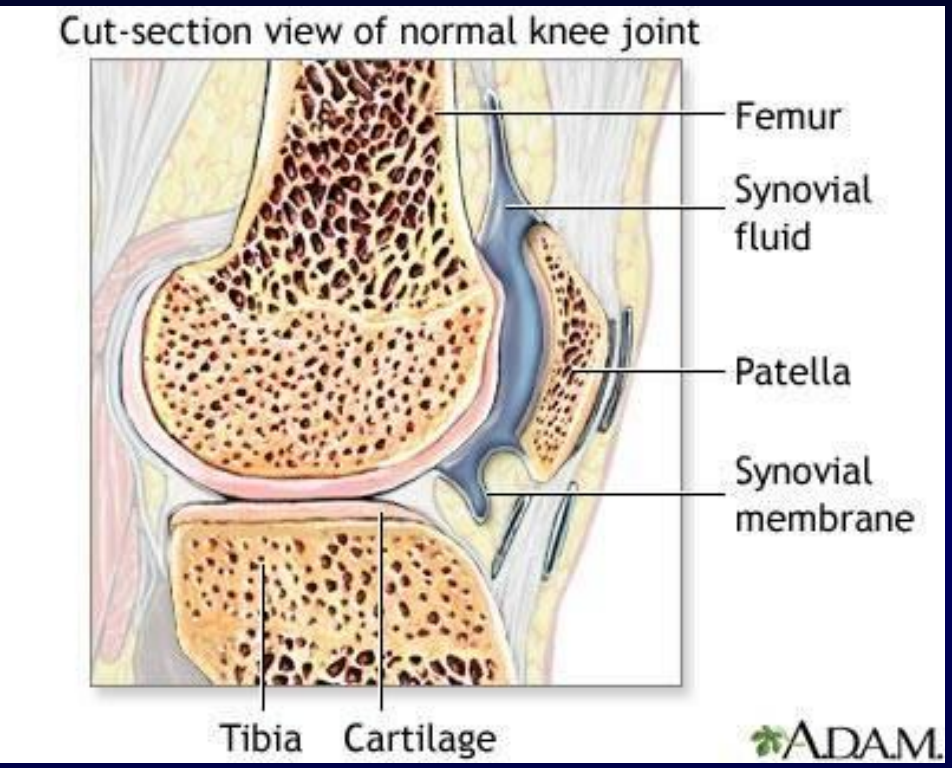
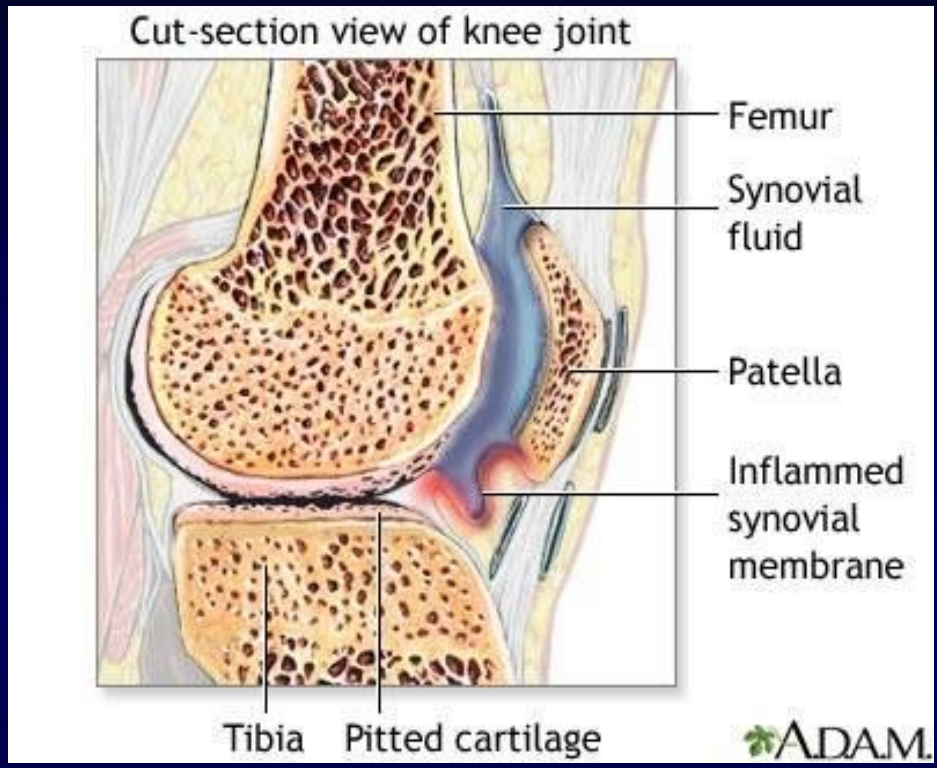
