Diagnosis and Treatment of Common Rheumatology Conditions

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Disclosures

Declaration Statement: I have relevant relationships with ineligible companies to disclose within the past 24 months. (Note: Ineligible companies are defined as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.)

- Abbvie: Speaker
- Amgen: Speaker
- Novartis: Consultant

*All of the relevant financial relationships listed for this individual have been mitigated.

Learning Objectives

At the conclusion of this session, participants should be able to:

1.) Discuss diagnostic approaches and treatment options for common rheumatic conditions encountered in primary care: RA, PsA, AS, Lupus

2.) Explain the 2021 ACR Treatment Guidelines for Rheumatoid Arthritis

3.) Identify evaluation strategies and treatment guidelines for patients with osteoporosis

RHEUMATIC DISEASES

Prevalence

- **Rheumatoid arthritis** – 1.3 million U.S. adults[3]
- **Juvenile arthritis** – 294,000 people in the U.S.[3]
- **Spondylarthritides** – 0.6 to 2.4 million U.S. adults over 15[3]
- **Systemic lupus erythematosus** – 161,000 to 322,000 U.S. adults[3]
- **Systemic sclerosis** – 49,000 U.S. adults[3]
- **Sjögren's syndrome** – 0.4 to 3.1 million adults [3]
- **Clinical osteoarthritis** – 27 million U.S. people age 25 and older[4]
- **Polymyalgia rheumatica** – 711,000 people in the U.S.[4]
- **Giant cell arteritis** – 228,000 people in the U.S.[4]
- **Gout** – 8 million people in the U.S.[4]
- **Fibromyalgia** – 5 million people in the U.S.[4]
- **Low back pain**– 59 million within the three months prior to the study[4]
- **Neck pain** – 30.1 million within the three months prior to the study[4]

[3] Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States- Part I. Arthritis & Rheum. 2008: 58(1):15-25.
[4] Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States- Part II. Arthritis & Rheum. 2008: 58(1):26-35.

Rheumatoid Arthritis

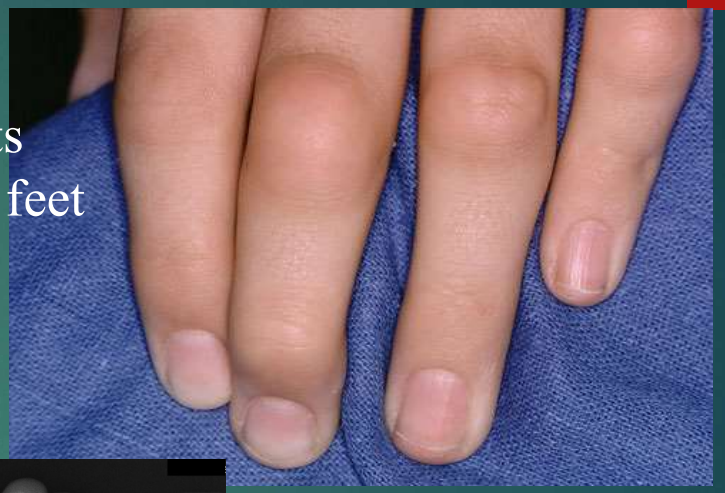
RA = chronic, systemic, autoimmune disease that causes pain, stiffness, swelling and limited motion and function of many joints. While RA can affect any joint, the small joints in the hands and feet tend to be involved most often. Inflammation sometimes can affect organs as well, for instance, the eyes or lungs.

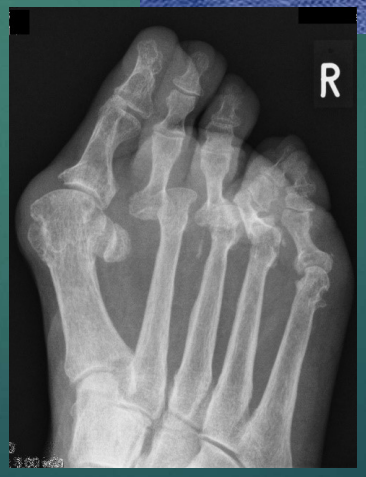
Facts

- About 1.3 million Americans suffer from RA
- Most common autoimmune arthritis*
- About 75% of RA patients are women
- Often diagnosed in middle-age
- Associated with high disability rate
- Cause??? Genetics? Environmental factors?

