Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #1

A 53 year old man had a 10 year history of Wegener's granulomatosis with features of disease that included episcleritis, a mass lesion on the underside of the upper eye lid, nasal, sinus, renal, lung involvement. Current medications included prednisone (20mg/d) and azathioprine (150mg/d). He was not receiving trimethoprim/sulfa because of sulfa allergy and he had not tolerated dapsone or inhaled pentamidine for Pneumocystis prophylaxis. Past medical history included bladder cancer requiring cystectomy and an ileal conduit.

When seen 1 month ago, he was in apparent remission. He called for today's appointment because of a 3-week history of left ankle pain that resolved, only to be followed by left thigh pain that resolved. Last week left lacrimal gland enlargement became more apparent and was associated with left periorbital pain. He had increased bloody nasal discharge and maxillary region discomfort. New occurrence of a dry cough and left sided chest pain present for 1 week.

Physical examination revealed BP 138/80, P 88, T 36.2 ºC, right conjunctivae were very injected and right lacrimal gland was enlarged, right periorbital edema; extraocular muscles were intact; the left eye was normal. Nasal crusting and bloody nasal mucosa was seen on right side only. Examinations of the ears, lungs, heard, and joints were unremarkable.

Laboratory studies: Hemoglobin 10.3 g/dL, WBC 7.57 k/uL (total lymphs 380), creatinine 1.40 mg/dl (123.9 mmol/l), ESR 40 mm/1st hr, CRP normal. Urine from ileal conduit – ostomy: abundant debris, 1+protein, 1+ Hgb (not changed - consistent with past).

Chest CT scan demonstrated scarring in areas of prior injury but no new disease.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #2

A 66 year old man with a 6 year history of Wegener's granulomatosis (WG) returned for follow-up evaluation.

In the past, sites affected included nose, sinus, ears (otitis media), eyes (conjunctivitis), joints, skin, lower extremity sensory neuropathy, mouth (oral ulcers), and kidney (glomerulonephritis). He had tested positive for C-ANCA/anti-PR3. When last seen (August 2003), he had been in remission. He had been off methotrexate for 15 months and off prednisone for 2 years.

Two months ago, he noted severe right knee pain. One month ago he had a severe nose bleed requiring cautery to control of epistaxis, subsequently noted little red spots on the back of his right leg, and 2 weeks ago his right hand was very painful and he could not use the hand for normal activities.

Current physical examination of his eyes, ears, nose, sinuses, heart, lungs, and joints are unremarkable. Skin examination reveals palpable purpura on both legs.

Laboratory studies: Hemoglobin 12.6 g/dL, WBC 6.2 k/uL, creatinine 1.10 mg/dl (97.4 mmol/l), ESR 40 mm/1st hr, CRP 6.6 (nl <2.0). Urinalysis: 3+ blood, 1+ protein, new observation of RBC casts.

Chest CT scan was fully unremarkable.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #3

A 66 year old man with Wegener's granulomatosis is evaluated urgently after reporting one day of severe right flank pain and gross hematuria.

He has a 4-year history of Wegener's granulomatosis involving the nose, sinuses, joints, kidneys (glomerulonephritis leading to end-stage renal disease and renal transplantation two years ago). He had tested positive for C-ANCA/anti-PR3. He was feeling well, getting back into exercise program since his last visit. Current medications include sirolimus 1 mg/daily, mycophenolate 1000 mg twice daily, prednisone 5 mg daily, and trimethoprim/sulfamethoxazole tablet daily.

Physical examination was remarkable only for a nasal septal perforation (unchanged), Cushingoid facies and right flank pain.

Urinalysis revealed gross blood, RBCs that were not dysmorphic, and no RBC or mixed cellular casts.

The patient underwent a cystoscopy revealing normal urethra, prostate, and bladder. A right renal stone was found.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #4

A 36 year old man with a 3-year history or Wegener's granulomatosis (WG) is seen in follow-up because of new symptoms. His WG has been characterized by sinusitis (biopsy revealed necrosis with granuloma formation, giant cells, and negative cultures), rhinitis, myalgias, arthralgias and arthritis, otitis media and conjunctivitis. He has been ANCA-negative.

