Choosing Wisely in Rheumatology:
5 Things Internists Need to Know and Practice

N. Lawrence Edwards, MD, MACP, MACR
Professor and Vice Chair
Department of Medicine
University of Florida

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American College of Rheumatology
EDUCATION • TREATMENT • RESEARCH

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Learning Objectives

1. Understand the origins of the ABIM Foundation's Choosing Wisely campaign
2. Distinguish use from abuse in anti-nuclear antibody (ANA) and ANA-subserology testing
3. Recognize the clinical manifestations of Lyme and Lyme-like disease and when it's appropriate to test
4. Understand which imaging studies are appropriate in diagnosing Rheumatoid Arthritis
5. Discuss the appropriate use of non-biologic disease-modifying drugs in early RA.
6. Observe guidelines for use of serial DXA scans in the management of osteoporosis.

Conflicts of Interest

- **None**

The Choosing Wisely Campaign

- Initiated in 2011 by the ABIM Foundation
  - Challenge all medical professional societies to construct "lists of 5"
    - tests, treatments, and services commonly used and frequently misused
- Response to the 2002 ***Principles of Professionalism*** laid out in the Physician Charter (ABIM, ACP, EFIM)
    - Patient welfare
    - Patient autonomy
    - Social justice
    - Promote fair distribution of health care resources
    - Engage in collective efforts to improve the health care system

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Don’t test ANA sub-serologies without a positive ANA and a good clinical suspicion of immune-mediated disease.

ANA in rheumatologic diseases

Disease	Sensitivity
• SLE	99
• SSc	85
• PM-DM	61
• Sjogren's	48
• Raynaud's	64
• JCA	57
• JCA with uveitis	80
• RA	40

ANA in non-rheumatologic diseases

- **Hashimoto's thyroiditis 40-50%**
- **Graves' disease 50%**
- **Autoimmune hepatitis 60-90%**
- **Primary biliary cirrhosis 10-40%**
- **Chronic infectious diseases 10-60%**
  - **Mononucleosis**
  - **Hepatitis C**
  - **SBE**
  - **TB**
- **<u>Normal Population</u> 5-10%**
  - **Higher in women, elderly**

The Clinical Utility of a Positive Antinuclear Antibody Test Result

Abeles AM, Abeles M. Amer J Med 126; 324-328, 2013

- **Patients referred to Rheumatology by non-rheumatologists for a positive ANA test result over a 2 year period (n=232).**
- **Positive predictive values for a "positive ANA test result" were calculated for all ANA-associated rheumatic diseases**
  - **PPV for Lupus 2.1%**
  - **PPV for any ANA-ard 9.1% (half were RA)**
  - **No ANA-assoc RD was present in patients with an ANA < 1:160**
  - **Most common reason for ordering ANA : widespread pain (54/232, 23.2%). PPV in this group was 0%.**
- **Conclusion: Poor predictive value of a + ANA attributable to unnecessary testing in patients with a low pretest probability for ANA-associated rheumatic disease**

When to Consider a Diagnosis of SLE

- **Usually seen in women of childbearing age**
- **Although 90% of patients are female, SLE can be seen at any age in either sex**

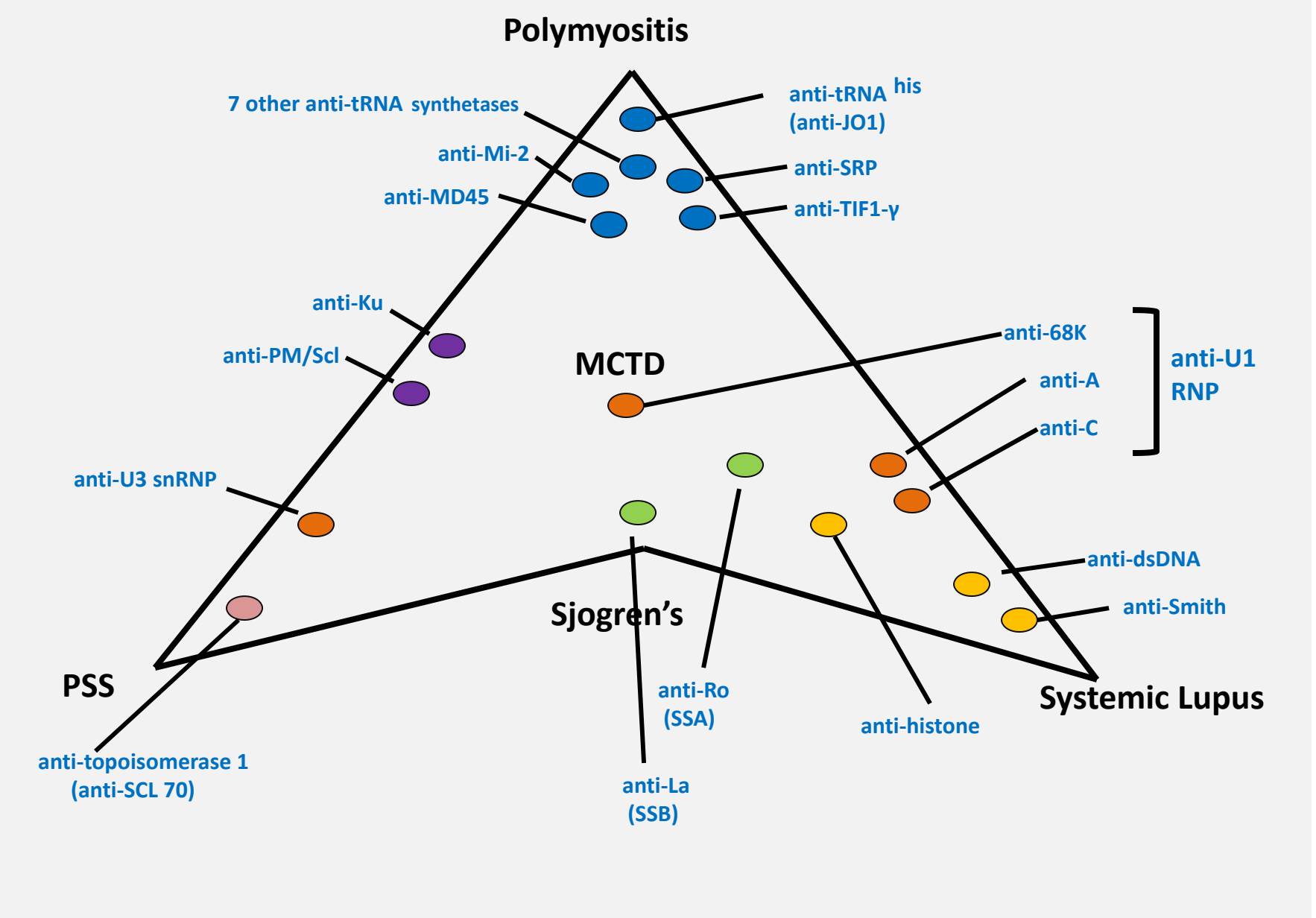
What symptoms or physical exam findings should prompt clinicians to consider lupus?

Criterion	Sensitivity (%)
• Acute rash (malar, photosensitive)	65
• Chronic rash (classic discoid)	20
• Oral or nasal ulcers	44
• Alopecia (non-scarring)	32
• Arthritis (synovitis/morning stiffness)	79
• Serositis (pleural or pericardial)	35
• Neurologic (seizure, psychosis, mm)	6
• Raynauds	15
• Chronic fatigue	80
• Fibromyalgia	30

XXXX

SLICC classification criteria, 2012

Clinical Associations of ANA sub-serologies and Connective Tissue Disease



Anti-Nuclear Antibodies

- **ANA testing should be used exclusively to confirm the presence of a clinically suspected connective tissue disease**
- **False (+) prevalence in the general population is 5%**
- **Prevalence of SLE is 0.1% (PM = 0.05%, PSS = 0.03%)**
- **Only 1 in 50 subjects with +ANA (≥1:80) in unscreened population would have SLE**
- **"Do not screen for ANAs in patients with non-specific symptoms, such as fatigue or myalgia, or in patients with fibromyalgia."**

Qaseem A, Alguire P, Dallas P, et al. Appropriate use of screening and diagnostic tests to foster high-value, cost-conscious care. Ann Intern Med. 156:147-9, 2012

