General Internal Medicine Review Course

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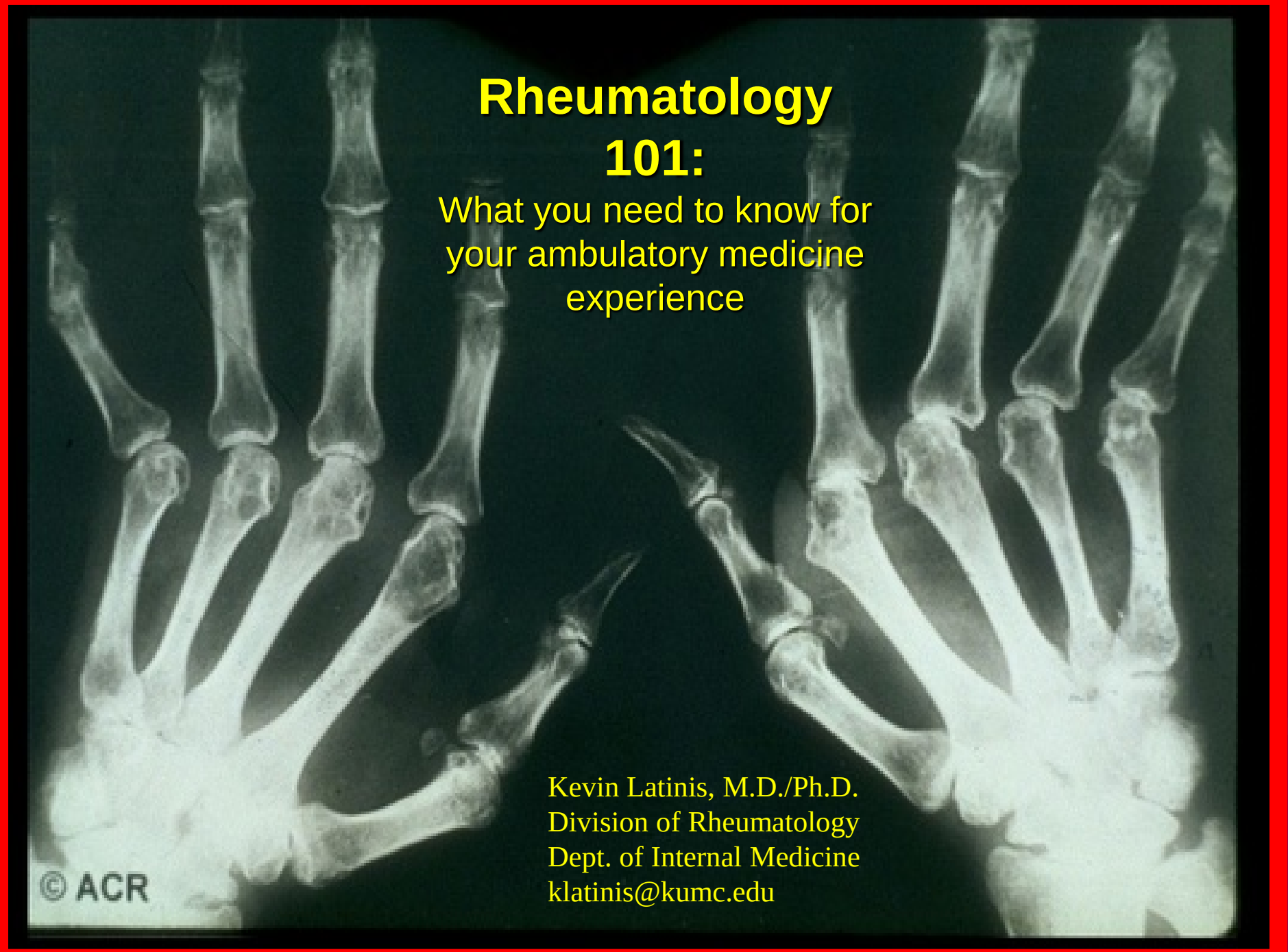
- DUE TO TIME CONSTRAINTS content of some slides will be only discussed briefly but is here so you can STUDY it on your OWN
- Each organ system has multi-year subspecialty training
- Expectations: establish a working diagnosis, initiate treatment, know when to refer to a specialist
- Limitations: diagnostic testing, availability of specialists
- Do the best you can (medical ethics)
  - If it’s key to the diagnosis, facilitate external testing
  - Give it your best guess and initiate treatment and assess for response
  - Refer to specialist when indicated
  - See them back to coordinate care

Rheumatology overview

- Pain and / or inflammation of the joints and/or soft tissues
- Wide variety of presentations
- Focus on identifying those with on-going inflammation
- Goal is improved functional capacity and limit on-going damage

- The following slides are selected from presentations found online



Rheumatology 101:

What you need to know for your ambulatory medicine experience

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Rheumatology 101

- Arthritis
  -Inflammatory (RA, spondyloarthropathies)
  -Mechanical (OA)
- Lupus
- Fibromyalgia
- Low back pain and other peri-articular complaints
- General musculoskeletal exam (time permitting)

Mechanical vs. Inflammatory Arthritis

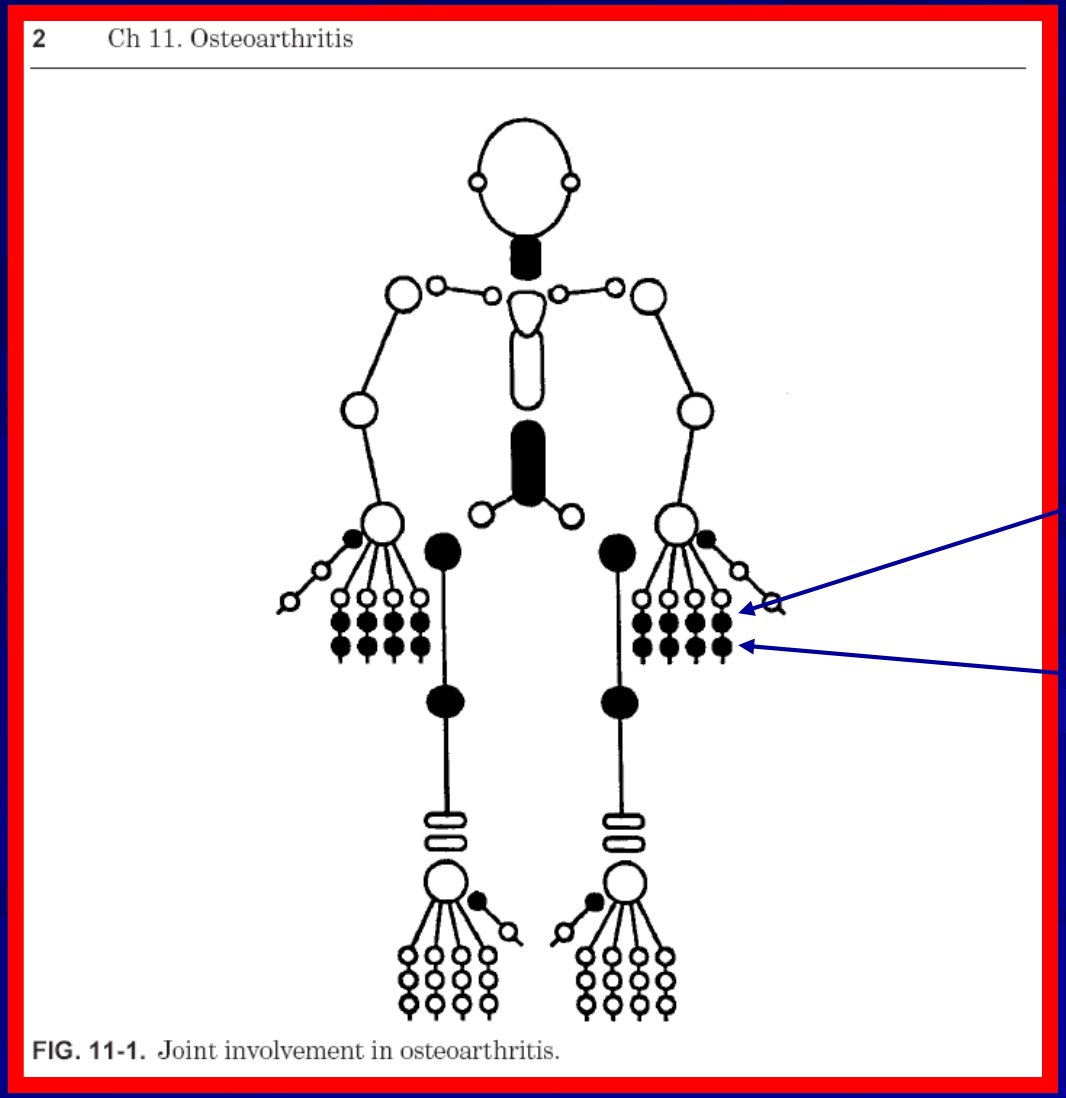
TABLE 1-1. NONINFLAMMATORY VS INFLAMMATORY DISORDERS

	Noninflammatory disorders (e.g., OA)	Inflammatory disorders (e.g., RA, lupus)
Symptoms		
Morning stiffness	Focal, brief	Significant, prolonged, >1 hr
Constitutional symptoms	Absent	Present
Peak period of discomfort	After prolonged use	After prolonged inactivity
Locking or instability	Implies loose body, internal derangement, or weakness	Uncommon
Symmetry (bilateral)	Occasional	Common
Signs		
Tenderness	Unusual	Over entire exposed joint area
Inflammation (fluid, tenderness, warmth, erythema, synovitis)	Unusual	Common
Multisystem disease	No	Often
Lab abnormalities	No	Often

Adapted from American College of Rheumatology ad hoc Committee on Clinical Guidelines. Guidelines for the initial evaluation of the adult patient with acute musculoskeletal symptoms. *Arthritis Rheum* 1996;39:1.

Latinis, K., et al *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.

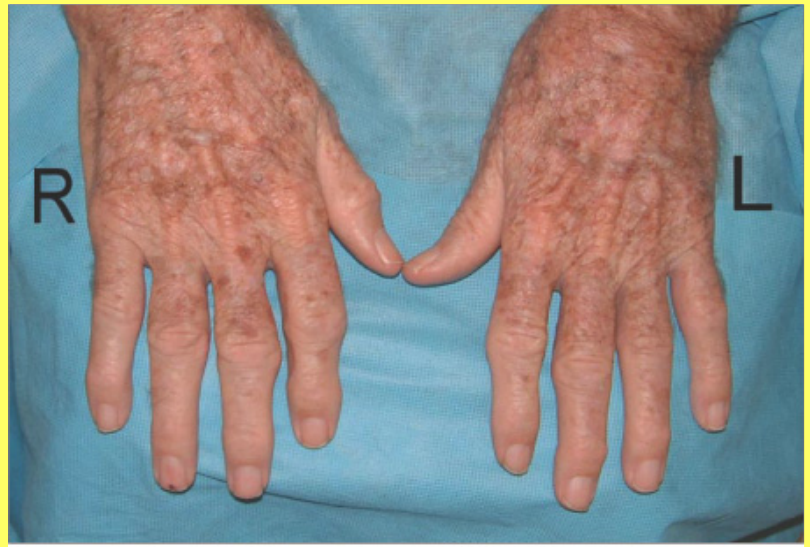
Osteoarthritis-Distribution



Bouchard's

Heberden's

Latinis, K., Dao, K, Shepherd, R, Gutierrez, E, Velazquez, C. *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.



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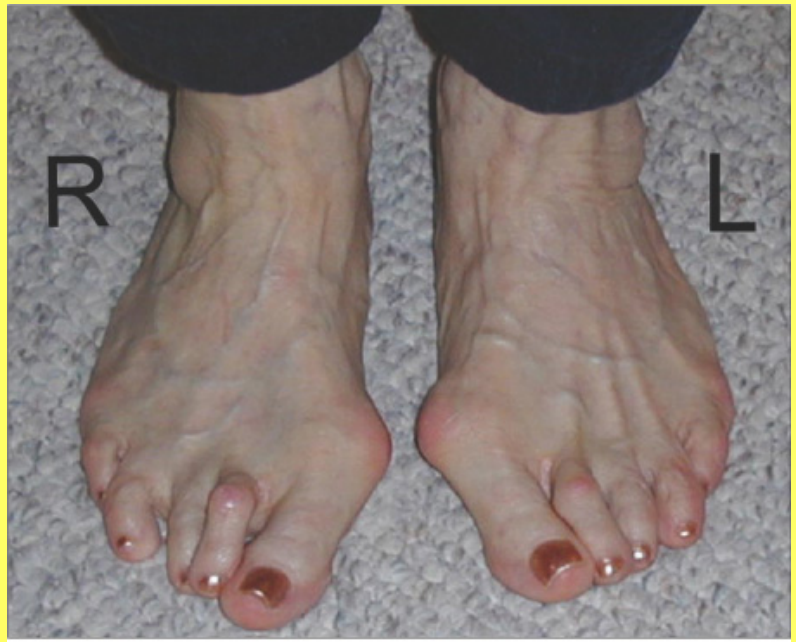

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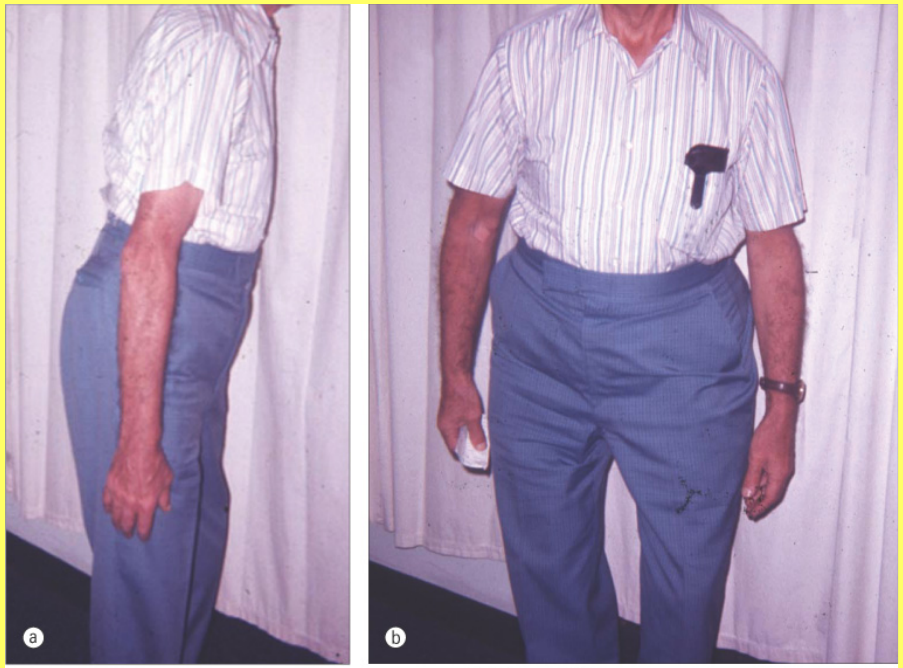

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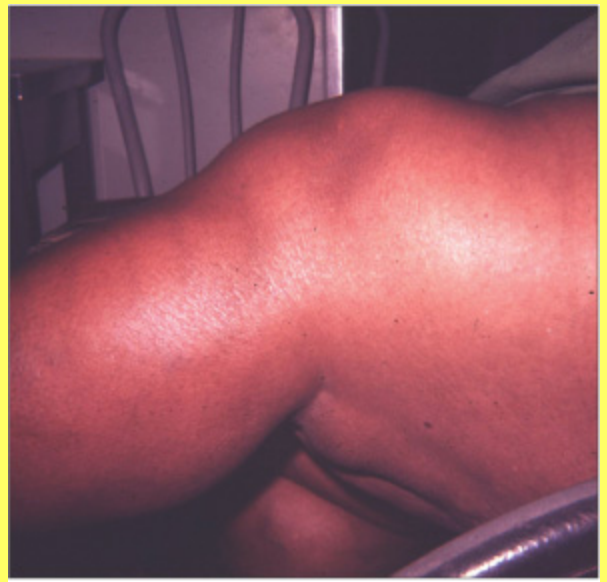
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Osteoarthritis-Diagnosis

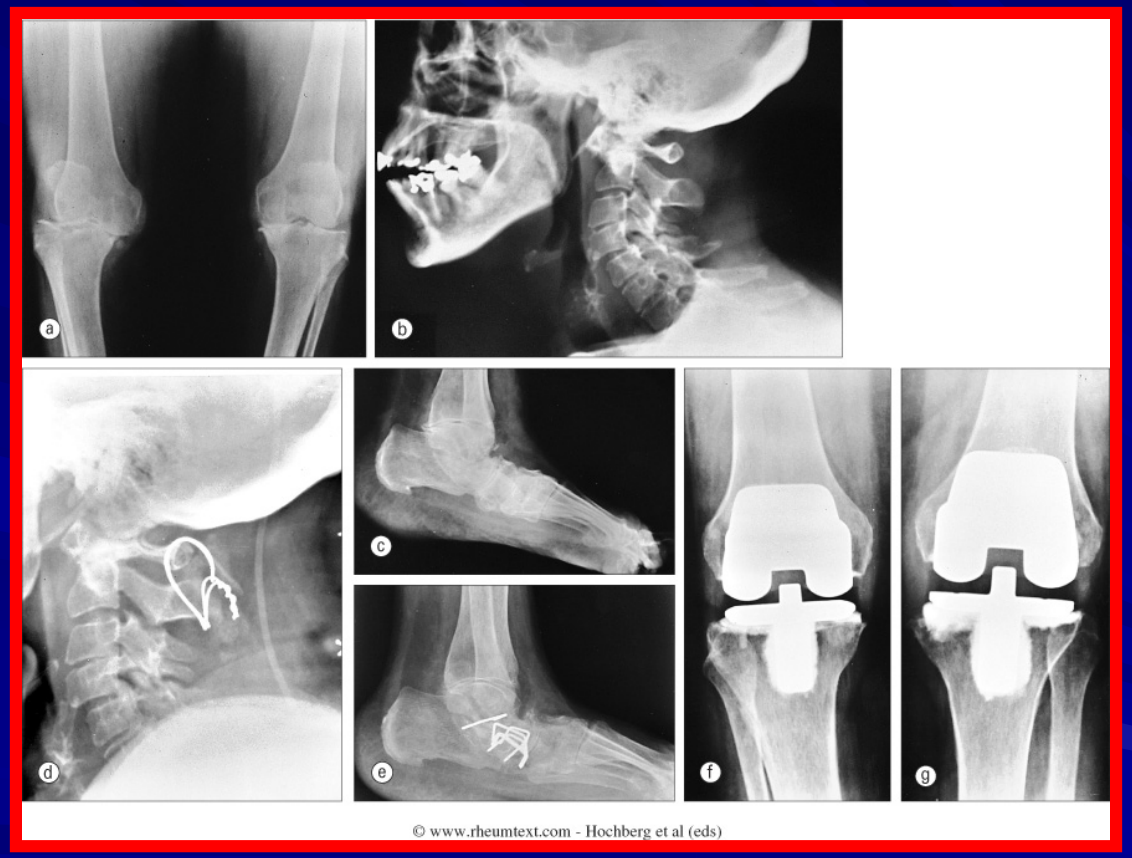
- Clinical
- Supported by X-rays
- Non-inflammatory lab data, if any

Osteoarthritis-Treatment

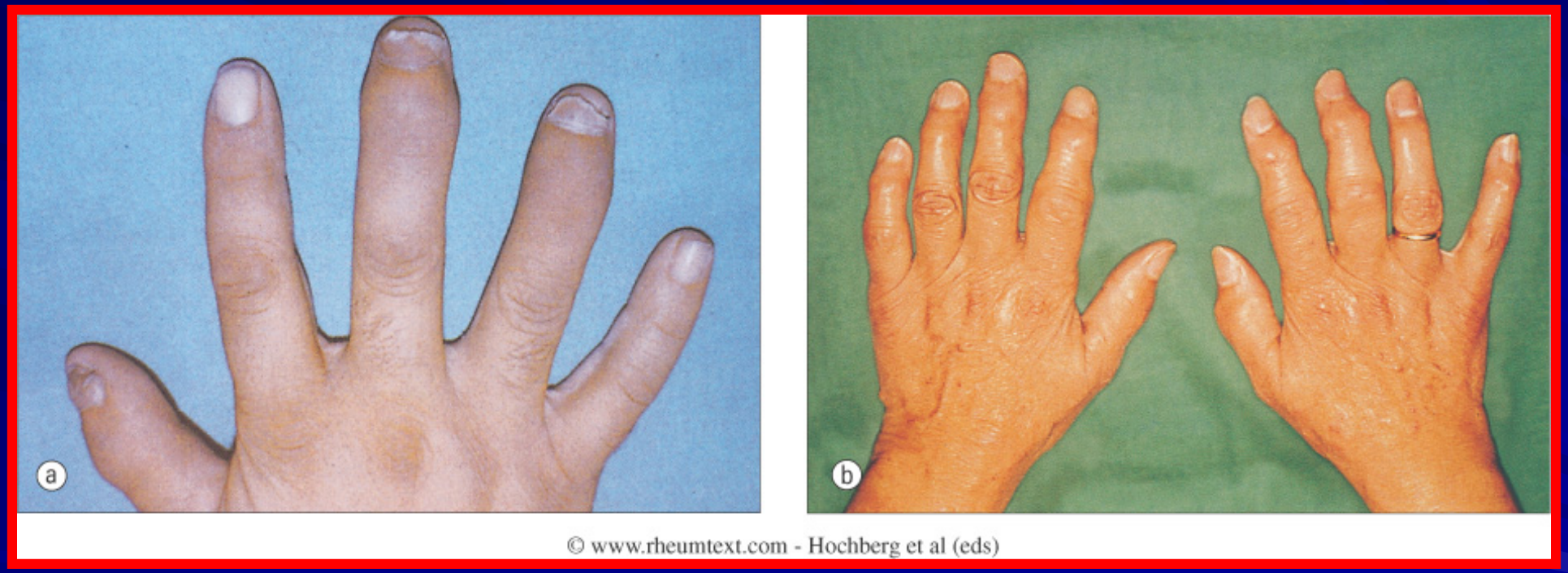
- Pain relief
  -Analgesics and NSAIDs/Cox-2 Inhibitors
- SMOADs (structure modifying osteoarthritis drugs)
  -Glucosamine Sulfate -see meta-analysis McAlindon et al. JAMA, 283: 3/2000, p. 1469
  -many under development
- Non-pharmacologic approaches
  -Reduce stress/load on joint
  -Strengthen surrounding muscles-PT/OT
  -Weight reduction
  -Patient education
- Limit disability and improve quality of life

