

Rheumatology Red Flags and Emergencies :Workshop

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Disclosures

- Amgen
- Janssen
- Roche
- BMS
- Pfizer
- UCB
- Novartis
- Merck

Advisory board, speaker, clinical trials....

Objectives

1. Recognize patterns of acute rheumatic scenarios that require timely management
2. Importance of early referral and treatment of patients with suspected acute inflammatory rheumatic syndromes
3. Update on current therapeutic options, and side effects to be aware of

Topics to be reviewed

- The hot joint(s)- acute mono and polyarthritis
- PMR and GCA
- The patient on biologics

The Hot Joint(s)

- Monoarthritis

- Polyarthritis

Case

- 67 year old man
- Type 2 diabetic, suffers with ulcers on legs, recent knee injection for OA.
- Presents with acute history (progressive over 48-72 hours) of painful, hot, swollen red knee
- Struggling to walk into clinic
- Feels feverish past 36 hours

Acute Monoarthritis - Etiology

- THE MOST CRITICAL DIAGNOSIS TO CONSIDER: INFECTION!

→ DDX:

- Crystal (Gout , Pseudogout)
- Hemarthrosis (heme disorders)
- Monoarticular onset of systemic disease or other inflammatory arthritis (ex: RA, Spondyloarthritis)
- Trauma

Joint aspiration



Send fluid for: Gm stain, C+S, Crystals, Cell count

Tests to Perform on Synovial Fluid

- Gram stain and cultures
- Total leukocyte count/differential
 - Inflammatory vs. non-inflammatory
- Polarized microscopy to look for crystals
- Not necessary routinely:
 - Chemistry (glucose, total protein, LDH) unlikely to yield helpful information beyond the previous tests.

Synovial Fluid Analysis

Joint Fluid	Appearance	Cell Count
Normal	Clear/Yellow	<200 WBC's
Non-Inflammatory	Clear/Yellow	<2000 WBC's
Inflammatory	Turbid/Yellow	<50,000 WBC's
Septic	Pus	>50,000 WBC's

Other Tests Indicated for Acute Arthritis

1. Almost always indicated:

Radiographs

CBC

ESR/CRP

2. Indicated in certain patients:

Blood Cultures

Serologic: ANA, RF, HLA-B27

Serum Uric acid level

Risk Factors for Septic Arthritis

- Previous arthritis
- Trauma
- Diabetes Mellitus
- Immunosuppression
- Bacteremia
- Sickle cell anemia
- Prosthetic joint /Recent IA injection

Pathogens

- 90% non-gonococcal
 - staph aureus 50-80%, streptococcus 15-20%, haemophilus influenzae b 20% (infants 6mo-2yrs), anaerobes 5%
- Gonococcal
 - young, sexually active
 - Pustular skin lesions (dermatitis-arthritis syndrome)
 - Tenosynovitis
 - Migratory arthralgias
 - Hand > knee, wrist, ankle, or elbow

INFECTIOUS (PYOGENIC) ARTHRITIS

- Assume any monoarticular arthritis is infectious until proven otherwise
- *Sudden* onset and *very* painful is more suggestive of crystalline disease – bacterial infection peaks over a few days
- If a nearby break in skin, or bacteremia, most definitely approach as infectious process
- Septic joint carries high morbidity and mortality
- Inflammatory arthritis can mimic septic joint!