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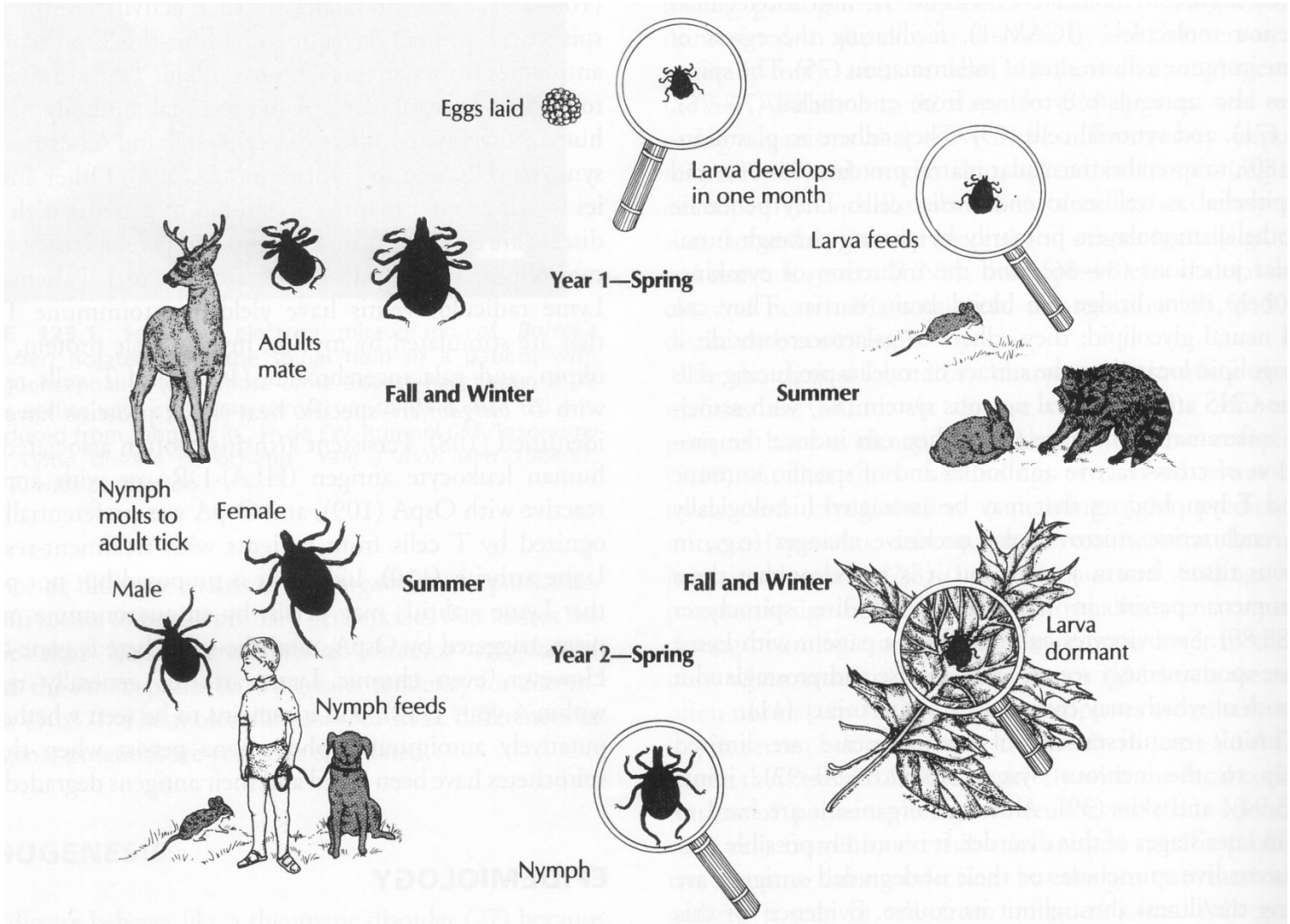
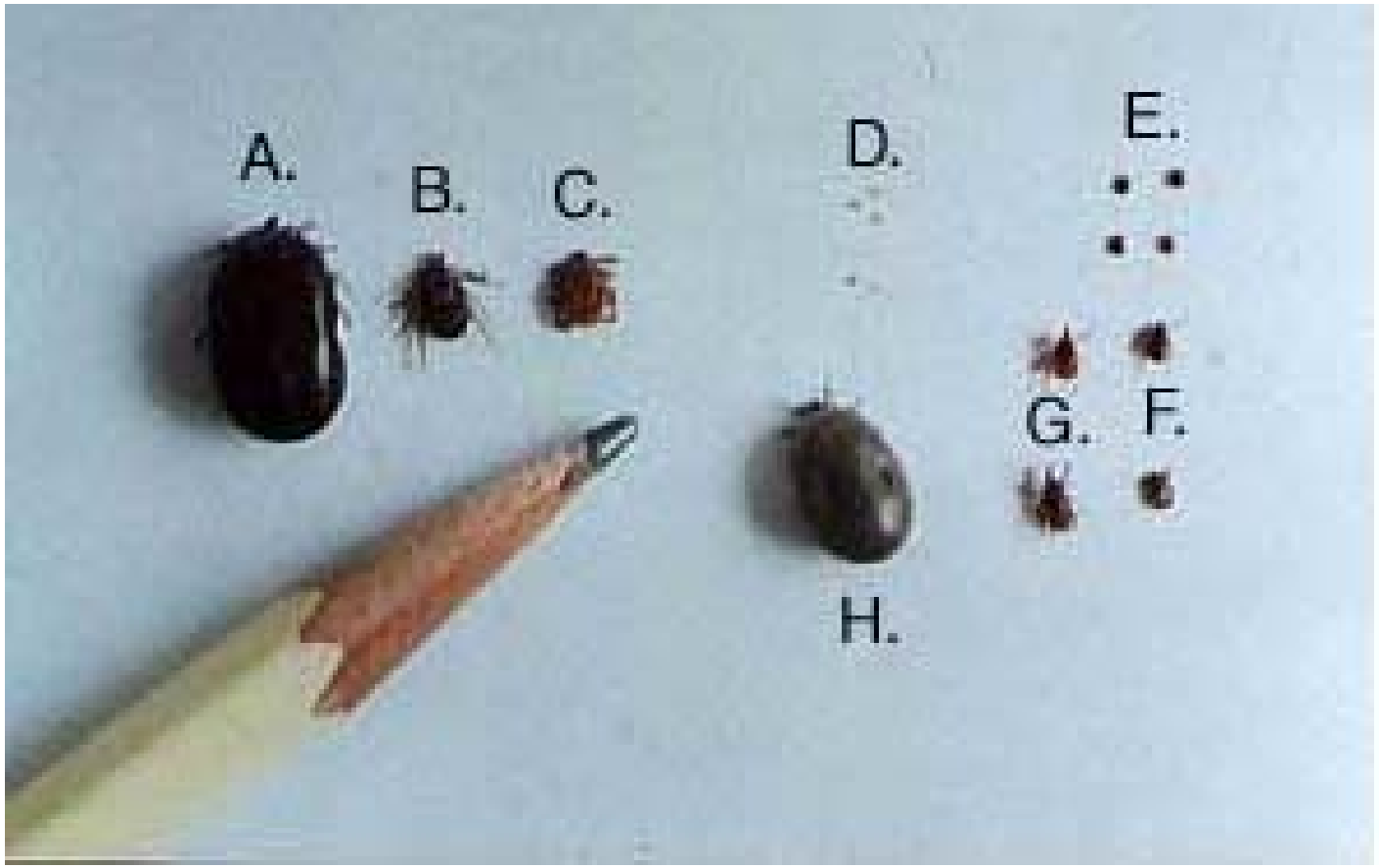
Don’t test for Lyme disease as a cause of musculoskeletal symptoms without an exposure history and appropriate exam findings.

