**Off to a Bad Start**
A 10 year-old boy presented with a one-week history of lower extremity edema. While on vacation, he and his parents noted indentations on his ankles from his socks.

His past medical history was significant for environmental allergies with nasal congestion and sneezing. He has asthma with 1-2 episodes of wheezing per year, generally in the fall season, sometimes with a respiratory infection.

Physical examination showed a blood pressure of 116/54 mmHg, clear lungs, mild ascites and 2+ pretibial and pedal edema. No rashes were present.

A urine dipstick shows a specific gravity of 1.030, pH 7, with no blood but 4+ protein. The urine protein/creatinine ratio was 6.5 (normal < 0.20, nephrotic range > 2.0). His electrolytes were normal. Other labs included: creatinine 0.6, albumin 2.3, calcium 8.1, C3 of 110 (normal: 80-210), C4 of 22 (normal: 15-45). ANA was negative.

The patient was started on prednisone 60 mg once daily. Four weeks later, his urinalysis showed negative protein. He was converted to alternate day prednisone, but 5 days later, he again had 4+ urine protein. A decision was made at that time to perform kidney biopsy.

**Pathology Report for Biopsy #1**

The kidney biopsy shows mild mesangial hypercellularity with low-grade mesangial IgM and C3 deposition (no IgG, IgA or C1q). Podocytes show diffuse foot process fusion (slide 2).

**What is the diagnosis at this time?**

After the biopsy, the patient was started on cyclosporine and continued on prednisone. Urine protein became negative within 3 weeks. Prednisone is weaned off over the next 3 months and he was maintained on cyclosporine.

He continued in remission for a total of 11 months. However, coincident with a viral respiratory illness, he had a relapse with 4+ urine protein. Prednisone was re-started with remission within 3 weeks. Over the next several months, the patient proved steroid-dependent on several cycles of attempted weaning and restarting. Ultimately, he became steroid-resistant.

With a urine protein/creatinine ratio at 6.2, albumin at 2.3 g/dl and serum creatinine at 0.8 mg/dl, a second renal biopsy was done.

**Pathology Report for Biopsy #2**

The biopsy shows areas of tubular atrophy with interstitial fibrosis and chronic inflammation. Occasional glomeruli show segmental areas of scarring (slides 1-2). Podocytes again show diffuse foot process effacement.

**What is the diagnosis?**

*Study Questions (no online answers required):*
  - What is the prognosis in this case?
**A Little Too Late**

HM is a 67-year old Native American man who presents with decreased vision in the right eye. The past history is significant for rheumatoid arthritis, which is still active. He has had weight loss of 80 pounds in the past year, which he attributes to decreased alcohol intake and the fact that he has been depressed by the death of his daughter.

Eye grounds show microvascular lesions thought to be consistent with hypertensive retinopathy. Blood pressure at the time was 180/100. There is some peripheral edema.

**Urinalysis:**
- 3+ proteinuria by dipstick and a 24-hour urine shows 12 grams of protein.
- No hematuria.
- Urine electrophoresis shows no evidence of paraprotein.

**Serum:**
- Rheumatoid factor positive at 1:2560.
- Normal electrolytes
- BUN 41, creatinine of 2.2, glucose 98, albumin 2.8 and cholesterol 199.

A renal biopsy was done.

**Pathology Report**

The light microscopy showed nodular mesangial sclerosis (slide 1). Congo red and thioflavin T stains were negative. Immunofluorescence was negative except for some linear staining of glomerular and tubular basement membranes for albumin and IgG. Electron microscopy showed increased mesangial matrix and thickened, homogeneous glomerular basement membranes (slide 2). There were no immune complexes and no amyloid.