Signs and Symptoms

- Swollen, tender, erythematous joints
  - Often small joints of hands and feet
- Symmetric joint involvement
  - (often migratory)
- Decreased joint ROM
- AM joint stiffness > 1 hour
- Fatigue
- Anemia
- Fever
- Weight loss
- Depression





2010 ACR Rheumatoid Arthritis Classification Criteria

Score of ≥ 6 = Definite RA

Classification criteria	Score
Target population (Who should be tested?): Patients who have at least 1 joint with definite clinical synovitis (swelling)* with the synovitis not better explained by another disease†	
Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of ≥ 6/10 is needed for classification of a patient as having definite RA)‡	
A. Joint involvement§	
1 large joint	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)#	2
4-10 small joints (with or without involvement of large joints)	3
> 10 joints (at least 1 small joint)**	5
B. Serology (at least 1 test result is needed for classification)††	
Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)‡‡	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
D. Duration of symptoms§§	
< 6 weeks	0
> 6 weeks	1

Diagnosis

Labs:

- Rheumatoid Factor (RF) → positive in 80% of people who have RA
- ACPA/anti-CCP → much more specific for RA
    - often indicates risk of more severe disease
- ESR and CRP
- TSH, HLA-B27, ANA

- Seronegative RA: laboratory studies (RF and ACPA/CCP) negative but patient has evidence of rheumatoid arthritis on x-ray, MRI, or exam. Treatment is virtually the same as seropositive RA.

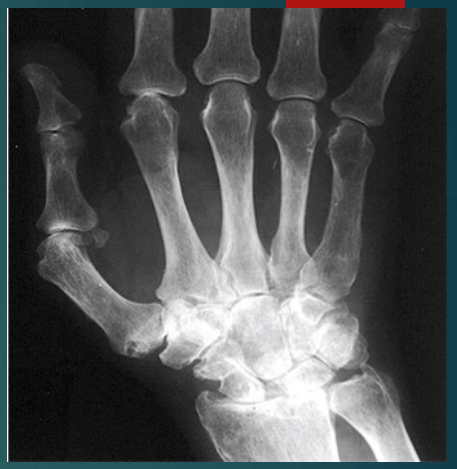
Imaging

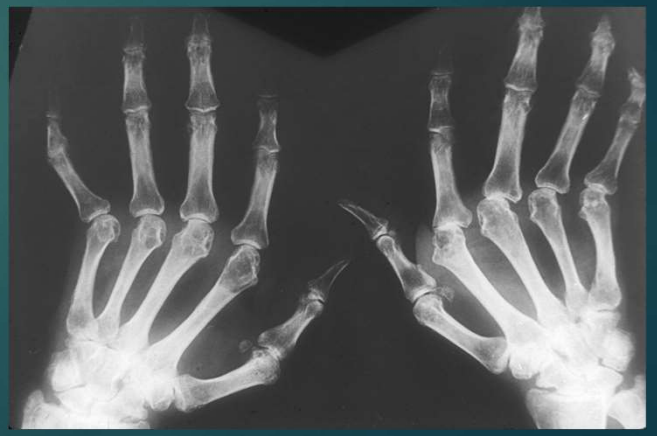
X-rays:

- Often normal in early disease
- Peri-articular osteopenia
- Marginal erosions

MRI:

- Often erosions are found that are not seen on x-ray
- Bone marrow edema
- Synovitis, capsulosynovitis
- Diffuse tendonitis