Life Cycle of Ixodes scapularis



Dog Ticks **Deer Ticks**



STAGES OF LYME DISEASE

I
Early
1 – 3 weeks

- **Erythema Migrans**
- **Flu-like symptoms**

II
Early Dissem
3 – 5 weeks

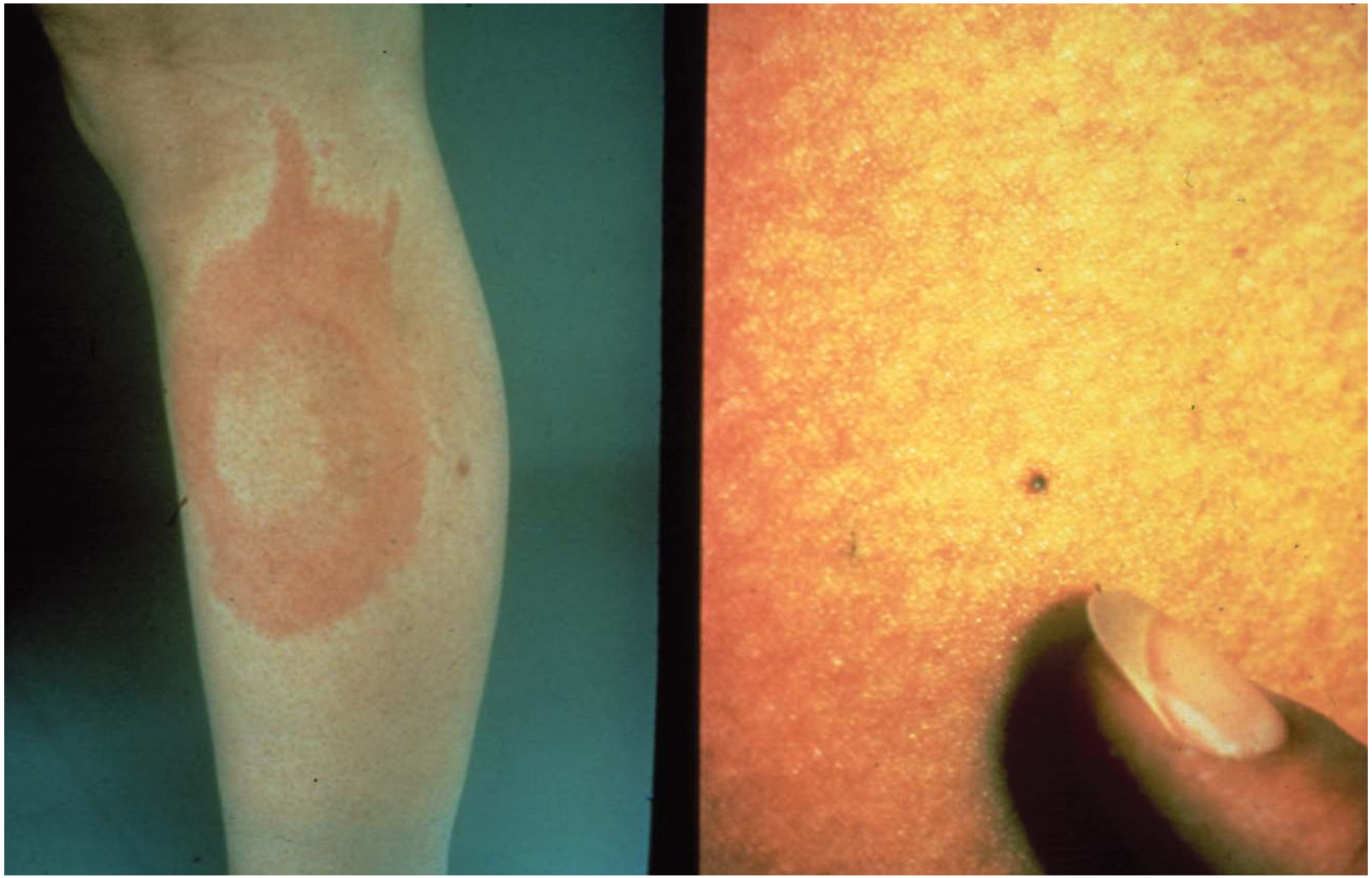
- **Multiple EM lesions**
- **Migratory arthritis**
- **Cardiac**
  - **AV block**
  - **Myocarditis**
- **Neurologic**
  - **Cranial neuropathy**
  - **Meningitis**

III
Late
2 months – years

- **Chronic meningo-encephalitis**
- **Sensorimotor neuropathies**
- **Intermittent or chronic oligoarthritis**

Embedded I. scapularis tick with local inflammatory reaction

Typical EM Lesion and Feeding Ixodes Nymph



EM Lesions in Lyme Disease

Spectrum of Atypical EM Lesions in LD

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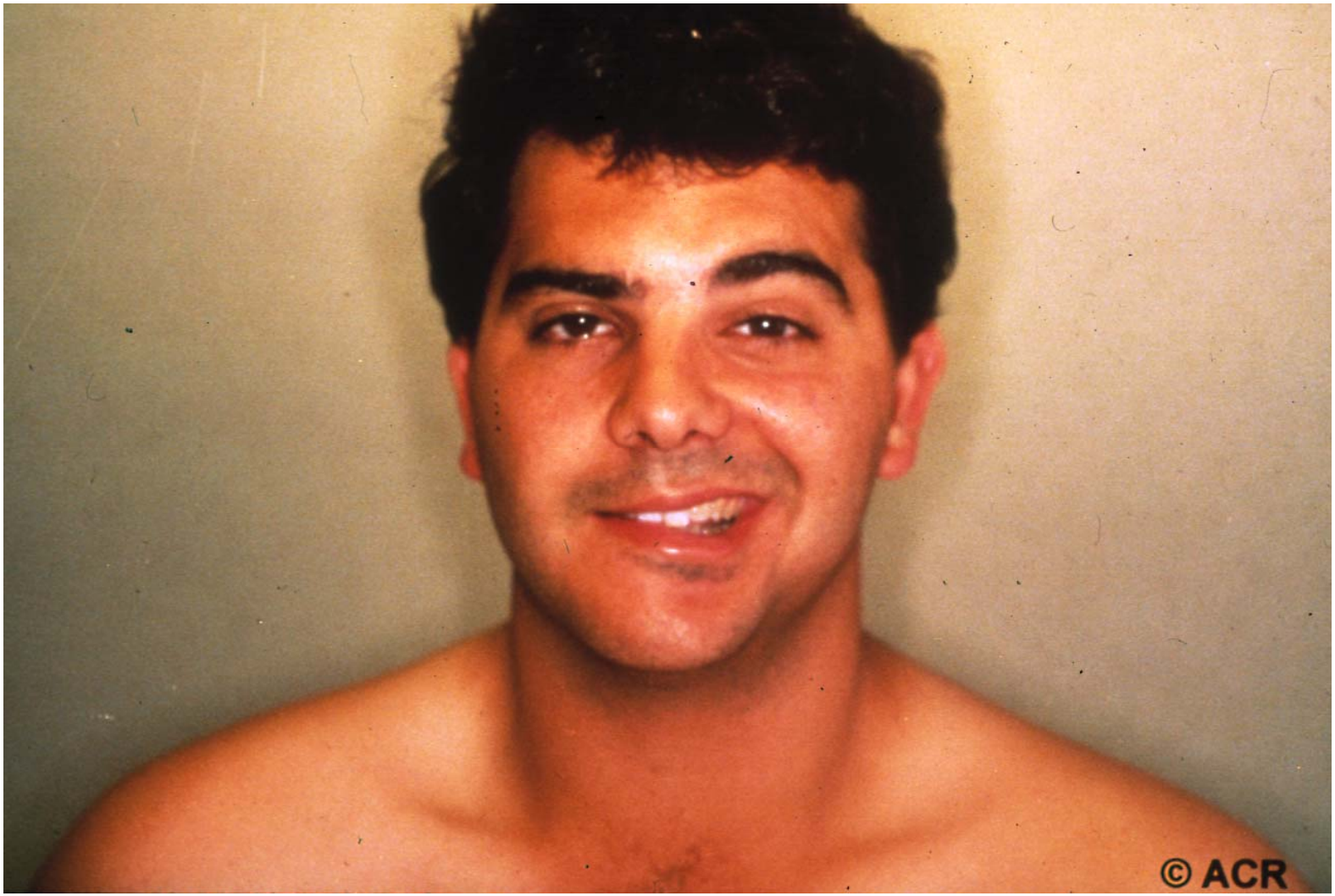
Late
2 months – years

- Chronic menigo-encephalitis
- Sensorimotor neuropathies
- Intermittent or chronic oligoarthritis

Satellite EM Lesions in Disseminated LD

Bell's Palsy in Early Disseminated LD



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  - **Meningitis**

III
Late
2 months – years

- **Chronic menigo-encephalitis**
- **Sensorimotor neuropathies**
- **Intermittent or chronic oligoarthritis (<10% of EM patients)**

Persistent Lyme Disease

- **Late Neuroborreliosis**
  - mild encephalopathy
  - memory/concentration deficits
  - antibiotic responsive
- **Post-Treatment Lyme Disease Syndrome (PTLDS)**
  - persistent non-specific complaints
  - antibiotic non-responsive
- **Lyme Anxiety**
  - common problem in endemic areas
  - occurs in both naïve and infected persons