**What is the diagnosis?**

*Study Questions (no online answers required):*
- What are the common causes of this renal syndrome in patients with rheumatoid arthritis?
- The diagnosis in this case seems at odds with the laboratory data. What is the natural history of this disease? What is your hypothesis about what happened here?
- How might we re-interpret the retinopathy and reconsider the cause of his presentation with visual problems at this point?
**Misfolded and Stuffed**
A 74 year-old man is referred to a nephrologist because of proteinuria. The patient has a history of hypertension, hypercholesterolemia and angina. Ten years ago, he had coronary angioplasty. Approximately one year ago, he first noted pedal edema and now is found to have non-selective proteinuria at 6.7g/day with hypoalbuminemia.

There is no past history of serious infection, TB or cancer other than removal of a basal cell carcinoma of the nose. The patient denies adenopathy, joint swelling, rash, anorexia, weight loss, fever, chills or night sweats.

Patient was a smoker until the time of the angioplasty. Social and family history are otherwise non-contributory. Physical exam was negative except for the edema. Lab data includes negative ANA, normal C3 and C4 complement, serum creatinine of 1.5 mg/dl, creatinine clearance of 30 cc/min and cholesterol of 382 mg/dl.

**Pathology Report**

![Pathology Images](slide1-slide7)

A renal biopsy was done and showed glassy acellular material filling the mesangium and thickening the capillary loops by light microscopy (slide 1). Electron micrographs (slides 2-4) show fibrillar material filling the glomerular mesangium and extending into capillary loops on both sides of the lamina densa (LD) of the glomerular basement membrane (GBM). The fibrillar nature of the infiltrating material is evident at higher magnification. Congo red stain is positive (slides 5-6). Immunofluorescence shows staining of the glomerular deposits with lambda but not kappa immunoglobulin light chains (slide 7).

**What is the diagnosis?**

*Study Questions (no online answers required):*
- What is non-selective proteinuria?
- How do you account for the low GFR with a borderline normal serum creatinine?
- What are the most likely causes for this renal presentation in this age group?
- What are some possible causes for acellular mesangial expansion and capillary loop thickening?
A Dread Sense of Inevitability and Helplessness

A 32-year old man reports episodes of gross hematuria for at least the past 2 years. The hematuria is usually associated with upper respiratory tract infections and disappears on its own. The patient is otherwise healthy and the physical examination is negative.

Urinalysis shows proteinuria (2.5 g/day) and RBC with only granular casts. Creatinine clearance is 85 cc/min.

A renal biopsy was done.

Pathology Report

Renal biopsy shows a mesangial proliferative immune complex glomerulonephritis (slide 1) with segmental necrosis (slide 2) or small cellular crescents in 15% of glomeruli, global sclerosis in 15% and segmental sclerosis in an additional 15% of glomeruli. The immune complexes are predominantly mesangial (slide 3) and stain for IgA ++ (slide 4), IgG + and C3+ [0 to +++ scale]. Some glomerular capillaries show subendothelial immune complex dense deposits and mesangial cell interposition (slides 5 and 6). There is moderate tubular atrophy and interstitial fibrosis. Arterioles show focally massive hyalinosis.

What is the diagnosis?

Study Questions (no online answers required):

• Is this the typical clinical presentation for this disease?
• What is the mechanism of proteinuria in this case? What other mechanism of proteinuria commonly occurs with this disease?
• What is the likely outcome in this patient?
• What are the major adverse prognostic indicators in this patient’s history and biopsy?
• Treatment for this disease is problematic. Everyone would agree with the importance of blockade of the renin-angiotensin system but, for decisions about immunosuppressive agents, antiplatelet agents, anticoagulants or fish oil, the evidence base is weak and there is only expert opinion, which is not in uniform agreement.
• Arteriolar hyalinosis is commonly seen in this disease and often appears in absence of systemic hypertension.

Orphan Andrew

A 14-year old boy presents with a history of six to seven years of hematuria and proteinuria which presently is 3 grams/day.

A renal biopsy is performed.

Pathology Report

Glomeruli show pronounced and diffuse basement membrane abnormalities (slides 1-3).

What is the diagnosis?
A New Test Brings Clarity
A 39-year-old man was referred to a nephrologist because of rising serum creatinine.