Osteoarthritis-Treatment

- Joint Replacement Surgery
  -Primarily of knee and hip, but also available in hands, shoulders,& elbows
  -Indications:
    1. pain at rest
    2. instability
  -patients benefit from aggressive PT before & after surgery
- Other surgical procedures



Clinical Pearl:
Arthritis of the DIP joint



Psoriatic Arthritis (inflammatory)

OA (non-inflammatory)

Inflammatory Arthritis

- Rheumatoid arthritis
- Spondyloarthropathies
  -Undifferentiated
  -Ankylosing spondylitis
  -Psoriatic arthritis
  -Reactive arthritis (formerly Reiter’s syndrome)
  -Enteropathic arthritis
- SLE, Sjogrens, Scleroderma, Polymyalgia rheumatica, Vasculitis, Infectious (bacterial, viral, other), Undifferentiated connective tissue disease

TABLE 1-3. CAUSES OF POLYARTHRITIS

- Inflammatory
  - Polyarticular peripheral (usually symmetric)
    - RA (usually presents insidiously, additive)
    - Viral arthritis (usually acute onset)
    - SLE
    - PsA (occasionally)
    - Palindromic rheumatism (recurrent attacks)
  - Oligoarticular with axial involvement (usually asymmetric, lower extremity joints)
    - Seronegative spondyloarthropathies (AS, ReA, PsA, and enteropathic arthritis)
  - Oligoarticular without axial involvement (usually asymmetric)
    - PsA
    - ReA
    - Enteropathic arthritis
    - Lyme disease
    - Polyarticular gout (more commonly monoarticular)
    - CPDD
    - Bacterial endocarditis
    - Septic arthritis (particularly in patients with RA)
    - Sarcoidosis
    - Behçet's disease and relapsing polychondritis (rare)
    - Rheumatic fever (usually migratory)
- Noninflammatory
  - OA
    - OA of the hands
    - Generalized OA
    - Posttraumatic OA
    - OA secondary to metabolic diseases (hemochromatosis, ochronosis, acromegaly)
  - Sickle cell disease
  - Hypertrophic osteoarthropathy
  - Other (rare)
    - Leukemia
    - Hemophilia
    - Amyloidosis

Latinis, K., et al *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.

Rheumatoid Arthritis-Background

- Symmetric, inflammatory polyarthritis
- Affects ~1% of our population
- Occurs in women 3x more than men
- Etiology
  -Genetic, class II molecules (HLA-DRB1)
  -Autoimmune
  -?Environmental

Rheumatoid Arthritis-Distribution

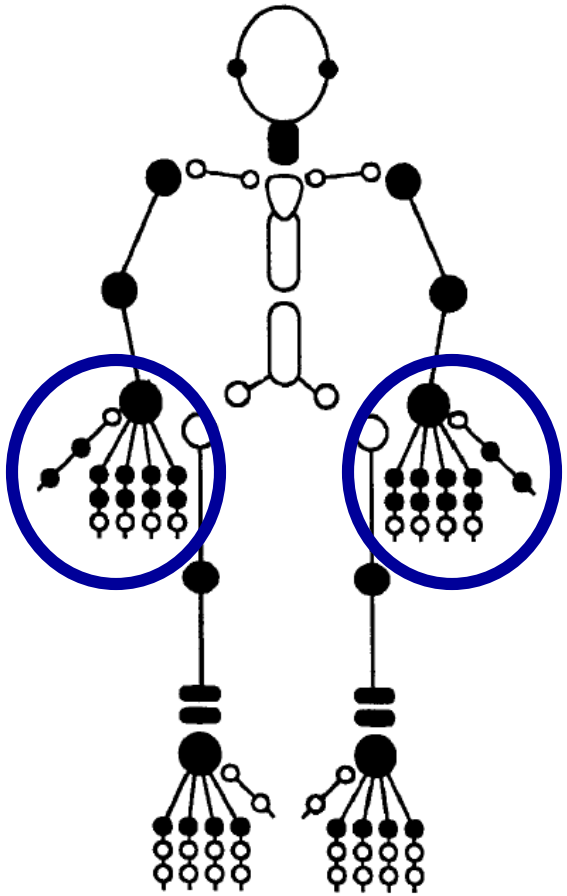


FIG. 10-1. Joint involvement in rheumatoid arthritis.

Latinis, K., et al
The Washington Manual Rheumatology Subspecialty Consult., LWW, 2003.

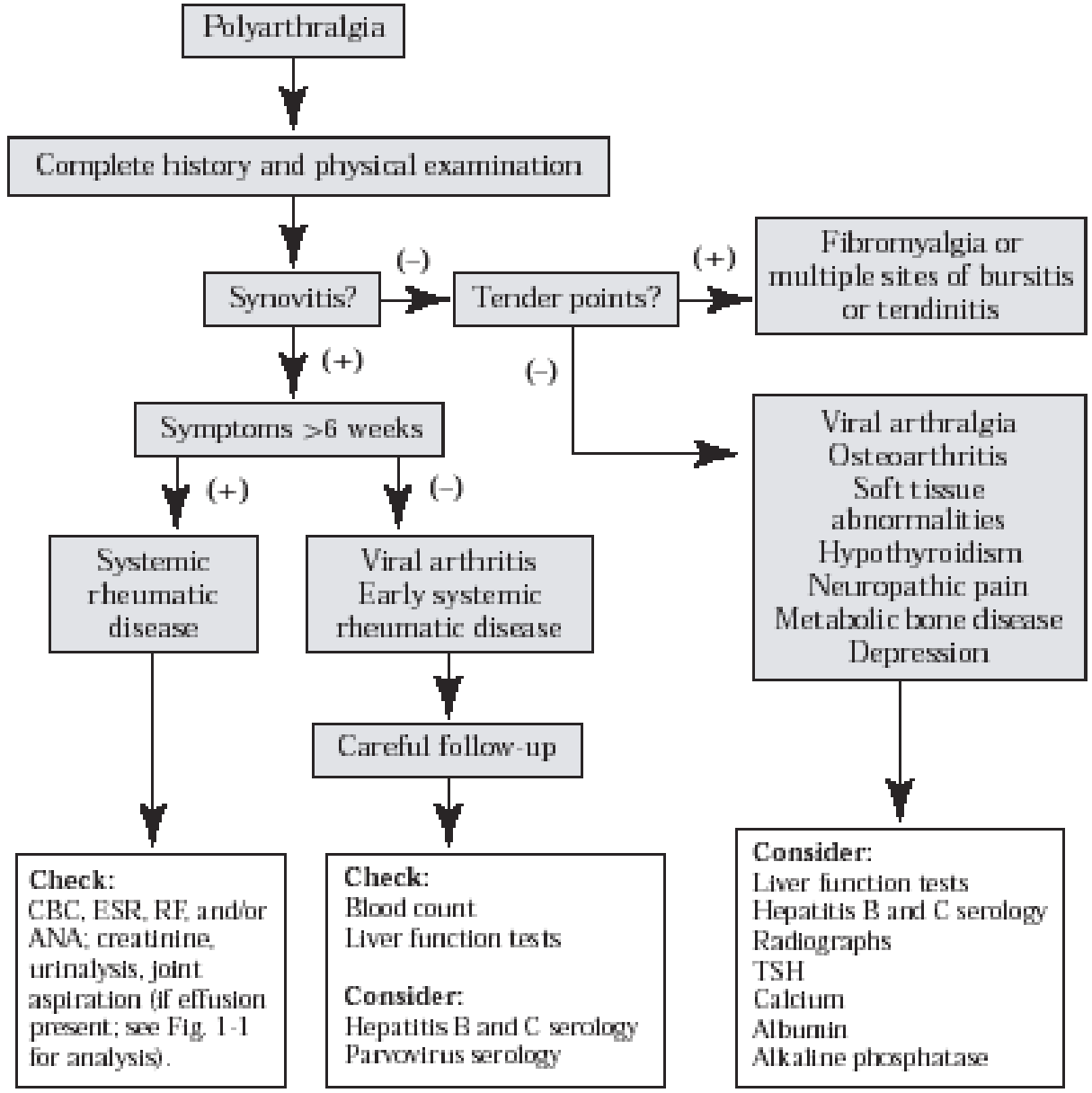


FIG. 1-2. Approach to polyarthritis. (Adapted from American College of Rheumatology ad hoc Committee on Clinical Guidelines. Guidelines for the initial evaluation of the adult patient with acute musculoskeletal symptoms. *Arthritis Rheum* 1996;39:1.)

Latinis, K., et al *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.

Systemic Lupus Erythematosus (Lupus)-Background

Definition

-An inflammatory multisystem disease of unknown etiology with protean clinical and laboratory manifestations and a variable course and prognosis.

-Immunologic aberrations give rise to excessive autoantibody production, some of which cause cytotoxic damage, while others participate in immune complex formation resulting in immune inflammation.

Systemic Lupus Erythematosus (Lupus)-Background

Clinical features

-Clinical manifestations may be constitutional or result from inflammation in various organ systems including skin and mucous membranes, joints, kidney, brain, serous membranes, lung, heart and occasionally gastrointestinal tract.

-Organ systems may be involved singly or in any combination.

-Involvement of vital organs, particularly the kidneys and central nervous system, accounts for significant morbidity and mortality.

-Morbidity and mortality result from tissue damage due to the disease process or its therapy.

Systemic lupus erythematosus classification criteria
(SOAP BRAIN MD)

1. ***S***erositis:
   (a) pleuritis, or
   (b) pericarditis
2. ***O***ral ulcers
3. ***A***rthritis
4. ***P***hotosensitivity

10. ***M***alar rash
11. ***D***iscoid rash

". ..A person shall be said to have SLE if four or more of the 11 criteria are present, serially or simultaneously, during any interval of observation."

5. ***B***lood/Hematologic disorder:
   (a) hemolytic anemia or
   (b) leukopenia of < 4.0 x 10^9
   (c) lymphopenia of < 1.5 x 10^9
   (d) thrombocytopenia < 100 X 10^9
6. ***R***enal disorder:
   (a) proteinuria > 0.5 gm/24 h or 3+ dipstick or
   (b) cellular casts
7. ***A***ntinuclear antibody (positive ANA)
8. ***I***mmunologic disorders:
   (a) raised anti-native DNA antibody binding or
   (b) anti-Sm antibody or
   (c) positive anti-phospholipid antibody work-up
9. ***N***eurological disorder:
   (a) seizures or
   (b) psychosis

53 yo BF with severe generalized weakness, weight loss, and chronic psychosis

Laboratory Data

139	106	16
4.3	21	1.4

101

7.7

3.9 298

22.3

MCV=83

Absolute lymph=0.5

24 hour urine

Protein=514

ESR=119

CH50=67 (118-226)

C3=31 (83-185)

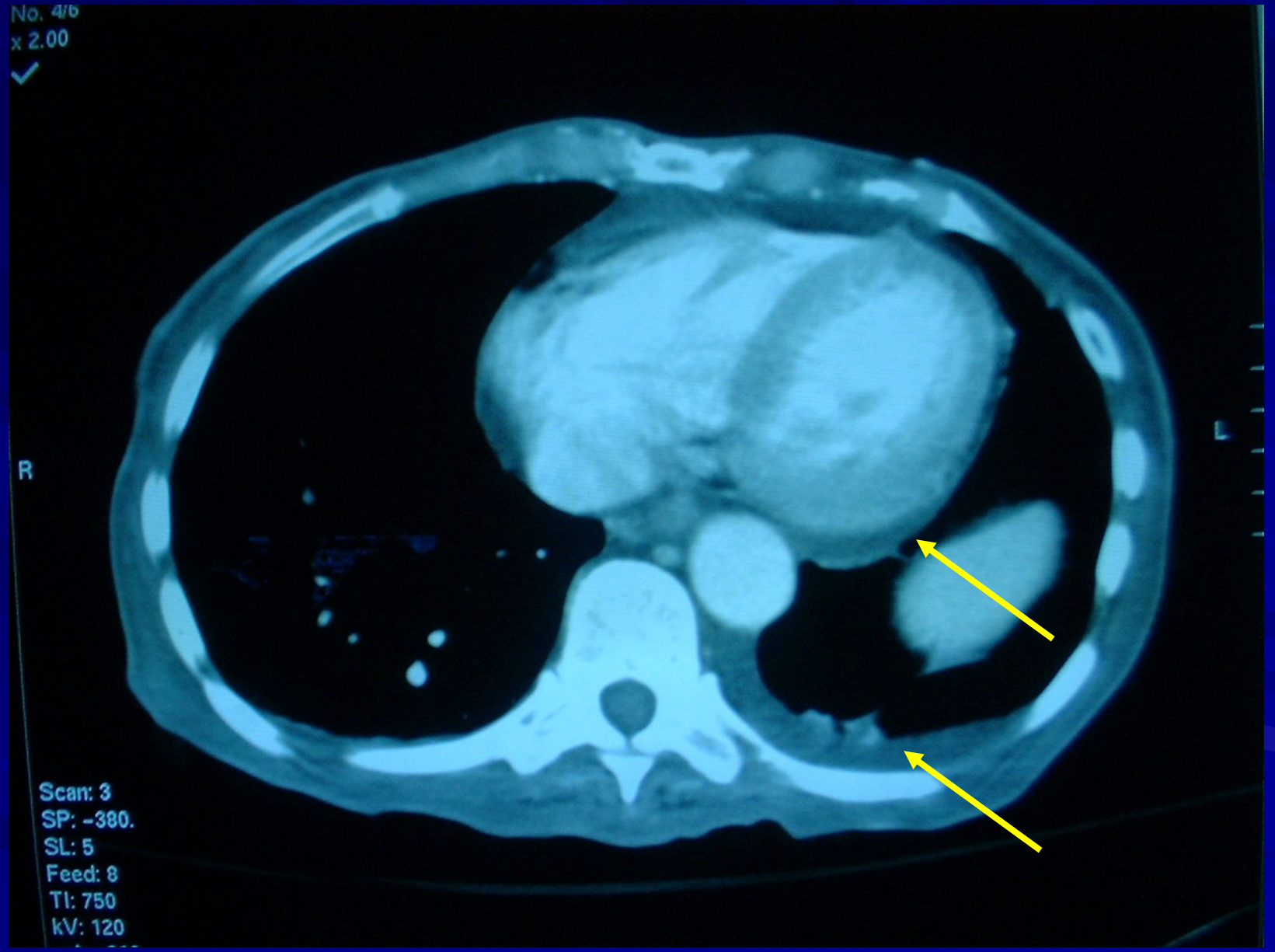
C4=18 (12-54)

ANA + 1:5280

Anti DNA +

Direct & Indirect Coombs +

Anti-IgG +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Treatment of SLE

- Arthritis, arthralgias, myalgias: NSAIDS, anti-malarials (eg. Plaquenil), Steroids-injections, oral methotrexate
- Photosensitivity, dermatitis
  - avoid Sun exposure
  - topical steroids
  - Plaquenil
- Weight loss and fatigue
  - steroids
- Abortion, fetal loss
  - ASA
  - immunosuppression
- Thrombosis
  - anti-coagulants
- Glomerulonephritis
  - steroids
  - pulse cytotoxics
  - mycophenylate mofetil
- CNS disease
  - anti-coagulants for thrombosis
  - steroids and cytotoxics for vasculitis
- Infarction (secondary to vasculitis)
  - steroids
  - cytotoxics
  - prostacyclin
- Cytopenias
  - steroids
  - IVIG-short term for thrombocytopenia
  - danazol
  - cytotoxics-if bone marrow status is known

Steroids in Lupus

- Steroid responsive
  - Dermatitis (local)
  - Polyarthritis
  - Serositis
  - Vasculitis
  - Hematological
  - Glomerulonephritis (most)
  - Myelopathies
- Steroid non-responsive
  - Thrombosis
  - Chronic renal damage
  - Hypertension
  - Steroid-induced psychosis
  - Infection

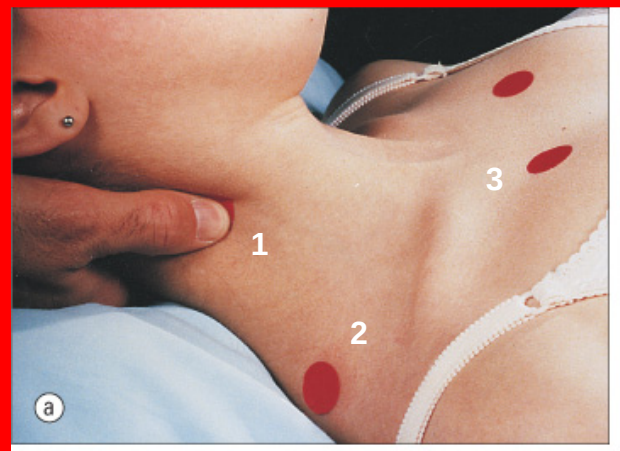
Fibromyalgia-Background

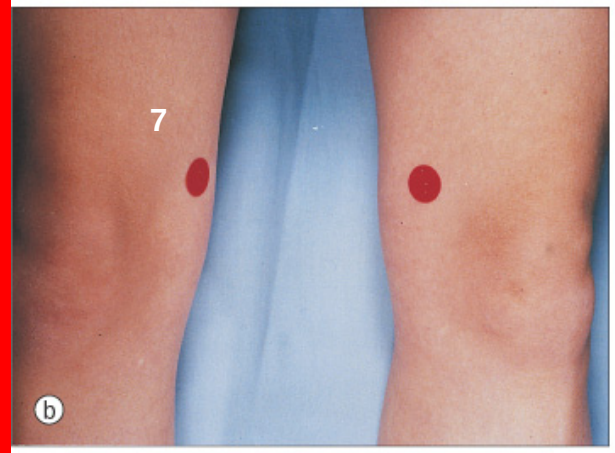
- Chronic musculoskeletal pain syndrome of unknown etiology
- Characterized by diffuse pain, tender points, fatigue, and sleep disturbances
- Prevalence is 2-5% with a female to male predominance of 8:1
- Mean age is 30-60

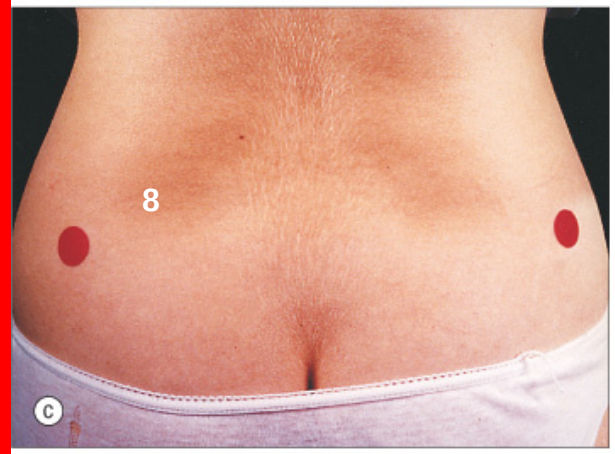
Fibromyalgia-Diagnosis

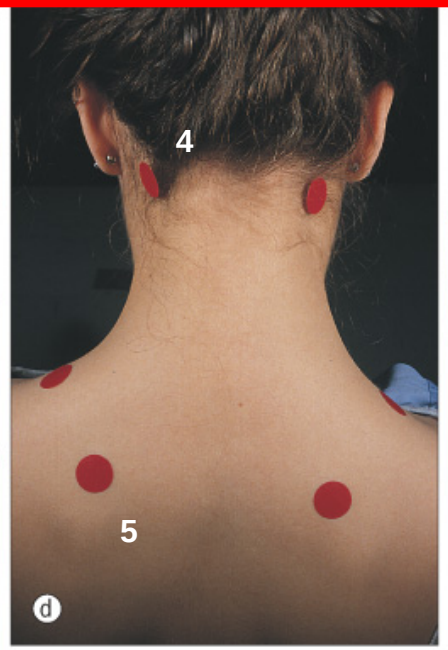
TABLE 62.1 DIAGNOSTIC FEATURES OF FIBROMYALGIA

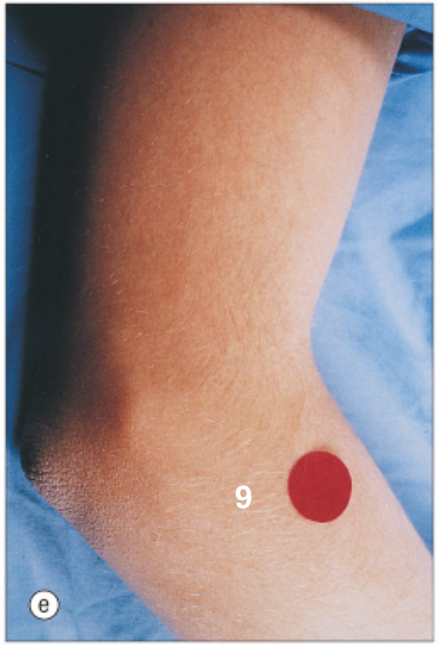
Cardinal features*
Chronic, widespread pain Tender points on examination
Characteristic features
Fatigue Sleep disturbances Stiffness Paresthesias Headaches Irritable bowel syndrome Raynaud's-like symptoms Depression Anxiety
*For classification criteria, patients must have pain for at least 3 months involving the upper and lower body, right and left sides, as well as axial skeleton, and pain in at least 11 of 18 tender points on digital examination.