Remission was induced with methotrexate and prednisone he was able to taper and discontinue prednisone. He was maintained on methotrexate 25mg/week for some time but has been tapered in recent months. Current dose of methotrexate is 10mg/week.

Three weeks ago he developed rhinorrhea, with clear discharge, sinus congestion, and a dry cough. This week the discharge became bloody and nasal crusts more frequent and copious. His nose has become sensitive to irrigating fluids. The right ear has also become painful. Muscle and joint pain began 4 days ago, with the focus being on his knees and right hip.

Current physical examination of his eyes, heart, and lungs, are unremarkable. Eears: TM's normal; tenderness over right mastoid process. Nose/Sinuses: nasal erythema, no ulcers, dry crusts, bilateral maxillary sinus tenderness. Musculoskeletal exam reveals tenderness in right hip/greater trochanteric region, pain with full range of motion of right knee and right hip.

Laboratory studies: Hemoglobin 14.7 g/dL, WBC 5.7 k/uL, creatinine 0.90 mg/dl (79.7 mmol/l), ESR 8 mm/1st hr, CRP 0.6 (nl <2.0). Urinalysis: negative.

Chest CT scan is normal. Sinus CT scan reveals mucosal thickening which essentially fills the entire right maxillary sinus. There is also substantial bony thickening, consistent with reactive osteitis. These findings are unchanged compared to prior imaging studies.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #5

A previously well 25 year-old woman was well until May 2003 when she noted fever and painful nodules of varying sizes on her arms and proximal thighs. Medical evaluation revealed a normal CBC, chemistry profile, creatinine, and urinalysis. Tests for HIV and hepatitis A, B, and C were all negative. A chest x-ray and PPD were negative. EKG and echocardiogram were normal. Multiple trials of antibiotics did not lead to clinical improvement.

In July 2003 she developed arthralgias of her fingers, wrists, elbows, knees, ankles and jaw, anorexia, and weight loss of 5 kg within a period of 2 weeks. She subsequently experienced hemoptysis and SOB and was hospitalized. Physical examination at that time: T 39ºC, respirations of 24/minute, BP 110/65, Pulse 120. Examinations of the eyes, ears, nose, pharynx, heart, abdomen, and nervous system were unremarkable. She was tachypneic with bilateral diffuse rales. Tender purpuric nodular lesions were present on both thighs. Joint exam revealed tenderness without swelling at MCP and MTP joints; pain with full flexion of knees.

Laboratory studies: Hemoglobin 11.5 g/dL, creatinine 1.10 mg/dl (97.4 mmol/l), ESR 93 mm/1st hr. Urinalysis: 3+ hematuria with RBC casts. Positive test for C-ANCA/anti-PR3. Anti-GBM test was negative. Chest CT revealed bilateral lung infiltrates, no adenopathy, no nodules. Sinus CT scan was negative

Skin biopsy (thigh) revealed leukocytoclastic vasculitis involving small and medium-sized vessels. The infiltrate was pleomorphic and there were no granulomatous changes.

Initial treatment with prednisone 60 mg/day was begun on July 24, 2003. By the next day she was feeling much better; she was pain-free, afebrile, and skin lesions were improving.

An 8/5/03 open lung biopsy demonstrated pulmonary hemorrhage, with abundant hemosiderin-laden macrophages and small vessel vasculitis/capillaritis. Granulomatous changes were not seen. Cultures of the biopsy were negative.

You now see the patient for the first time in consultation (mid August).

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #6

A 57 year old woman was referred with a purpuric skin rash involving her lower limbs, intermittent large joint oligoarthritis, and deteriorating renal function. She had been diagnosed with microscopic polyangiitis one year previously on the basis of a renal biopsy with a necrotizing, crescentic glomerulonephritis and positive P-ANCA/anti-MPO. After treatment with cyclophosphamide and prednisolone her serum creatinine stabilized at 2.27mg/dl (200umol/l) and she was switched to azathioprine.

The patient now reports profound fatigue and malaise.