He had presented weeks earlier with a migratory polyarthritis involving ankles, wrists, elbows and shoulders and the work-up had shown a positive ANA (1:64 speckled) with an erythrocyte sedimentation rate of 54 mm/hr. Serum creatinine then was 1.5 mg/dl and urinalysis showed 1+ proteinuria and 30-50 RBC/HPF. The patient had been put on low dose prednisone at this point and during the following week developed a purpuric skin rash on the legs. A biopsy of the rash showed leukocytoclastic vasculitis (slide 1). Over the following week, the serum creatinine rose to 2.3 mg/dl with urinalysis showing an “active sediment” with RBC casts. Proteinuria was measured at 800 mg/day. Serum complement (C3 and C4) was normal.

A renal biopsy was done.

Pathology Report

Slide 1  Slide 2  Slide 3

Renal biopsy showed a focal necrotizing glomerulonephritis (slides 2 and 3). Immunofluorescence was negative ("pauci-immune") and electron microscopy showed no immune complexes, no abnormal fibril depositions and no evidence of hereditary glomerular basement membrane abnormalities.

What is the diagnosis?

Study Questions (no online answers required):
- This patient has a multisystem disease including small vessel vasculitis involving skin. Does he meet criteria for a diagnosis of SLE?
- What additional testing would you order?

Conventional Folly
LC is a 59 year-old woman admitted to the hospital with complaints of vomiting and progressive weakness. For the past two months, she has had general malaise, anorexia, and right flank pain (treated with non-steroidal anti-inflammatory drugs (NSAIDs)).

On admission, she is noted to have gross hematuria and a serum creatinine of 4.2 mg/dl. Her serum creatinine is known to have been normal two months earlier. Blood pressure is 150/84. There is no edema.

Urinalysis shows red blood cells and 2+ protein. No casts were seen. The chest X-ray is negative. The patient developed anuria and a rapidly rising serum creatinine.

A renal biopsy was done.

Pathology Report

Slide 1  Slide 2  Slide 3  Slide 4

Nearly all of the glomeruli were obliterated by necrosis and crescents (slides 1 (Masson-Trichrome), 2 (Jones Silver) and 3 (immunofluorescence for fibrinogen)). Immunofluorescence was strongly positive for IgG and C3 in a linear GBM pattern (slide 4).

What is the diagnosis?

Study Questions (no online answers required):
- What considerations impact on the decision to treat in this case?
**Leaping Before Looking**

A 13 year-old boy presented to the Emergency Room with seizures (falling backward and experiencing a transient loss of consciousness) on the day of admission. While the ER, he had another seizure.

His past medical history is significant for chronic sinusitis for which the patient is being followed by an allergist. He had presented to his pediatrician three times in the previous two months with complaints of headaches, congestion, sore throat, and most recently (three days prior to the seizures) with a cough productive of yellow sputum associated with anorexia and nausea. He had been treated with various antibiotics and nasal inhalers for these complaints.

On examination, his blood pressure was 160/116 and his temperature was 98.4 deg F. There was marked boggy nasal mucosa consistent with allergic rhinitis. His throat was normal without lesions or exudate, and his ears were clear.

Labs showed a WBC count of 17.4K with 79% polyps and 5% bands. Electrolytes were normal. BUN was 45, serum creatinine was 1.7, albumin was 2.9 and the cholesterol was 137. A rapid strep throat swab was negative. ANA, rheumatoid factor and cryoglobulin are also negative, as were cultures of blood, sputum and lumbar puncture.

ANCA was positive at 1:160 with a p-ANCA pattern. C'3 complement was decreased at less than 16; C'4 was 49, C1q binding assay was elevated at 22. Streptozyme titer was slightly elevated at 200.

Urinalysis showed light brown urine with 3+ blood and positive protein (7.4 grams per 24 hours).

Chest x-ray showed left lower lobe infiltrate. An MRI performed the day after admission showed lesions involving bilateral medial parietal-occipital regions interpreted as ischemic and possibly due to vasculitis.

Treatment with cytoxin and prednisone was begun, and a renal biopsy was done.