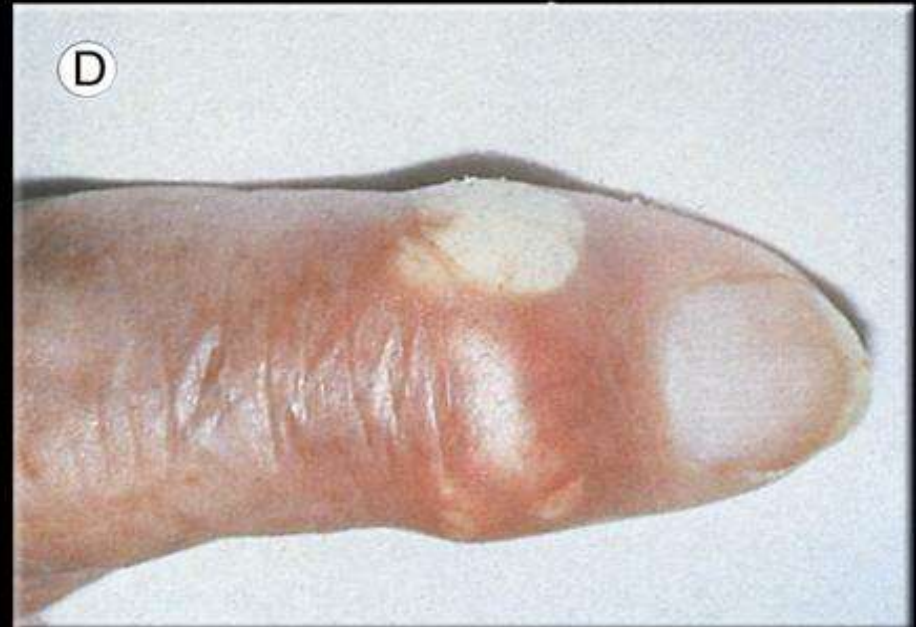
Empiric Therapy for Septic Arthritis

- You must cover Staph and Strep
 - Oxacillin, cephazolin
 - Vanco if PCN-allergic or if concern for MRSA
- If infection is hospital acquired or prosthetic joint-cover gram negatives
 - 3rd generation cephalosporin
- Empiric coverage for GC is recommended if clinical suspicion
- Frequent aspiration of joint, Ortho consult → may need debridement/lavage
- Treat 2-4 weeks iv, then 2-4 weeks po

Acute Gouty Arthritis

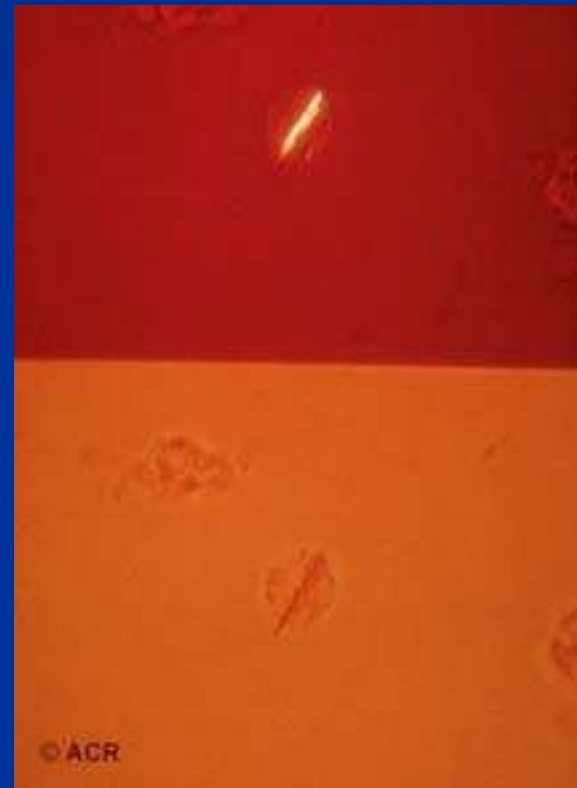


Gouty Arthritis



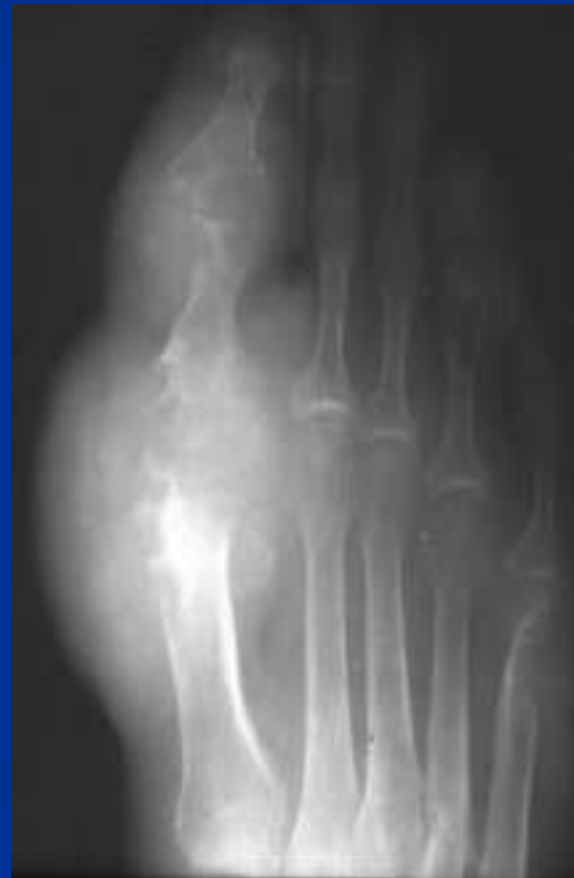
Urate Crystals

- Needle-shaped
- Strongly negative birefringent



PREVENT THIS.....