Laboratory Assessment of LD

- **Biopsy culture: only definitive diagnosis**

  Early - marginal EM lesion on BSK2 medium

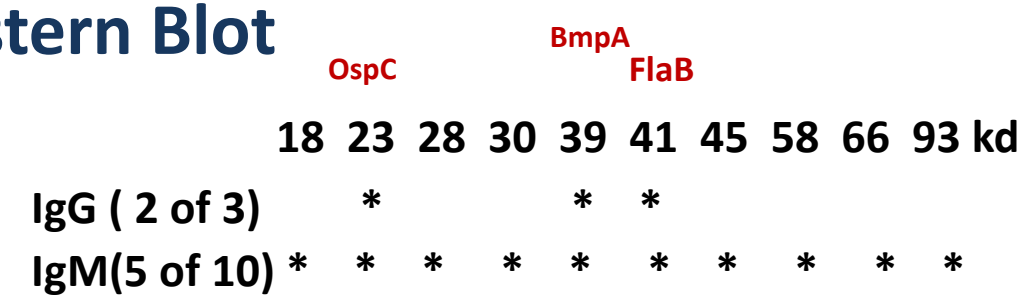
  Late - PCR is better

- **Serodiagnosis testing: 2-step (ELISA/WB)**

  Early (1-3 wks) IgM only , 20-30% +

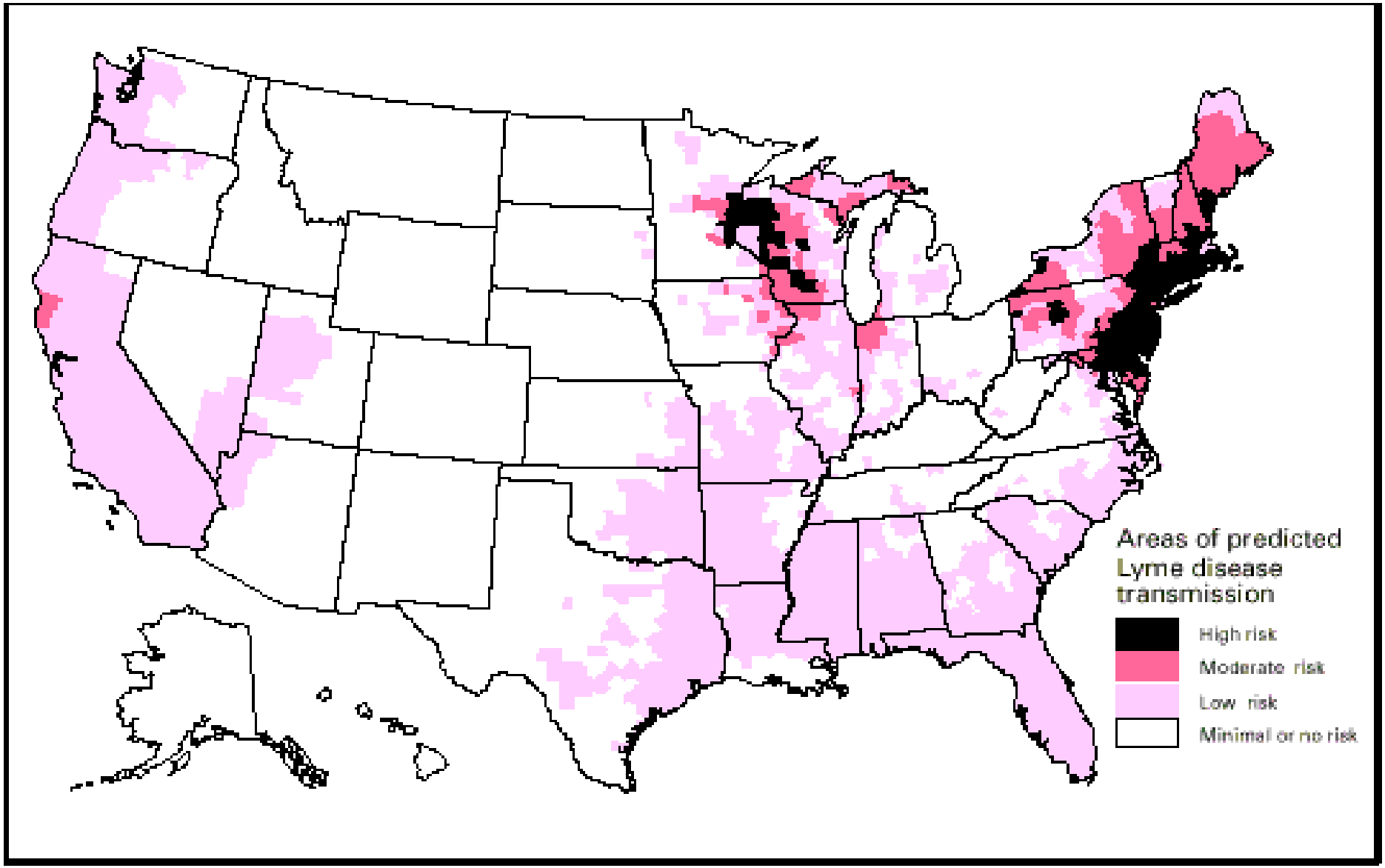
  Convalescent (4-8 wks) IgG +/- IgM , >80% +

- **Western Blot**

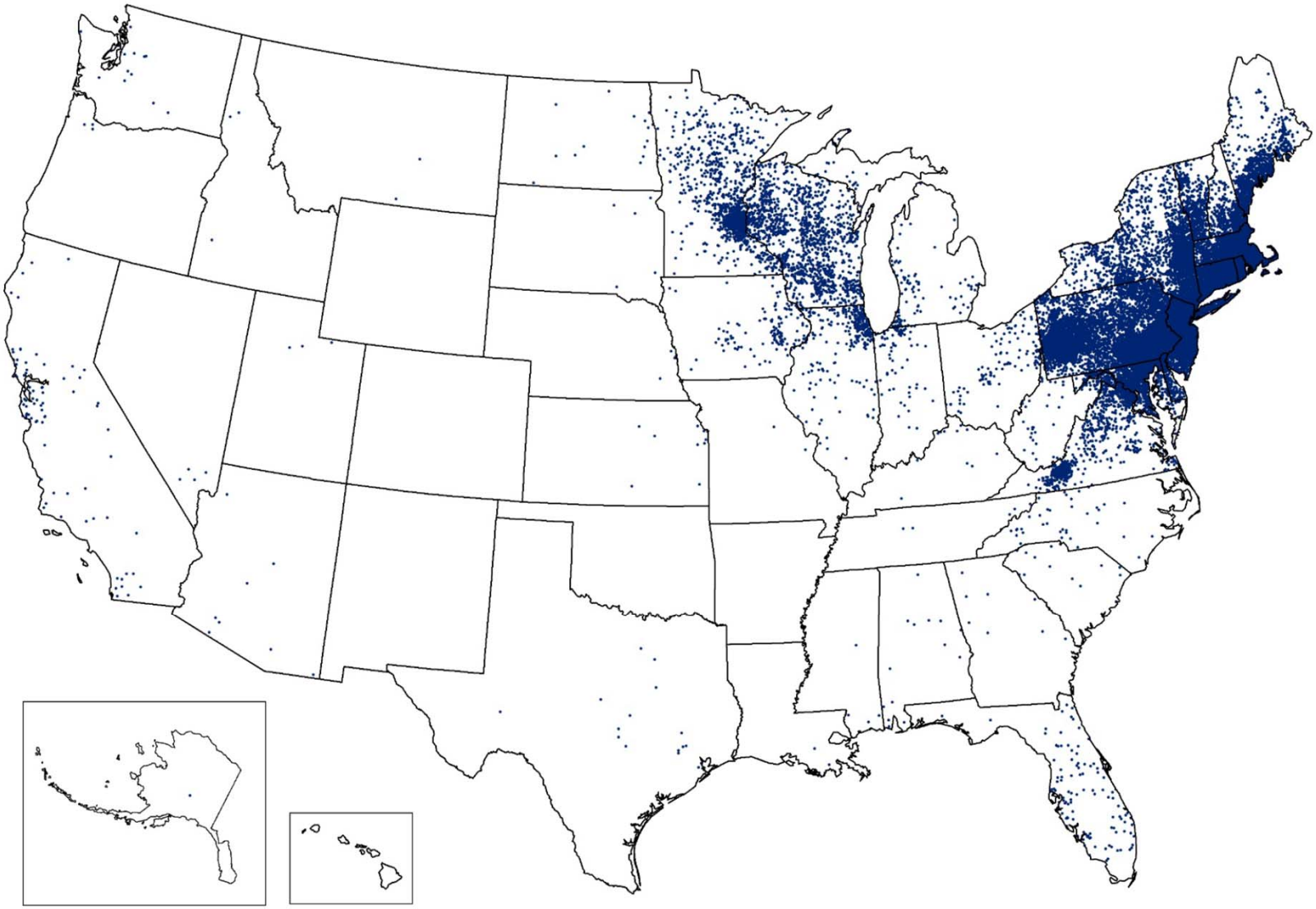


Treatment of Lyme Disease

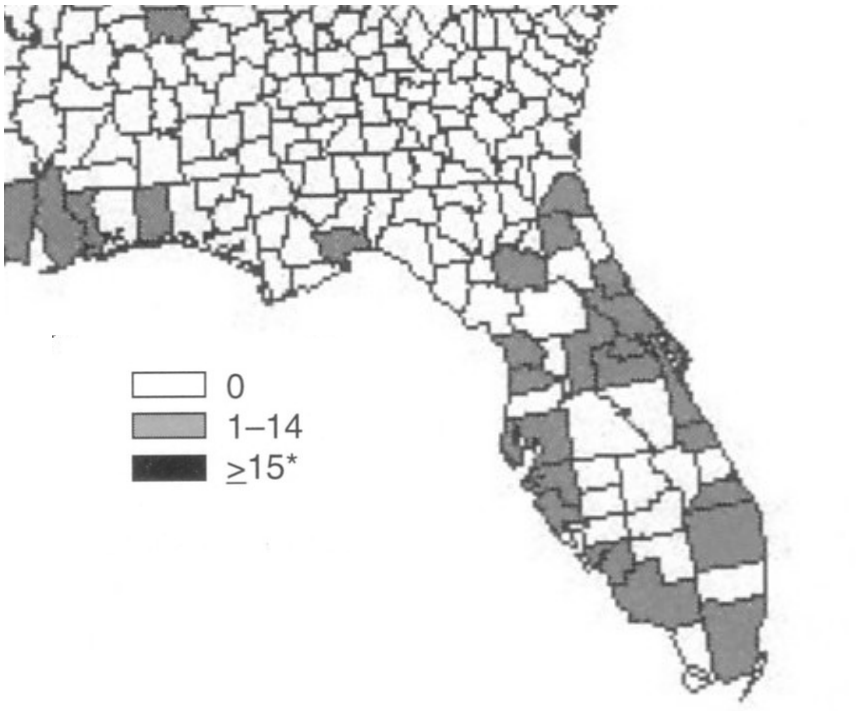
	I Early	II Early Dissem	III Late
Post exposure	1-3 weeks	3-5 weeks	1+ months
First Line	▪**Doxycycline 100 mg po q 12h X 14-21 days**	▪**Ceftriaxone 2gm IV daily X 14-28 d** ▪**Cefotaxime 2gm IV q8h X 14-28d** ▪**Doxycycline 100mg po TID X 30d**	▪**Ceftriaxone 2gm IV daily X 14-28d**
Alternate	▪**Amoxicillin 500mg po q8h X 14-21d** ▪**Cefuroxime 500mg po q12h X 14-21d**	**Oral regimine adequate for facial palsy, AV block or arthritis alone**	** **Avoid Doxycycline in pregnancy**