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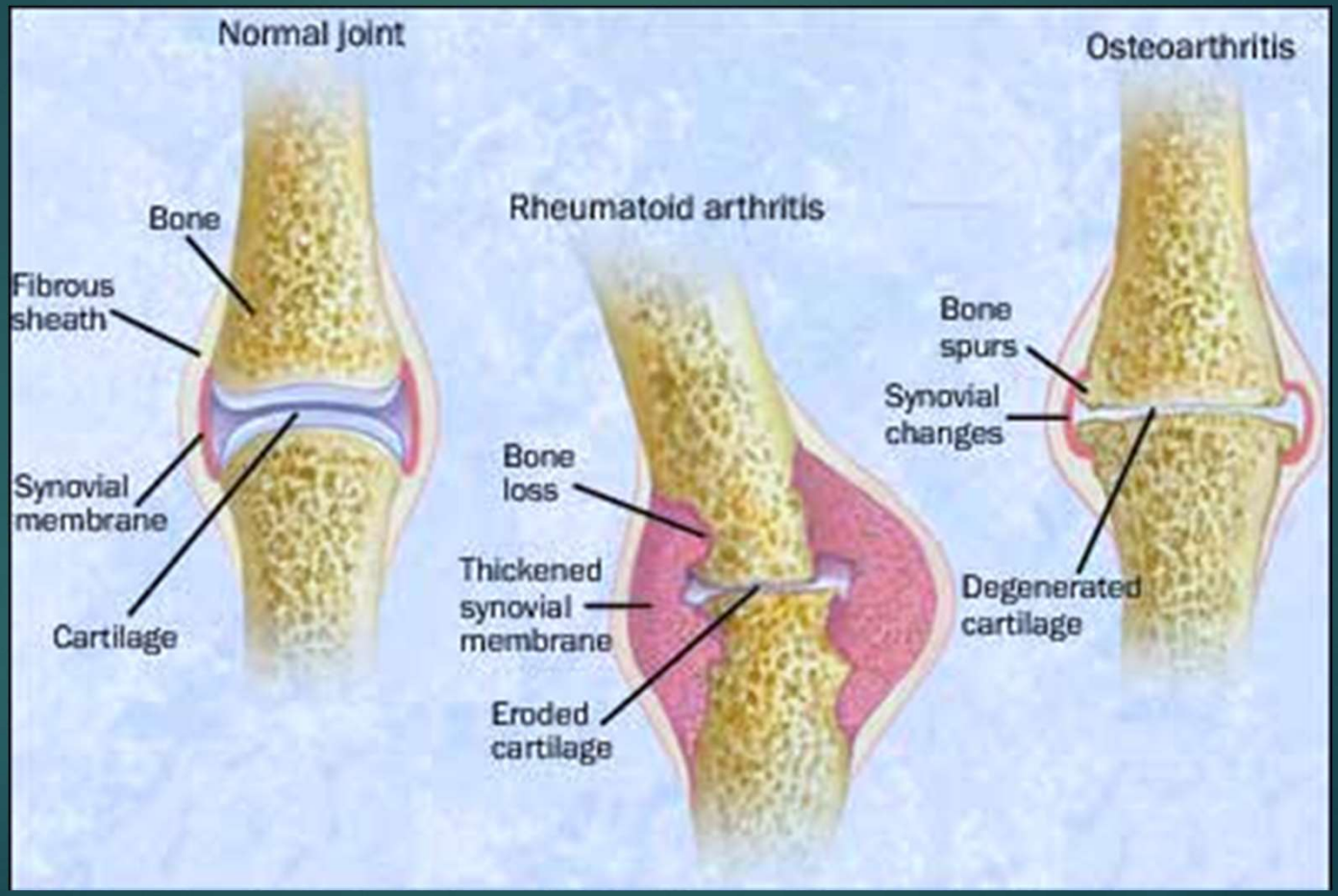
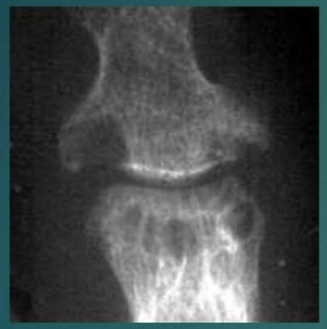
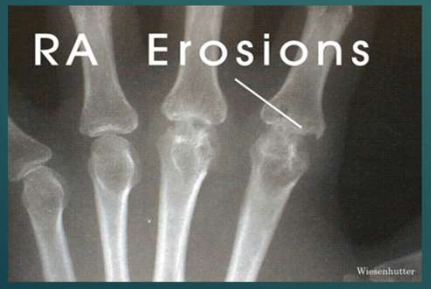
Rheumatoid Arthritis vs Osteoarthritis