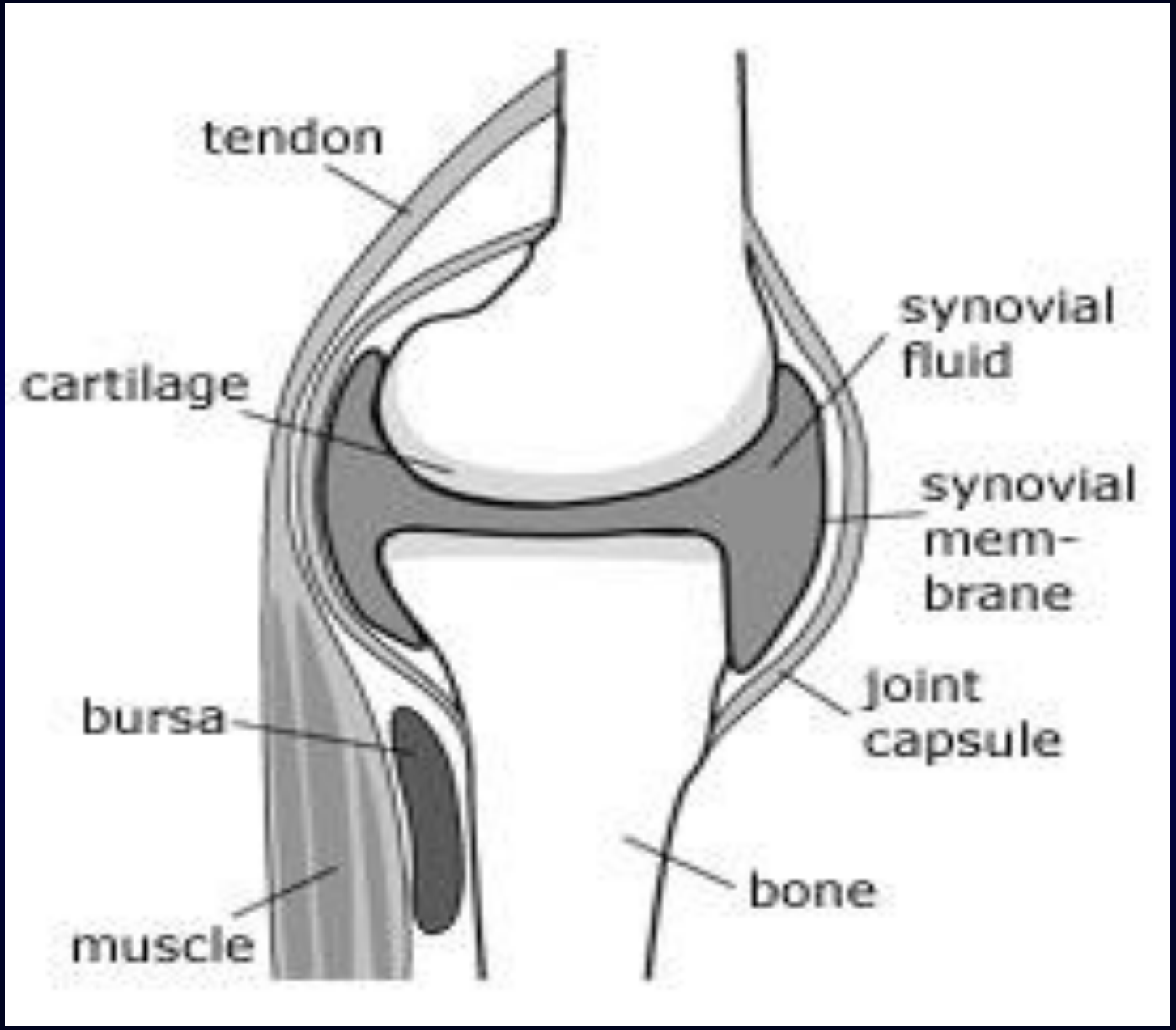
Approach Patient with Rheumatological Diseases