Areas of predicted
Lyme disease
transmission
High risk
Moderate risk
Low risk
Minimal or no risk

CDC Surveillance of Incident Lyme Disease - 2015



Confirmed Lyme Cases in Florida - 2014



63 confirmed cases

17 locally acquired

24/67 counties +

- Palm Beach 12/3
- Pinellas 15/6
- Hillsborough 8/3
- Volusia 5/2
- Orange 6/1

CDC Confirmed Cases of LD in Florida 2010 - 2015

- **Average # cases per year : 67***
  - 77% acquired in endemic areas
  - 23% acquired in FL
- **Peak incidence in July**
- **Demographics**
  - Average age 42 (1-87)
  - 87% white

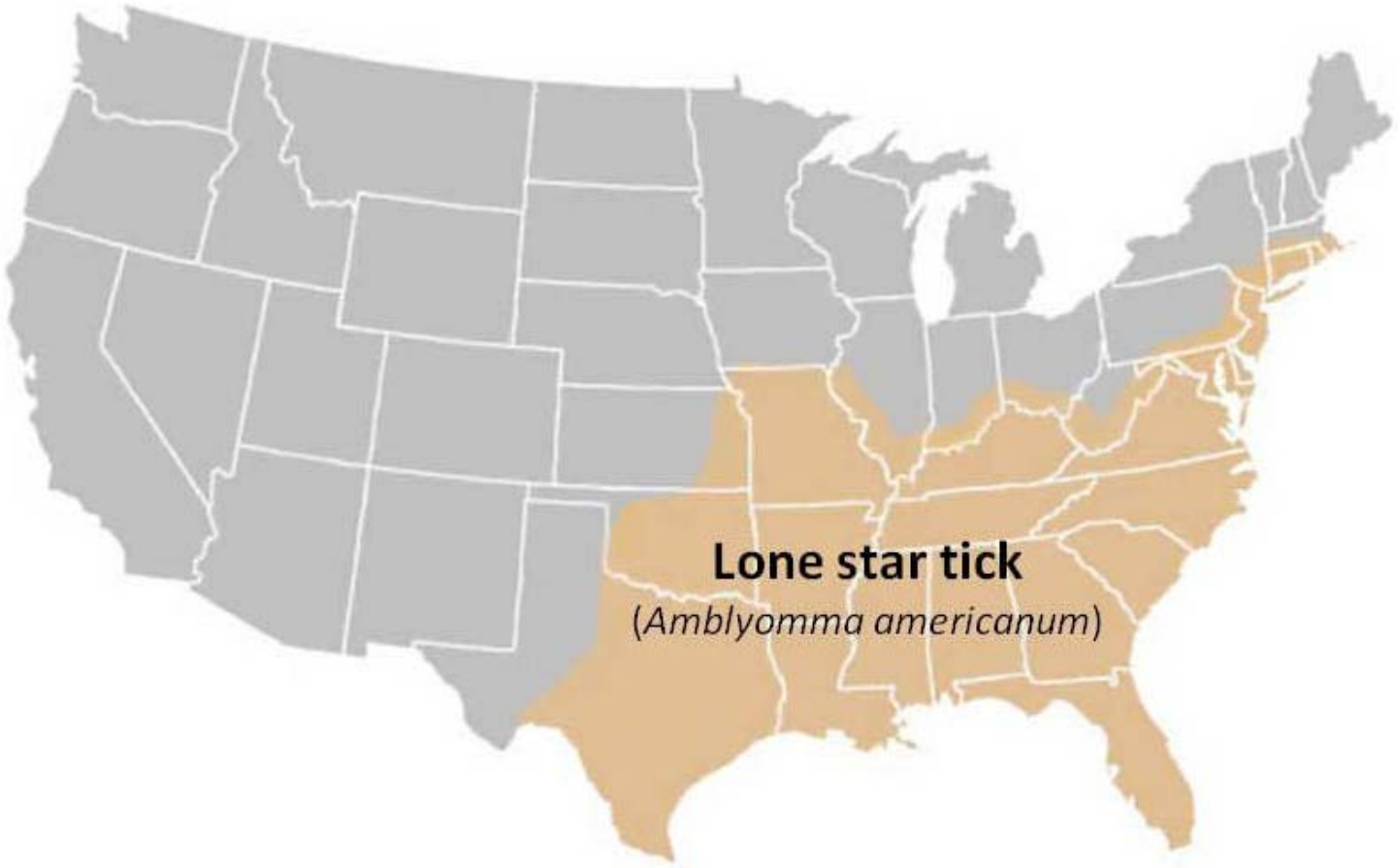
* 16,000 reported cases in US/yr

Southern Tick-Acquired Rash Illness

STARI

Lyme Disease vs EM-Like Disorder

	Lyme Disease	STARI
Etiol Agent	*B. burgdorferi*	*? B. lonestari*
Tick Vector	I. scapularis I. pacificus	Ambylomma ameicanum
Geography	NE, NC, far west	SE, SC
Rash (EM)	+ (non-pruritic)	+ (pruritic)
Cardiac/Neurol	+	?
Arthritis	+	?
B. burgdorferi ELISA	+	+
B. burgdorferi immunoblot	+	-
B. burgdorferi culture	50 – 80%	0%


Lone star tick
(Amblyomma americanum)

STARI Rash

Other Human Tick-Borne Diseases

	Babesiosis	Ehrlichiosis	RMSF
Agent	*Babesia microti* (protozoa)	*Ehrlichia sp.* (richettsia-like)	*R. richettsii*
Vector	**Ixodes**	**Ixodes** **Dermacentor** **Ambylomma**	**Dermacentor (Amblyomma)**
Signs and symptom	**Malaria-like illness, fever, chills, fatigue , headache. Occ fatal in elderly, asplenic & immunodeficient**	**Fever, HA, myalgia, N/V, pneumonitis, decr. WBC, ataxia, seizure, meningitis. Death if untreated.**	**Flu-like illness, high fever, photo-sensitive. Measles-like rash**

Others: Relaping fever, Colorado tick fever, Tick paralysis, and Tularemia

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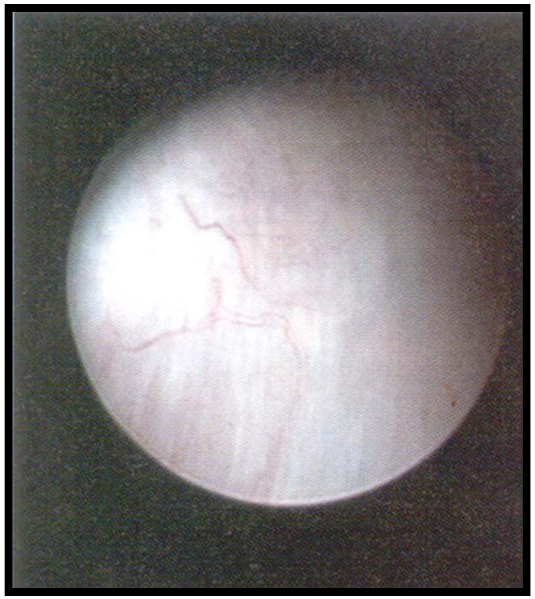
Don’t perform MRI of the peripheral joints to routinely monitor inflammatory arthritis.