Current treatment was Azathioprine 100mg/day and prednisolone 25mg daily.

Current physical examination: Blood pressure 170/110. A non-blanching purpuric rash with one area of confluence and pre-ulceration I present. One wrist was swollen and tender, both ankles are swollen with pitting edema, and there is elevated central venous pressure.

Urinalysis reveals 3+ hematuria and 4+ proteinuria.

Creatinine now is 4.43mg/dl (390umol/l), ESR 48mm/1st hr, CRP 6mg/l, albumin 25g/l, , P-ANCA/anti-MPO is positive.

A renal biopsy is performed yielding 5 glomeruli; 4/5 were sclerosed with extensive intersitial fibrosis; active necrosis or cellular crescents are not seen.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #7

A 21 year old woman had a two year history of Wegener's granulomatosis with ENT, lung and renal involvement, and C-ANCA/anti-PR3 positivity returns for a routine follow-up visit. She had been in remission for 18 months with a stable serum creatinine of 2.27mg/dl (200umol/l).

Symptoms of intermittent nasal obstruction, occasional nasal crusting and unilateral deafness are unchanged from her previous review. She reports exertional dyspnea without cough but can swim 400m without difficulty.

Current medications include azathioprine 150mg, prednisolone 5mg, sulfamethoxazole trimethoprim 960x2, and ramipril 10mg.

Blood pressure is 140/90.

A chest X-ray demonstrates linear atelectasis and pleural thickening in the right upper zone unchanged from the previous examination.

Urinalysis reveals no hematuria but does show 2+ proteinuria. Serum creatinine is 5.1mg/dl (450umol/l) and renal ultrasound show kidneys with lengths 8.9 and 9.5cm and reduced cortical thickness. She was C-ANCA weak positive, PR3-ANCA negative.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #8

A 38 year old man with Wegener's granulomatosis for five years presents for evaluation of joint pains and a non-productive cough. He had a history of ENT and pulmonary disease with at least three emergency admissions for diffuse alveolar hemorrhage and respiratory failure. His cumulative cyclophosphamide exposure was 27g. Current therapy was mycophenolate mofetil 2g/day, and prednisolone 30mg/day.

In clinic he was mildly Cushingoid and comfortable at rest. There was no obvious joint inflammation but he had increased his prednisolone to 30mg/day five days earlier and was now pain free.

Chest-X ray was unchanged from his previous assessment with evidence of bilateral basal fibrosis and volume loss. A fiberoptic bronchoscopy discovered an inflamed tracheal and bronchial mucosa with contact bleeding, microbiological isolates were negative and transbronchial biopsy revealed a dense neutrophil infiltrate and occasional giant cells with possible loosely formed granulomata.

Urinalysis had 1+ hematuria and no proteinuria. Blood pressure and serum creatinine were normal. ANCA was negative and ESR and CRP modestly elevated but unchanged from the previous review.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #9

A 29 year old woman was referred for evaluation of joint pains. She gave a six-month history of pain and swelling in her wrists, shoulders, hips, and knees that responded to NSAIDs. Over the same period she had become tired and lacked energy, she had had several nosebleeds and complained of nasal stuffiness. There were no symptoms of sinus involvement apart from a non-specific left temporal headache also relieved by NSAIDs. There was no hearing loss or respiratory symptoms. She had lost 2.5 kg in weight but may have been dieting to lose weight. She was on no other medication apart from an oral contraceptive pill. She had occasional night sweats in the past month. She is a smoker but has no other prior medical problems.

Examination revealed a pale woman. Blood pressure was normal. Two nail fold infractions were seen. There was no joint tenderness but scleral injection and thickening were seen in both eyes.

Urinalysis demonstrated hematuria (++), proteinuria (+) but no neutrophils or organisms. Echocardiogram, renal ultrasound, and serum creatinine were normal. She declined a renal biopsy. ENT examination and sinus and chest X-rays were normal.

Hgb was 10.2g/dl, platelets 530, WBC 11.2, ESR 49mm/1st hr, CRP 16g/l, P-ANCA/anti-MPO positive. Rheumatoid factor, ANA and multiple blood cultures were negative.