Anatomy of the Joint

- **Articular/Hyaline cartilage**
  - Acts as a shock absorber
  - Allows for friction-free movement
  - Not innervated!
- **Synovial membrane/Synovium**
  - Secretes synovial fluid
  - Nourishes cartilage
  - Cushions the bones


Cut-section view of normal knee joint
Femur
Synovial fluid
Patella
Synovial membrane
Tibia
Cartilage
A.D.A.M.


Cut-section view of knee joint
Femur
Synovial fluid
Patella
Inflammed synovial membrane
Tibia
Pitted cartilage
A.D.A.M.


tendon
cartilage
synovial fluid
synovial mem-brane
bursa
joint capsule
bone
muscle

Introduction..

- Is it Arthritis or Arthralgia?
- Musculoskeletal emergencies
  - Infection
  - Sepsis
  - Compartment syndrom.
- Self Limited
- Disabling and life-threatening.

Arthralgia..

- Fibromyalgia
- Bursitis
- Tendinitis
- Hypothyroidism
- Neuropathic pain
- Metabolic bone disease
- Depression

Monoarthritis

- Trauma
- Infection:
  - Nongonococcal bacterial infections: large joints.
  - Mycobacterial and fungal infection.
- Crystal induced arthritis
  - Monosodium Urate crystals (MPJ)
  - Ca pyrophosphate dihydrate crystals (knee)
- Lyme disease
- Systemic Rheumatoid diseases:
  - Seronegative spodyloarthropathy (Reactive arthritis, psoriatic) arthritis, Inflammatory BD..)
  - Sarcoid periarthritis
  - RA
- Osteoarthritis

Polyarthritis

- Rheumatoid Arthritis
- Systemic Lupus Erythrematosus
- Viral arthritis
- Reiter's disease
- Psoriatic arthritis
- Reactive arthritis

Migratory Arthritis

- Rheumatic fever
- Gonococcemia
- Meningococcemia
- Viral Arthritis
- SLE
- Acute Leukemia

Rheumatic Fever..

- **Majer Criteria:**

  1- Carditis 2- Polyarthritis 3- Chorea

  4- Erythema Marginatum 5- Subcutaneous nodules

- **Minor criteria:**

  1- Arthralgia 2- Ferver 3- Acute phase reactant

  4- Prolong PR interval 5- Evidence of group A streotococcal infection (AST, Throat culture…)

History.. Age

- **<30=** SLE, Ankylosis spodylitis, Reactive Arthritis.
- **30-50=** RA, Systemic sclerosis, Gout.
- **>50=** OA, Pseudogout, PMR
- **Any Age group=** Psoriatic arthritis, Enteropathic arthritis

History.. Sex

- **>Female:**
  - SLE, RA, OA, Systemic sclerosis, Ankylosis spodylitis, PMR.
- **Male=Female:**
  - Psoriatic arthritis, Enteropathic arthritis Pseudogout.
- **>Male:**
  - Gout, Reactive Arthritis.

History Symptoms

- **Site:**
  - Symmetrical= RA, SLE, Systemic sclerosis
  - Asymmetrical=OA
  - Large joints=OA
  - DIP= OA, Psoriatic arthritis
  - MCP, PIP= RA, SLE
  - 1st MTP= Gout, OA
  - Spine= OA, Ankylosis spodylitis, Psoriatic arthritis, Reactive arthritis
  - Shoulder= PMR

History Symptoms

- **Pain character:**
  - Aggravated by motion= Mechanical
  - Relieved by motion= Inflammatory.
- **Duration:**
  - <6 wks= viral arthritis, systemic rheumatic diseases
  - >6 wks=systemic rheumatic diseases
- **Associated Symptoms :**
  - **Morning stiffness: >1hr= RA, PMR, Inflammatory : > 30 Minutes = OA**

History Symptoms

- **Associated Sx:**
  - Multi-system involvement= Systemic rheumatic diseases.
- **Past Medical history:**
  - Trauma, Fracture, Surgical procedures…
- **Medication list:**
  - Drug induced lupus.
  - Diuretics.

Phyisical Examination

- **Joint:**
  - Soft tissue swelling, warm, effusion…= Inflammation.
  - Inflammation signs extended= Septic arthritis, Crystal induced arthritis, Fracture.
  - Passive motion (N), active(↓↓)= Bursitis, Tendinitis, muscle injury.
  - Passive motion (↓↓), active(↓↓)= Synovitis

