsy for cholesterol emboli
> E. Anti-double stranded DNA antibody
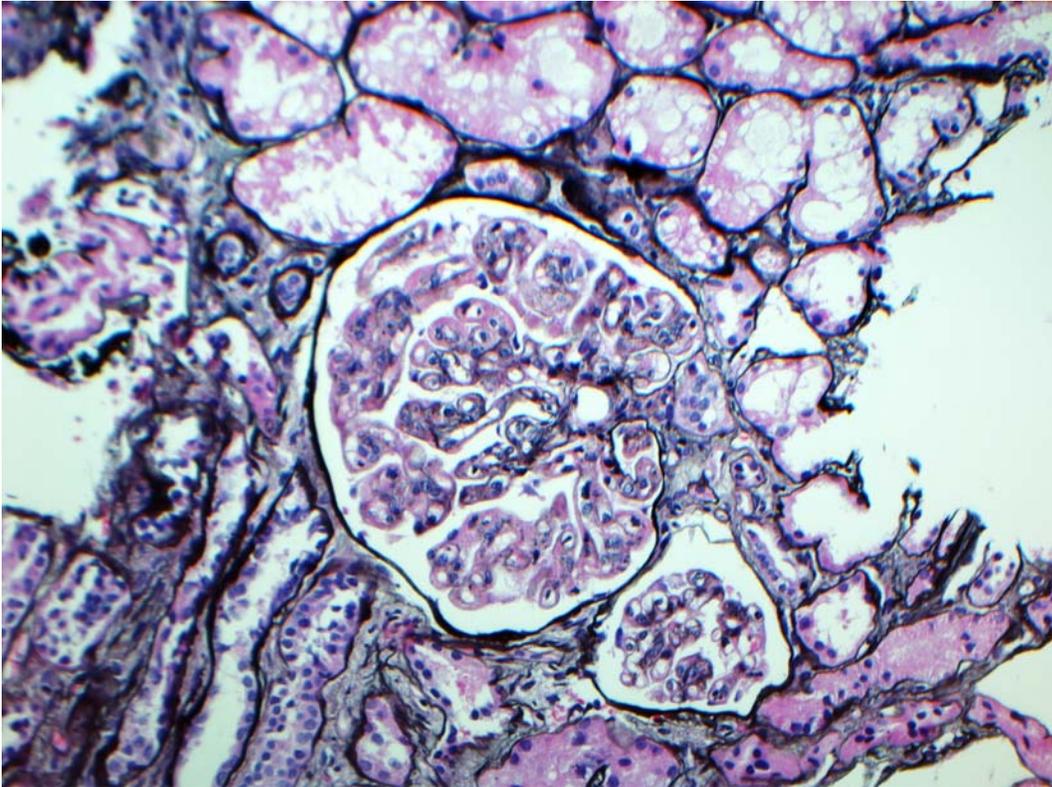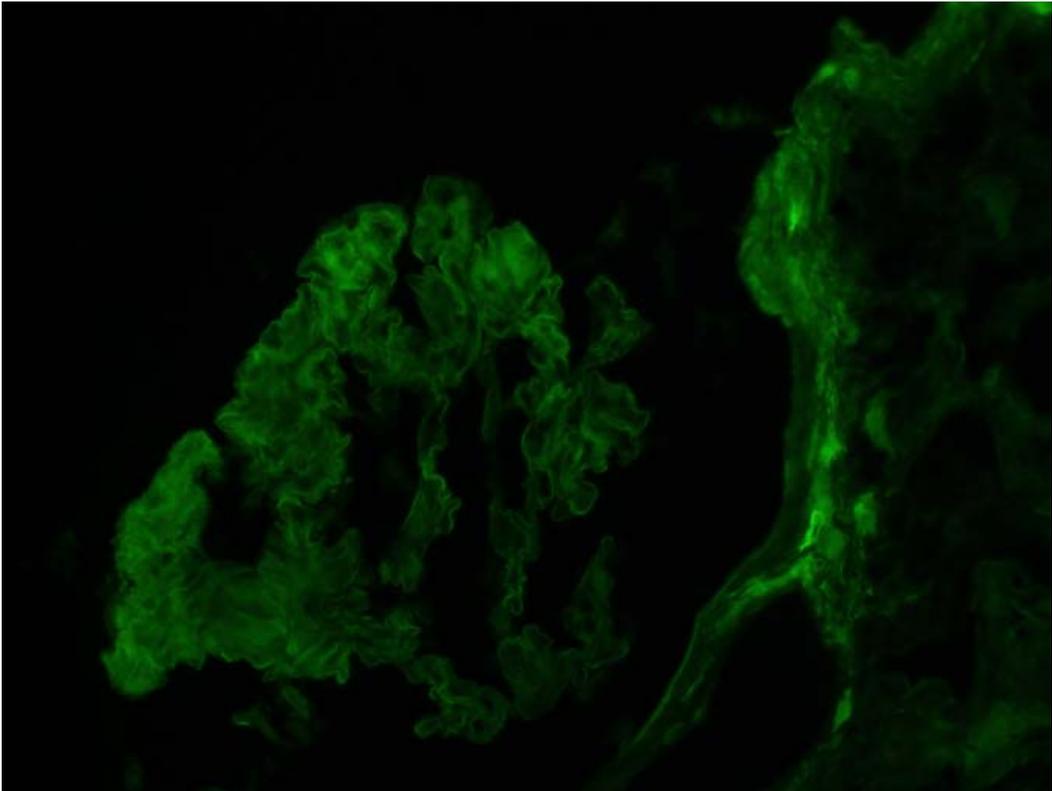