Classic “overhanging edge”



Gout Management Approach

TREAT Acute Flare¹

Treat the flare early with low doses of colchicine or with an NSAID or coxib or robust doses of corticosteroids (oral, IM or i.a.)



Identify and treat comorbidities and consider cause of hyperuricemia

INITIATE Urate-Lowering Therapy¹

Initiate urate-lowering therapy (ULT), once the flare has passed, in those with:¹

- frequent flares (≥ 2 per year)
- tophi
- uric acid overproduction
- chronic kidney disease
- history of urolithiasis
- difficult to treat gout

Initiate concomitant gout-flare prophylaxis¹



Treat to serum urate target of $<360 \mu\text{mol/L}$



Do not stop ULT because of flares and do not start UTL during a flare.

Advise lifestyle and diet adjustments: Help optimize weight, modify diet, and limit alcohol intake. Promote physical fitness. Ensure adequate hydration and achieve good control of hypertension, diabetes, and dyslipidemia. Also suggest smoking cessation.

Pseudogout

(Chondrocalcinosis on x-ray)



CPPD: Associated Diseases

■ Definitely Associated

- Hemochromatosis
- Hyperparathyroidism
- Hypophosphatemia
- Hypomagnesemia
- Wilson's disease

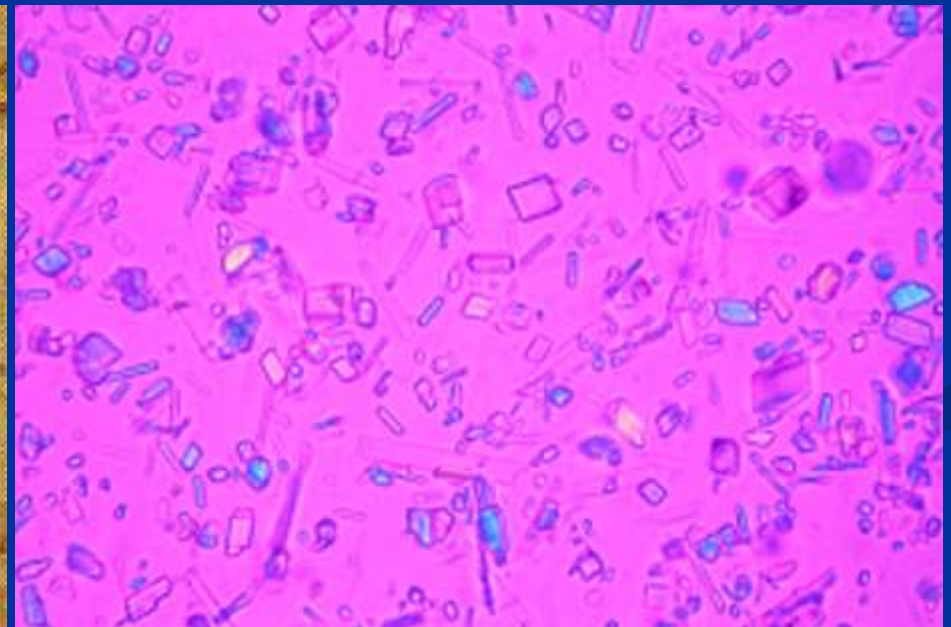
■ Possibly Associated

- Hypothyroidism
- Gout
- Ochronosis

Think about it when you see OA in atypical joints not usually associated with primary OA (ex: shoulder, ankle, MCP's) !

CPPD Crystals on Polarizing Microscopy

Rod or rhomboid shaped, weakly positive birefringent



Pseudogout

- Can cause monoarthritis clinically indistinguishable from gout.
- Often precipitated by illness or surgery, may have underlying metabolic disease.
- Pseudogout is most common in the knee (50%) and wrist.
- CPPD disease may be asymptomatic (deposition of CPP in cartilage).