A diagnosis of microscopic polyangiitis was made and she was commenced on azathioprine 150mg/day and prednisolone 20mg/day.

You are now seeing her six weeks later she feels considerably better. She has had no joint pains or sweats, or nose bleeds, weight was up 3kg, eyes were quiet and urinalysis showed trace proteinuria only. ESR and CRP were normal.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #10

A 72-year-old man presented with dialysis-dependent renal failure, purpura, polyarthritis, pulmonary infiltrates, and a positive P-ANCA/anti-MPO in November 2001. Renal biopsy confirmed vasculitis and he was treated with plasma exchange, cyclophosphamide, and prednisolone. He recovered renal function, entered clinical remission, but proved intolerant of azathioprine and was maintained on mycophenolate and prednisolone with a stable creatinine between 2.27-2.84 mg/dl (200 and 250umol/L).

Throughout 2002 he complained of non-specific constitutional symptoms, inflammatory markers were near normal and MPO-ANCA was negative. At the end of 2002, mycophenolate was temporarily withdrawn in case it was contributing to his symptomatology.

In February 2003 he presented acutely complaining of non-productive cough and dyspnea. This episode was preceded by weight loss of 2kg, night sweats and more malaise. He had no ENT or eye symptoms. Exam was notable for hypoxemia at rest, normal blood pressure, and fine crackles present at both lung bases.

CT chest scan demonstrated a complex picture with fine reticular shadowing at both bases, widespread alveolar infiltrates, and a more dense 4cm opacity close to the right hilum.

Urinalysis showed 1+ hematuria and 1+ proteinuria, and no casts. Creatinine was 4.77mg/dl (420umol/l); CRP 120mg/l; ESR > 100mm/1st hour

Bronchoscopy was unremarkable; bronchial lavage did not demonstrate blood; brushings and biopsy were negative for PCP. CMV PCR was normal and extensive microbiological work-up was negative. In addition to prednisolone 5mg/day he had been receiving, irbesartan, alendronate and lansoprazole. He was treated with high dose trimethoprim-sulfamethoxazole and additional intravenous anti-bacterial drugs without benefit. A diagnosis of vasculitis relapse was then made and he received three grams of IV methylprednisolone and re-introduction of cyclophosphamide. After a transient improvement, respiratory failure progressed and he died two weeks later. Request for post mortem was declined.

On the assumption that the presentation in February was caused by a flare of his vasculitis, please evaluate this patient's disease activity.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #11

A 47-year-old man was seen in follow-up of Wegener's granulomatosis (WG).

WG had been diagnosed 2 years earlier based on the deterioration of his general condition, recurrent sinusitis, cutaneous nodules, abdominal tenderness, acute renal insufficiency with serum creatinine at 4.75 mg/dl (420 μmol/l) and positive C-ANCA/anti-PR3. Renal biopsy showed pauci-immune crescentic glomerulonephritis and a skin biopsy demonstrated a granulomatous infiltrate. Pulmonary imaging was normal but a CT scan of the sinuses showed right maxillary sinusitis. Intravenous cyclophosphamide (CYC) and glucocorticoids (GCS) were administered and led to regression of the general symptoms, fading of the cutaneous lesions, and reduction of serum creatinine to 3.74 mg/dl (331 μmol/l). Six months later, while still taking CYC and GCS, the patient experienced sudden intense abdominal pain. Diagnostic work-up yielded signs of peritonitis prompting an emergency laparotomy that showed massive infarction of the small intestine. Histological analysis of the resected bowel was non-specific. CYC and GCS were maintained, and the subsequent event-free disease course allowed the progressive tapering and then withdrawal of GCS. However, renal function remained poor with serum creatinine reaching 5.13 mg/dl (454 μmol/l) 19 months after diagnosis.