MCP, PIP and Wrist Involvement in RA

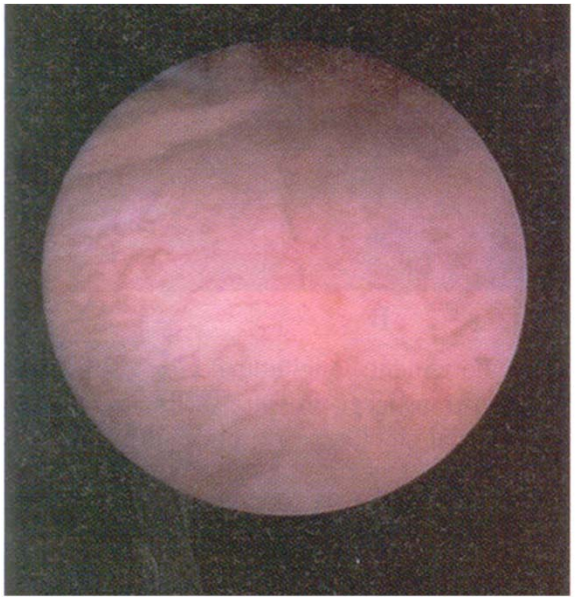
EARLY

ADVANCED

Arthroscopic Progression of Synovitis



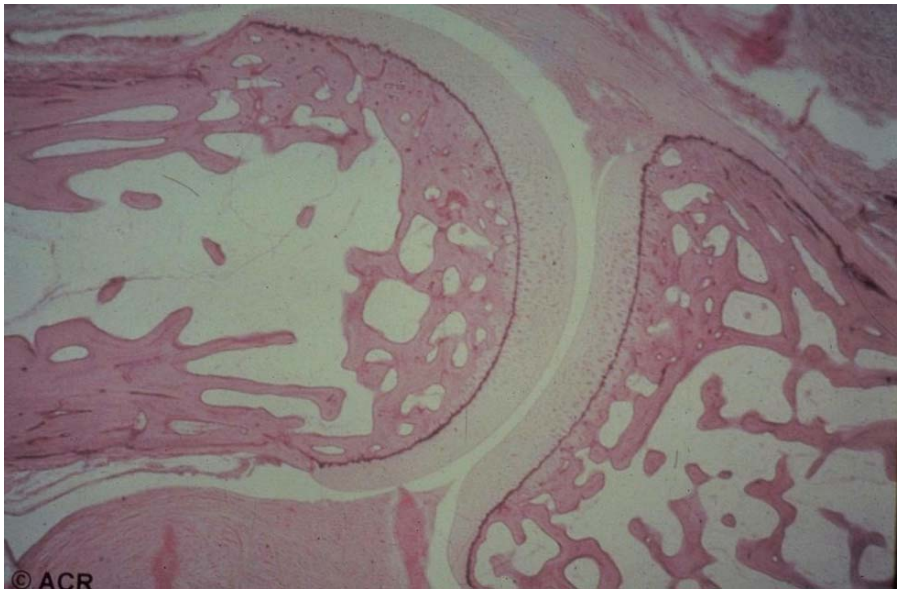
Normal Synovium



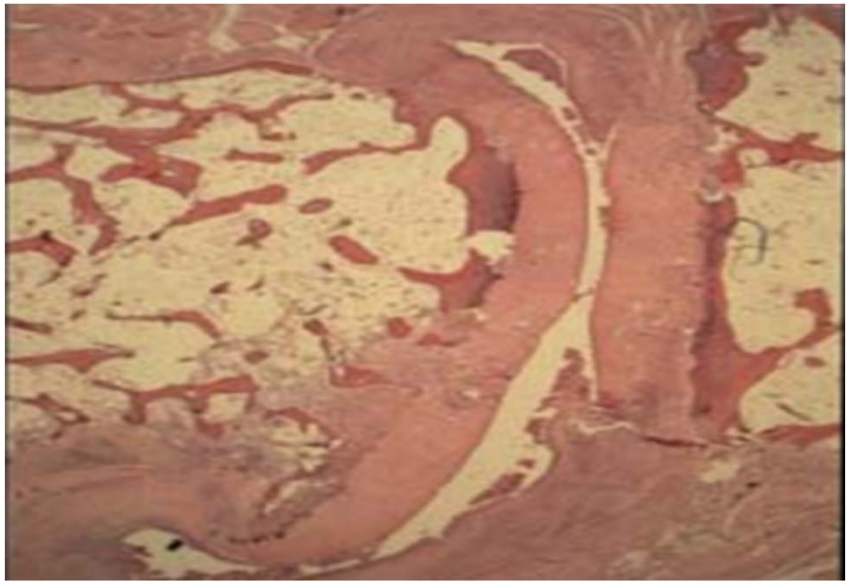
RA at 4 Months

RA at 16 Months

Sagittal View of Diarthrodial Joint

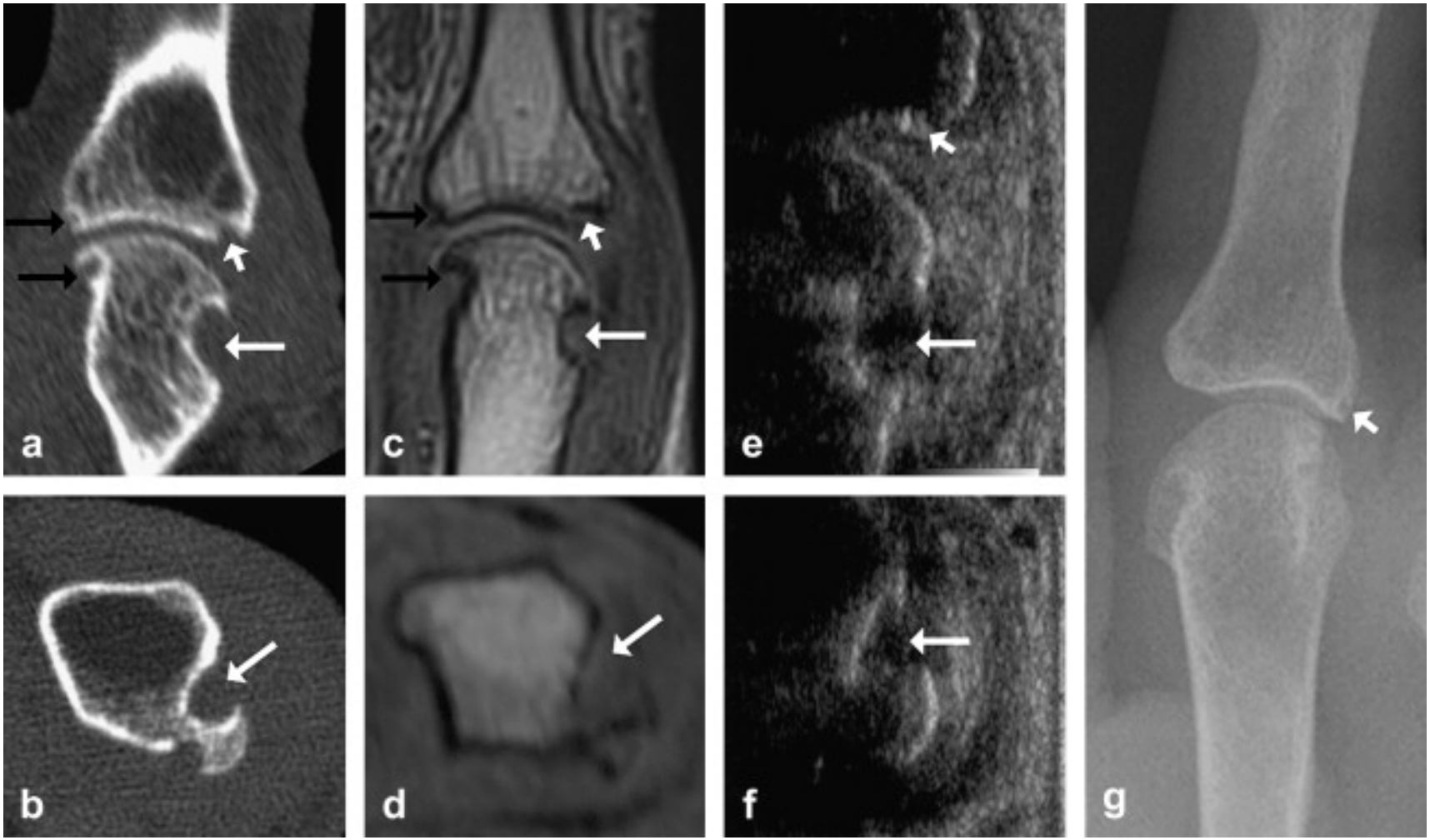


Normal Joint



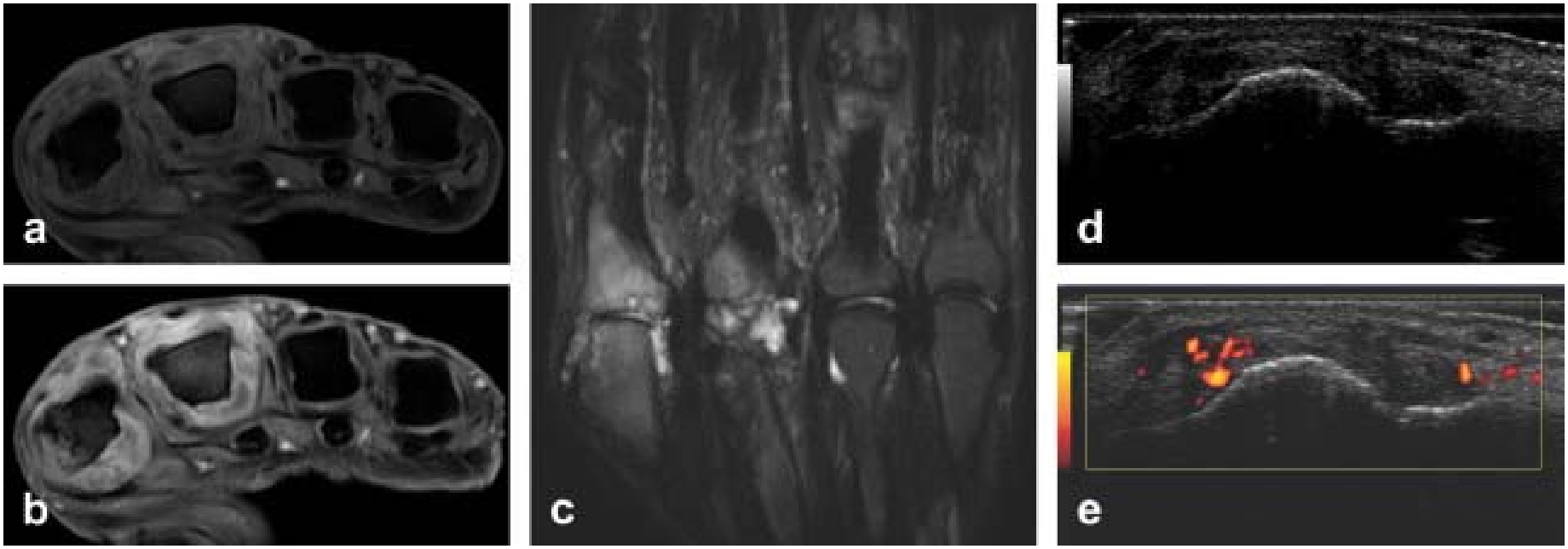
Rheumatoid Arthritis

Assessment of RA bony erosions in 2nd MCP by CT (a,b), MRI (c,d), US (e,f) and plain radiograph