Common Errors in Diagnosing Acute Monoarthritis

The problem is in the joint, because the patient complains of "joint pain."

The soft tissues around the joint can be the source of the pain (e.g., prepatellar bursitis of the knee).

Crystal-proven diagnosis of gout or pseudogout rules out infection.

Crystals can be present in a septic joint.

The presence of fever is useful in distinguishing infectious causes from other causes.

Fever may be absent in patients with infectious monoarthritis but can be a presenting feature in acute attacks of gout or pseudogout.

A normal serum uric acid level makes gout a less likely diagnosis.

Serum uric acid levels often are lowered in patients with acute gout (30%). There may be unrelated hyperuricemia in patients with other conditions.

Gram staining and culture of synovial fluid are sufficient to exclude infection.

Culture results may be negative in early infection

Acute Polyarthritis

Infection

- Gonococcal
- Meningococcal
- Lyme disease
- Rheumatic fever
- Bacterial endocarditis
- Viral (rubella, parvovirus, Hep. B)

Inflammatory

- RA
- JRA
- SLE
- Reactive arthritis
- Psoriatic arthritis
- Polyarticular gout
- Sarcoid arthritis

Temporal Patterns in Polyarthrititis

- **Migratory pattern:**
 - Rheumatic fever, gonococcal (disseminated gonococccemia), early phase of Lyme disease
- **Additive pattern**
 - RA, SLE, psoriasis
- **Intermittent:**
 - Gout, reactive arthritis

DISSEMINATED GONORRHEA

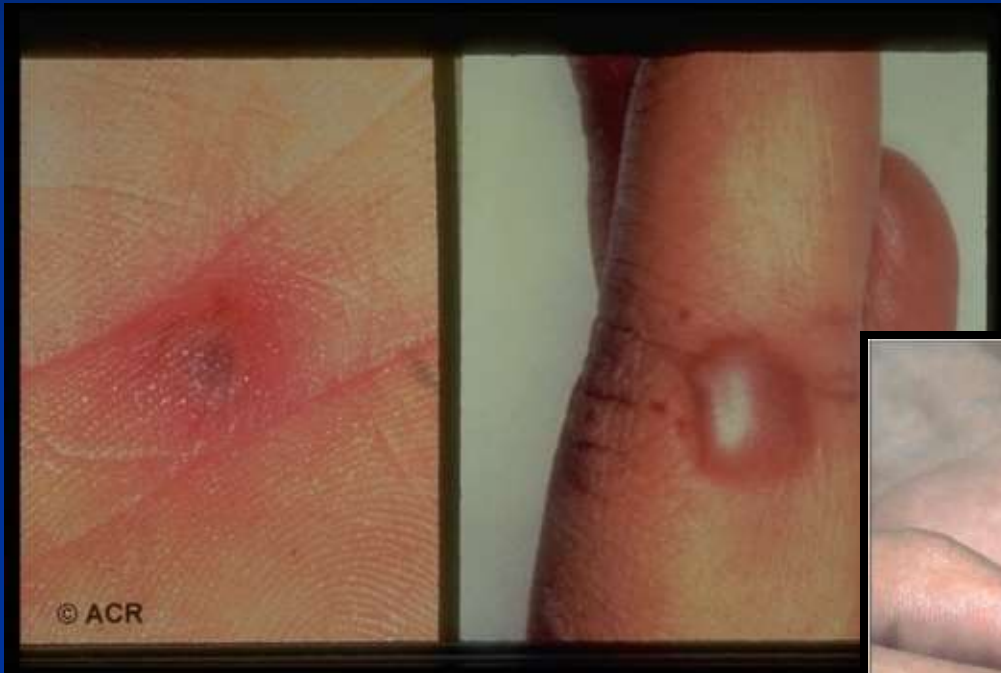
- Most common cause of septic arthritis and tenosynovitis in young adults in N.A.
- Complicates less than 1% of all GC cases
- Often have an asymptomatic mucosal infection
- Major risk factor is absence of C5-8 complement

DISSEMINATED GONORRHEA

■ Clues:

- Migratory or additive acute oligo (<4) arthritis
- Tenosynovitis of wrists / ankles / foot
- Fever / chills
- Females more commonly affected than males and often within 1 week of menses
- 2/3 have rash but it may be scant

DGI



May have only *ONE* vesicle or pustule – so look carefully...