During the current visit, the patient complained of persistent fatigue, arthralgia of the peripheral joints, myalgia, and an intermittent nasal discharge. Physical examination revealed: normal temperature, stable body weight, blood pressure of 170/110 mm Hg and otherwise normal findings. The results of laboratory analyses were: CRP, 12 mg/l; Hb, 9.6 g/dl; serum creatinine, 6.22 mg/dl (550 μmol/l); positive C-ANCA/anti-PR3 test. Urinalysis was normal and proteinuria was 1.26 g/day. CT scan of the sinuses documented persistent right maxillary sinusitis. Thoracic CT scan images were normal.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #12

A 53-year-old woman was hospitalized with a 6-month history of weight loss (7 kg, > 10% of her normal body weight), arthralgias of both ankles and subsequent development of a purpuric rash on her legs.

At her admission physical examination, she was febrile (38°C), had swollen joints in both feet with synovitis of the ankles, pitting edema of both lower limbs, and infiltrated purpura of both legs. Laboratory investigations yielded: ESR, 81 mm/1st h; CRP, 142 mg/l; Hb, 9.4 g/dl; serum creatinine, 0.75 mg/dl (66 µmol/l) and positive P-ANCA/anti-MPO test. Initially, urinalysis was normal with no proteinuria. Skin biopsy of the purpura found leukocytoclastic angiitis of a small arterioles with no IgA deposits. Serial urinalyses over several days revealed hematuria (100 RBS per HPF) with proteinuria of 0.42 g/day. A renal biopsy was performed and showed focal and segmental glomerulonephritis with no immune deposits. At that time, serum creatinine was 1.24 mg/dl (110 µmol/l).

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #13

A 48-year-old man presented with a 3-month history of fever, poor general condition, arthralgias, ENT symptoms, conjunctivitis, and diarrhea.

At admission, the patient complained of fatigue, facial pain with no nasal discharge, tenderness of the right ankle, left knee, right elbow, and both shoulders, and diarrhea without blood or mucus. Physical examination detected fever (38°C), bilateral non-purulent conjunctivitis, swollen eyelids considered to be a consequence of bilateral dacryocystitis and numerous ulcers of the oral mucosa. No signs of arthritis or synovitis were noted. Examination of the abdomen was normal. Laboratory studies revealed: ESR, 105 mm/1st h; CRP, 299 mg/l; Hgb 9.5 g/dl; serum creatinine 1.27 mg/dl (112 µmol/l), and a positive C-ANCA/anti-PR3 test. Urinary sediment was normal.

CT scan of the sinuses revealed pansinusitis predominantly involving the right ethmoidal sinuses, and bilateral otitis media and mastoiditis. Chest CT scan demonstrated numerous small nodules in both lungs with no cavitation and a moderate pericardial effusion that was confirmed by echocardiography.

Because of persistent diarrhea, colonoscopy was performed that detected ulcerative inflammation of the colon and the terminal ileum. Histological analysis of the samples taken from the colon and ileum was consistent with inflammatory changes of the bowel wall and vasculitis of 2 medium-sized arteries with fibrinoid necrosis of the vessel walls.

Concomitantly, the patient developed acute renal insufficiency with serum creatinine rising to 3.01 mg/dl (266 µmol/l) and Urinalysis showing 2+ proteinuria and 3+ hematuria. A renal biopsy revealed pauci-immune crescentic glomerulonephritis.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #14

A 32-year-old man was seen in follow-up to evaluate the status of his Wegener's granulomatosis (WG).

WG had been diagnosed 12 months earlier based on ENT symptoms, palsy of the VIIth cranial nerve due to compression by adjacent mastoiditis, several cavitary lung nodules, serology positive for C-ANCA/anti-PR3 and biopsy of the nasal cavity containing a granuloma with giant cells. Eight months later, this patient had been transferred to our institution because WG was considered to be refractory to several therapeutic lines including immunosuppressants and monoclonal antibodies (e.g., anti-TNFα and anti-CD20). At that time, he complained of fever, weight loss, and severe ENT symptoms. CT scan showed the involvement of maxillary, sphenoidal, and ethmoidal sinuses, and 4 large pulmonary masses with cavitation with the largest mass in the apex of the right lobe measuring 6 cm in diameter. Intermittent intravenous cyclophosphamide (CYC) combined with oral glucocorticoids and analgesics were prescribed.