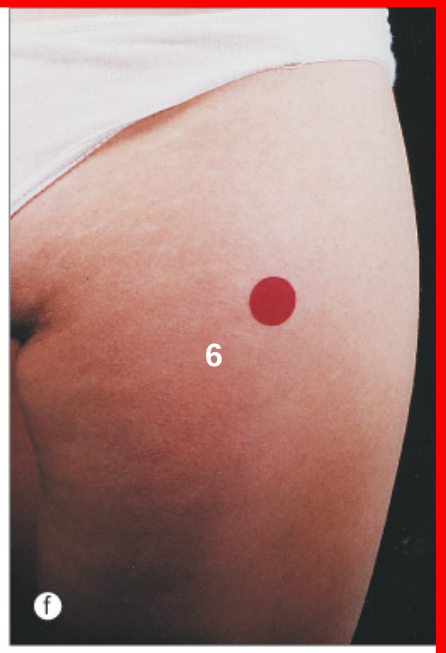












TENDER POINTS IN FIBROMYALGIA

Pain on digital palpation must be present in at least 11 of the following 18 tender point sites:

Occiput: bilateral, at the suboccipital muscle insertions (d)

Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5–C7 (a)

Trapezius: bilateral, at the midpoint of the upper border (d)

Supraspinatus: bilateral, at origins, above the scapula spine near the medial border (d)

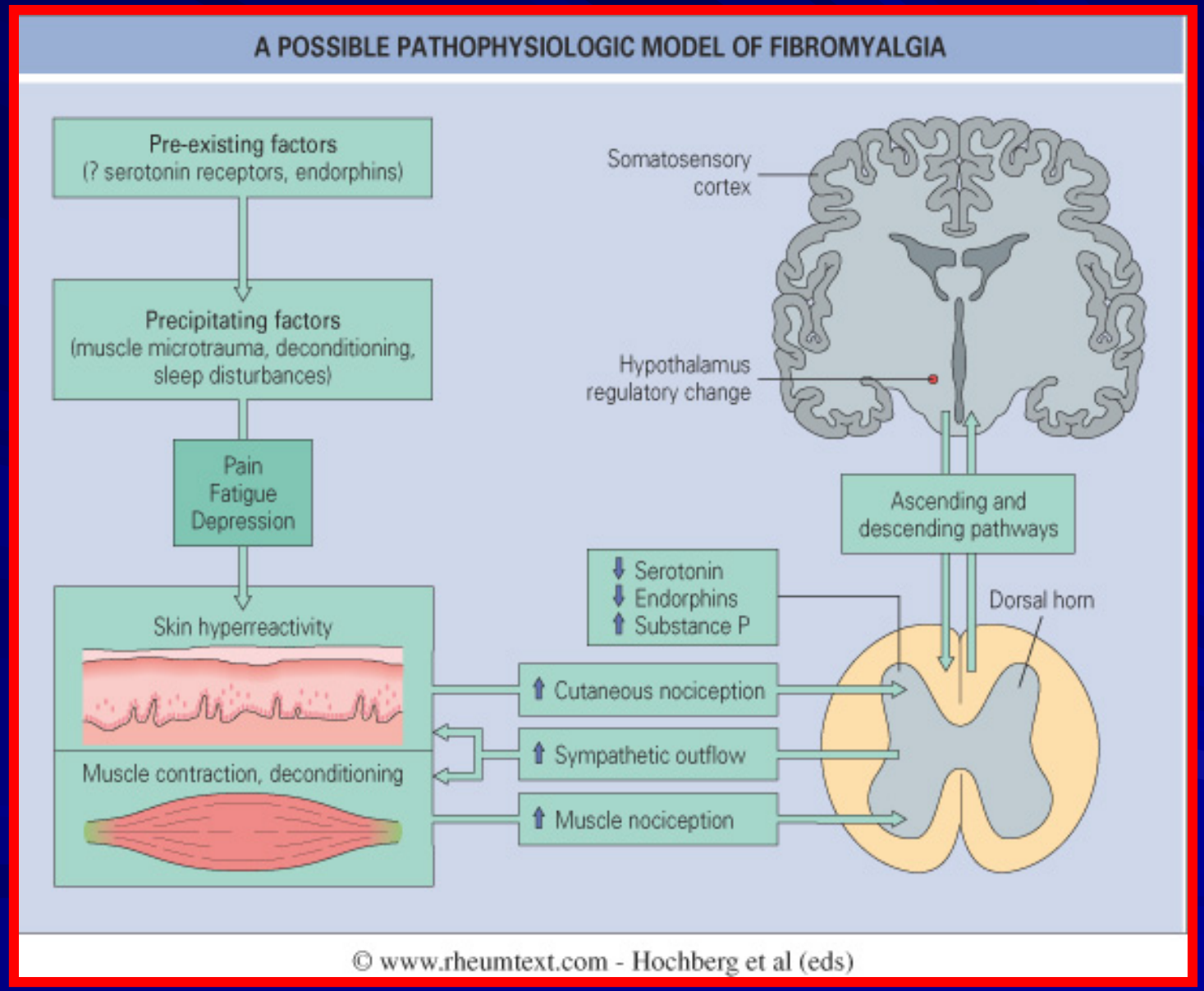
Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces (a)

Lateral epicondyle: bilateral, 2cm distal to the epicondyles (e)

Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle (c)

Greater trochanter: bilateral, posterior to the trochanteric prominence (f)

Knee: bilateral, at the medial fat pad proximal to the joint line (b)


A POSSIBLE PATHOPHYSIOLOGIC MODEL OF FIBROMYALGIA
Pre-existing factors
(? serotonin receptors, endorphins)
Precipitating factors
(muscle microtrauma, deconditioning, sleep disturbances)
Pain
Fatigue
Depression
Skin hyperreactivity
Muscle contraction, deconditioning
Somatosensory cortex
Hypothalamus regulatory change
Ascending and descending pathways
Serotonin
Endorphins
Substance P
Dorsal horn
Cutaneous nociception
Sympathetic outflow
Muscle nociception
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Fibromyalgia-Treatment

TABLE 62.7 STEPWISE APPROACH TO FIBROMYALGIA TREATMENT

First-line treatment
Medications: simple analgesics, NSAIDs, low-dose tricyclic antidepressants* or serotonin receptor inhibitors Education* Exercise*: low impact, such as walking, water exercises If mood disturbances, treat with appropriate medications
Second-line treatment
Medications: tramadol*, combinations of antidepressants* or other analgesics Cognitive behavioral program*, stress management therapy* Structured exercise program* Physical medicine and rehabilitation program Trigger point injections, acupuncture Pain management program

* Evidence of efficacy in controlled clinical trials.
NSAIDs, non-steroidal anti-inflammatory drugs.

Low back pain and other peri-articular complaints- background

- Very common, one of the most frequent reasons to visit primary care physicians
- Articular vs peri-articular problems
  -Articular pain is generally deep or diffuse and worsens with active and passive motion
  -Periarticular pain usually exibits point tenderness and increased tenderness with active, but NOT passive motion

TABLE 8-5. DIFFERENTIAL DIAGNOSIS OF LOW BACK PAIN

- Mechanical low back pain (97%)
  - Idiopathic low back pain (lumbago, lumbar strain)
  - Degenerative disk disease
  - Herniated disk
  - Spinal stenosis
  - Spondylolisthesis
  - Trauma
- Neoplasia (<1%)
  - Metastatic lesions
  - Multiple myeloma
  - Lymphoma and leukemia
  - Primary vertebral tumors
  - Spinal cord tumors
- Infection (<1%)
  - Osteomyelitis
  - Paraspinous abscess
  - Epidural abscess
  - Septic diskitis
  - Bacterial endocarditis
- Rheumatic diseases (<1%)
  - Ankylosing spondylitis
  - Psoriatic arthritis
  - Reactive arthritis
  - Inflammatory bowel disease-related arthritis
- Visceral disease and referred pain (<1%)
  - Aortic aneurysm
    - GI disease (pancreatitis, cholecystitis)
    - Genitourinary (nephrolithiasis, pyelonephritis, pelvic inflammatory disease)
  - Hip disease

Latinis, K., et al *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.

TABLE 8-6. EVALUATION OF SELECTED CAUSES OF LOW BACK PAIN

	Idiopathic low back pain	Herniated disk	Spinal stenosis	Ankylosing spondylitis	Metastases	Spinal infection
Characteristics of pain	Dull, lower back; may radiate to buttocks; improves with rest	Sudden, sharp, intense; radiates below the knee (sciatica); usually unilateral	Pseudoclaudication: bilateral pain (buttocks, thighs, legs) brought on by standing or walking and relieved by sitting or flexing spine	Insidious, chronic, worse in the morning, improves with exercise	Chronic, severe, not improved with bed rest	Severe, sharp; may radiate to thighs
History	History of lifting or straining	History of lifting or straining	Occurs in patients >60 yrs with degenerative disease of the spine	Occurs in patients <40 yrs; may have family history, or history of uveitis or axial arthritis	Age >50 yrs, history of cancer, weight loss, failure of conservative management	Immunocompromised patients; history of IV drug abuse, alcohol abuse, infections; fever not always present
Physical exam	May have pain with movement or in certain positions; neurologic exam is normal.	Pain with straight-leg raise; may have altered dermatomal sensation, weakness or decreased reflexes; 95% S1 root.	May have sensory, motor and reflex abnormalities.	Decreased range of motion, arthritis.	May show evidence of primary tumor; rule out spinal cord compression in patients with neurologic findings.	Neurologic findings present and depend on the level of involvement.
Lab studies	None needed.	None needed.	None needed.	ESR often elevated; HLA-B27 may be present but is not a good screening test.	ESR may be elevated.	ESR often elevated; positive blood cultures, leukocytosis not always present.
Imaging	None needed.	MRI recommended in patients with neurologic deficits.	MRI may be needed for diagnosis.	X-rays may show sacroiliitis; "bamboo spine" is a late finding.	CT or MRI; emergent imaging needed in suspected cord compression.	MRI indicated.

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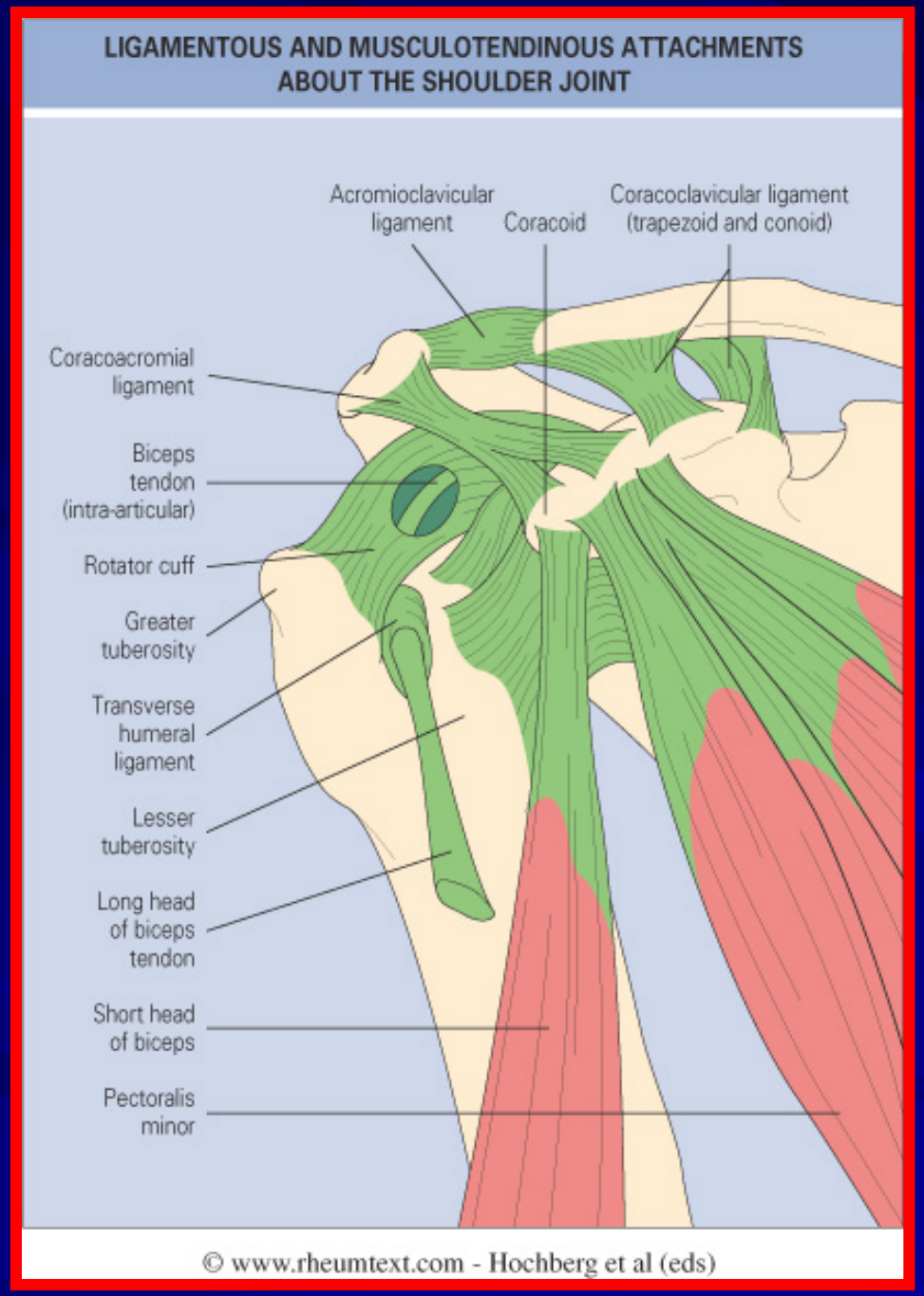
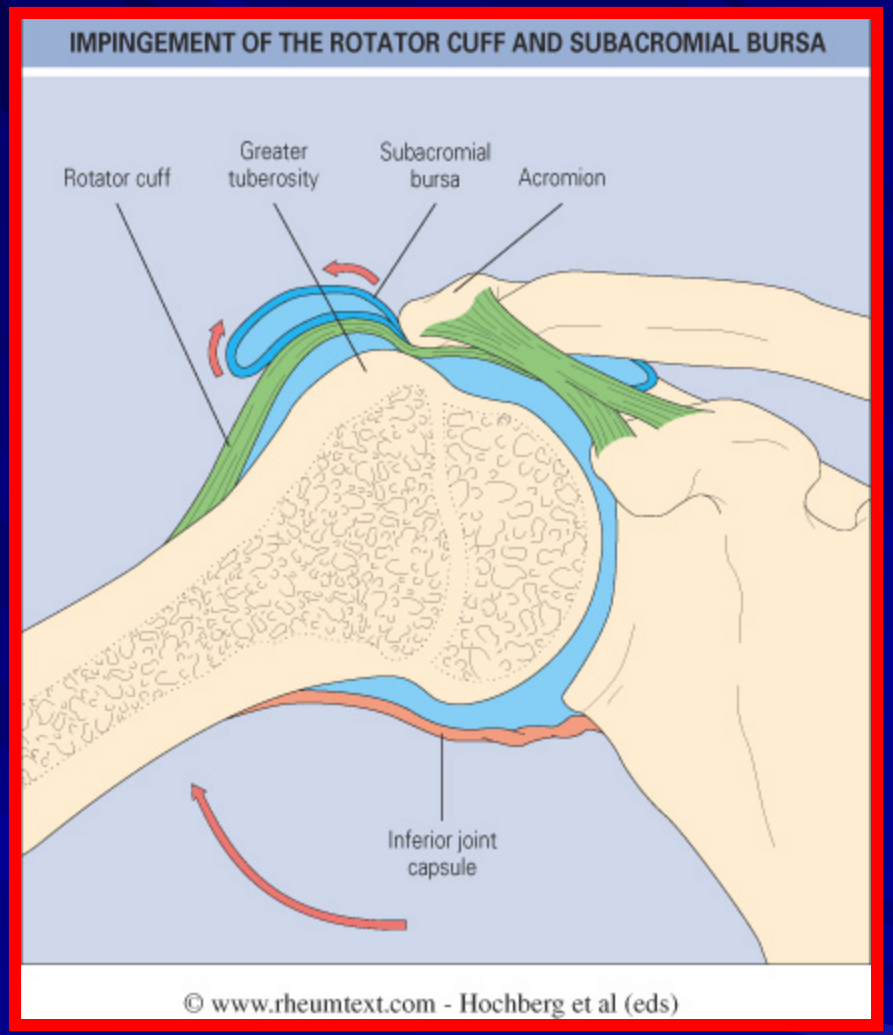
TABLE 8-8. CAUSES OF SHOULDER PAIN

Periarticular disorders
Rotator cuff tendinitis
Calcific tendinitis
Rotator cuff tear
Subacromial bursitis
Bicipital tendinitis
Adhesive capsulitis
Articular disorders
Inflammatory arthritis (rheumatoid arthritis)
Glenohumeral arthritis
Acromioclavicular arthritis
Sternoclavicular arthritis
Septic arthritis
Osteonecrosis (of humeral head)
Fractures, dislocations
Neurovascular diseases (usually have neurovascular symptoms)
Brachial plexopathy
Suprascapular nerve entrapment
Thoracic outlet syndrome
Referred pain (should be suspected in cases with normal range of motion)
Cervical spine disease
Intrathoracic or intrabdominal disease
Other
Polymyalgia rheumatica (usually bilateral)
Fibromyalgia
Reflex sympathetic dystrophy

Latinis, K., et al *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.