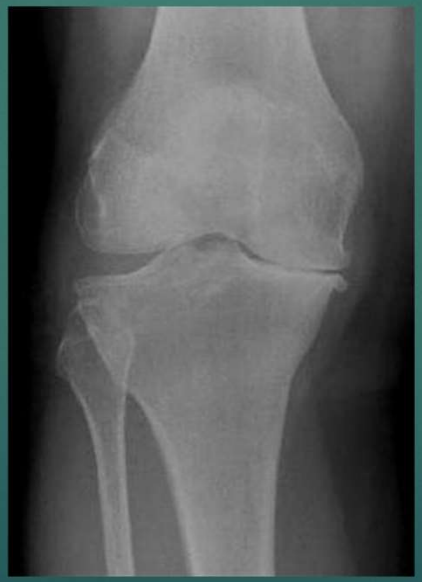
Rheumatoid Arthritis vs Osteoarthritis

Rheumatoid arthritis
MCPs, PIPs
Cervical spine – rarely
MTPs
Any joint

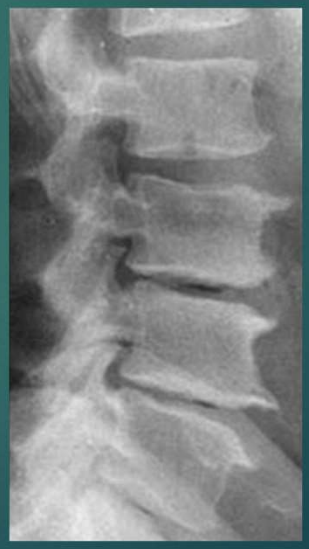


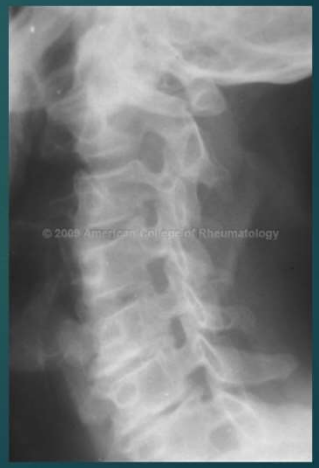


Osteoarthritis
CMCs, PIPs, DIP
Hips
Knees
1st MTP



Degenerative disc disease
Cervical spine
Thoracic spine
Lumbar spine





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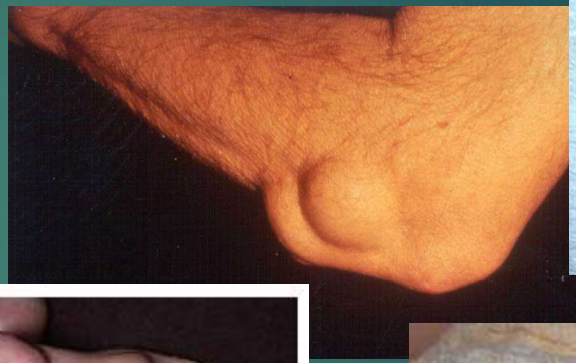
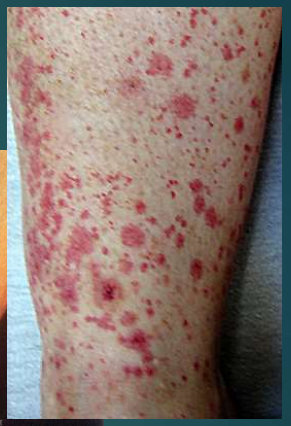
Synovial Fluid Analysis