Now, four months later, the patient is in good general condition. He has no complaints except tenderness of the right shoulder that started 2 days ago after a trauma. In particular, the patient has no ENT symptoms. Physical examination reveals stable body weight at 91 kg, no fever, and otherwise unremarkable findings. Examination of the right shoulder was consistent with tendonitis of the long head of the biceps. Laboratory analyses revealed: ESR, 12 mm/h; CRP, 45 mg/l; serum creatinine, 0.96 mg/dl (85 μmol/l). Urine dipstick analysis showed no hematuria or proteinuria. He is still positive for C-ANCA/anti-PR3. CT imaging detected persistent pansinusitis; thoracic CT scan showed a cavitated lung nodule, 3 cm in diameter, in the right apex, and a nodule, 1 cm in diameter, in the left lower lobe. These changes all represent improved or stable lesions in the lung compared to prior CT scan.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #15

A 77-year-old man was seen for evalution of a 2-month history of deteriorating general condition (fatigue, anorexia), exertional dyspnea, and suspected acute renal insufficiency.

Physical examination was unremarkable, except for pitting edema of both lower limbs and fine inspiratory crackles over the basal parts of both lungs. Laboratory results included: ESR > 100 mm/1st h; CRP, 96 mg/l; leukocytosis, 23,200/mm^3; serum creatinine, 2.11 mg/dl (87 µmol/l), proteinuria varying between 0.85 and 2.68 g/day. Urinalysis showed numerous red cells. ANCA testing was positive for P-ANCA/anti-MPO. Chest radiograph and high-resolution chest CT scan demonstrated bibasilar undifferentiated interstitial pneumonia. Bronchoalveolar lavage fluid contained 160,000 cells/ml, with 31% lymphocytes, consistent with lymphocytic alveolitis. A renal biopsy showed crescentic glomerulonephritis with no immune deposits and vasculitis of the arterioles.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #16

A 30 year old man returns for reassessment of vasculitis disease activity and treatment recommendations. He was diagnosed 10 years ago with manifestations that included severe alveolar hemorrhage, severe anemia, pauci-immune glomerulonephritis (renal biopsy), arthralgias, skin vasculitis, nasal inflammation, and positive tests for both C-ANCA /anti-PR3 and anti-GBM antibodies. He responded well to combination therapy of prednisone and cyclophosphamide but developed severe hemorrhagic cystitis.

A minor flare nine months ago presented with recurrence of skin vasculitis of and arthralgias. Azathioprine and prednisone were restarted. Three weeks ago, when the prednisone dose was 5 mg every other day, he had recurrence of migratory large joint arthralgia/arthritis, recurrent skin vasculitis, sinus congestion and pain, epistaxis, a cough with occasional hemoptysis, and an increase in his proteinuria and microhematuria. He was started him back on prednisone 20 mg twice daily. In the past 24 hours he coughed up blood-tinged sputum.

Physical examination reveals palpable purpura over both lower extremities, sinus tachycardia and grade 1 pitting edema of both ankles but is otherwise completely unremarkable. Otorhinolaryngology consultation noted only punctate submucosal erythema in the adenoid bed, but no other abnormalities of nasopharynx, oral cavity, ears, or subglottic region.

Chest roentgenogram obtained 2 days ago shows a hazy lingular infiltrate. High-resolution chest CT performed today demonstrates scattered areas of groundglass alveolar infiltrates in both lungs, consistent with alveolar hemorrhage. Most of the lung is not involved. The largest areas are in the lower lobes on the right and on the left. Small nodular densities are present in an area of presumed hemorrhage in the left apex.