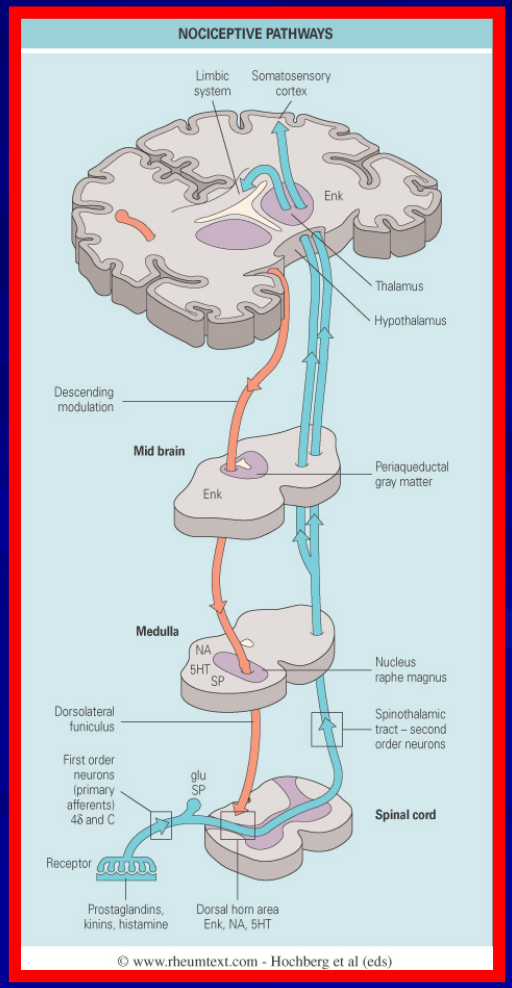
Muscles of the rotator cuff:
Supraspinatus
Infraspinatus
Subscapularis
Teres Minor

TABLE 55.1 DIFFERENTIAL DIAGNOSIS OF SHOULDER PAIN: CLINICAL AND RADIOGRAPHIC FEATURES OF COMMON CAUSES OF SHOULDER PAIN

Diagnosis	Age	Type of onset	Location of pain	Night pain	Active range of motion	Passive range of motion	Impinge-ment signs	Radiation of pain	Paras-thesia	Weakness	Instability	Radio-graphic changes	Special features
Rotator cuff tendinitis	Any	Acute or chronic	Deltoid region	+	↓↓ guarding	Normal	+++	–	–	Only due to pain	Look for	In chronic cases	Painful arc of abduction
Rotator cuff tears (chronic)	Over 40 years	Often chronic	Deltoid region	++	↓↓↓	Normal (may ↓ later)	++	–	–	++	–	+	Wasting of cuff muscles
Bicipital tendinitis	Any	Overuse	Anterior	–	↓ guarding	Normal	+	Occasionally into biceps	–	Only due to pain	Look for	None	Special exam-ination tests
Calcific tendinitis	30–60 years	Acute	Point of shoulder	++	↓↓↓ guarding	Normal except for pain	+++	–	–	Only due to pain	–	++	Tenderness ++
Capsulitis 'frozen shoulder'	Over 40 years	Insidious	Deep in shoulder	++	↓↓	↓↓	+	–	–	–	–	–	Global range of motion ↓
Acromioclavicular joint	Any	Acute or chronic	Over joint	Lying on side	↓ full elevation	Normal	–	–	–	–	–	In chronic cases	Local tenderness
Osteoarthrosis of glenohumeral joint	Over 40 years	Insidious	Deep in shoulder	++	↓↓	↓↓	–	–	–	May have mild	–	+++	Crepitus
Glenohumeral instability	Usually <25 years	Episodic	Anterior or posterior	–	Only appre-hension	Only appre-hension	Possible	–	+ with acute episodes	+ with acute episodes	+++	Often	Stress tests
Cervical spondylosis	Over 40 years	Insidious	Supra-scapular	Often	Normal	Normal	–	++	+++	+	–	In cervical spine	Pain with neck movement
Thoracic outlet syndrome	Any	Usually with activity	Neck shoulder arm	–	Normal	Normal	–	++	++	++	–	–	Special exam-ination tests

Low back pain and other peri-articular complaints-Treatment

- RICE
  -Rest
  -Ice
  -Compression
  -Elevation
- NSAIDs and analgesics
- Time
- Other



General Musculoskeletal Exam

- Underutilized by primary care providers
- Should be simple and quick
- Goal is to recognize signs of rheumatological diseases and determine if it is appropriate to refer to a rheumatologist or manage independently

High Impact Rheumatology

Rheumatology at a Glance

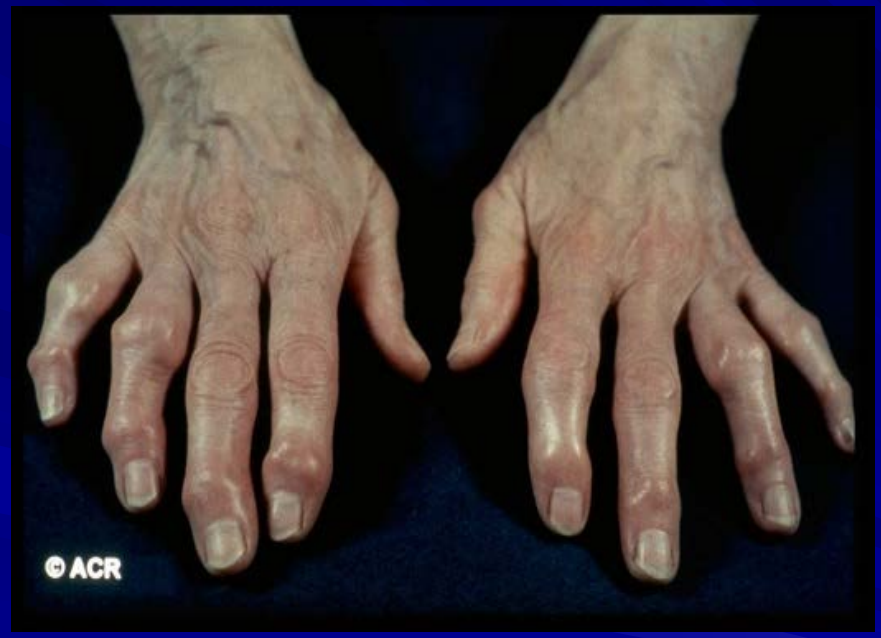
Know It When You See It

*

Know It When You See It

Osteoarthritis: Typical hand

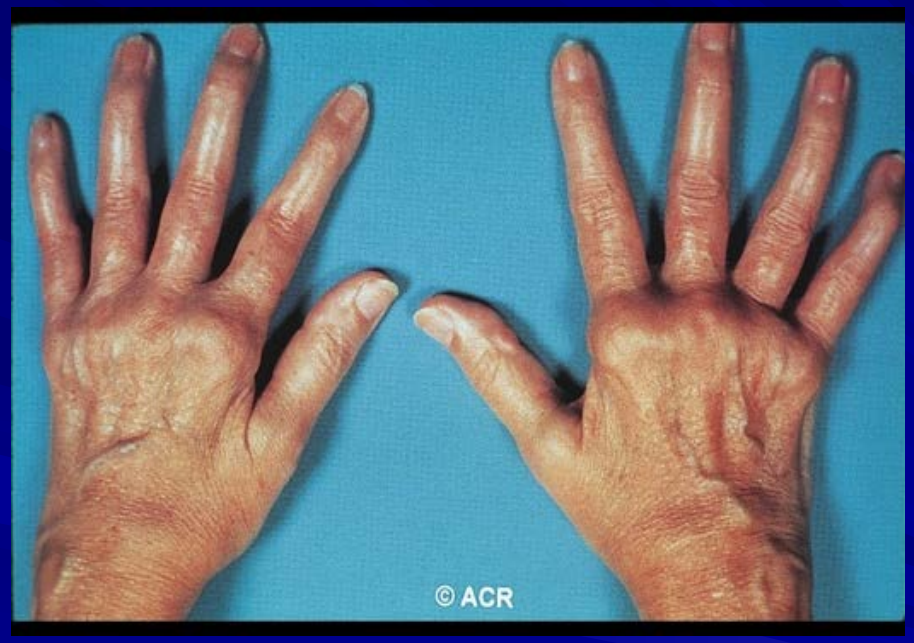
- Hard boney enlargements
- Heberden's nodes at the DIP joints
- Bouchard's nodes at the PIP joints
- Often have "squared" first CMC joint due to osteophytes at that joint



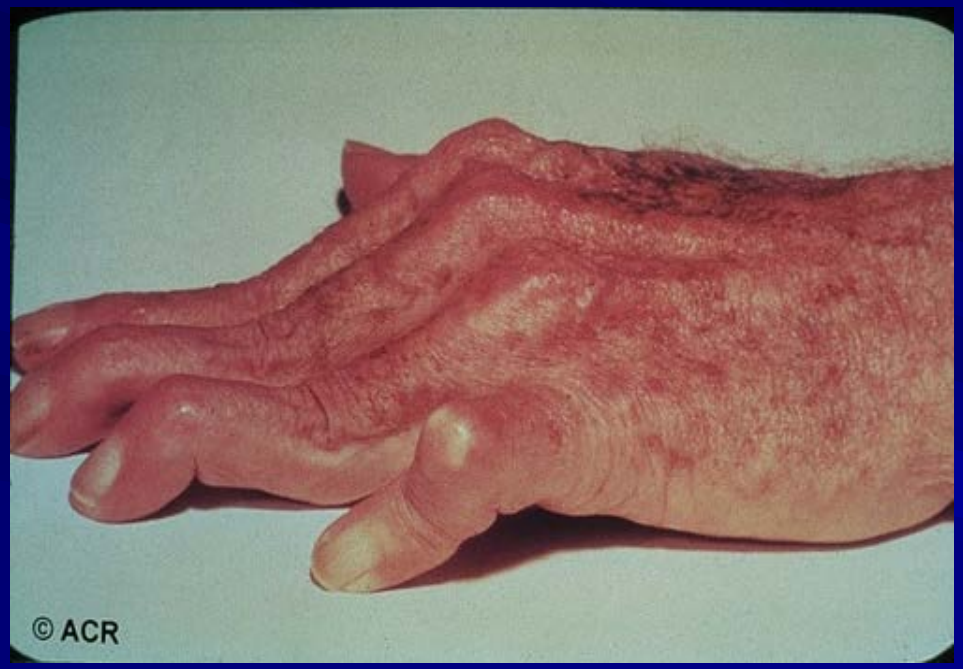
Know It When You See It

Rheumatoid arthritis

- Soft synovial swelling
- Synovitis and volar subluxation at the MCP joints
- Synovitis of the wrists
- Synovitis of the PIP joints with early swan neck deformities



Rheumatoid Arthritis: Swan Neck and Boutonnière Deformities

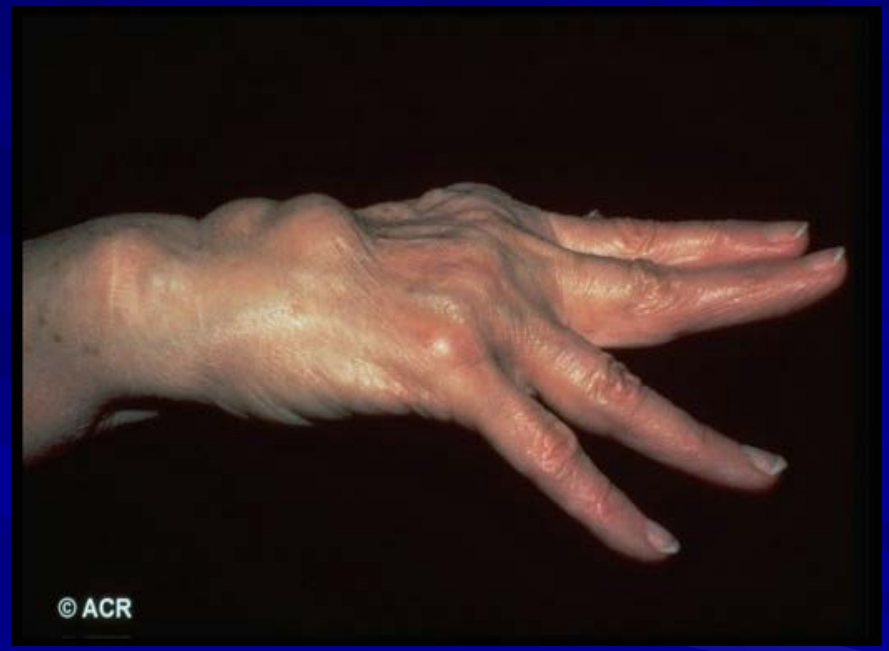


- Late-stage findings indicating serious changes in the joints
- Swan neck (digits 2 to 4) PIP extension DIP flexion
- Boutonnière (digit 5) is the reverse; PIP flexion DIP extension

Know It When You See It

Tendon rupture in RA

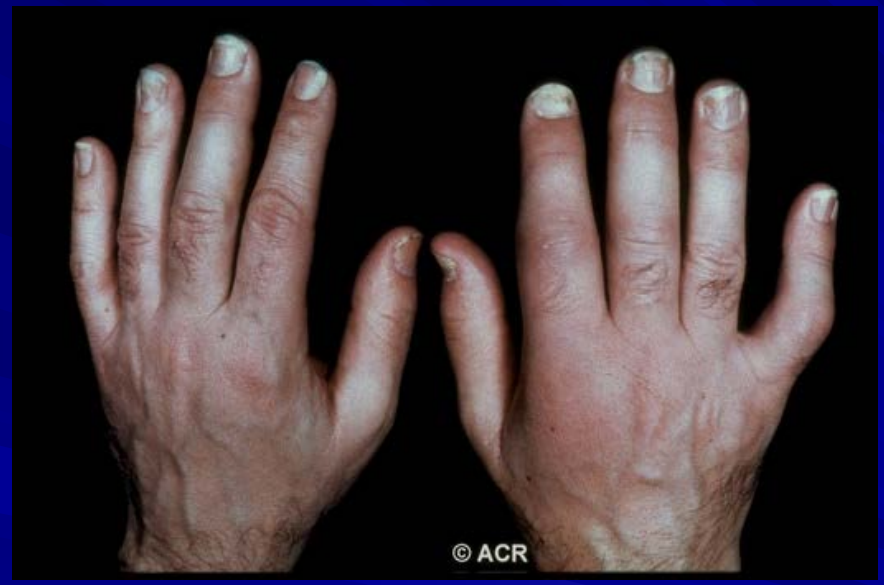
- Inability to extend fourth and fifth digits
- Due to deformity and inflammation at the wrist causing excess wear of the extensor tendons



Know It When You See It

Psoriatic arthritis

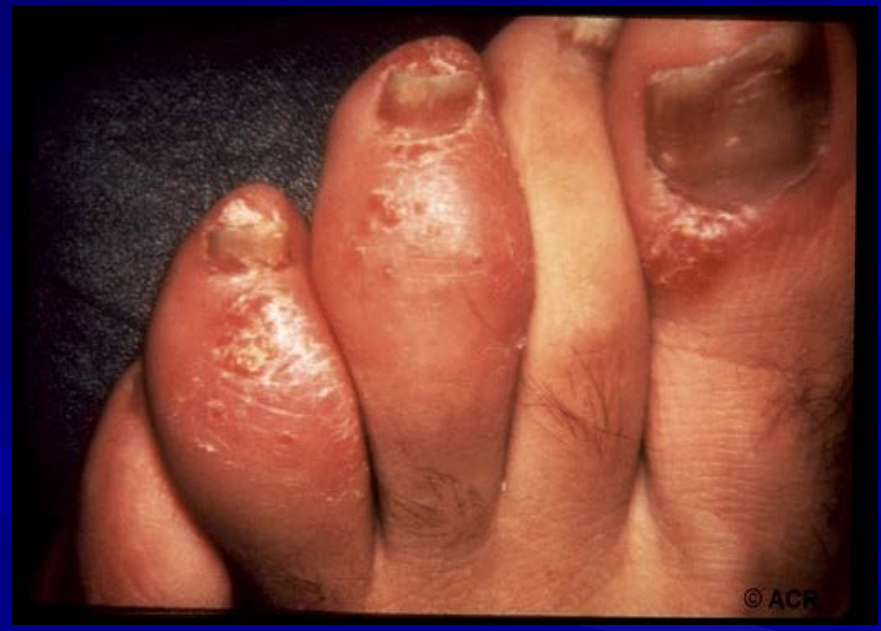
- Inflammation of the DIP joints
- Sausage fingers
- Joint involvement shows radial pattern
- Nail changes
- Psoriatic patches
- Arthritis may start before the skin



Know It When You See It

Psoriatic arthritis

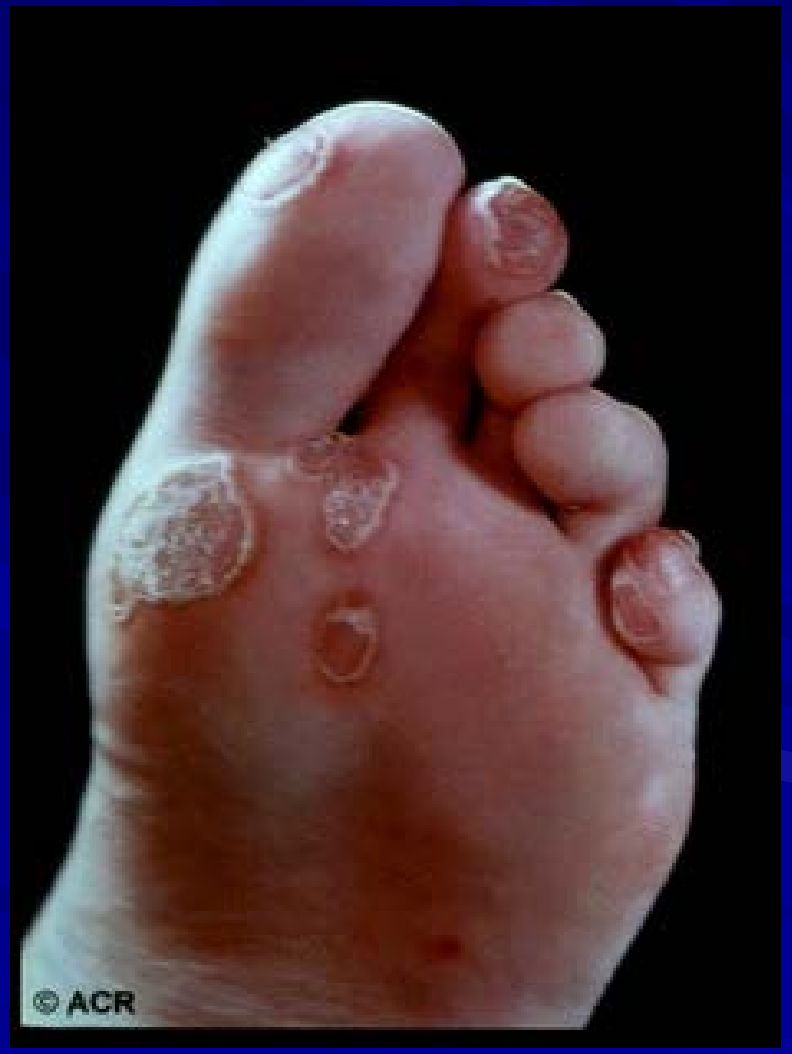
- Sausage toes
- IP joint involvement of a toe suggests a rheumatoid variant
- Psoriatic arthritis and Reiter’s disease are the most common causes



Know It When You See It

Reiter’s syndrome

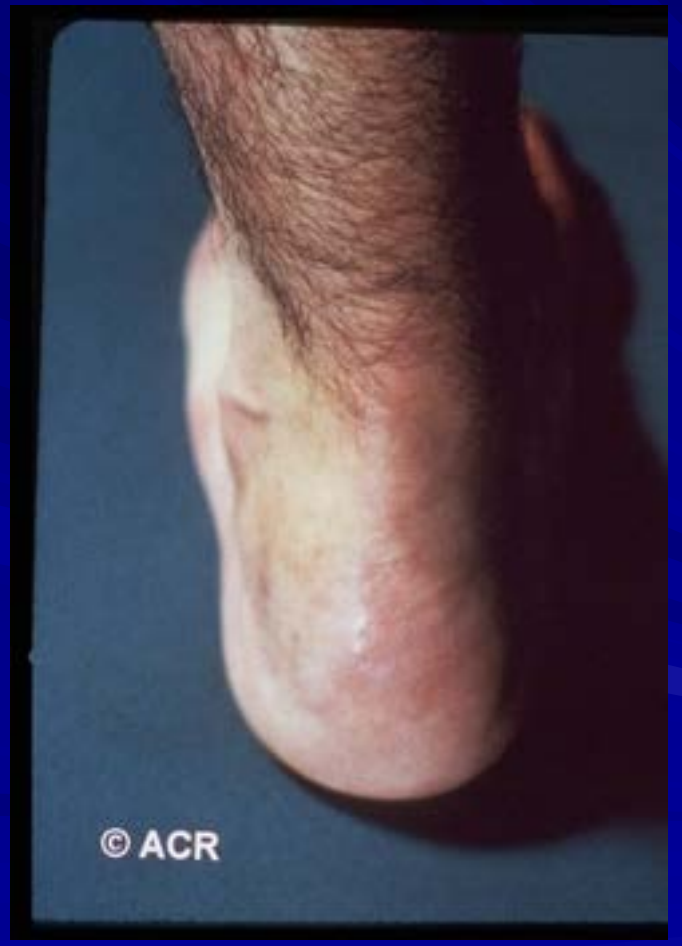
- Keratoderma blennorrhagica
- May look like psoriasis or syphilis
- Can occur in patches or as sterile pustules



Reiter's Syndrome (Reactive Arthritis)

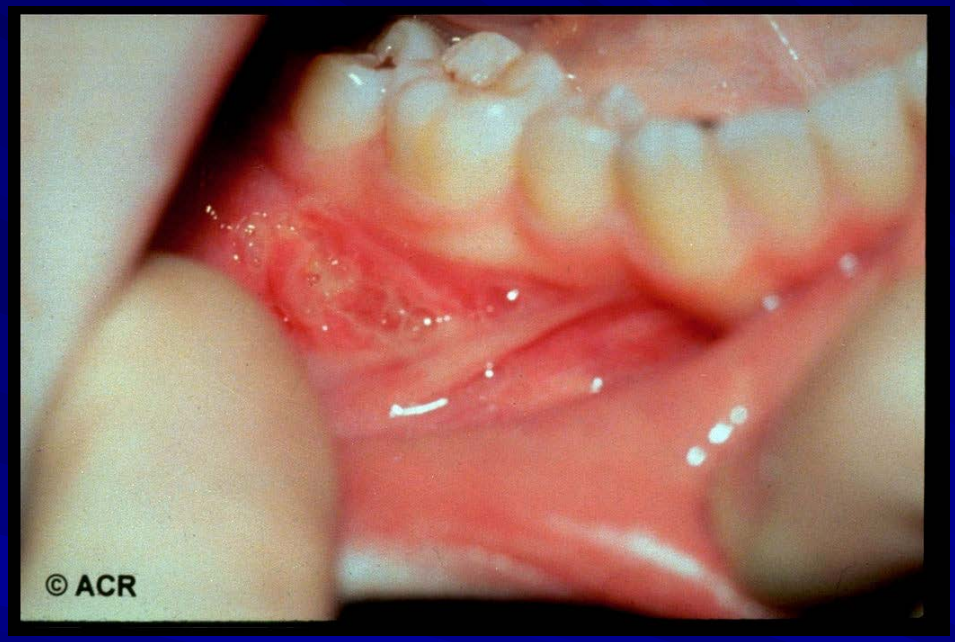
Seronegative asymmetric arthritis

- Following:
  - Urethritis or cervicitis
  - Infectious diarrhea
- Often associated with:
  - Inflammatory eye disease
  - Balanitis, oral ulceration, or keratoderma
  - Enthesopathy
  - Sacroiliitis