DISSEMINATED GONORRHEA



DISSEMINATED GONORRHEA

■ Approach:

- Less than 25% of synovial cultures are positive
- Less than 10% of blood cultures are positive
- Skin biopsy culture is hardly ever positive but may be able to see on gram stain
- Best yield is to cultures/DNA probe the mucosal site
- Remember the concomitant infection (HIV, syphilis, NSU)
- Rx with 3rd generation cephalosporin
- **Often add doxycycline to cover for Chlamydia**

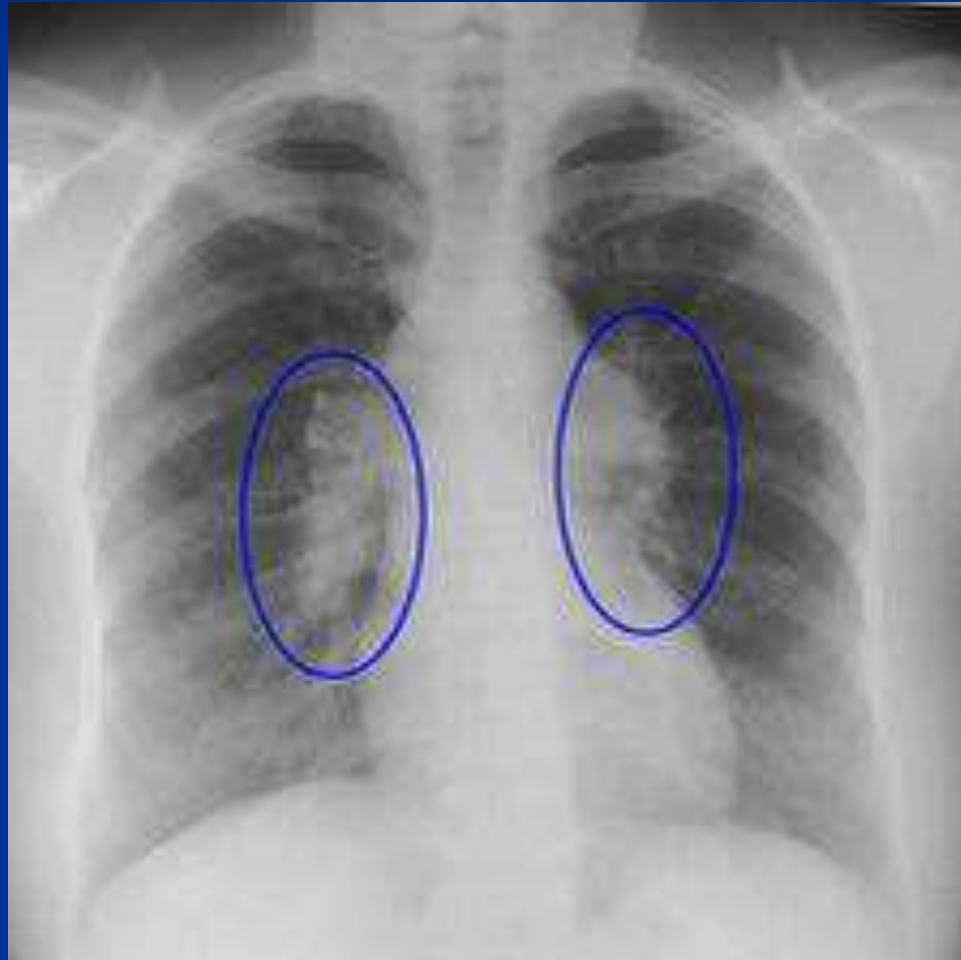
Parvovirus B-19

- The virus of “fifth disease”, erythema infectiosum (EI).
- Children “slapped cheek”; adults flu-like illness, maculopapular rash on extremities.
- Joints involved more in adults (20% of cases).
- Frequently RF +
- Abrupt onset symmetric polyarthralgia/polyarthritits with stiffness in young women exposed to kids with E.I.
- May persist for a few weeks to months.