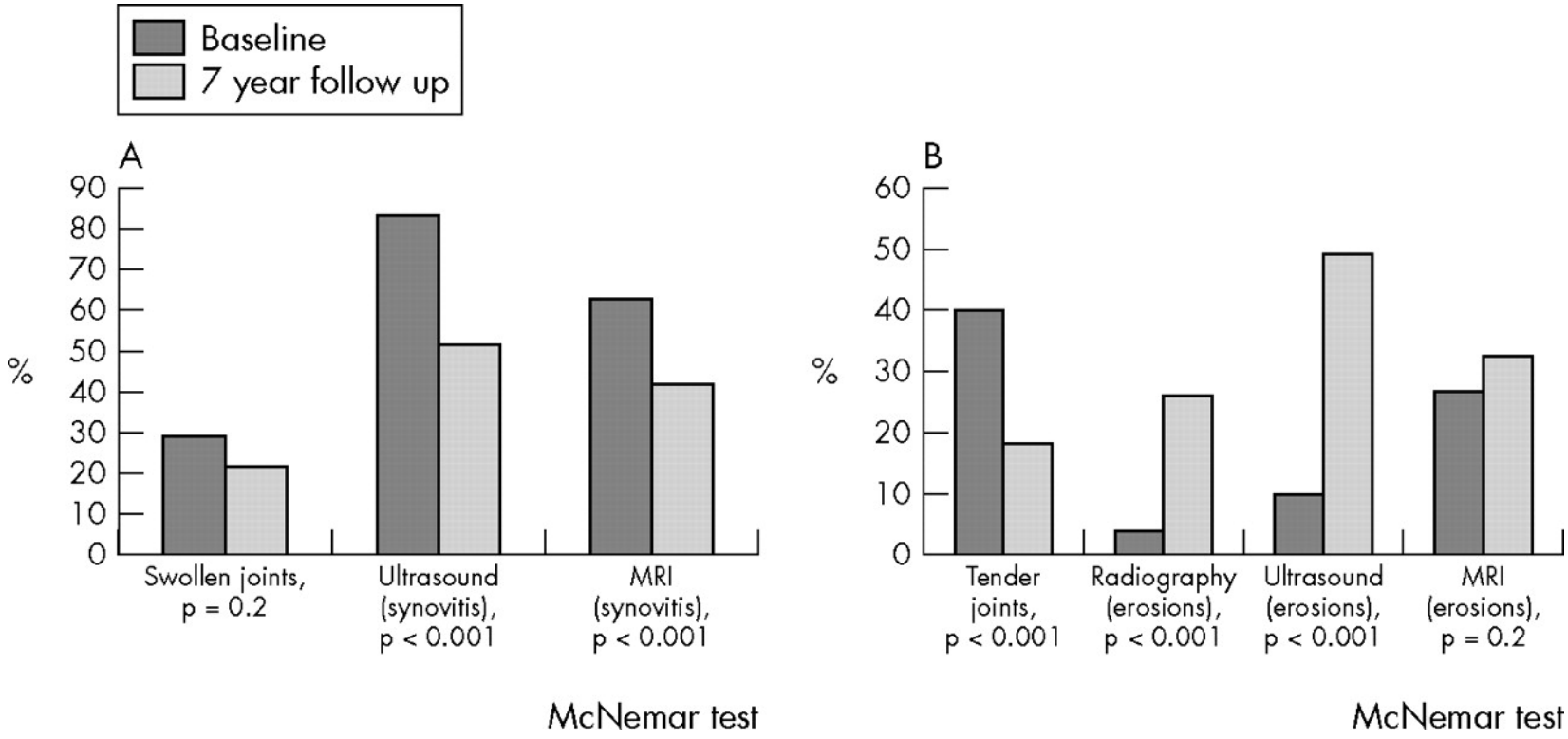
Mikkel Østergaard , Susanne Juhl Pedersen , Uffe Møller Døhn ; Research Clinical Rheumatology, Volume 22, Issue 6, 2008, 1019 - 1044

Assessment of inflammation in RA by MRI (a, b-gadolinium, c-STIR) and US (a-gray scale, b-power Doppler)



Mikkel Østergaard , Susanne Juhl Pedersen , Uffe Møller Døhn ; Research Clinical Rheumatology, Volume 22, Issue 6, 2008, 1019 - 1044

(A) Detection of soft tissue lesions (synovitis/effusion) by CE, US, and MRI in 128 finger joints.



A K Scheel et al. Ann Rheum Dis 2006;65:595-600

ARD

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Don’t prescribe biologics for rheumatoid arthritis before a trial of methotrexate (or other conventional non-biologic DMARDs)

Rheumatoid Arthritis: Scope of the Problem

- **1,293,000 Americans ages 18 and older have rheumatoid arthritis**
- **Across most developed countries the incidence is similar, at approximately 0.5% to 1% of adults**

Reference: Helmick C, et al "Estimates of the prevalence of arthritis and other rheumatic conditions in the United States" *Arthritis Rheum* 2008; 58: 15-25.

The Methotrexate Era

- **Before the mid 1980s treatment of active RA consisted primarily of gold or penicillamine**
- **RA is frequently severe and debilitating; the side effects of DMARDs were problematic**
- **In 1988 methotrexate was approved for use in RA which was a quantum leap forward**
- **Methotrexate remains the cornerstone of therapy of RA today**

The Tumor Necrosis Factor (TNF) Era

- **The first biologic for RA, etanercept (Enbrel), was approved in the U.S. in 1998**
- **There are now six TNF inhibitors on the market**
- **The TNF inhibitors were a significant addition to our armamentarium which has led to dramatic improvements in patient outcomes**

2012 ACR Recommendations for use of biologics in RA with pre-existing co-morbidities

Comorbidity/clinical circumstance	Recommended	Not Recommended
Hepatitis		
Hepatitis C	*Etanercept*	
Untreated Chronic Hep B		*Any biologic agent*
Malignancy		
Treated solid malignancy >5 yrs ago	*Any biologic agent*	
Treated solid malignancy within 5 yrs	*Rituximab*	
Treated skin melanoma	*Rituximab*	
Treated lymphoproliferative malignancy	*Rituximab*	
Congestive Heart Failure		
NYHA class II/IV and EF < 50%		*Anti-TNF biologic*

Singh JA, et al. Arth Care Res. 64;625-639, 2012

ACR Recommendations for Vaccines use in RA

	Killed vaccines			*Recombinant vaccines*	*Live attenuated*
	Pneumo-coccal	**Influenza - intramuscular**	**Hepatitis B**	**Human Papillomavirus**	**Herpes zoster**
Before initiating therapy					
DMARD monotherapy	√	√	√	√	√
DMARD combination	√	√	√	√	√
Anti-TNF biologic	√	√	√	√	√
Non-TNF biologic	√	√	√	√	√
While already taking therapy					
DMARD monotherapy	√	√	√	√	√
DMARD combination	√	√	√	√	√
Anti-TNF biologic	√	√	√	√	**Not Recommended**
Non-TNF biologic	√	√	√	√	**Not Recommended**