**Pathology Report**

By light microscopy, all of the glomeruli looked similar and were characterized by diffuse endocapillary hypercellularity with some neutrophil exudation (slide 1). Immunofluorescence was positive for IgG and C3. A glomerulus stained for C3 is shown (slide 2). Electron microscopy shows immune complex deposits in the mesangium and capillary loops (slide 3). The capillary loop deposits are both subendothelial and subepithelial. The subepithelial deposits are characteristic "humps" without GBM reaction. (slide 4).

**What is the diagnosis?**

**Study Questions (no online answers required):**

- What type of pathogenesis is suggested by the low C'3 and the positive C1q binding assay?
- What diagnosis is suggested by the positive p-ANCA and how does this fit in with the biopsy findings?
- What is the pathogenesis of the seizures?
A Rock and a Hard Place
A 66-year-old man with metastatic colon cancer is referred to a nephrologist because of rising serum creatinine.

Ten months previously, the patient presented because of fatigue and abnormal bowel movements. Work-up resulted in discovery of an adenocarcinoma of the colon. At the time of segmental resection of the colon 6 months ago, liver metastases were found and chemotherapy with intrahepatic infusion of 5-fluorodeoxyuridine (FUDR) and mitomycin C was begun. Following surgery and the first course of chemotherapy, his discharge serum creatinine was 1.8 mg/dl. He had received 4 courses of FUDR and 3 of mitomycin C over the ensuing months. One week ago, he had another course of chemotherapy with mitomycin C. His serum creatinine at that time was 2.2 mg/dl. Now the serum creatinine is found to be 5.2 mg/dl.

On examination, the blood pressure was 156/94 mm Hg and he had mild edema.

Urine showed microhematuria (without cellular casts) and 3+ proteinuria (urine protein/creatinine ratio was approximately 1.0). Labs showed WBC 13K, hematocrit 32, platelets 182K and LDH 956. Ultrasound shows normal size kidneys without hydronephrosis.

A renal biopsy was done.

Pathology Report

The main finding is occlusion of glomeruli capillaries by fibrin thrombi (slides 1-4).

What is the diagnosis?

Study Questions (no online answers required):

- What is the differential diagnosis of acute renal failure prior to the biopsy and how does work-up help sort among the possibilities?
- What additional clinical information might have been helpful?
- What are some common causes of renal injury related to cancer?
- What is the probable cause of renal injury in this case?

The Eternal Return
A 42-year-old woman had end-stage renal disease secondary to dense deposit disease and had a living-related-donor kidney transplant in March 2005. She presents now with an elevated creatinine over the course of 4 weeks. Her creatinine with the allograft reached a baseline of 1.3 mg/dl in April of 2008 but has progressively risen (slide 1). Her past history includes hypertension and antiphospholipid syndrome (on coumadin). Her immunosuppression is Neoral and Myfortic. Urinalysis shows 4+ proteinuria and 3+ hematuria. A biopsy of the transplant kidney was done (arrow in slide 1 indicates time of allograft biopsy).

Pathology Report

The biopsy (slides 2 and 3) shows minimal interstitial inflammation but diffuse mesangial expansion and hypercellularity and capillary loop thickening. There was prominent C3 complement deposition. The electron microscopy (slide 4) showed a diagnostic change in the basement membranes.

What is the diagnosis?
**Long Way Around**

A 70 year-old man is referred to nephrology. Labs from today showed a serum creatinine of 3.8 mg/dl. Three weeks ago, routine labs in his physician's office showed a creatinine of 3.1 mg/dl. His creatinine 6 months ago was 1.5 mg/dl.

The patient reports reduced appetite for the last 5 to 6 weeks and thinks that he has lost about 6 to 7 pounds. The patient has anemia, which is getting worse (hematocrit 27.8%). He has a history of B12 deficiency for which he receives monthly B12 shots. He also has a history of longstanding hypertension (controlled with Benicar, hydrochlorothiazide and Toprol) and hypercholesterolemia (on Crestor and Tricor). Other meds include aspirin, Vitamin B complex and Nexium. He denies using any nonsteroidal anti-inflammatory medications or any over-the-counter herbal products.