Laboratory studies today: Hgb 12.8 g/dl; WBC 7.5 k/ml; Plat 252 K; creatinine 1.0 mg/dl (88.5 mmol/l); ESR 25 mm/1st hr; CRP 0.483 mg/dl. C-ANCA/anti-PR3 is positive. Urinalysis shows hematuria (20 RBCs/HPF), 2+ proteinuria (estimated 0.565 g/24hrs), and red cell casts.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #17

A 50 year-old woman with a history of non-Hodgkin's lymphoma (diagnosed in 1996 and treated with 6 cycles of CVP; in complete remission ever since) presents for follow-up of Wegener's granulomatosis (WG). She was diagnosed with WG in 2000 based on: nasal and sinus inflammation (biopsy: nonspecific acute and chronic inflammation), iritis, arthralgias and synovitis, palpable purpura (biopsy: subacute dermatitis with perivascular lymphocytic inflammation), and a positive test for C-ANCA/anti-PR3. All symptoms resolved with therapy consisting of prednisone and cyclophosphamide.

She was maintained on prednisone and mycophenolate mofetil (methotrexate and azathioprine were contraindicated because of chronically elevated liver function tests attributed to fatty liver). Over the past few years she had intermittent flares of the disease variably involving eyes, nose and sinuses, joints and skin, requiring increased prednisone dose.

She now returns for a reevaluation prompted by a 2 weeks of signs and symptoms consistent with an acute flare of her Wegener's granulomatosis despite being maintained on mycophenolate mofetil 1000 mg bid and prednisone 20 mg daily. She complains of arthralgias.

Physical examination reveals tender swelling and redness of both ankle, a petechial rash and some palpable purpura. Chest x-ray is normal. Despite complaints of nasal stuffiness and sinus pressure, examination of the oropharynx, nose and sinuses by an otorhinolaryngologist reveals no sign of active inflammation. Eye exam is also normal.

Laboratory testing: normal ESR, normal Hgb, WBC, and platelet count; slightly elevated CRP and AST; Creatinine of 1.10 mg/dl (97.4 mmol/l). C-ANCA/antiPR3 is positive. Urinalysis: hematuria (5 RBCs/HPF), 1+ proteinuria (estimated 0.194 g/24hrs), occasional hyaline, granular, and RBC casts, as well as >25% dysmorphic red cells.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #18

A 23 year old woman was diagnosed with Wegener's granulomatosis in January 2002. Initial presentation consisted of nasal and sinus inflammation resulting in saddle nose deformity, serous otitis, and an ulcerated, non-tender skin lesion on her back. Nasal and sinus biopsy showed necrotizing granulomatous inflammation and vasculitis (negative fungal and mycobacterial stains). She was C-ANCA/anti-PR3 positive. There was no other organ involvement. She responded promptly to treatment consisting of prednisone and methotrexate.

She returns now in August 2003 for a reevaluation of disease activity and the possibility of a repair of her saddle nose deformity. She is asymptomatic. Medications include MTX 25 mg/wk, folic acid 1 mg/d, TMP/SMX 1 SS/d. Otorhinolaryngology evaluation reveals no sign of active inflammation in the nose and sinuses, ears, larynx, subglottic region. ENT surgeon states: "ready to do the nose anytime you give the green light".

Physical examination is normal with the exception of the saddle nose deformity. Chest x-ray is normal. Urinalysis is normal. ESR 33 mm/1st hour, CRP 3.14 mg/dl (nl 0.02-0.8), Hgb 11.5 g/dl, WBC and platelets normal, creatinine normal; C-ANCA/anti-PR3-ANCA positive.

Pulmonary function testing (PFT) reveals a normal total lung capacity (95% of predicted), increased residual volume (130%), a reduced FEV1 (73%), a normal FEV1/FVC ratio, normal diffusing capacity and a slight abnormality in the shape of the expiratory flow-volume loop. These subtle PFT abnormalities in a young never-smoker in combination with abnormal markers of inflammation and persistently positive ANCA prompted a bronchoscopy. This revealed focal erythema, friable mucosa and substantial narrowing of the right upper lobe bronchus; mucosal biopsy from the affected site revealed "necrotizing granulomatous inflammation consistent with active Wegener's (negative fungal and mycobacterial stains)".

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #19

A 63 year-old woman was healthy until December 1998, when he developed a flu-like illness but had normal breathing. During January and February 1999 he developed migratory muscle cramps and dyspnea with exertion. This resolved spontaneously by summer. By September 1999 he had gradually worsening dyspnea with exertion. Currently (November 5, 1999) he can walk two flights and then he is out of breath. He also noticed anorexia, fatigue, some cough, and over the course of the last month has noticed occasional blood tinged sputum. Physical exam is entirely unremarkable.