Inflammatory Bowel Disease

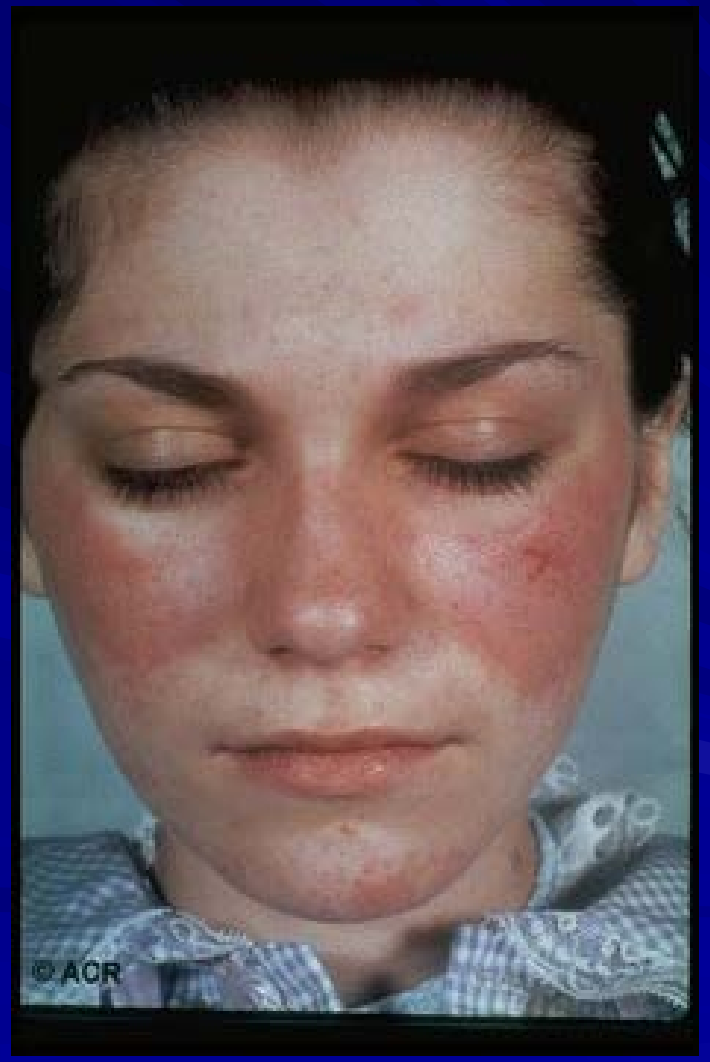
- Ulcerative colitis
- Regional enteritis (Crohn's disease)
- ? Whipple's
- ? Behçet's



Know It When You See It

Systemic lupus erythematosus

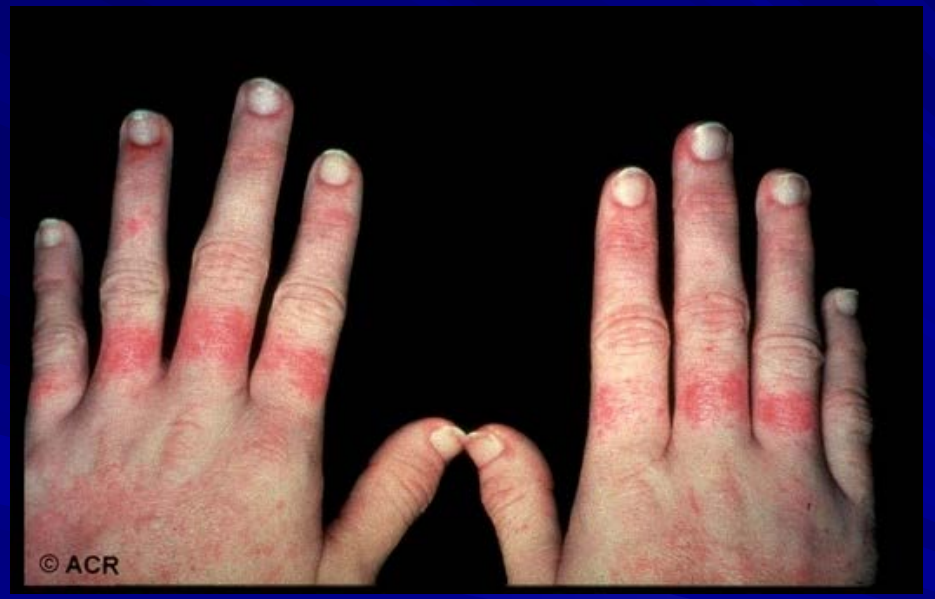
- Butterfly rash
- Involves cheeks and nose
- Patient also has rash on chin and some telangiectasia



Know It When You See It

Systemic lupus erythematosus

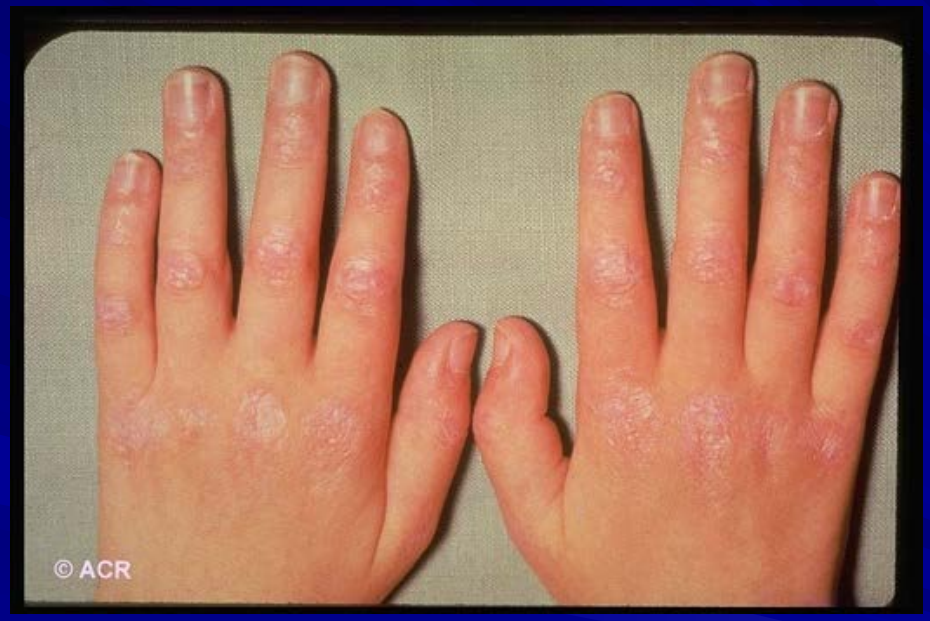
- Interarticular dermatitis
- Also has periungual erythema
- This rash is distinct from that seen in dermatomyositis that occurs over the joints



Know It When You See It

Dermatomyositis

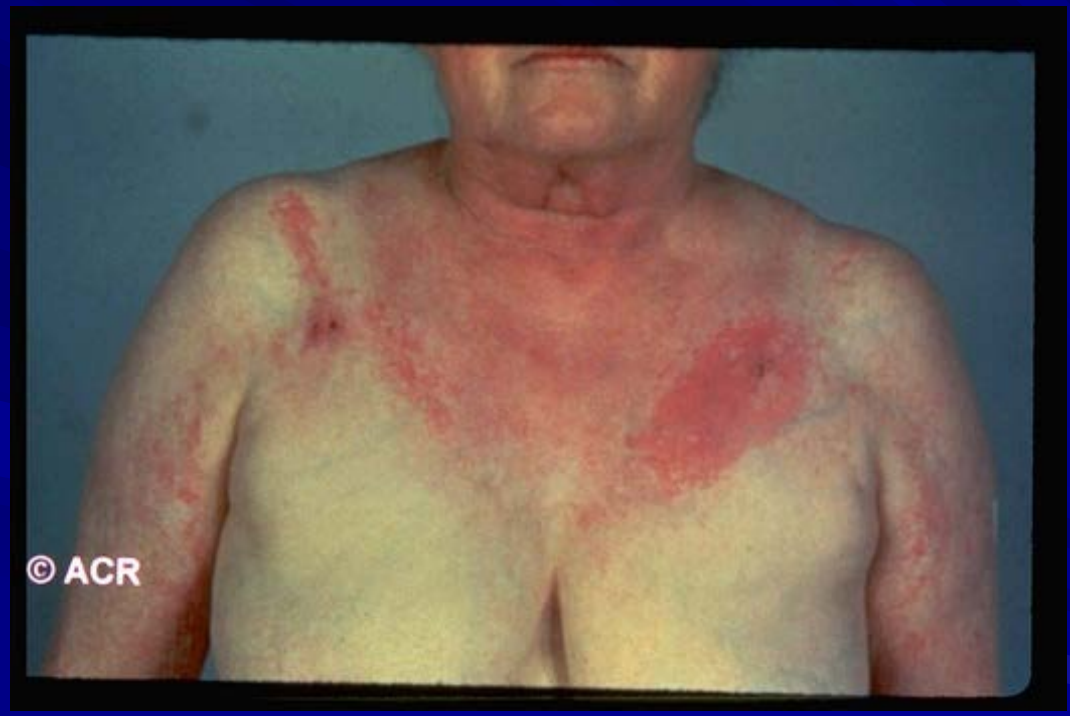
- Scaly rash over the extensor surfaces of the interphalangeal joints



Know It When You See It

Dermatomyositis

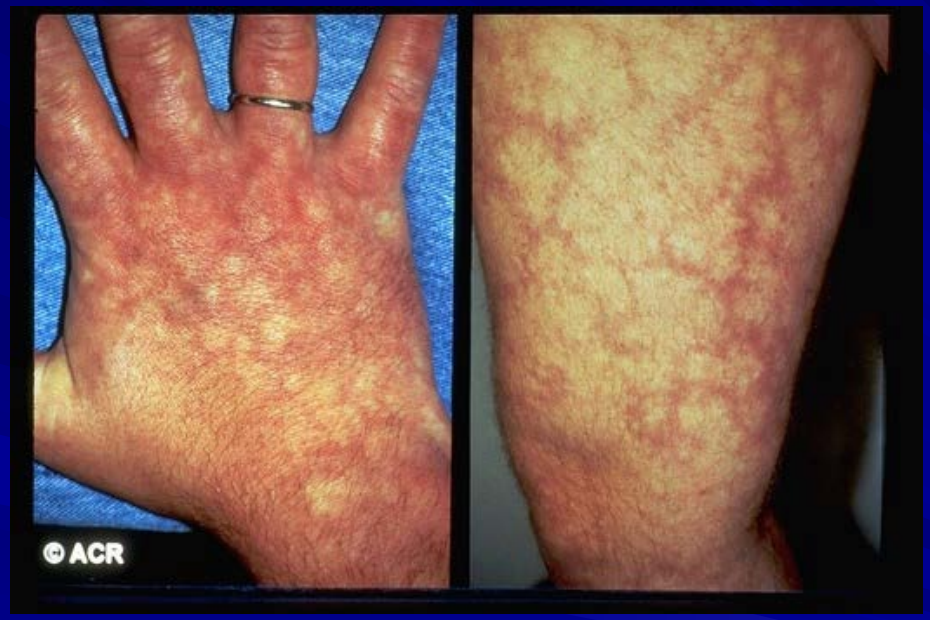
- Mantle or shawl distribution of rash



Know It When You See It

Livedo reticularis

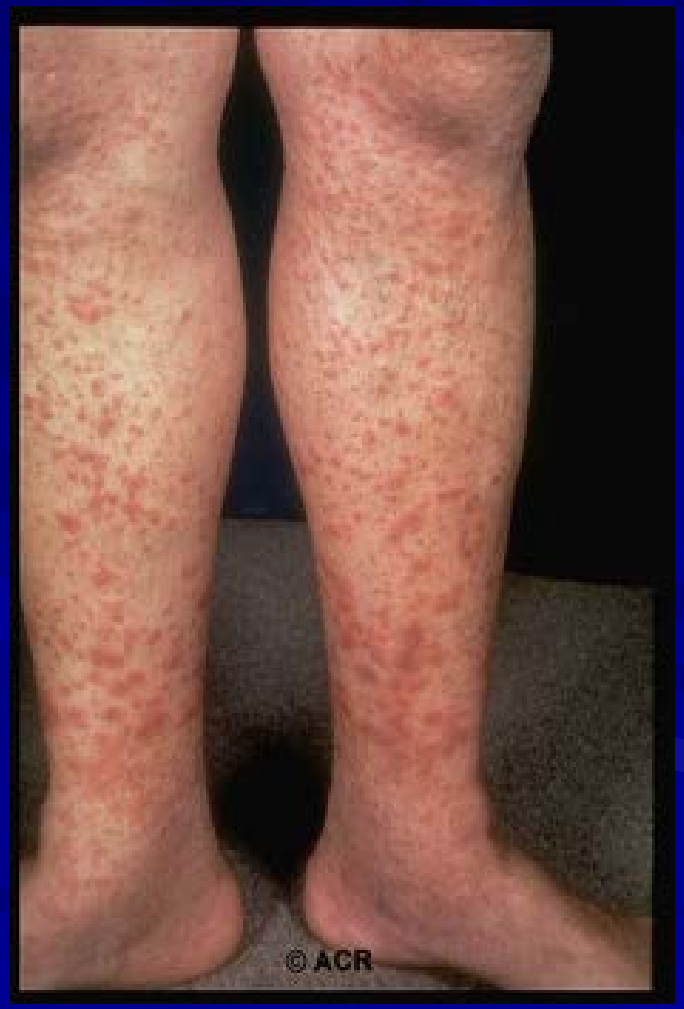
- Appears in a broad-based interrupted pattern in systemic vasculitis, including SLE
- May occur as a fine, connected, lacy pattern in normals



Know It When You See It

Palpable purpura

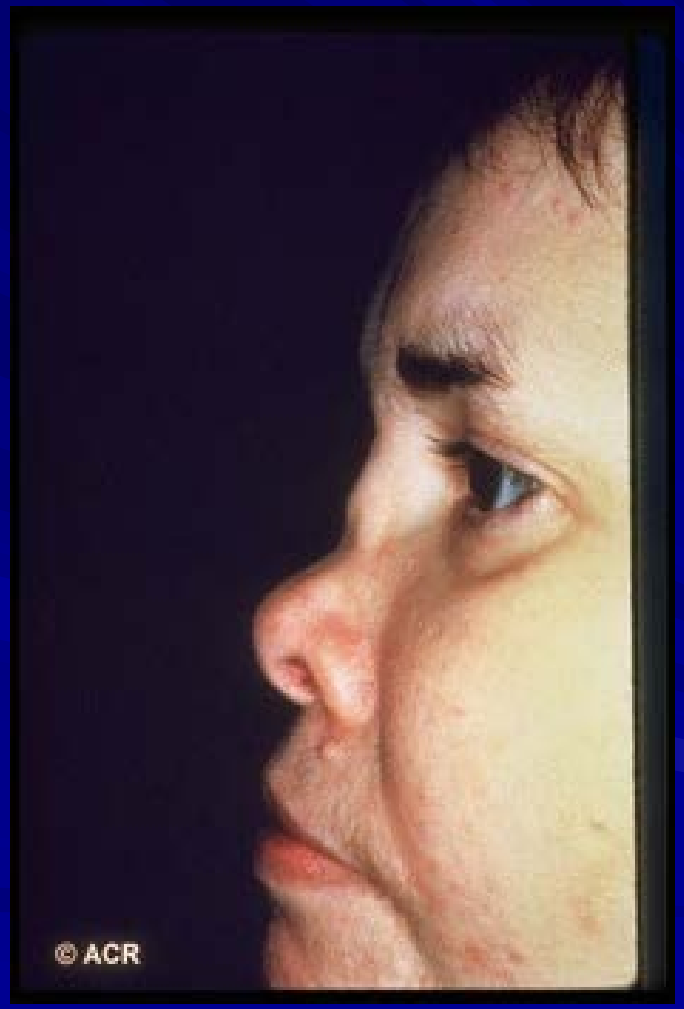
- Characteristic of dermal vasculitis in Henoch-Schönlein purpura



Know It When You See It

Saddle nose deformity

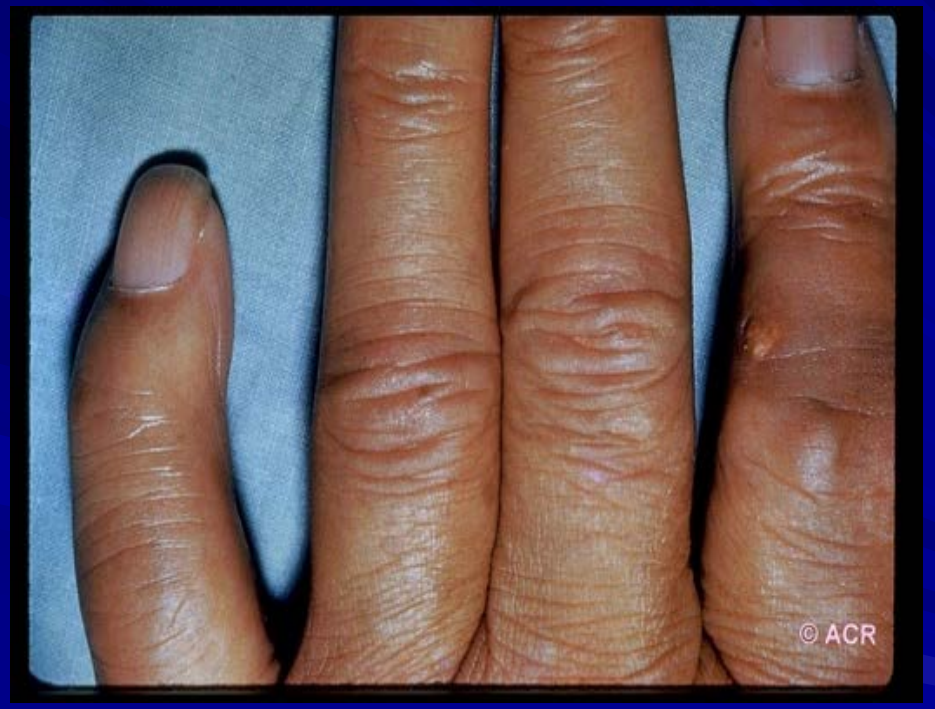
- Relapsing polychondritis
- May also occur in Wegener's granulomatosis and syphilis



Know It When You See It

Gouty tophus on finger

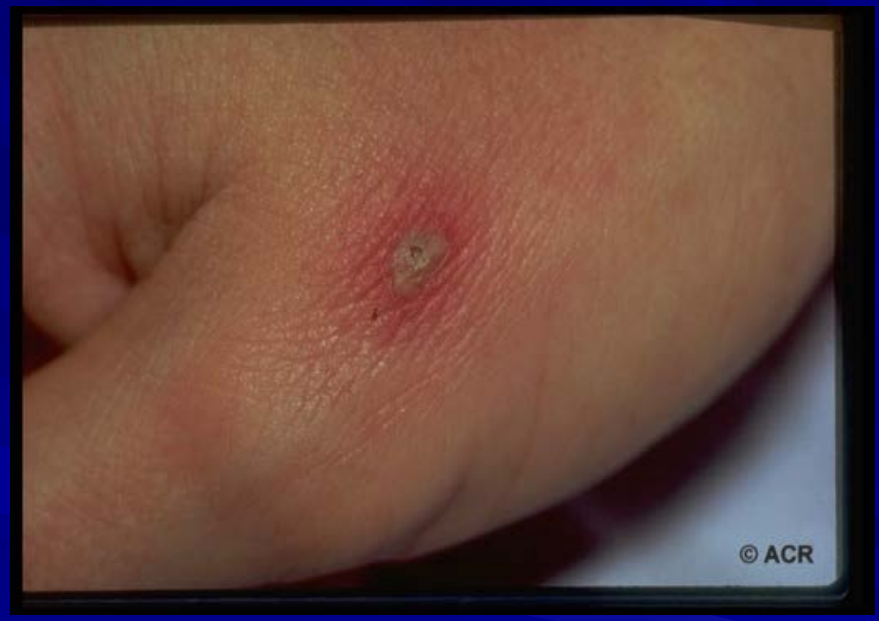
- Note the yellow-orange color typical of a tophus
- Patient also has swelling of the PIP of the index and fifth digits