He has a history of prostate cancer and he underwent seed implant and radiation therapy as well as Lupron and this has been in remission. His prostatic specific antigen recently is normal.

He reports taking 6 to 7 alcohol drinks per day either in the form of beer, vodka or wine.

Urinalysis shows 2+ protein, 1+ blood. The urine sediment shows several dysmorphic RBCs but no red blood cell or white blood cells casts. He did have an occasional granular cast.

Prerenal and post-renal causes were ruled out and a renal biopsy was done.

**Pathology Report**

![Slide 1](image1)
![Slide 2](image2)
![Slide 3](image3)

The biopsy showed prominent tubular obstruction by cast material (*slides 1-3*). Glomeruli and larger blood vessels showed only hypertensive changes.

**What is the diagnosis?**

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**Monday's Child**

The patient is an 18-year-old woman with a history of cystinosis had a living-related kidney transplant 12 years earlier. She was found to have an increased creatinine up to 4.6 from a baseline of 1.4 mg/dl. She was also noted to be hyperkalemic and anemic. The patient says she has been completely asymptomatic with no recent changes in her medication list.

Urinalysis showed cloudy urine with some protein, WBC too numerous to count and a small amount of bacteria. With intravenous hydration, the creatinine started improving and trended down to 3.0. A kidney biopsy was done (arrow in *slide 1* indicates time of biopsy).

**Pathology Report**

![Slide 1](image4)
![Slide 2](image5)
![Slide 3](image6)

Biopsy of the transplant kidney shows generally intact glomeruli. There is interstitial nephritis with prominent neutrophils and some “pus casts” (*slides 2-4*).

**What is the diagnosis?**

**Study Questions (no online answers required):**

- What is cystinosis and how does it cause end-stage renal disease?
**The Sad Truth**

The patient is a 38-year-old woman who was diagnosed with type 1 diabetes mellitus at age 9 and developed end-stage renal disease secondary to diabetic nephropathy. She had a deceased-donor combined kidney-pancreas transplant 9 years ago with good function and a baseline serum creatinine of 1.6 mg/dl until she stopped her immunosuppressive medications 3 weeks ago because she believed they were causing GI distress. She had been on Imuran, Medrol and tacrolimus and she discontinued all three of them. She comes to the emergency room now complaining of back pain and is found to be in renal failure. On exam, she had tenderness in the left lower quadrant over the transplant kidney and in the right lower quadrant over the transplant pancreas.

Bloodwork showed: potassium 5.3 mmol/L, creatinine 4.4 mg/dl, BUN was 53 mg/dl, albumin 2.3 g/day, amylase 169 U/L and lipase 483 U/L. Glucose was initially 94 but rose over the next day to 252 mg/dl. Urinalysis shows a specific gravity of 1.006, 1+ proteinuria and 1+ glucosuria. The urine sediment shows 17 white blood cells/high power field.

A kidney biopsy was done.

**Pathology Report**

![Slides 1-6]

A biopsy of the transplant kidney showed inflammatory infiltrates, including lymphocytic tubulitis and lymphocytic endovasculitis (slides 1-5). Most of the lymphocytes in the tubulointerstitial area and in the arteries stained as CD8 positive T cells (slides 3 and 5). C4d staining is positive in the peritubular capillaries (slide 6).

**What is the diagnosis?**

**Flooded Lowlands**

A 74 year-old man presented with acute onset of abdominal pain and weakness. He was found to be hypotensive (BP 60/40 mmHg), tachycardic (pulse 130/min) and severely anemic (hematocrit 28%) with a large tender pulsatile abdominal mass and intact peripheral pulses. The clinical impression was ruptured abdominal aortic aneurysm which was confirmed at surgery where a Dacron graft was inserted.

The patient was hypotensive and oliguric despite fluid administration for several hours after surgery. The urine output returned to 60 cc/hour over the next few days but blood urea nitrogen and serum creatinine rose.