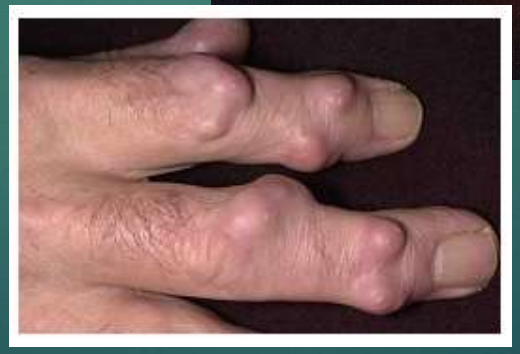
Condition	Appearance	WBC's/mm	% PMN's	Glucose: % Serum Level	Crystals Under Polarized Light
Normal	Clear	<200	<25	95-100	none
Non-inflammatory (e.g. DJD)	Clear	<400	<25	95-100	none
Acute Gout	Turbid	2000-5000	>75	80–100	negative birefringence; needle-like crystals
Pseudogout	Turbid	5000-50,000	>75	80-1000	positive birefringence; rhomboid crystals
Septic Arthritis	Purulent/turbid	>50,000	>75	<50	none
Inflammatory (e.g Rheumatoid arthritis)	Turbid	5000-50,000	50-75	approx 75	none

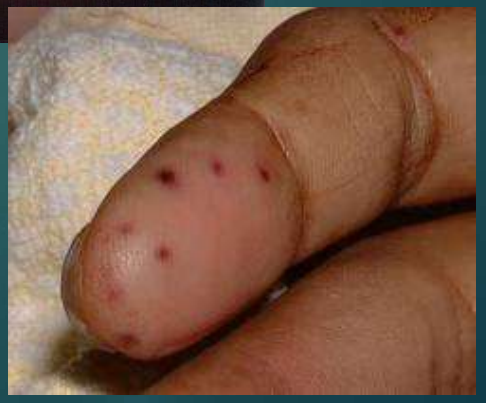
Extra-articular Complications of RA

- CVD - #1 cause of death in patients with RA
- Rheumatoid lung
- Rheumatoid nodules
- Osteoporosis
- Anemia of chronic disease
- Pleurisy/Pericarditis
- Increased infections
- Neuropathy
- Carpal tunnel syndrome
- Vasculitis
- C1/C2 subluxation









Rheumatoid Arthritis Treatment

Conventional DMARDs

	Hydroxychloroquine	Sulfasalazine	Methotrexate	Leflunomide	Azathioprine
Mechanism of Action	EXACT MECHANISM IS UNKNOWN				
Route (standard dosing)	Oral 400 mg daily	Oral 1000 mg bid	Oral or Parental 7.5mg-25mg weekly	Oral 20 mg daily	Oral 50-150 mg daily
Potential Risks	Retinal toxicity Photosensitivity	Hepatoxicity Hematological abnormalities Oligospermia	Hepatoxicity Pulmonary toxicity Hematological abnormalities Fetal toxicity	Hepatoxicity Pulmonary toxicity Hematological abnormalities Fetal toxicity	Pancreatitis AML Hematological abnormalitlies

Almost all above DMARDs have multiple possible side effects including but not limited to nausea, diarrhea, hair loss, headache, fatigue, increased risk of infection, hypersensitivity reactions, etc.

Rheumatoid Arthritis Treatment

Biologic Treatment

TNF inhibitor	T-Cell inhibitor	B-cell inhibitor	Il-6 inhibitor	Il-1 inhibitor
Injectable or Infusion	Injectable or Infusion	Infusion	Injectable or infusion	Injection
Adalimumab (Humira) Etanercept (Enbrel) Infliximab (Remicade) Golimumab (Simponi) Certolizumab (Cimzia)	Atabacept (Orencia)	Rituximab (Rituxan)	Tocilizumab (Actemra) Sarilumab (Kevzara)	Anakinra (Kineret)
Serious infections, Malignancies TB or Hepatitis B reactivation Worsening MS Worsening CHF Lupus-like syndrome	Serious infections Malignancies COPD worsening	Serious infections PML	Serious infections Malignancies ↑ Hepatoxicity cholesterol levels Bowel perforation	Serious infections Malignancies Hematological abnormalities