Acute Sarcoid Arthritis

- Löfgren's syndrome: acute arthritis, erythema nodosum, bilateral hilar adenopathy
- Chronic arthritis- (15-20%)
 - Symmetrical: wrists, pip's, **ankles**, knees
- Chronic inflammatory disorder – non-caseating granulomas at involved sites
- Common with hilar adenopathy

Sarcoid



Erythema Nodosum



Learning points

1. In acute inflammatory mono or polyarthritis, an appropriate history and physical will narrow the Ddx, and help guide the investigations.
1. Don't miss septic arthritis! Aspirate when possible!!
1. In acute inflammatory monoarthritis, symptoms reaching their maximum within 6-12 hours are highly suggestive of a crystal arthropathy. Beware that gout and sepsis can co-exist.
4. Acute monoarthritis (but no history of trauma) or polyarthritis with systemic features → refer to Rheumatology

Case Study

- 67 y.o. woman
- Several weeks proximal > distal myalgias and arthralgias
- Malaise, low grade fever, loss appetite
- Hard to get out of bed in am
- Rolling over wakes her at nite
- ESR 86, CRP 58



Clinical Features of PMR

- Pain in the muscles of the shoulder girdle, pelvic girdle, and neck (commonly bilateral and symmetrical, of at least 4 weeks in duration)
- Stiffness am, nite pain
- Elevation of the ESR and CRP
- Frequent constitutional features including anemia, weight loss, fever, and general malaise
- Prompt clinical response to corticosteroid treatment

PMR/RA Overlap in the Elderly

- RA may present as PMR in the “elderly onset” subgroup of RA
- Difficult to tell apart initially, often seronegative
- Watch for peripheral, small joint involvement as taper steroids- this may be the clue

Differential Diagnosis of Polymyalgia Rheumatica

- Arthropathies
 - Rheumatoid arthritis
 - Other inflammatory joint diseases in the elderly
 - Degenerative joint disease
 - Shoulder disorders
- Inflammatory muscle disease
- Malignant diseases
- Infection
- Hypothyroidism
- Parkinson's disease
- Functional myalgias

Treatment of PMR

- Prednisone 10-20 mg per day for 1st month
- i.m. Depomedrol 120 mg q 3 weeks
 - Dasgupta, Br. J. Rheum. 1998; 37: 189-195
- Decrease 2.5 mg q 2 weeks until 10 mg/day, then decrease by 1 mg/month
- Follow the ESR and CRP, but treat the patient!
- Treat 1-2 years

Do you need to perform Temporal Artery Biopsy in PMR?

<10% are biopsy positive in PMR
without symptoms of arteritis, so
perform only in patients who have
cranial symptoms or signs

Case Study

- 67 y.o. woman
- T.I.A. resolved, put on ASA
- Malaise, myalgias, weight loss, low grade fever few months
- Left arm feels weak , achy with use
- Left subclavian bruit on exam
- ESR 86, CRP 58



GCA- (Giant Cell Arteritis) : Clinical Features & Epidemiology

- Mean age is 70
- 75% females
- Onset often abrupt
- Wide spectrum of symptoms
- PMR in 40 - 60%

GIANT CELL ARTERITIS

■ Clues:

- > 50 yo
- **NEW** headache
- Jaw claudication or arm claudication
- Sudden visual loss, diplopia
- Systemically ill with many markers of systemic inflammation, increased CRP, Ferritin, ESR

■ Approach:

- **TREAT** and then biopsy !!
- You have 2 weeks to get the biopsy

Treatment of GCA

- Prednisone 40-60 mg/day
- i.v. pulse methylprednisolone for patients with visual symptoms
- Treat full dose 4-6 weeks, then reduce by 10% every 2 weeks; more slowly once 20 mg/day has been reached
- Alternate day therapy NOT recommended
- Add ASA 80 mg
- Steroid sparing drugs- MTX, Tocilizumab

Side Effects: Corticosteroids

Osteoporosis:

- Osteoporosis Society of Canada (OSC) recommends Bisphosphonate therapy for all patients who take >7.5 mg/day of Prednisone for >3 months
- Calcium 1200-1500 mg/day and Vitamin D 1000 u/day

The Patient on Biologics



MCQ

Which of the following statements is true?

1. Patients who take non anti-TNF biologics do not need to have TB screening done prior
2. Patients on biologics can safely receive any vaccines
3. Anti-TNF biologic agents are classified as Category B drugs for pregnancy
4. If a patient becomes pregnant on a biologic drug, abortion should be recommended

MCQ

Which of the following is false:

Biologic agents have been associated with which all of the following?

- 1. increased risk of infection
- 2. increased risk of demyelinating disease
- 3. increased risk of MI and CVA
- 4. increased risk of skin cancers