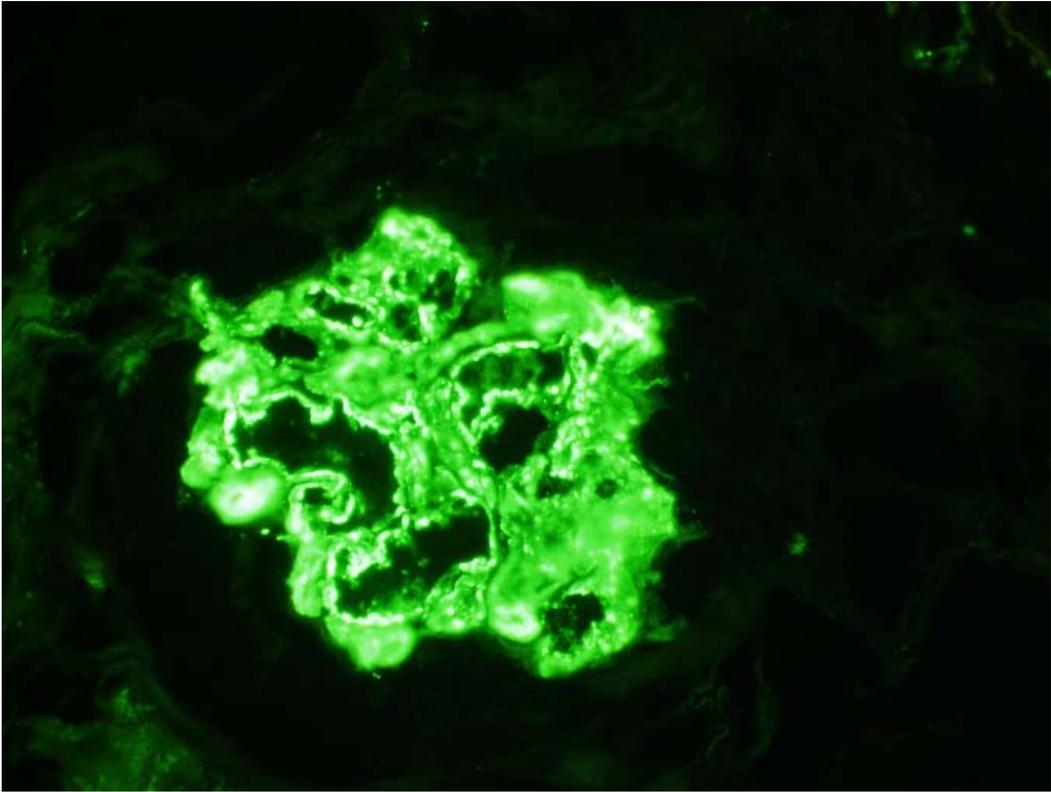
Figure 2a - Silver 400X

Figure 2b – IgG

Figure 2c – C3

Figure 2d – Electron Microscopy