<table>
<thead>
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<th></th>
<th>BP (mmHg)</th>
<th>BUN (mg/dl)</th>
<th>Serum Creatinine (mg/dl)</th>
<th>Serum Potassium (mEq/l)</th>
<th>Urine Sodium (mEq/l)</th>
<th>Urine Osm (mosmol/kg)</th>
<th>Urine Volume</th>
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<tr>
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<td>1.0</td>
<td>WNL</td>
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<td>Oliguria</td>
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<tr>
<td>3 days post-op</td>
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<td>6.9</td>
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<td>336</td>
<td>60 cc/hr</td>
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</tr>
</tbody>
</table>

Urinalysis had been normal before surgery. Sodium excretion was initially low but increased and by day 3 post-op urine sediment showed many granular casts and occasional renal tubular epithelial cells.

**Pathology Report**

No renal biopsy was performed.

**What is the diagnosis?**

**Study Questions (no online answers required):**

- Define "oliguria."
- What additional information would be needed to calculate FE_{Na}?
- Why was a renal biopsy not thought to be necessary?
- What is the prognosis for this patient?
Crossing Boundaries

A 31-year old woman developed proteinuria at 30-weeks gestation of her second pregnancy. The proteinuria was associated with severe peripheral edema but only minimal hypertension (with BP up to 140/80 mmHg). Delivery was induced at 37-weeks gestation because of the proteinuria.

Ten days after delivery, she is referred to a nephrologist for persistent proteinuria (urine protein:creatinine ratio of 11.7). She was previously healthy with no personal or family history of kidney or urinary tract disease except for an uncle who had had post-infectious glomerulonephritis. She has no arthritis, serositis, rash or any other systemic signs or symptoms of vasculitis. BP is 124/61 mmHg. There is still severe peripheral edema. Urinalysis shows proteinuria with only occasional RBCs and WBCs. The patient is anemic (hematocrit 23.2%). Serum albumin is 0.7 g/dL. Serum creatinine is 0.7 mg/dL. ANA is positive at 1:160 in a speckled pattern. VDRL is positive, but FTA is negative.

The patient was treated with diuretics and followed. Three months later, a renal biopsy was done for persistent, high-grade proteinuria (7 g/24 hrs) and edema. The biopsy findings are shown.

Pathology Report for Biopsy #1

The kidney is generally intact by light microscopy (slides 1 and 2). Glomeruli show only a suggestion of hypercellularity and capillary loop thickening without active inflammatory lesions. Immunofluorescence shows granular mesangial and capillary loop staining most prominent for IgG (slide 3). There is staining in the same pattern but weaker for IgA and C3. There is mesangial only staining for IgM. Electron microscopy shows capillary loop deposits (slides 4 and 5).

What is the diagnosis at this time?

The patient was managed conservatively (diuretics and an ACE inhibitor) and had a spontaneous remission of the proteinuria (urine protein:creatinine ratio down to 0.3).

Three years later, she developed edema again with proteinuria (protein:creatinine ratio of 11), hypoalbuminemia (albumin of 1.2 g/dL) and hyperlipidemia (cholesterol of 331). Review of systems and physical exam were negative except for the leg edema. There was no rash, arthritis, serositis or alopecia.

Urine showed microscopic hematuria, as well as proteinuria, and labs showed hypocomplementemia (low C3) and anti-double stranded DNA antibodies. The patient was anemic and had a positive Coombs' test. Renal function was normal, with a serum creatinine of 0.7 mg/dL. A second renal biopsy was done. The findings are shown.

Pathology Report for Biopsy #2

The biopsy shows diffuse endocapillary hypercellularity (slides 1 and 2). Immunofluorescence (slide 3) and electron microscopy (slide 4) show more extensive immune complex deposition than in the previous biopsy. The staining is strongest for IgG (shown in slide 3) but there is a "full house" (three antibodies and a pair of complements, IgG, IgA, IgM, C3 and C1Q) pattern of staining with staining for all immunoreactants in the mesangium and capillary loops.