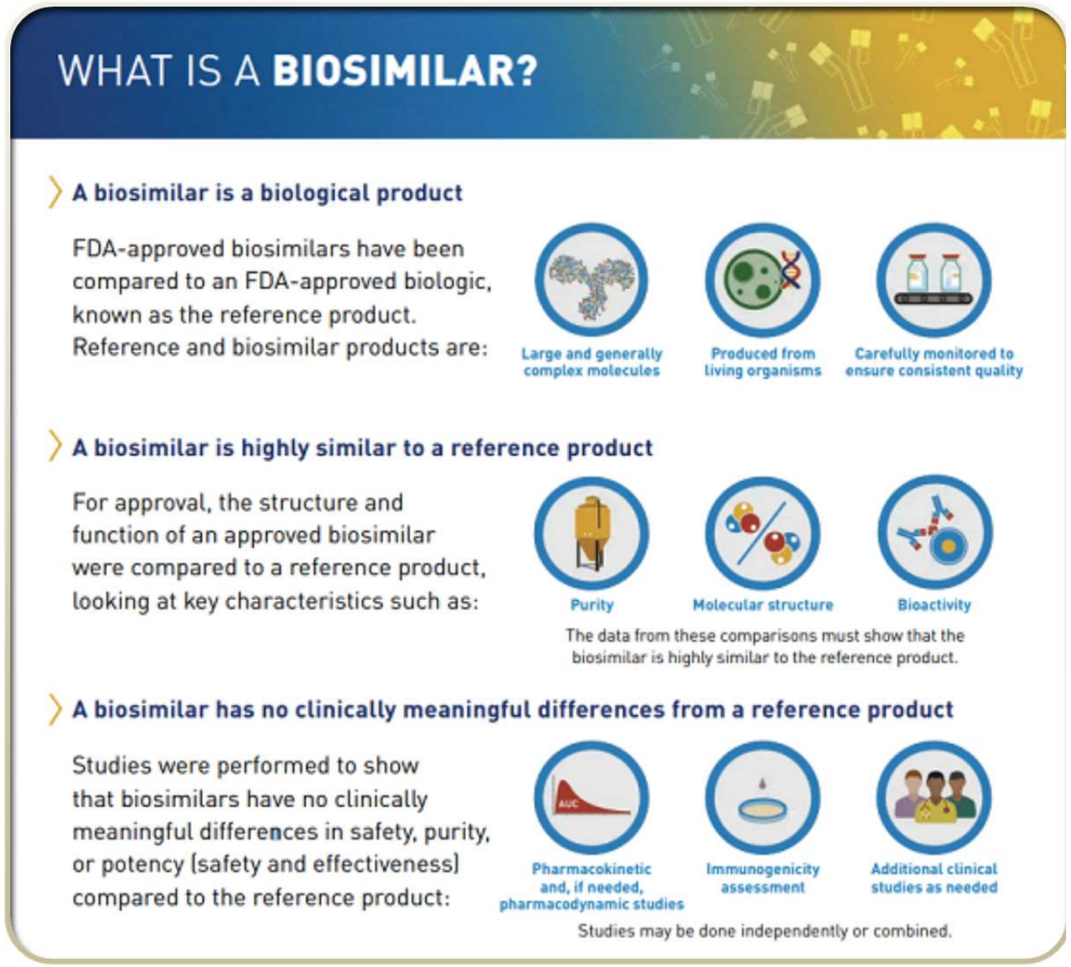
Self injections → possible injection site reactions Infusions → possible infusion reactions

Rheumatoid Arthritis Treatment

Targeted synthetic DMARDs

JAK inhibitor
Oral
Tofacitinib (Xeljanz) Baricitinib (Olumiant) Upadacitinib (Rinvoq)
Serious infections Malignancies Hepatoxicity Elevated cholesterol levels Bowel perforation Thrombosis New Black Box Warning*