Know It When You See It

Skin pustule with disseminated gonorrhea

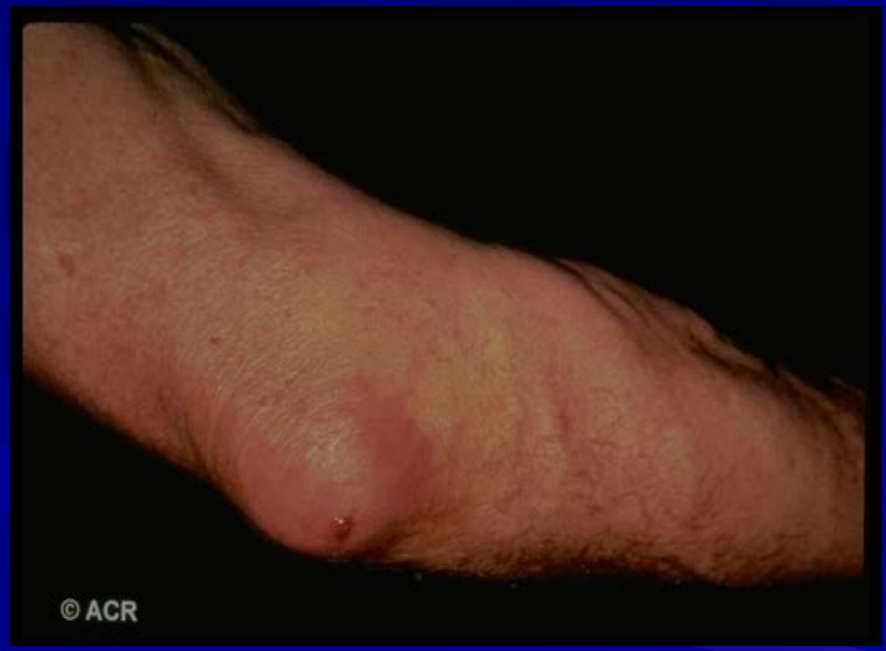
- Usually a few lesions
- Usually found on the extremities



Know It When You See It

Septic olecranon bursitis

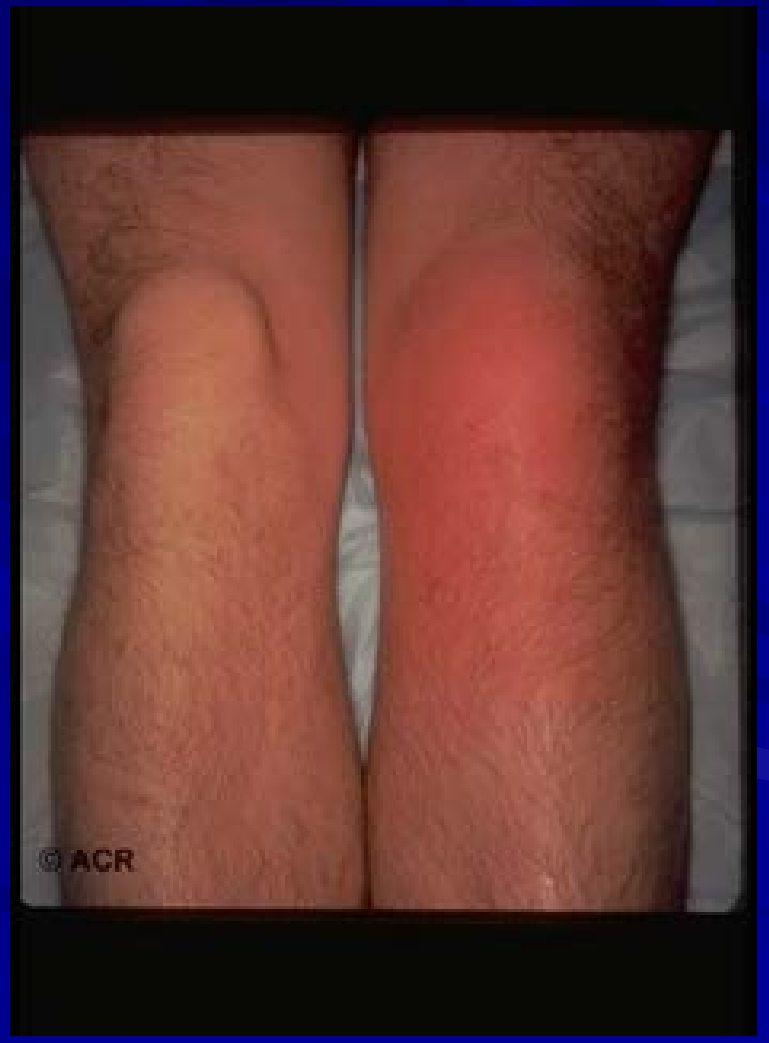
- Swelling of the bursa
- Erythema and tenderness
- If it looks ugly, tap it



Know It When You See It

Septic prepatellar bursitis with cellulitis

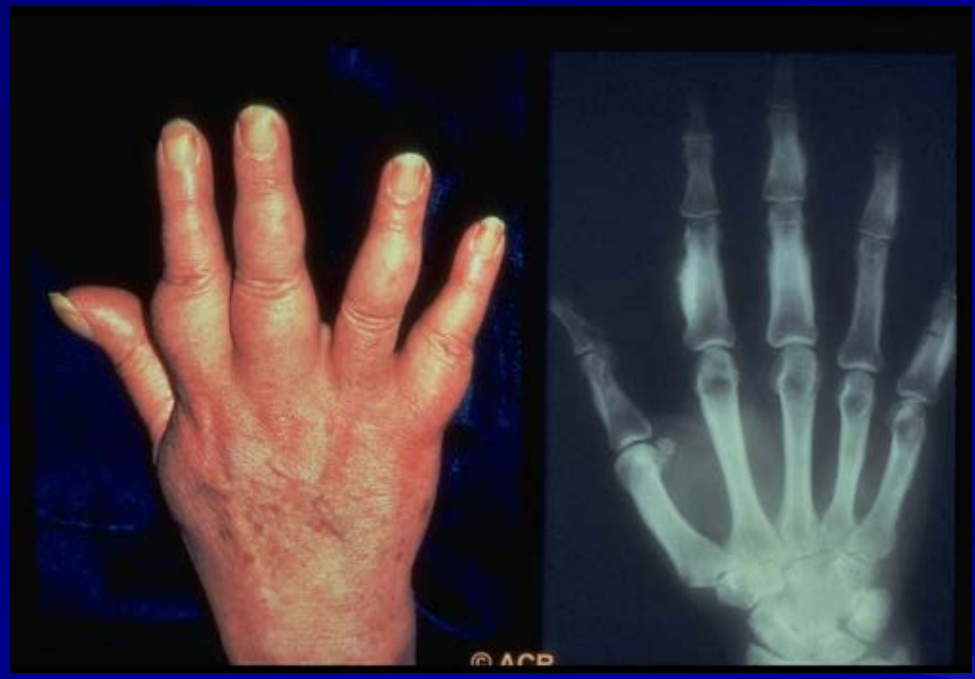
- Rubor, calor, dolor over the patella and adjacent tissue
- Lack of joint involvement evident from nontender suprapatellar pouch and popliteal area
- Don’t tap a normal knee through cellulitis



Know It When You See It

Hyperthyroidism

- Acropachy
- Right: Soft tissue swelling between joints
- Left: Periosteal new bone formation



High Impact Rheumatology

When It Really Hurts

When It Really Hurts:  Don’t Blow It

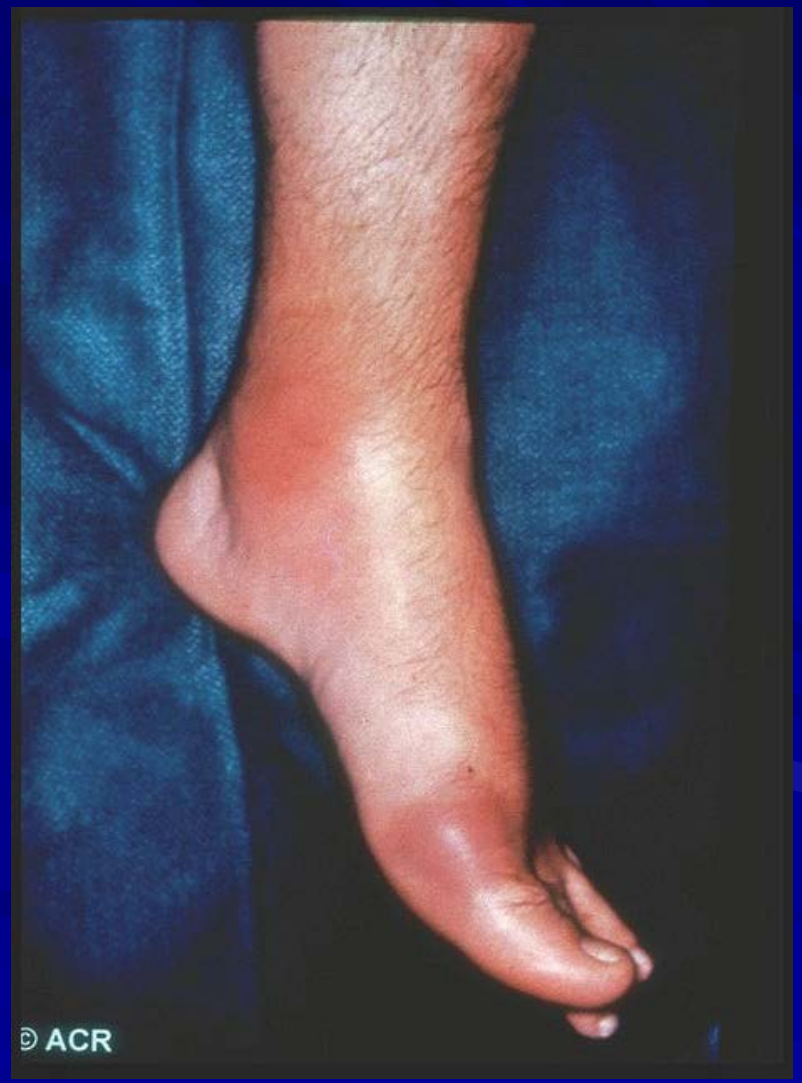
- Focused history and physical exam
- X-ray first
- Aspirate the Joint—The Eye of the Needle is the key to the diagnosis
- A few lab tests

When It Really Hurts: Case 1

- A 39-year-old man presents with severe pain in the forefoot and ankle that awakened him from sleep that morning. He twisted his ankle the day before at work while welding at the Johnson Battery factory. He has had hypertension treated with hydrochlorothiazide for 5 years. Over the past week, he has consumed 1 quart of whiskey per day in a “falling down bender.”
- BP 160/105, temperature 100.5°F

When It Really Hurts: Case 1

- General physical exam is normal
- Intense erythema over the ankle and first MTP
- Severe pain with active and passive motion
- Marked tenderness to palpation of ankle and MTP joint lines
- No inguinal or femoral lymphadenopathy



Question 1: What Is Differential Dx?

A. Reiter’s syndrome
B. Rheumatoid arthritis
C. Infection
D. Trauma
E. Crystalline arthritis

Question 1: Correct Answers

C. Infection, D. Trauma, and E. Crystalline are all possible based on the history and exam

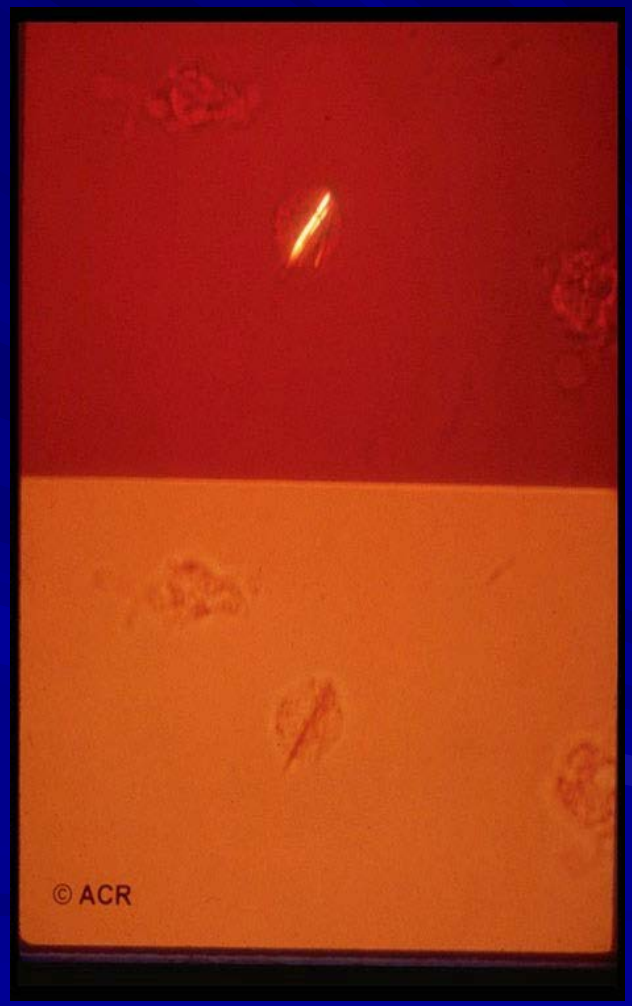
Incorrect Answers:

A. Reiter's syndrome includes acute arthritis and conjuctivitis, urethritis, or diarrhea

B. RA also may be acute but is usually more insidious in onset and tends to involve multiple small joints in a bilaterally symmetrical pattern

Initial Test Results

- Creatinine 1.8 mg/dL
- Synovial fluid analysis
  - WBC 50,000, 90% PMNs
  - Gram stain: No organisms
  - Culture sent
  - Compensated polarizing microscopy
    - Many crystals



Question 2: What Will You Prescribe?

- Probenecid
- Aspirin, 1 g/d
- Colchicine
- Indomethacin
- Prednisone
- Allopurinol

Question 2: Answer

Don’t Blow It: The diagnosis of acute gout is correct, but hypouricemic therapy with probenecid or allopurinol should not be started during an acute attack

- ASA (1 g/d) would further elevate the uric acid level

Treatment of Acute Gout

- The earlier the better
- NSAIDs are effective but may be hazardous in this patient with mildly elevated creatinine
- Oral, IV, IM, or IA corticosteroids are effective with minimal toxicity in short course
- Colchicine: Used less often now because of side effects (intravenous injection probably should not be used)

Follow-Up Management of Gout

- Patient is seen 4 weeks after the acute attack. Pain and all signs of inflammation are gone. No tophi are seen and there is no history of renal stones. Possible lead exposure in battery factory. Creatinine is normal. Uric acid is 8.9 mg%
- Key point now:  Don’t Overtreat
  - Change to different antihypertensive
  - Stop alcohol binging
  - Monitor for and treat recurrences promptly with abortive therapy: Low dose po colchicine or an NSAID

Six Months Later

- The patient returns and reports four additional acute gouty attacks that responded to indomethacin, but he lost 2 days of work with each attack. He is now in AA and not drinking at all. BP is 130/80 with lisinopril. BUN and creatinine are normal. Uric acid is 9 mg% and urine uric acid is 650 mg/24 h

- Key question now:
  - Is the patient overproducing or under-excreting uric acid?

Determinants of Uric Acid Level

- 10% overproduction of uric acid: Urine uric acid >700 to 1000 mg/24 h
  - HGPRTase deficiency/PRPP synthase overactivity
  - Lymphoproliferative and myeloproliferative disorders, solid tumors
  - Drugs: Cytotoxic agents, pancreatic extracts, vitamin B_{12}
  - Alcohol consumption (especially beer)
  - Obesity, psoriasis, and tissue necrosis

Determinants of Uric Acid Level (cont'd)

- 90% under-excretion of uric acid: Urine uric acid <700 mg/24 h
  - Renal defect: Reduced GFR, tubular defect
  - Drugs: Cyclosporine, diuretics, nicotinic acid, salicylates (low dose), pyrazinamide, and ethambutol
  - Ethanol
  - Dehydration, acidosis, starvation
  - Lead nephropathy

Treatment for Overproducers

- For overproducers
  - Allopurinol: 100 to 300 mg/d; use the lowest dose to keep uric acid level <6.5 mg/dL. Use 100 mg/d in patients with renal insufficiency
    - Adverse effects
      - Mild to potentially serious dermatitis
      - Toxic hepatitis, nausea, diarrhea
      - Cytopenias

Treatment for Under-Excretors

- For under-excretors
  - Probenecid: 0.5 to 2.0 g/d
    - Adverse effects
      - Rash
      - Cytopenias
      - Reduces excretion of other drugs, eg, penicillin
  - Sulfinpyrazone: Rarely used

Summary of Allopurinol Therapy

- When to use it
  - Recurrent episodes of acute gout:
    >3 Attacks per year
  - Tophaceous gout
  - Nephrolithiasis
- When NOT to use it
  - During an acute attack
  - For asymptomatic hyperuricemia
  - In full dose in combination with azathioprine
  - In full dose in patient with renal failure

Use low dose colchicine or an NSAID for prophylaxis when starting hypouricemic therapy

When It Really Hurts: Case 2

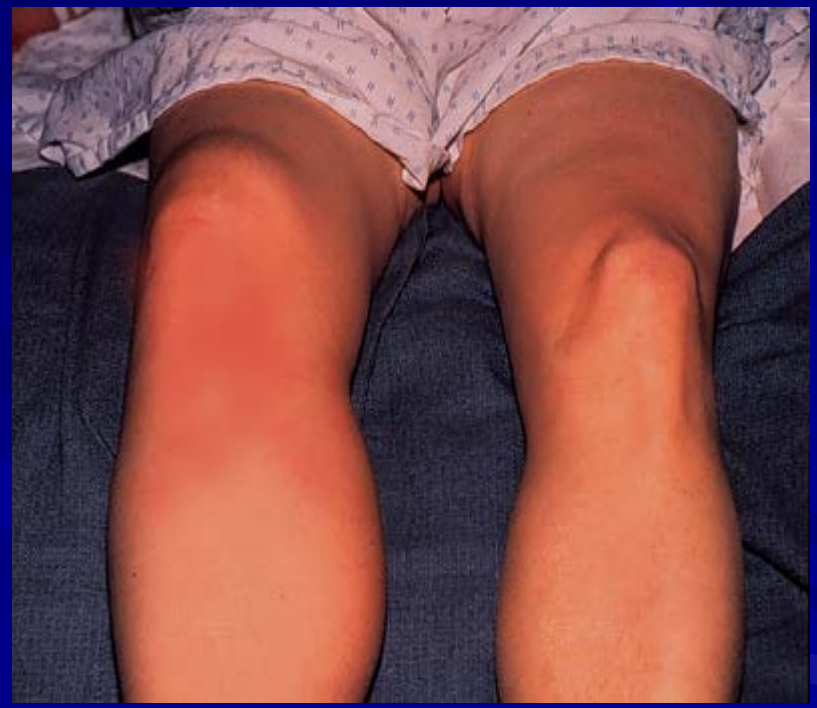
- A 35-year-old man with diabetes who has been on hemodialysis for 6 years developed severe pain and swelling in the right knee several hours after playing volleyball. He also noted that during the dialysis run that morning he had had a chill but felt well
- Past history includes three attacks of gout in the left great toe and the right knee 2 years before starting dialysis

When It Really Hurts: Case 2

- He has difficulty getting onto the examination table because of knee pain. Temperature 101°F, pulse 100 bpm, BP 150/90. He is diaphoretic over the face and arms. The skin over the AV fistula is slightly erythematous, but the bruit is strong. There are two small abrasions over the left elbow. Examination of HEENT, chest, and abdomen are normal

Physical Findings

- The right knee is swollen, slightly reddened, warm, and tender to palpation over the medial and lateral joint margins. Both active and passive flexion and extension are limited by pain. There is no laxity, but the exam is limited by pain



Step 1: Characterize This Illness

- Acute inflammatory monoarticular arthritis and fever within 24 hours of dialysis, vigorous physical activity, and perhaps trauma in a patient with a history of gout
- Signs of systemic illness: Fever, diaphoresis
- Initial laboratory tests: WBC 22,000 with 95% PMNs, Hgb 10 g%

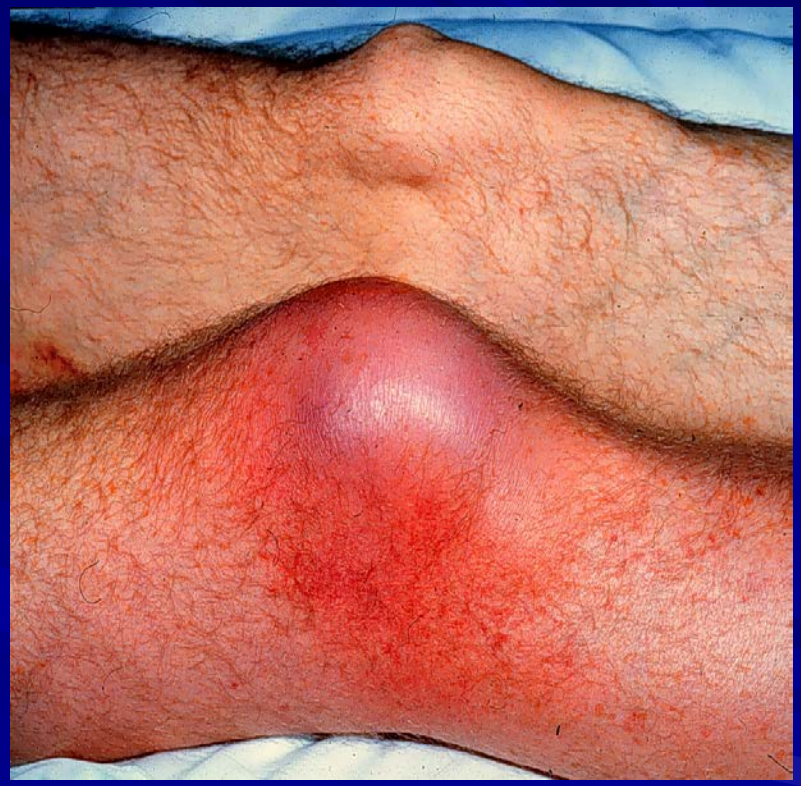
Question 1: What Is Differential Dx?