What is the diagnosis at this time?

The patient was treated with the NIH protocol (“pulse” solumedral for 3 days followed by 6 months of IV cytoxan and prednisone). At the end of the six months of therapy, urine protein:creatinine ratio was 0.6 and serum albumin was 3.4 g/dL. Serum creatinine was 0.6 mg/dL. BP was 118/80 mmHg.
A third renal biopsy was done to assess the effects of therapy. The results are shown.

Pathology Report for Biopsy #3

Slide 1  Slide 2  Slide 3

There is significant resolution of the glomerular inflammation with residual thickening and irregularity of the glomerular capillary loops (slide 1). Ultrastructure shows immune complexes in various stages of resolution (slides 2 and 3).

What is the diagnosis?

Study Questions (no online answers required):

- The patient has a systemic disease and underwent three renal biopsies. The World Health Organization (WHO) has a classification system for renal involvement in this disease. What is the WHO classification in this case?
- Do the findings at each stage move the patient across boundaries of this classification?
- What is the significance of classification for therapy or prognosis?
- What features in the renal biopsies indicate "activity" or "chronicity" of disease?
- How do these features figure into therapeutic decisions?

Lucky Strike

Patient is a 63-year-old man with a history of steroid-dependent asthma for the past 40 years. He presented with daily low-grade fevers (100-101 degrees F), shortness of breath and a productive cough. In addition, he had vague upper abdominal discomfort accompanied by early satiety and a 14-lb weight loss over a 1-month period.

His past medical history is also significant for chronic sinusitis, steroid-induced osteoporosis, and a 40 pack/year smoking history (quit nine years ago). His family history reveals that his father died in his 70s of multiple myeloma.

Current medications include flovent, theo-dur, prevacid, prilosec, naprosyn and fosamax.

Physical exam revealed a BP of 150/92, neck and axillary adenopathy, a 2/6 systolic ejection murmur, a fine erythematous raised rash on his upper back, oral thrush, and periorbital and pedal edema.

Lab results included a WBC count of 28,000 with 60% eosinophils, high serum IgE, a slightly positive rheumatoid factor, cryoglobulins and toxoplasmosis titers. He had an ESR of 120. Anti-DNA Ab, ANCA, serum and urine protein electrophoresis were negative. Urinalysis showed 3+ protein (2.1 g/day), 1+ blood, hyaline and fine granular casts. The serum creatinine was 1.3 mg/dL.

The patient underwent a renal biopsy shortly after admission.

Pathology Report

Slide 1  Slide 2

There is a transmural fibrinoid necrosis and inflammation in one larger artery and its branch. The inflammatory infiltrate in the vessel wall is rich in eosinophils and there are some multinucleated giant cells. Glomeruli show only ischemic changes. Immunofluorescence is negative.

What is the diagnosis?
It All Comes Back to Me Now

The patient is a 57 year-old woman with a history of vasculitis who was referred to a nephrologist due to possible renal involvement. Her medical history also includes remote IV drug use, extended tobacco use (1 pack/day), and up until ten months ago, a history of "binge" drinking (2-3 pints of liquor on the weekends).

She has a long history of an episodic purpuric skin rash, mainly over her lower extremities and trunk, which has worsened in recent years. Two years prior to biopsy, she had an abrupt onset of joint pain, stiffness and swelling bilaterally in her knees and ankles, as well as her right hand. Work-up at that time revealed dipstick positive proteinuria and hematuria, positive ANA, positive cold agglutinins, low C3 and C4, negative cryoglobulins, and a possible M spike on serum protein electrophoresis. A skin biopsy showed leukocytoclastic vasculitis with IgG, IgM and C3 deposition, with no detectable IgA. She was placed on high doses of prednisone with moderate response, but the patient was noncompliant and lost to follow-up.

She presented to her physician six months ago with pleuritic chest pain and worsening skin lesions (ecchymotic/purpuric raised lesions on the legs and abdomen, becoming confluent in some areas, with sparing of the face and plantar surfaces of the feet). Steroids were restarted.