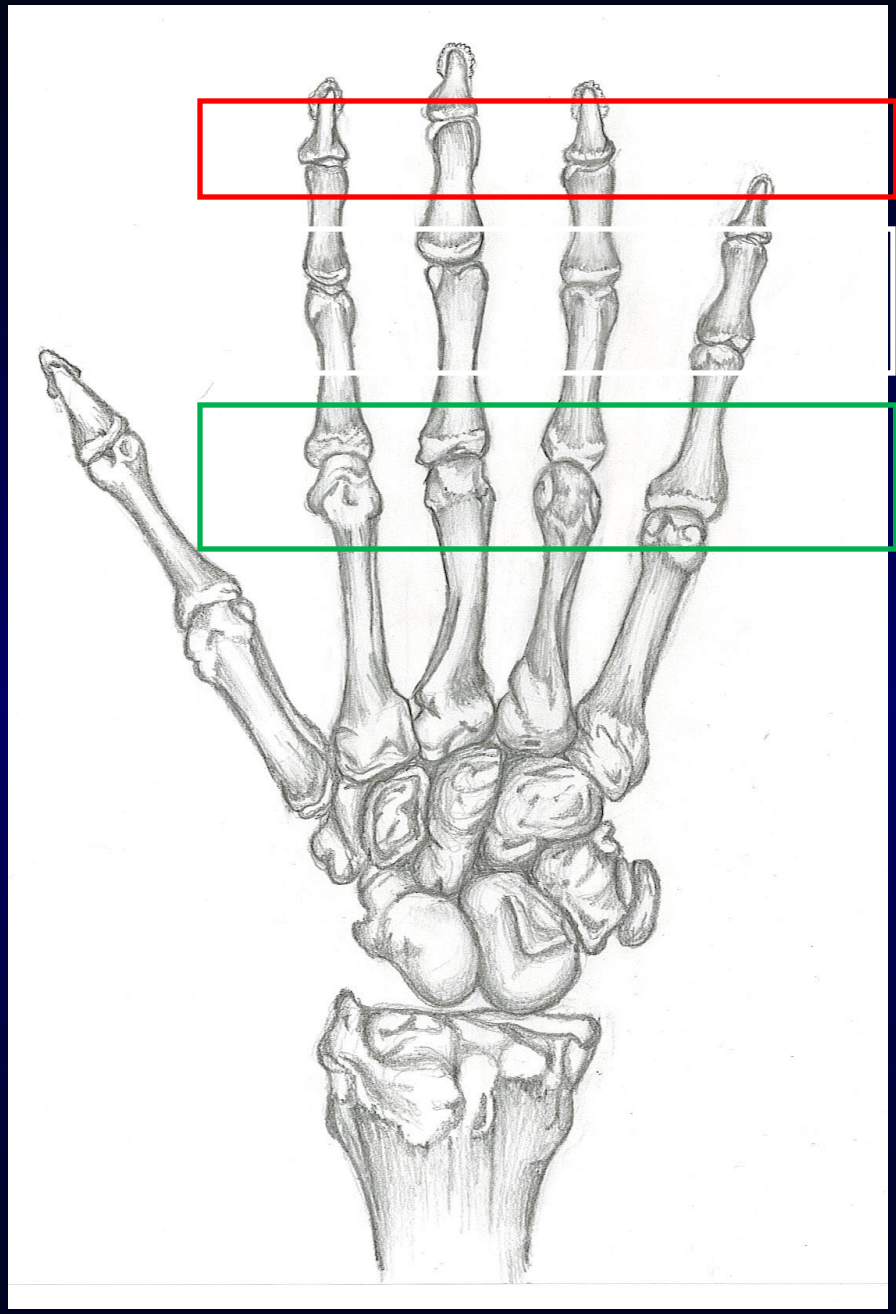
Phyisical Examination

- **General Examination:**
  - Parotid enlargement, Oral ulceration, Heart murmurs, Pericardial or Pleural friction rubs, Crackle…= Systemic disease.
  - Fever= Infection, Reactive arthritis, RA, SLE, Crystal induced arthritis…
  - Subcutaneous nodules= RA, RHD, Gout (Tophi)
  - Skin manifestations= Psoriasis, RA, SLE…
  - Eye disease (Keratoconjunctivitis sicca, Uveitis. Conjunctivitis, episcleritis…)

Raynauds in Rheumatology

Table 2
Relationship of Raynaud's phenomenon (RP) with connective tissue diseases (CTD).

CTD	Prevalence of RP in CTD (%)	Occurrence of CTD in primary RP		
		Mean follow-up (years)	(%)	Reference
SSc	96.3	3.2–4.8	8.6–12.6	[31,38,39]
MCTD	86	4.8	0.8	[33,38]
SLE	31–46	4.8	4.7	[33,34,38]
UCTD	30	7	12	[35,59]
RA	3–22	4.8	3.5	[36,38,62]
SS	13	4.8	3.4	[37,38]



DIP: Psoriatic Arthritis, Osteoarthritis (Heberden's nodes)

PIP: Osteoarthritis (Bouchard nodes) Rheumatoid arthritis, SLE

MCP: RA, SLE, Hemochromatosis

	WBCs	Diff	Micro/Polarization	Glucose
DJD, SLE, Traumatic arthritis	< 1000 to 2000	Monos + Lymphs	Negative	Normal
RA, Spondyloarthropathies	5000 to 50,000	PMNs	Negative	Normal/low
Gout	5000 to 75,000	PMNs	Monosodium Urate/Strongly negative	Normal
Pseudogout (CPPD)	5000 to 75,000	PMNs	CPPD/Weakly positive	Normal
Septic Arthritis	50,000 to > 100,000	PMNs	Gram stain abnormal in most	Normal

Laboratory Studies

- Uric acid concentration= Gout
- Synovial fluid analysis= Infection, Crystal induced arthritis, Inflammatory..
- Hepatitis B and C
- Parvovirus serology

Laboratory Studies..