Singh JA, et al. Arth Care Res 64; 625-639,2012

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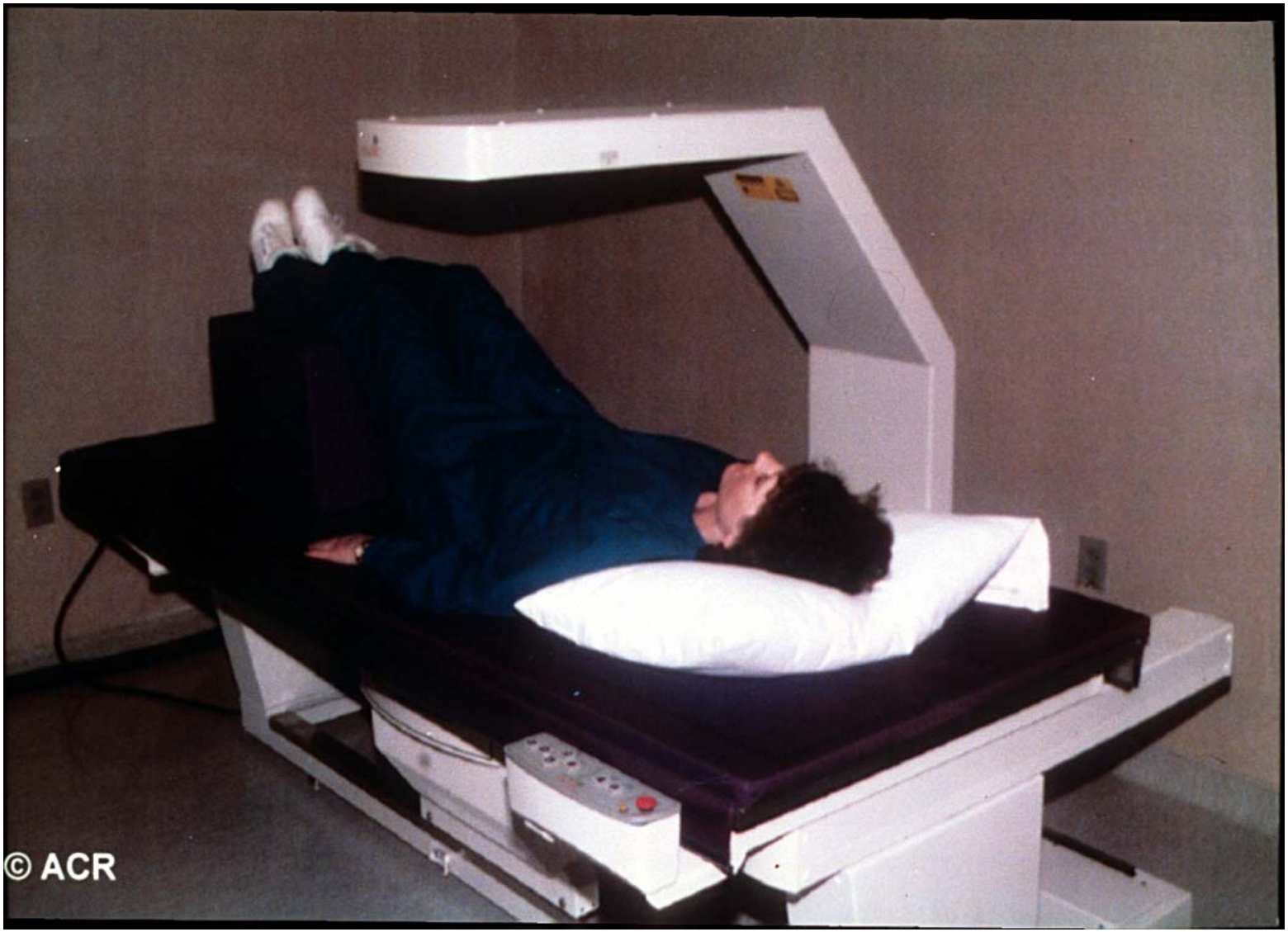
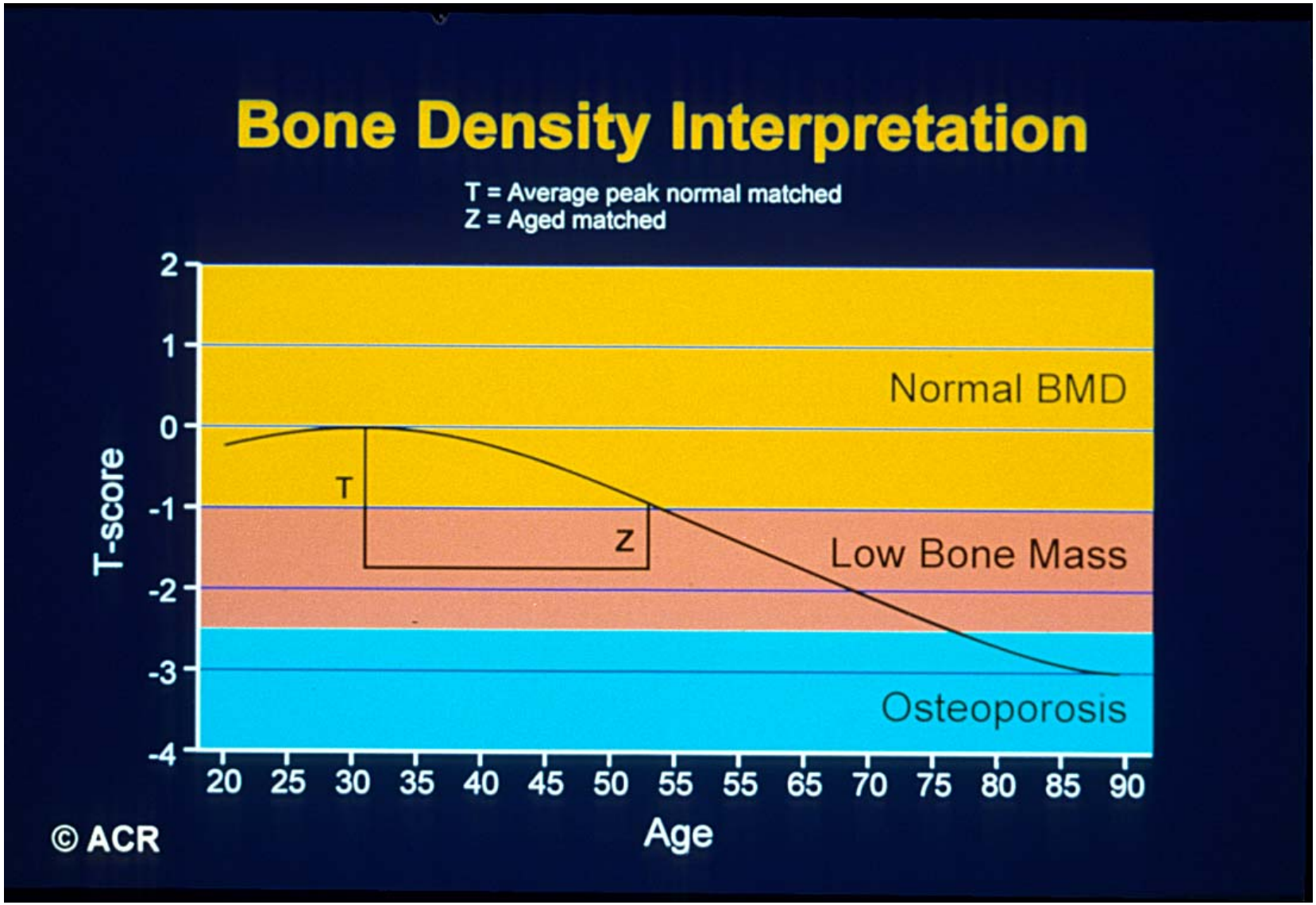
Don’t routinely repeat DXA scans more often than once every two years


© ACR


Bone Density Interpretation
T = Average peak normal matched
Z = Aged matched
T-score
2
1
0
-1
-2
-3
-4
Normal BMD
Low Bone Mass
Osteoporosis
T
Z
20 25 30 35 40 45 50 55 55 65 70 75 80 85 90
Age
© ACR

- **DXA remains the standard for measuring BMD**
  - **Under-utilized in many populations (family hx, tobacco abuse, glucocorticoid use)**
  - **Over-utilized in office practices with DXA scanner**
- **DXA helps in clinical decision making**
  - **2008 National Osteoporosis Foundation Clinician's Guide treatment eligibility based on:**
    - **Prior spine/hip fracture, or**
    - **BMD T-score ≤ -2.5, or**
    - **BMD T-score -1 to -2.5 plus a ≥3% hip fx or ≥20% other major fx 10 year risk by WHO's FRAX prediction**
- **Changes in bone density over short periods (<2 years) are usually below detection by most DXA.**
- **Treatment may decrease fracture risk even when no apparent BMD change**

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Summary

- Have a real clinical suspicion of an auto-immune disease when ordering an ANA.
- Test for Lyme Disease only in patients with a good history of exposure and appropriate exam findings.
- Don’t use expensive imagining studies if they won’t change management.
- Observe the recommended treatment algorithms for RA.
- Frequent BMD testing (e.g. <2 years) is unnecessary in most patients.
- Promote fair distribution of health care resources through high value care.

Which of the following tick-borne disease is transmitted by the same tick vector as Lyme Disease?

A. Tick-borne Relapsing Fever (TBRF)
B. Rocky Mountain Spotted Fever (RMSF)
C. Southern Tick-Acquired Rash Illness (STARI)
D. Erhlichiosis
E. Colorado Tick Fever (aka, American Tick Fever)

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E. Colorado Tick Fever (aka, American Tick Fever)

Tick vectors for above diseases: TBRF/ornithodoros (soft tick); RMSF/dermacentor; STARI/ambylomma; Erhlichiosis/Ixodes; Colorado Tick Fever/dermacentor