In follow-up four months ago, she was noted to have a serum creatinine of 1.6 mg/dL, a creatinine clearance of 53 cc/min and 1.5 g protein/24 hr.

In the past two months, the patient has developed progressive renal insufficiency (serum creatinine now 2.2 mg/dl), hypertension (blood pressure up to 178/90 mmHg), proteinuria (urine protein to creatinine ratio of 3.25), hematuria and hypocomplementuria (low C'4 with normal C'3). Erythrocyte sedimentation rate was high at 73 and rheumatoid factor was positive. ANCA, anti-double stranded DNA and cryoglobulins were negative.

A renal biopsy was done.

Pathology Report

Glomeruli show marked mesangial expansion, endocapillary hypercellularity and peripheral capillary loop thickening (slide 1) with double-contour capillary loops on silver stain (slide 2). Some capillaries are occluded by hyaline thrombi (slide 3, arrows pointing to thrombi). Approximately one-third of the glomeruli show cellular crescents (slide 4). There is moderate interstitial fibrosis and tubular atrophy. Immunofluorescence shows peripheral rim staining for IgM (++), C3 (+), IgG (+) and C1q (+/-). Electron microscopy shows massive subendothelial and intraluminal deposits with some substructure (slides 5-6).

What is the diagnosis?

Study Questions (no online answers required):
- Does this patient fit criteria for a connective tissue disease?
- What is the probable underlying systemic illness?
**Bloody Catastrophe**

A 47 year-old woman with a history of substance abuse (alcohol and cocaine), hypertension and chronic lower back pain (requiring large doses of Motrin and Advil and recently Darvon) presented to the ER with complaints of generalized weakness, headache, abdominal discomfort and bright red blood per the rectum. While in the ER, she suffered a generalized seizure, the first ever for the patient.

Two months prior, she had presented to her primary physician with a 4-month history of arthralgias, malaise and increasing weakness. ANA was positive and a tentative diagnosis of SLE was given. Creatinine at that time was 1.1 mg/dL. She was treated with prednisone.

In the past two weeks, she had noted oliguria. Review of systems revealed dysphagia. Physical exam showed hypertension (BP of 170/100). She had smooth, tight skin over her face, hands and feet. Rectal exam showed heme positive stools and a post-ictal neuro exam revealed no focal deficits.

Laboratory results included a BUN of 104, creatinine of 8.9, hemoglobin of 7, hematocrit of 21 and an ESR of 31. Urinalysis was positive for blood and albumin. A CT of the head showed no acute disease.

A work-up of her GI bleeding included an upper endoscopy, which showed esophagitis, esophageal stricture and a bleeding duodenal ulcer.

A renal biopsy was done to investigate the cause of her renal failure.

**Pathology Report**

The glomeruli show diffuse, severe collapse and wrinkling of the glomerular basement membrane (slide 1). There is moderate tubular atrophy and interstitial fibrosis. Arteries show microangiopathic changes and focal thrombosis (slides 2 and 3; slide 3 is immunofluorescence stained for fibrin). Immunofluorescence of the glomeruli is negative for immune complexes. By electron microscopy, there is massive widening in the sub-endothelial region of the GBM and diffuse epithelial foot process fusion (slide 4).

What is the diagnosis?

*Study Questions (no online answers required):*
- What is the relationship of the gastrointestinal bleeding to the other problems in this patient?

**A Dry Eye in the House**

A 52-year old woman with Sicca syndrome and a probable distal renal tubular acidosis has a history of diabetes and hypertension and previous gastric bypass surgery. She presents now with a sub-acute progression of renal insufficiency with a serum creatinine currently at 2.7 mg/dl.

A renal biopsy was performed.

**Pathology Report**

Glomeruli are generally intact. The interstitium is massively widened by inflammatory cell infiltration. The predominant cell type appears to be plasma cells and there are significant numbers of lymphocytes with some lymphocytic tubulitis.

What is the diagnosis?