Biosimilars



www.FDA.gov

Biosimilars in Rheumatology

(FDA Approved)

Reference Drug	Biosimilars
Infliximab (Remicade)	Avsola (infliximab-axxq) Inflectra (infliximab-dyyb) Renflexis (infliximab-abda)
Rituximab (Rituxan)	Truxima (rituximab-abbs) Ruxience (rituximab-pvvr) Riabni (rituximab-arrx)
Adalimumab (Humira) *all coming to market in 2023 in US	Hadlima (adalimumab-bwwd) Cyltezo (adalimumab-adbm) Amjevita (adalimumab-atto) Abrilada (adalimumab-afzb) Hulio (adalimumab-fkjp) Hyrimaz (adalimumab-adaz) Yusimry (adalimumab-aqvh)

Many other biosimilars approved and used in other countries – patent disrupts in the US prohibit biosimilar companies from marketing and using in the US.

Rheumatoid Arthritis Treatment

Symptom relief

- NSAIDs
  - OTC (Aleve, Advil) vs. Prescriptive (many)
  - Possible side effects: Ulcers, renal damage, fluid retention, prolonged bleeding
  - Increased risk of cardiovascular events
- Corticosteroids
  - Daily vs. PRN vs. tapers
  - Possible side effects → see next slide
- Analgesics
  - OTC vs. tramadol vs. narcotics
  - Possible side effects and risks: many + dependence/abuse
- Corticosteroid injections
  - Possible side effects: hypopigmentation, skin atrophy, osteonecrosis

Side effects of corticosteroids

- Increased appetite → weight gain
- Increased blood glucose → diabetes
- Osteoporosis
- Cataracts
- Glaucoma
- Insomnia
- Immunosuppression
- Increased BP
- Nervousness/agitation
- Flushing
- Bruising
- Irritation of emotional/mental conditions
- Cushing's Syndrome
  - moon facies, central obesity, hyperhidrosis, skin atrophy, hirsutism

****Goal:** Use corticosteroids only when needed and at the smallest dose possible for shortest period possible

2021 ACR Treatment Guidelines for Rheumatoid Arthritis

Summary:

- For DMARD-naïve patients with moderate to severe disease activity, start methotrexate.
  - Oral methotrexate is suggested over subcutaneous methotrexate
  - Initiation/titration of methotrexate to 15 mg weekly within 4 to 6 weeks is conditionally recommended over initiation/ titration to <15 mg weekly
  - Switch to SQ MTX before switching to another DMARD if failing oral MTX
- In DMARD-naïve patients with low disease activity:
  Hydroxychloroquine > sulfasalazine > methotrexate > leflunomide
- When starting a conventional DMARD in patient DMARD-naïve patient, it is recommended not to start short-term (or long term) glucocorticoid treatment

*Very low to low evidence for most recommendations

2021 ACR Treatment Guidelines for Rheumatoid Arthritis

Summary:

- A treat-to-target approach is recommended
- Treatment goal of low disease activity is suggested over remission
- Adding bDMARD or tsDMARD is suggested over triple therapy
- Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients who are not at target

- Continuing treatment at same doses is recommended over dose reductions
- Dose reduction > gradual discontinuation > abrupt discontinuation
- Gradual discontinuation of MTX > gradual discontinuation of bDMARD/tsDMARD

*Very low to low evidence for most recommendations

2021 ACR Treatment Guidelines for Rheumatoid Arthritis

Summary:

- If a patient necessitates continuous or frequent glucocorticoids or IA glucocorticoid injections, it is recommended to add or change DMARD treatment
- Special population recommendations: SQ nodules, pulmonary nodules, fatty liver disease, hepatitis B infection, heart failure, etc.

What do the treatment guidelines not include?