- **Can be misleading.**
- Basic: CBC, Urinalysis, U&E, LFT.
- Acute phase reactant: ESR, CRP.
- Antibody tests:
  - ANA= SLE
  - Anti-dsDNA= SLE
  - Anti-native DNA, anti-Sm= SLE
  - RF= RA
  - Anti-CCP antibody=RA

Rheumatoid Factor

- Rheumatoid Arthritis
- Connective tissue diseases
- Viral infection
- Leishmaniasis
- Leprosy
- Tuberculosis
- Sarcoidosis
- Liver diseases
- Subacute bacterial endocarditis

Anti-Nuclear Antibody (ANA) and CTD's

- ANA's are antibodies that target human DNA as antigen.
- Different patterns of fluorescence will emerge:
  - Homogenous, Speckled, Peripheral and Nucleolar.
- It is common to all CTD and is the first test ordered when you suspect CTD.
- It is sensitive for CTD, but not specific:
  - 95% of patients with CTD will have a positive ANA
  - But there are many other diseases which will have it as well.
  - ~ 5% of normal blood donors will have positive ANA.
- Positive ANA include Neoplasms, liver disease, Active chronic infections and use of Birth control pills.

Sensitivity of ANA in Rheumatology

TABLE 1: Sensitivity of the ANA in Autoimmune and Nonrheumatic Disease

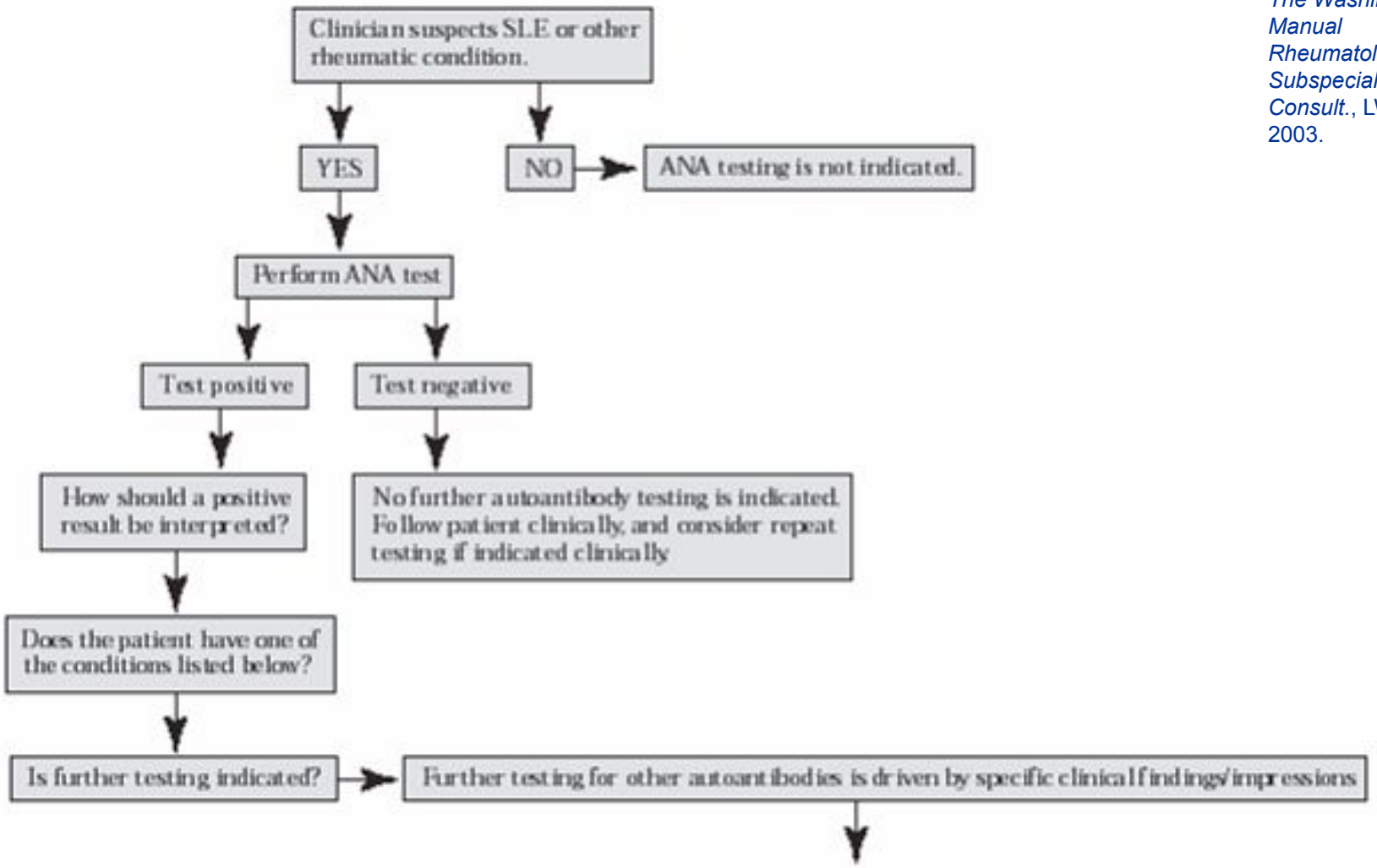
Autoimmune Disease

- SLE: 95–100%
- Scleroderma: 60–80%
- Mixed connective tissue disease: 100%
- Polymyositis/dermatomyositis: 61%
- Rheumatoid arthritis: 52%
- Rheumatoid vasculitis: 30–50%
- Sjögren's syndrome: 40–70%
- Drug-induced lupus: 100%
- Discoid lupus: 15%
- Pauciarticular juvenile chronic arthritis: 71%

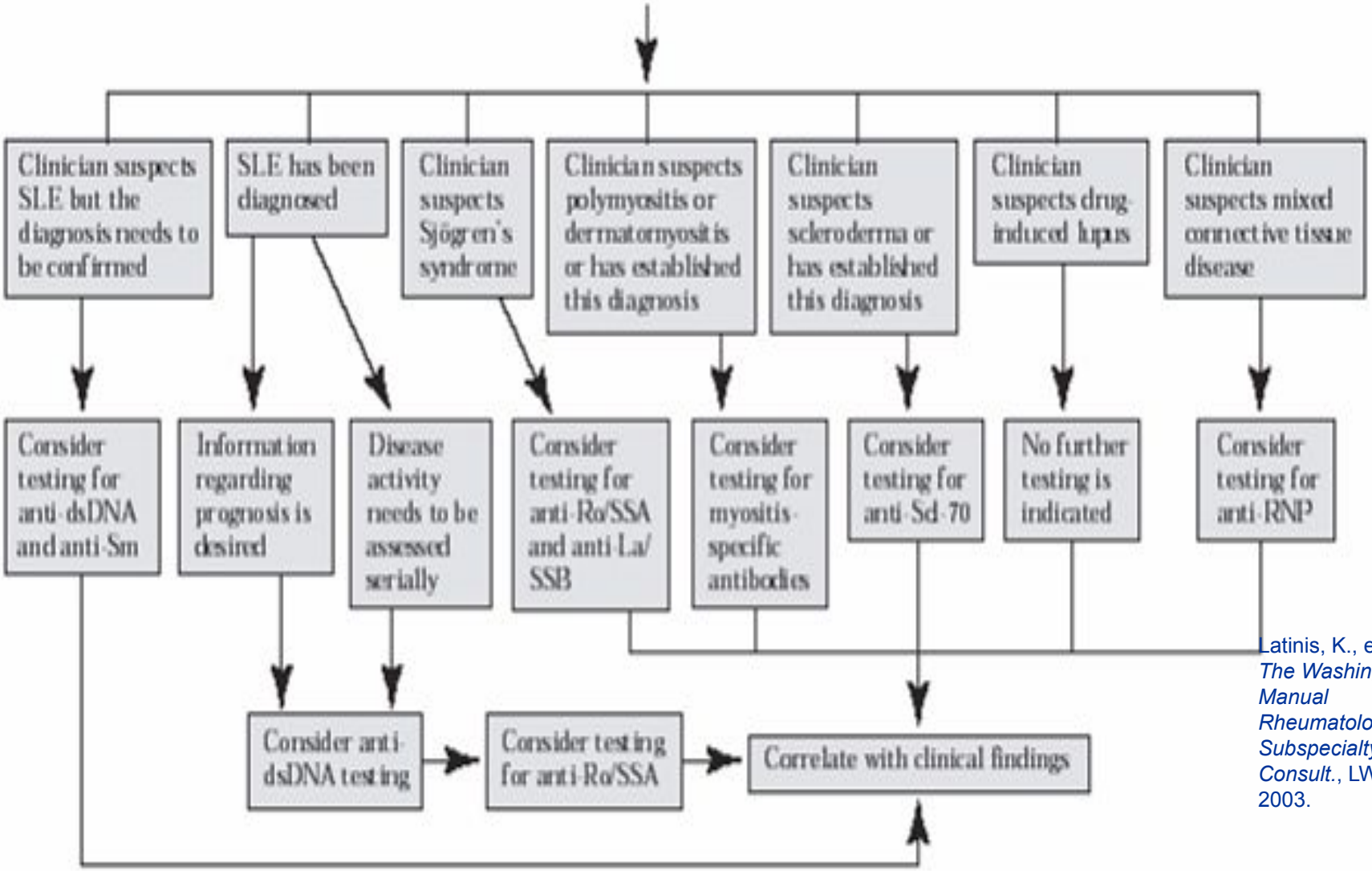
Nonrheumatic Disease

- Hashimoto's thyroiditis: 46%
- Graves' disease: 50%
- Autoimmune hepatitis: 100%
- Primary autoimmune cholangitis: 100%
- Primary pulmonary hypertension: 40%