Chest x-ray shows bilateral, predominantly basilar peripheral interstitial infiltrates. Comparison with a February 1999 x-ray indicates the peripheral interstitial infiltrates are unchanged; however, there is a new superimposed alveolar infiltrate in the right mid-lung.

Pulmonary function testing obtained yesterday indicates stable lung volumes and flows when compared to March 1999. However, there is a significant drop in diffusing capacity (corrected for Hgb) from 21.6 in March to 16.7 now.

Laboratory studies: ESR=88 mm/1st hr; creatinine has risen from 1.00 mg/dl (88.5 mmol/l) in March to 1.90 mg/dl (168.2 mmol/l) on October 21, and 2.00 mg/dl (177.0 mmol/l) on November 1. His Hgb was 13.9 g/dl in March 1999, 10.9 g/dl on October 21, 1999, and now on November 5, is 10.1 g/dl. WBC and platelets are normal. Urinalysis reveals 11-20 RBC's/HPF, >25% dysmorphic, 2+ proteinuria (estimated 1.39 g/24hrs), but no casts. P-ANCA/anti-MPO is positive.

Past medical history is significant for a pyeloplasty in 1963 for a mal-positioned left ureter. He has had persistent low-grade proteinuria and leucinuria since that time.

Renal biopsy demonstrates focal segmental necrotizing, crescentic glomerulonephritis (3 of 12 glomeruli) and early segmental sclerosis (2 of 12 glomeruli with no immune deposits.

Vasculitis Outcome Measure Initiative
Comparative Outcome Measure Exercise-Study Cases

Case #20

A 50 year old man is now (June 10, 2003) being evaluated for his Wegener's granulomatosis (WG). Disease onset was 2001 with lung (infiltrates and nodules) and renal involvement (biopsy-documented pauci-immune glomerulonephritis), and positive C-ANCA/anti-PR3. He was treated only with oral prednisone until December 2002 when he developed headaches, thirst and polydipsia for the first time. He was diagnosed with diabetes insipidus and placed on DDAVP.

He was first seen at our institution in January 2003. An MRI-scan revealed enlargement of the pituitary gland. It was concluded that this represented pituitary involvement of his WG, the prednisone dose was increased and oral cyclophosphamide (CYC) was added to his regimen. Hormone replacement therapy was also initiated. He did not tolerate the oral CYC and it was replaced by intravenous CYC.

An echocardiogram in March, performed to determine the etiology of progressive dyspnea, showed regional wall motion abnormalities in a distribution atypical for coronary artery disease. Therefore, it was concluded that these regional wall motion abnormalities were likely caused by WG although it was unclear whether these represented old or new lesions. A repeat brain MRI in March revealed reduction in size of the pituitary tumor. There was also initial symptomatic improvement and reduction in size of the lung lesions (x-ray). His prednisone dose was tapered an he briefly reached the dose of 25 mg daily but subsequently, in early May, the lung lesions were documented to again be increased in diameter. Over the last few weeks he noticed progressive frontal headaches, fatigue, poor appetite, and thirst with polyuria.

Current medications include prednisone (40 mg/d), IV monthly CYC (2.0 g; last dose exactly a month ago), trimethoprim-sulfamethoxazole.

On exam, the patient appears markedly cushingoid. Eye, ENT, heart, lung and abdominal examination reveal no abnormality. He has grade 2 pitting edema of the lower extremities and livedo reticularis of the lower extremities.

Chest x-ray today confirms significant enlargement of bilateral, multiple, partially cavitated lung lesions. Repeat brain MRI reveals enlargement of the pituitary tumor compared to the March study.

Laboratory studies now: ESR 29 mm/1st hr; CRP 1.92 mg/dl (nl 0.02-0.8). Hgb, WBC, platelets, creatinine, and urinalysis are all normal. C-ANCA/anti-PR3 is positive.