A. Knee trauma with hemarthrosis
B. Crystalline arthritis
C. Beta 2 microglobulin amyloidosis
D. Prepatellar bursitis
E. Septic arthritis

Incorrect Answers

C. Beta 2 microglobulin amyloidosis occurs in dialysis patients producing periarthritis, tenosynovitis, bone cysts, and pathologic fractures

D. Prepatellar bursitis produces pain, swelling, and erythema but does not limit extension of the knee



Differential Dx

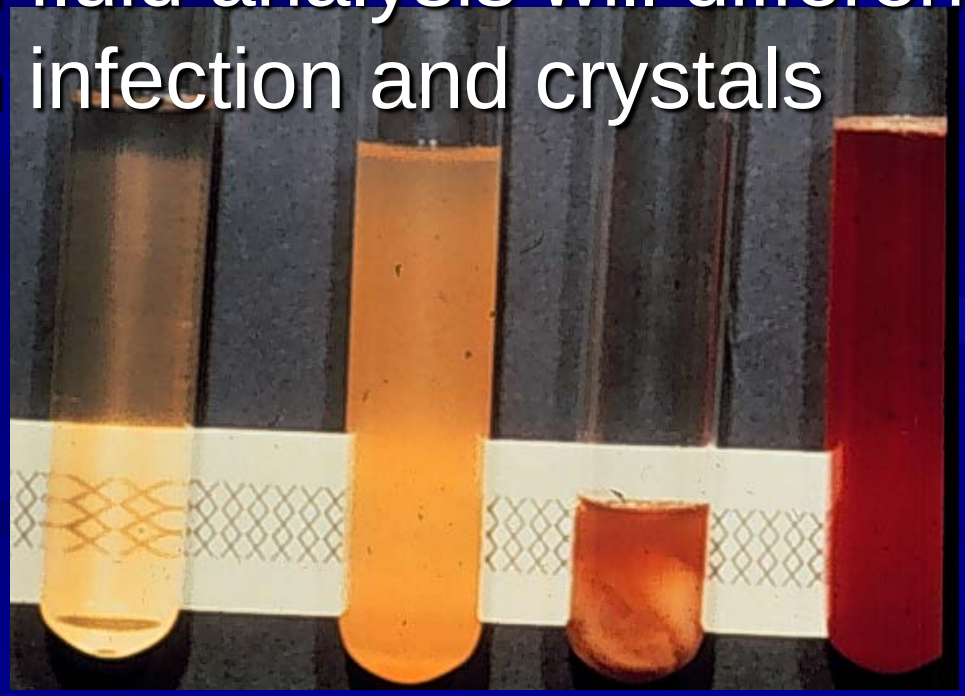
- The differential diagnosis includes A, B, and E
  - A. Hemarthrosis with mild trauma could occur in renal failure because of tissue fragility and platelet dysfunction
  - B. Patients with crystalline arthritis in renal failure may show uric acid, oxalate, apatite (BCP), or CPPD crystals
  - E. Bone and joint infections are common in dialysis patients because of vascular access and impaired immune defenses

Question 2: What Diagnostic Tests?

A. Bone scan
B. X-ray of knee
C. Arthroscopy
D. MRI of knee
E. Arthrocentesis and synovial fluid analysis

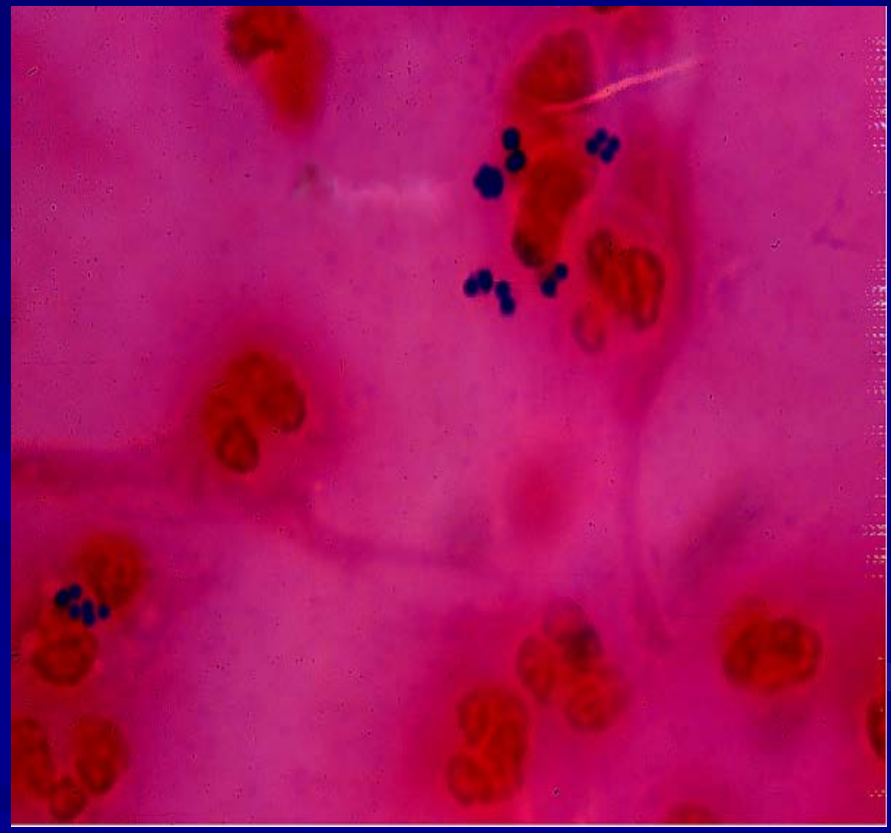
Question 2: Answer

- Key point: TAP THE JOINT! Diagnosis must be made immediately. X-ray of the knee should be done if the tap is bloody. Synovial fluid analysis will differentiate between infection and crystals



Synovial Fluid Findings

- Synovial fluid WBC 60,000 with 98% PMNs
- No crystals seen on polarizing microscopy
- SF culture and sensitivity test request sent to the microbiology lab
- Blood cultures sent
- SF gram stain



Organisms Causing Septic Arthritis

	Adults (%)	Children (%)
Gram-positive cocci		
S. aureus	35	50
S. pyogenes, S. pneumoniae	10	20
Gram-negative cocci		
N. gonorrhoeae, *meningitidis*	50	8*
H. influenzae	<1	<5
Gram-negative bacilli		
E. coli, Salmonella	5	20
and *Pseudomonas species*		
Mycobacteria and Fungi	<1	<1†

*Requires special media
†Requires synovial tissue

Question 3: What Treatment?

A. Penicillin
B. Tetracycline
C. Nafcillin
D. Vancomycin
E. Aminoglycoside

Question 3: Answer

- The most common cause of gram-positive septic arthritis in adults is *Staphylococcus aureus*
- Most *S. aureus* isolates are penicillin resistant
- An increasing number are methicillin resistant
- Initial treatment should be with one dose of vancomycin until sensitivity test results are available
- SF should be aspirated daily, or
  - If needle drainage inadequate, arthroscopy

Key Points

- With acute arthritis and fever and an identified source of bacteremia, the most likely dx is septic arthritis

Don’t Blow It!

  - Tap the joint!
  - Search for crystals
  - Do SF gram stain immediately
  - Send SF for culture and sensitivity before starting antibiotics

Key Points (cont'd)

- Must treat immediately with antibiotics selected according to SF gram stain and clinical setting
- Adjust antibiotics when sensitivity tests available
- Needle or arthroscopic drainage

High Impact Rheumatology

Diffuse Arthralgias
and Myalgias

Case 1: History

- A 48-year-old woman presents with diffuse muscle pain, weakness, and significant fatigue. She reports
  - Symptoms for over 3 years that have become slightly worse in past 6 months
  - Generalized pain and fatigue that limit her ability to work
  - Increasing sleep difficulty due to the pain

Case 1: Objective Findings

- General physical examination is unremarkable
- Diffuse muscle tenderness is noted
- Some tenderness around the joints, but no synovitis
- No objective muscle weakness
- Normal neurologic examination
- CBC, ESR, and chemistry profile are normal

How Should You Approach This Patient With Diffuse Musculoskeletal Complaints?

- Ask yourself the following questions:
  - Is this a systemic inflammatory rheumatic syndrome?
  - Does this represent rheumatic symptoms of an endocrinopathy?
  - Is this a toxic/drug reaction?
  - Is this a generalized soft-tissue pain syndrome?

NOTE: Do not overlook regional rheumatic pain syndromes (physical examination is critical)

Characteristics of Inflammatory Disease

- History
  - Associated with significant morning stiffness (>45 min)
  - Pain often better with movement
  - Insidious onset of the pain
- Physical exam
  - Objective findings of inflammation
    - Swelling, erythema, warmth, detectable joint fluid
  - Muscle weakness
  - Focal neurologic abnormalities

Characteristics of Inflammatory Disease (cont'd)

- Laboratory studies
  - ESR and C-reactive protein are indicators of generalized inflammation
  - Autoantibodies can be helpful in selected cases
  - Organ specific tests can suggest internal organ involvement
    - Liver function tests
    - Renal function tests
    - Muscle-specific enzymes

Inflammatory Causes of Musculoskeletal Pain: Specific Diagnoses

- Rheumatoid arthritis
- Systemic lupus erythematosus
- Polymyositis
- Scleroderma/eosinophilic fasciitis
- Polymyalgia rheumatica
- Duration of symptoms is important for diagnosis
  - <6 months = may be early rheumatic disease
  - 1 year = diagnostic clinical signs and lab abnormalities usually present
  - >2 years = abnormalities almost always present

Musculoskeletal Pain in Older Patients

- Think polymyalgia rheumatica when
  - Age >60
  - Proximal muscle myalgias and stiffness without specific muscle weakness
  - High ESR
  - Anemia

Think About the Musculoskeletal Pain of Endocrine Diseases

- Must consider
  - Thyroid disease
  - Parathyroid disease
  - Adrenal disease
  - Diabetes mellitus
  - Acromegaly
- Diagnosis suggested by history and appropriate screening lab studies
  - TSH, calcium, phosphorous, glucose, sodium/potassium

Don’t Forget

- Patients with hypothyroidism can present with diffuse and nonspecific arthralgias and myalgias. CKs may be elevated

Think About Toxic Drug Reactions That Can Cause Musculoskeletal Pain

- Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitor
- Zidovudine (AZT)
- Ethanol
- Clofibrate
- Cyclosporin A
- Penicillamine

Don’t Forget

- Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors can cause severe myalgias with or without evidence of objective myositis

Hsu I, et al. *Ann Pharmacother*. 1995;29:743–759.

Think About Generalized Soft-Tissue Pain Syndromes

- Fibromyalgia syndrome
- Major depression associated with musculoskeletal pain
- Somatoform pain disorders

Soft-Tissue Pain Syndromes: Major Depression With Musculoskeletal Pain

- Significant depression is seen in
  - 49% of patients with chronic soft-tissue pain
  - 37% of patients with rheumatoid arthritis
  - 33% of patients with osteoarthritis
- Depression is associated with increased pain levels in arthritis
- Depression is more prevalent with loss of valued activities

Bradley LA. *Primer on Rheum Dis*. 11th edition. 1997:413–415.
Huyser BA, Parker JC. *Rheum Dis Clin North Am.* 1999;25:105–121.

Case 1: Follow-up

- The laboratory studies were all normal
- The patient's symptoms were present for 3 years
- Signs of focal, inflammatory, or organic disease were not found on physical exam
- PRIME-MD screening did not reveal evidence of significant depression or somatization
- Thus, the diagnosis of fibromyalgia was made
  - Remember: Systemic rheumatic syndromes have objective abnormalities

Case 2: History

- A 48-year-old woman presents with complaints of diffuse muscle pain, weakness, and fatigue.
  She reports
  - Gradual onset over past 6 months
  - Morning stiffness lasting 2 to 3 hours
  - Difficulty with getting up out of a chair and combing her hair
  - No problems with holding a brush or standing on her toes

Case 2: Objective Findings

- Minimal muscle tenderness
- No joint tenderness or swelling
- Significant proximal muscle weakness in both upper and lower extremities
- No focal neurologic abnormalities

Case 2: Question

- Based on these findings, which of the following diagnoses should be initially considered?

A. Fibromyalgia
B. Polymyalgia rheumatica
C. Inflammatory myositis
D. Noninflammatory myopathy

Case 2: Answer

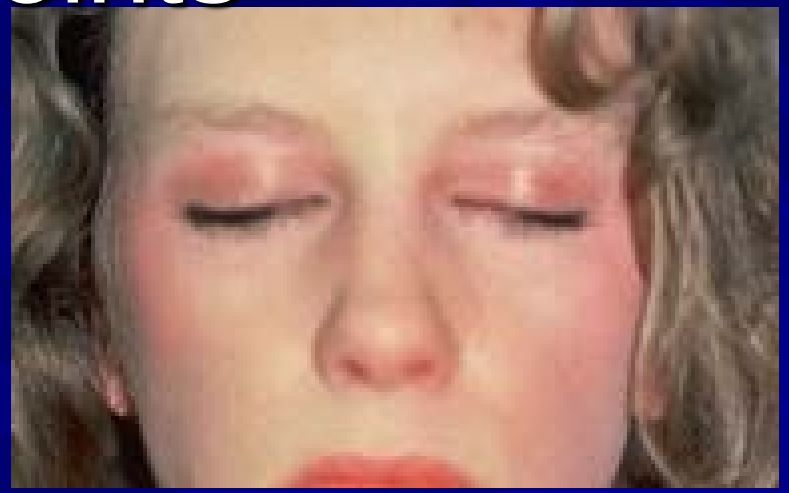
- *C and D. Inflammatory myositis or noninflammatory myopathy*
  - The recent onset of symptoms (6 months) makes consideration of an inflammatory process likely
  - Proximal muscle weakness suggests a myopathy
  - PMR is characterized by muscle pain and stiffness, not objective weakness

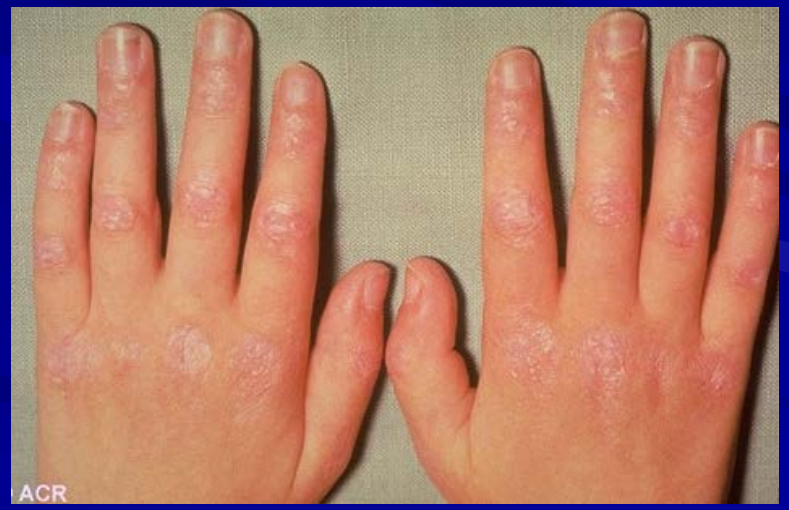
Common Causes of Proximal Muscle Weakness With Elevated CK

- Inflammatory myositis
- Noninflammatory myopathies
  - Hypothyroidism
  - Hypokalemia
  - Alcoholism
  - Drugs
    - AZT
    - HMG-CoA reductase inhibitors (the “statins”)

Polymyositis/Dermatomyositis: Key Points

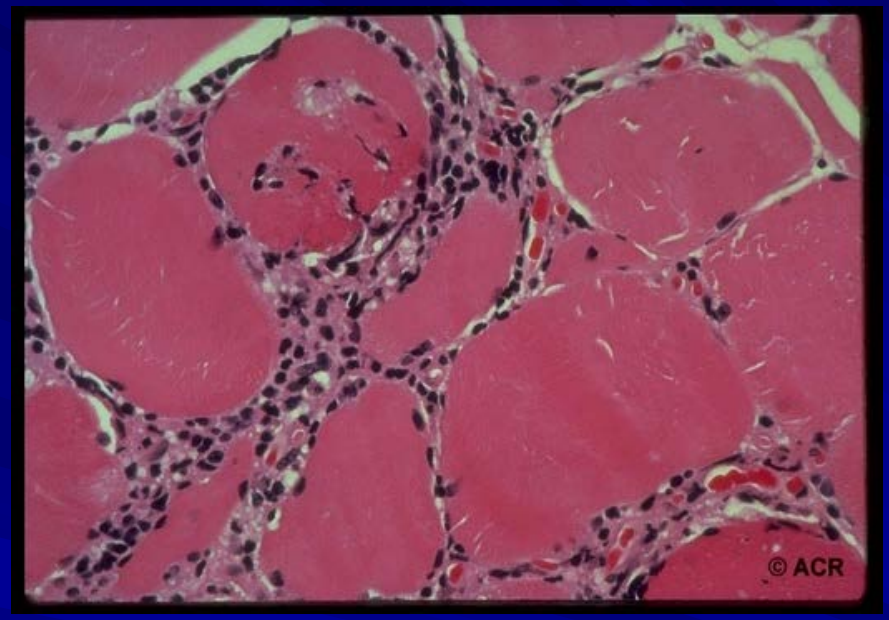
- Proximal muscle weakness
- May have characteristic skin involvement
  - Heliotrope eyelids
  - Gottron's sign





Polymyositis/Dermatomyositis

- Diagnosis confirmed by
  - CK levels
  - EMG findings
  - Muscle biopsy



Polymyositis/Dermatomyositis (cont'd)

- Therapy
  - Prednisone 1–2 mg/kg, as initial therapy
  - Methotrexate or azathioprine is often added
  - Intravenous immunoglobulin in rapidly progressive or refractory cases

Olsen NJ. *Primer on Rheum Dis*. 11th edition. 1997:276–282.

Don’t Forget

- Symptoms of muscle weakness require a careful muscle strength and neurological examination

Don’t Hesitate to Refer

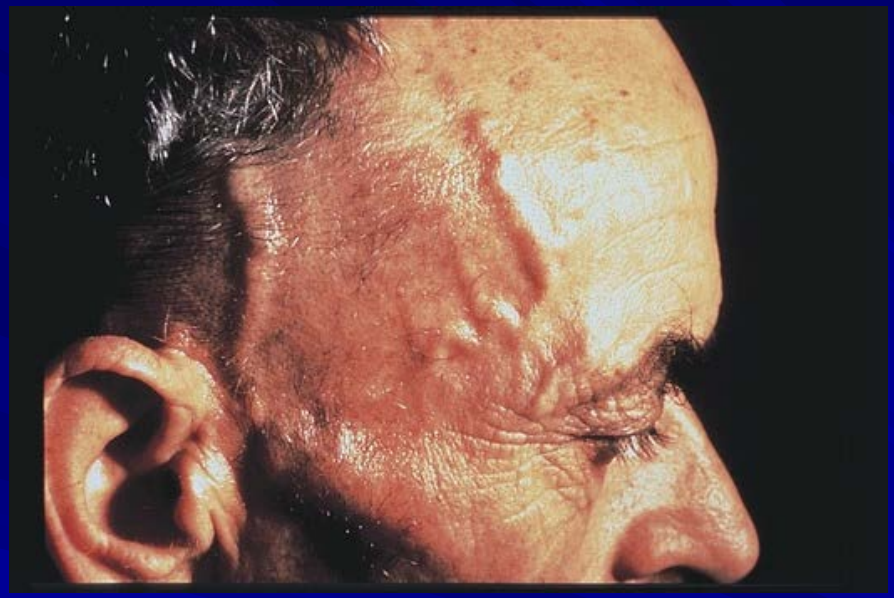
- The diagnosis of inflammatory muscle disease is difficult
- Prednisone therapy can cause a steroid myopathy with weakness
- Cytotoxic therapy is hazardous
- Failure to respond to therapy may suggest
  - Inclusion body myositis
  - Neoplasm-related myopathy

Case 3: History

- A 68-year-old man presents with complaints of diffuse muscle pain, weakness, and total body fatigue. He reports:
  - Gradual onset over past 6 months
  - Morning stiffness lasting 2 to 3 hours
  - Difficulty with getting out of a chair and combing his hair
  - Recent onset of right-sided headache
  - Recent onset of jaw pain when eating

Case 3: Objective Findings

- Proximal muscle tenderness without objective weakness
- Tender right temporal scalp region
- Normal visual acuity
- Hgb 9.8; ESR 85; CK 32



Case 3: Question

- Based on the clinical findings, what is the most important next step?
  - A. Treat now with prednisone 5 mg bid, and observe
  - B. Schedule a temporal artery biopsy for tomorrow morning and use the results to determine whether prednisone will be used
  - C. Start an NSAID at maximal dose
  - D. Treat now with prednisone at 40 to 60 mg per day and schedule temporal artery biopsy in the next few days

Case 3: Answer

- *D. Treat now with prednisone at 40 to 60 mg per day and schedule temporal artery biopsy for next week*
  - Patients with symptoms of PMR may have temporal arteritis
  - Sudden visual loss may occur in TA
  - The visual loss is usually not reversible

Nordberg E, et al. *Rheum Dis Clin North Am*. 1995;21:1013–1026.