ANA-When to order a Positive Test



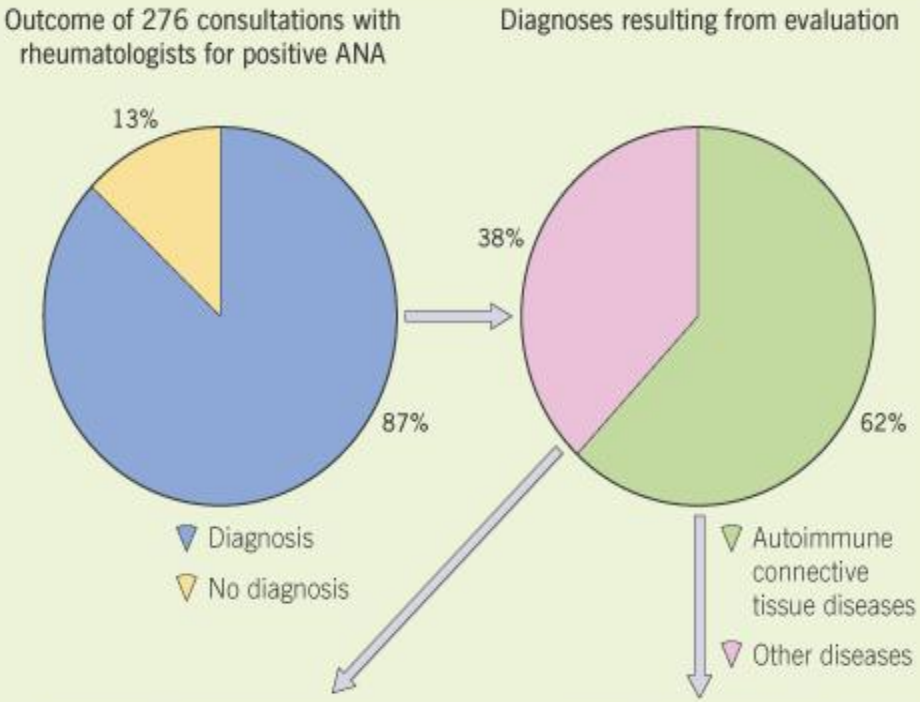
Latinis, K., et al *The Washington Manual Rheumatology Subspecialty Consult.*, LWW, 2003.



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

FIG. 1-3. Approach to a positive ANA. dsDNA, doublΘstranded DNA. (Adapted from Kavanaugh A, Tomar R, Reveille J, et al. Guidelines for clinical use of the antinuclear antibody test and test for specific autoantibodies to nuclear antigens. *Arch Pathol Lab Med* 2000;124:71-81.)

DIAGNOSTIC OUTCOME OF POSITIVE ANA TESTS



Non-autoimmune connective tissue diseases

Organ-specific autoimmune diseases (e.g autoimmune thyroiditis) – 10%

Infectious diseases – 8%

Neoplasia – 3%

Miscellaneous – 11%

Autoimmune connective tissue diseases (AI-CTD)

Systemic lupus erythematosus – 19%

Drug-induced systemic lupus erythematosus – 11%

Undifferentiated AI-CTD – 6%

Rheumatoid arthritis – 4%

CREST – 4%

Others – 7%

Specific Antibodies in Rheumatology

TABLE 2:
ANA Disease Associations

Sensitivity and Specificity of Different Antinuclear Antibodies

	Antibody							
	ds DNA	ss DNA	Histone	Nucleoprotein	Sm	RNP	Ro	La
SLE								
Sen	70%	80	30–80	58	25–30	45	40	15
Spec	95%		50	mod	mod	99	87–94	
Drug LE								
Sen	1–5%	80	95	50	1%		low	low
Spec		50	high	mod				
RA								
Sen	1%	mod	low	25	1%	47	low	low
Spec		mod		low				
Scleroderma								
Sen	<1%		<1%	<1%	<1%	20		
Spec		low						
PM/DM								
Sen	<1%		<1%	<1%	<1%		low	
Spec		low						
Sjögren's								
Sen	1–5%	mod	low	mod	1–5%	5–60	8–70	14–60
Spec		mod	low	mod			87	94

Sen: sensitivity; Spec: specificity
Other associations: RNP: MCTD; Ro: SCLE, bilary cirrhosis, vasculitis, CHB

Imaging Studies

- **X-ray:**
  - RA
  - Chronic Gout
  - OA
  - Ankylosing spondylosis.
- **MRI:**
  - Ankylosing spondylosis.

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

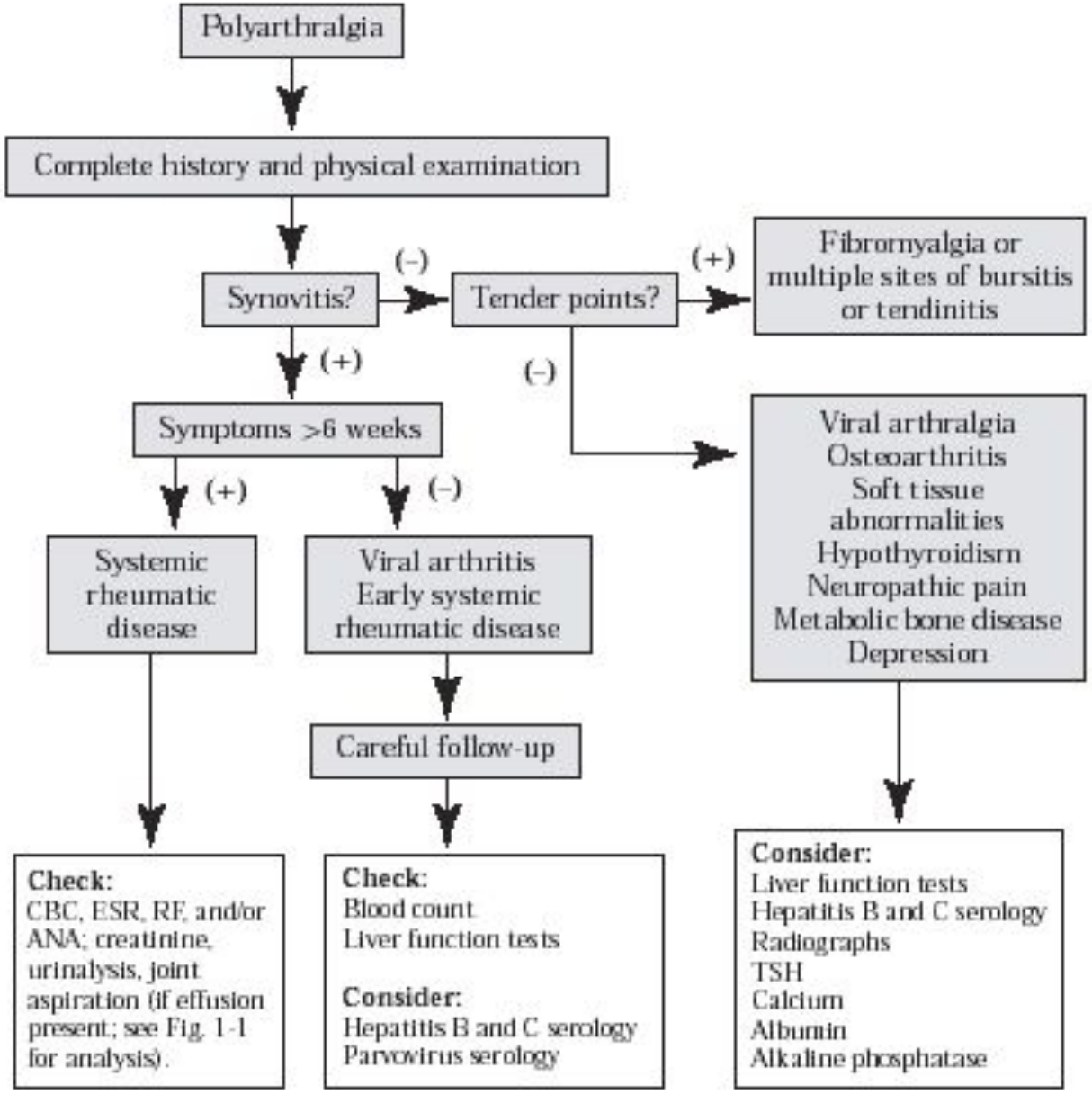


FIG. 1-2. Approach to polyarthritis. (Adapted from American College of Rheumatology ad hoc Committee on Clinical Guidelines. Guidelines for the initial evaluation of the adult patient with acute musculoskeletal symptoms. *Arthritis Rheum* 1996;39:1.)

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

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.

Distinguish Inflammatory and Non-inflammatory arthritis

Feature	Inflammatory	Noninflammatory
Joint inflammation (warmth, erythema, effusion)	+++	--- (bony proliferation in OA)
Morning Stiffness	generally > 1 hour	generally < 1 hour
Systemic Symptoms	+++	----
Synovial fluid	> 2000 Leuks, >50% PMN	< 2000 Leuks, < 50% PMN
Other labs findings	++++ (Elevated ESR, CRP, ACD, +RF or + CCP)	----
Radiographs	Erosions, periostitis	Osteophytes, subchondral sclerosis

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.

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

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