Temporal Arteritis and Polymyalgia Rheumatica

- Patients with PMR should be evaluated for symptoms of TA
  - Headache
  - Scalp tenderness
  - Visual changes
  - Jaw claudication
- Treatment approaches
  - TA: prednisone 40 to 60 mg qd
  - PMR: prednisone 10 to 15 mg qd

Don’t Hesitate

- For probable temporal arteritis:

  TREAT NOW! BIOPSY LATER!

- Biopsy as soon as possible

Hunder GC. *Primer on Rheum Dis*. 11th edition. 1997:294–300.

Case 4: History

- A 48-year-old woman presents with complaints of diffuse muscle pain, weakness, and fatigue. She reports:
  - Gradual onset over past 12 months
  - Recent separation from her husband
  - Difficulty sleeping
  - A 10-lb weight loss
- The physical exam and screening laboratory tests are normal

Case 4: Question

- Based on this clinical information, which of the following diagnostic studies are now indicated?

A. Abdominal CT to look for tumors
B. ACTH stimulation test
C. CPK, ANA, rheumatoid factor
D. PRIME-MD Patient Questionnaire

Case 4: Answer

- *D. PRIME-MD Patient Questionnaire*
  - A simple outpatient tool for the screening of mental disorders in the primary care setting
  - Presence of core symptoms of depression on this questionnaire correlates with DSM-IV diagnostic criteria
    - 97% sensitive
    - 94% specific

Brody, et al. *Arch Intern Med.* 1998;158:2469.

Screening for Depression in a Busy Clinic

- Screening question
  - “During the past month, have you often been bothered by the following?”
    - Little interest or pleasure in doing things (anhedonia)
    - Feeling down, depressed, or hopeless (depressed mood)
- If one answer is “yes,” probe for core symptoms of depression

Brody, et al. *Arch Intern Med.* 1998;158:2469.

Screening for Depression in a Busy Clinic (cont'd)

- Core symptoms of depression = *SALSA*
  - "Have you experienced any of the following feelings nearly every day for the past 2 weeks?"
    - Sleep disturbance
    - Anhedonia
    - Low self-esteem
    - Appetite decrease
- The presence of 2 or more core symptoms correlates with a diagnosis for major depression

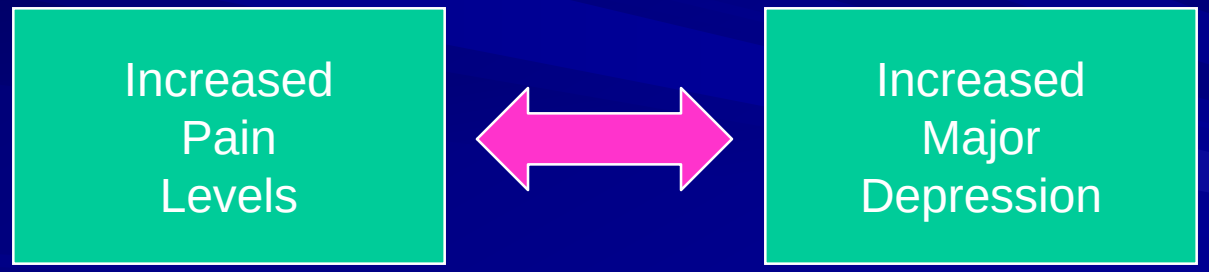
Common Presenting Complaints With Major Depression

- Excessive worry over physical health
- Complaints of pain
  - Joint pain
  - Headaches
  - Abdominal pain
- Tearfulness and irritability
- Brooding and anxiety

DSM-IV. 1994:323.

Don’t Forget

Musculoskeletal pain and the presence of major depression may be interrelated



Huyser BA, Parker JC. *Rheum Dis North Am.* 1999;25:115.

Case 5: Question

- 40-year-old woman with diagnosis of fibromyalgia has quit her job because of pain and fatigue. Which of the following therapies is most important?

A. NSAIDs
B. Low-dose tricyclic agents at night (amitriptyline, cyclobenzaprine)
C. Instruction in general physical conditioning exercises
D. Encourage her to return to work

Case 5: Answer

- *C. Conditioning exercises*
  - NSAIDs a little better than placebo
  - Amitriptyline a little better than NSAIDs
  - NSAIDs plus amitriptyline a little better than amitriptyline alone
  - Duration of response to pharmacological agents is usually limited
  - But exercise is BEST of all - to increase function in spite of pain not to eliminate pain.

Therapy of Fibromyalgia Syndrome

- Goal of therapy
  - Keep patient functional in spite of pain
- Therapeutic techniques
  - Listen to the patient and reassure
  - Educate regarding the nondestructive nature of the disease
  - Aggressively treat coexisting depression
  - Emphasize appropriate sleep hygiene
  - Instruct in a regular conditioning exercise program
  - Encourage social interactions and employment

Don’t Start It

- Use of corticosteroids or narcotic agents is not indicated in fibromyalgia

Things to Remember Tomorrow

- In patients with diffuse arthralgias and myalgias
  - Think about an inflammatory rheumatic syndrome
  - Think about an endocrine abnormality
  - Think about drug or toxic reactions
  - Think about a soft-tissue pain syndrome
    - Fibromyalgia
    - Depression
    - Somatoform pain disorder

Things to Remember Tomorrow (cont'd)

- Systemic rheumatic inflammatory syndromes have objective abnormalities on examination
- Symptoms of muscle pain and/or weakness require a careful examination of muscle strength and focal neurological abnormalities
- Screen for common, treatable mental disorders (PRIME-MD)

High Impact Rheumatology

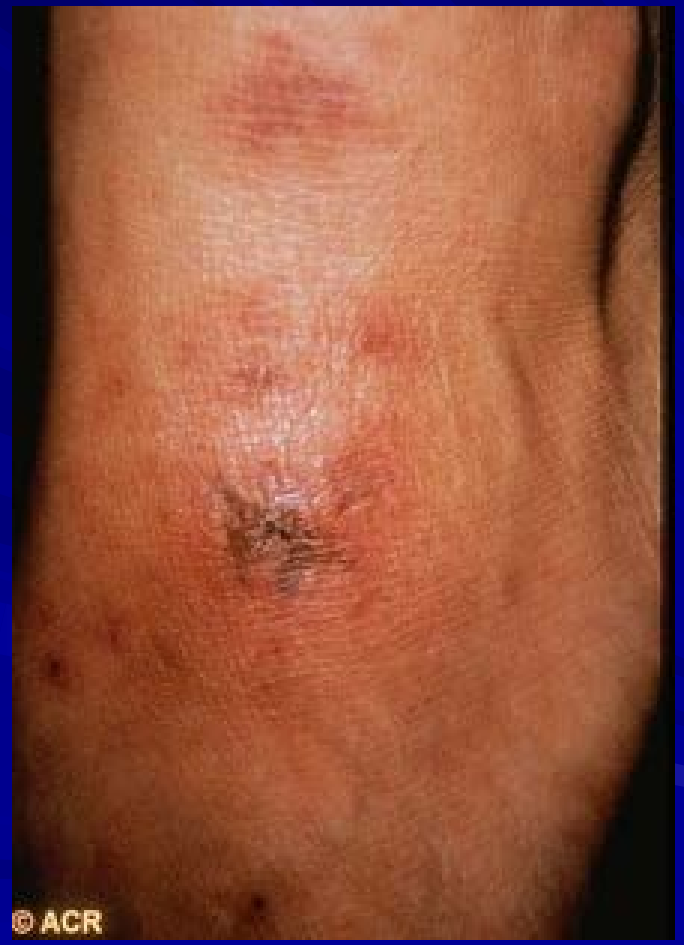
Multisystem Inflammatory Disease

Case 1: History

- A 45-year-old man presents with severe dyspnea and cough. He was in excellent health until 4 weeks ago when he developed a sore throat and fever. Over the past 2 weeks, he has noticed reddish ulcers on his legs, episodes of dark urine, and migratory arthralgias. He reports a past history of heavy alcohol use and acknowledges occasional “recreational” drug use

Case 1: Objective Findings

- Diffuse pulmonary rales and rhonchi
- No detectable heart murmurs or S_3
- Palpable ulcerative rash over the legs
- No synovitis
- Hgb = 9.8; WBC = 23,000; ESR = 68; Creatinine = 2.8
- UA = 50 RBCs with casts
- Oximetry = 85% O_2 saturation



Approach to Multisystem Inflammatory Disease

- How should you approach a patient who presents with multisystem inflammatory disease?

Diagnostic Considerations in Patients With Multisystem Inflammation

- Systemic lupus erythematosus (SLE)
- Systemic vasculitis
- Vasculitis mimics

Systemic Lupus Erythematosus

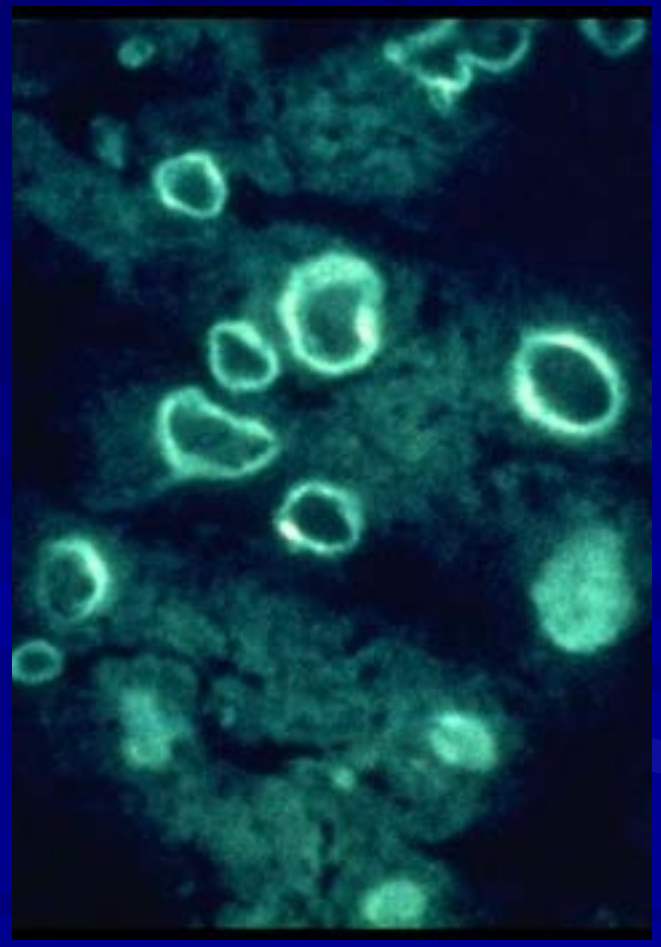
- Inflammatory multisystem disease primarily seen in females
- Highly variable course and prognosis
- Often has significant constitutional symptoms
- Associated with characteristic autoantibodies

Systemic Lupus Erythematosus (cont'd)

- Clinical symptoms related to the degree of inflammation in various organs
  - Skin and mucous membranes
  - Synovium (joints)
  - Serosal membranes
  - Kidneys
  - Central nervous system
  - Lungs
  - Heart
  - Hematopoietic system

Autoantibodies in SLE

- ANA
  - Seen in 95% of SLE
  - Not specific for SLE
  - Seen in many inflammatory, infectious, and neoplastic diseases
  - Seen in 5% to 15% of normal persons



Autoantibodies in SLE

- Anti-ds DNA
  - Seen in 60% of patients with SLE
  - Highly specific for SLE
  - Low titer rarely seen in other inflammatory conditions
  - Strongest clinical association is with nephritis
- Anti-Sm (Smith)
  - Seen in 10% to 30% of SLE patients
  - Highly specific for SLE

When to Consider a Diagnosis of SLE

- Usually seen in women of childbearing age with:
  - Constitutional symptoms of fever, weight loss, malaise, and severe fatigue
  - Skin rash and/or stomatitis
  - Arthritis
  - Renal disease
  - Cytopenias
- Although 90% of patients are female, SLE can be seen at any age in either sex

Diagnostic Classification of Vasculitis—I

- Large-vessel involvement
  - Giant cell arteritis
  - Takayasu's arteritis
- Medium-vessel involvement
  - Polyarteritis nodosa
  - Kawasaki disease of childhood

Jennette JC, Falk RJ. *N Engl J Med.* 1997;337:1512-1523.

Diagnostic Classification of Vasculitis—II

- Small-vessel involvement with immune complex deposition
  - Hypersensitivity vasculitis
  - Henoch-Schönlein purpura
  - Behçet's syndrome
  - Cryoglobulinemia
  - Vasculitis of rheumatic diseases (SLE, RA)

Jennette JC, Falk RJ. *N Engl J Med.* 1997;337:1512-1523.

Diagnostic Classification of Vasculitis—III

- Small-vessel involvement without immune complex deposition (pauci-immune)
  - Wegener's granulomatosis
  - Churg-Strauss vasculitis
  - Microscopic polyangiitis

Jennette JC, Falk RJ. *N Engl J Med.* 1997;337:1512-1523.

Clinical Features Suggesting Vasculitis

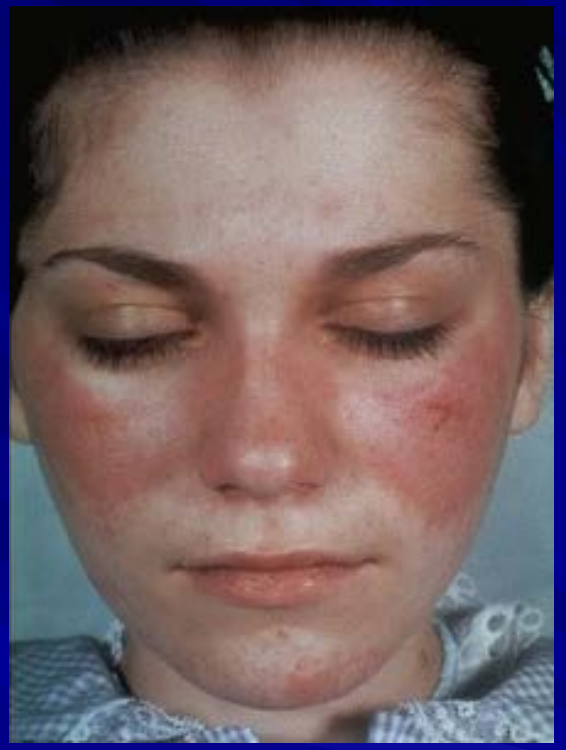
- Multisystem inflammatory disease
- Rapidly progressive major organ dysfunction
- Constitutional symptoms (fever, weight loss)
- High ESR, severe anemia, thrombocytosis
- Evidence of small-vessel inflammation:
  - In the kidneys = active urinary sediment
  - In the lungs = hemoptysis, dyspnea
  - In the skin = palpable purpura/hemorrhage
- Acute neurologic changes
  - Footdrop
  - Altered mental status

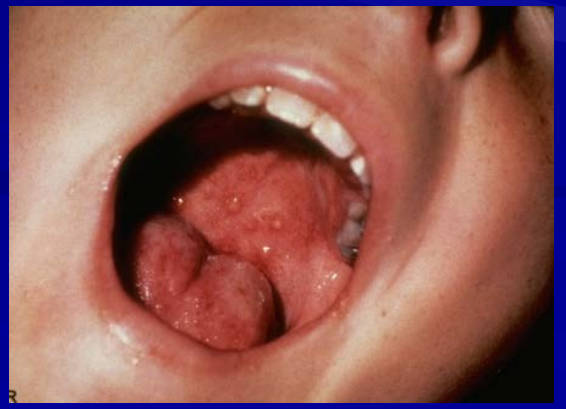
Case 2: History

- A 36-year-old female is seen for migratory arthritis of 6 months' duration. She also reports some fatigue and a photosensitive skin rash. ROS notes:
  - Patchy hair loss 4 months ago that regrew
  - Aphthous-like mouth ulcers every 4 to 6 weeks
  - A diagnosis of "walking pneumonia" made last month based on symptoms of pleuritic chest pain

Case 2: Objective Findings

- Pain with mild synovitis over the MCPs and PIPs
- Rash over her face, legs, and trunk
- Hgb = 12.1; ESR = 33
- UA = 3+ protein
- ANA = 1:640 titer





Case 2: Question

- With this clinical history, what is the most important thing to do now?
  A. Start an NSAID for the joint pain
  B. Start hydroxychloroquine to treat the rash and prevent recurrent pleurisy
  C. Fully evaluate her renal status and initiate appropriate therapy
  D. Start prednisone at 80 mg qd

Case 2: Answer

- *C. Fully evaluate her renal status*
  -  Don’t Wait
    - Aggressively evaluate renal status if the urinalysis is abnormal in SLE patients

Case 3: Clinical Findings

- A 26-year-old woman presents with progressive weight loss, fevers to 103.5°F, arthralgias, and ischemic ulcers on the fingers
- Physical examination reveals an enlarged spleen and a harsh midsystolic murmur
- Hgb 9.3 mg%, ESR 82 mm/s
- Urinalysis shows 15 to 20 RBCs

Case 3: Question

- Which of the following would you do first?
  - A. Echocardiogram and blood cultures
  - B. Renal biopsy
  - C. Anti-ds DNA antibody levels
  - D. C-reactive protein level

Case 3: Answer

- *A. An echocardiogram and blood cultures*
  - Echocardiogram showed vegetations on the valves
  - Blood cultures were positive for *Staph aureus*

Don’t Guess

- ALWAYS look for mimics of vasculitis that have specific treatments

Case 7: Clinical Findings

- A 51-year-old man is seen for complaints of hives, skin rash, and ulcers over his shins
- Physical exam reveals
  - Palpable purpura, ulcers, and urticarial lesions over the arms and legs
  - Palpable cervical and axillary adenopathy
  - Hepatosplenomegaly

Case 7: Diagnostic Studies

- Laboratory studies
  - ESR = 64; RF = 489 iu; C_3 = 24; AST = 876; ALP = 234
  - UA shows 20 to 30 RBCs, negative protein, no casts
  - Cryoglobulins = positive
- Skin biopsy reveals leukocytoclastic vasculitis

Case 7: Question

- What is the most probable etiology for this vasculitic syndrome?

A. Parvovirus infection
B. Drug reaction
C. Hepatitis C infection
D. *Staph* sepsis

Case 7: Answer

C. Hepatitis C infection

"Essential cryoglobulinemic vasculitis
is not so essential anymore"

Hepatitis C Virus-Associated Vasculitis

- The cause of most cryoglobulinemic vasculitis
- Cryoglobulins lead to tissue damage
- Patients are rheumatoid factor positive
- Prednisone and/or cytotoxic agents may increase virion load
- Alpha interferon may improve vasculitis and infection
- Despite therapy, relapses are common

Agnello V. *Rheum Dis Clin North Am*. 1996;22:1–21.

Hepatitis B Virus-Associated Vasculitis

- Seen in 10% to 50% of polyarteritis nodosa cases
- Presents as a systemic vasculitis with abnormal liver function tests
- Tissue damage is due to immune complexes
- Therapy includes steroids, antiviral agents, and occasionally apheresis

HIV Virus-Associated Vasculitis

- Masquerades as many rheumatic syndromes
  - Polyarteritis nodosa
  - Churg-Strauss vasculitis
  - Hypersensitivity vasculitis
  - Systemic lupus erythematosus
  - Sjögren's syndrome
  - Primary CNS vasculitis
- Primary therapy is antiviral
- Careful use of immunosuppressive agents may be considered

Cueller ML. *Rheum Dis Clin North Am*. 1998;24:403–422.

Don’t Miss It

- Viral infections can mimic many rheumatic and vasculitic syndromes
- Key associations
  - Hepatitis B—polyarteritis nodosa
  - Hepatitis C—cryoglobulinemia
  - HIV—“seronegative” rheumatic syndromes

General Concepts About Vasculitis Treatment

- Tissue damage with vasculitis requires early diagnosis and treatment
- Combinations of high-dose steroids and cytotoxic drugs are commonly used
- Effective treatment can improve outcome
- There is a delicate balance between treatment efficacy and toxicity
- Well-defined clinical outcomes are needed to guide the intensity and duration of treatment

Points to Remember

- When a patient has a complex multisystem inflammatory picture—think vasculitis
- If a vasculitic disorder is considered, search for its cause
- Employ tests and biopsies when indicated, but remember to treat the patient, not the test
- Rapid diagnosis and treatment is often organ or lifesaving
- Consider viral associated rheumatic/vasculitis syndromes when the autoantibody results are not typical

- The above slides were selected from presentations found online