- Recommendations of certain bDMARD/tsDMARDs over other bDMARD/tsDMARDs

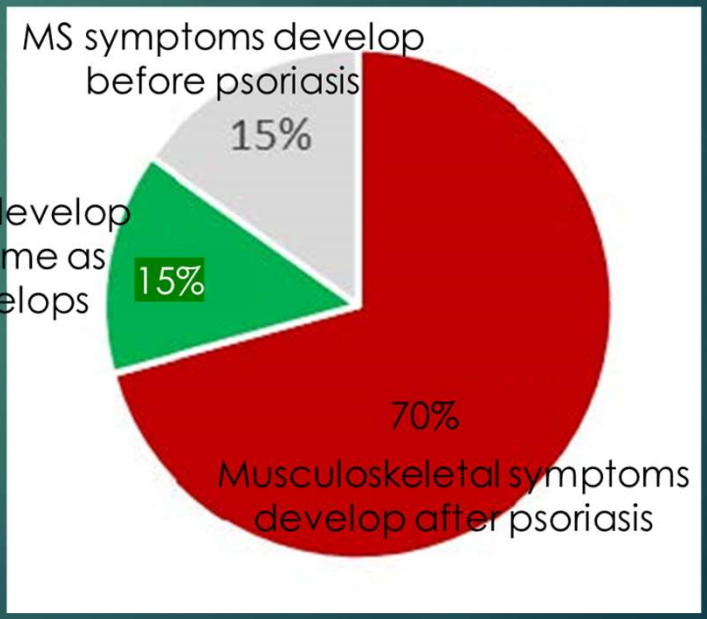
Differential Diagnosis

	RA	PsA	AS	OA
Type	Inflammatory	Inflammatory	Inflammatory	Degenerative
Age of onset	30-60	30-50	20-40	40-70
Sacroiliitis	No	Asymmetric	Symmetric	No
Stiffness	Morning > 1 hr	Morning > 1 hr	Yes	Morning < 30 min
Female:male ratio	3:1	1:1	1:3	Varies by site
Enthesitis	No	Yes	Yes	No
Nail lesions	No	Yes	No	No
Psoriasis	No	Yes	No	No

PsA = Psoriatic Arthritis AS = Ankylosing Spondylitis

Psoriatic Arthritis

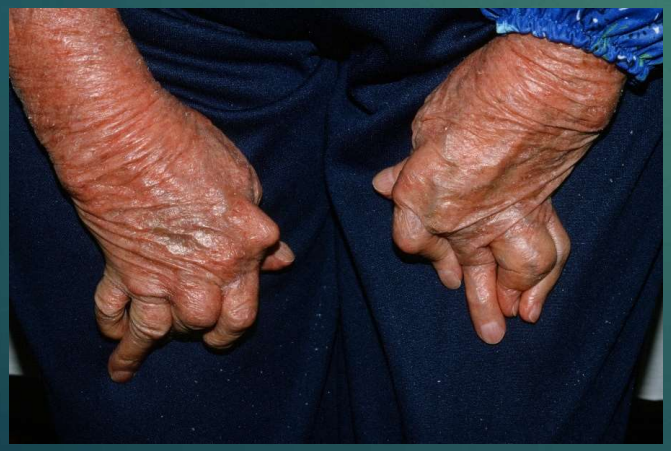
- Autoimmune inflammatory arthritis associated with skin psoriasis
  - Occurs in approximately 15%-30% of those with psoriasis
  - Usually diagnosed between 30-50 years of age
  - Male = female predominance
  - Not all patients have psoriasis at time of presentation

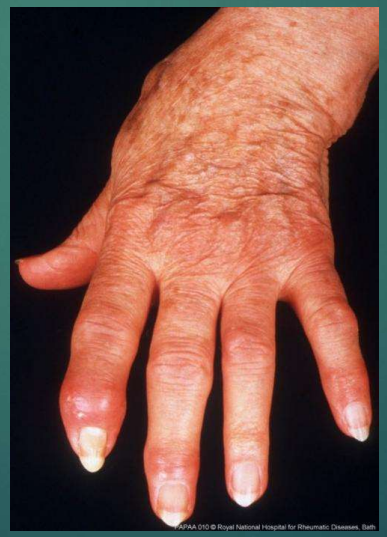


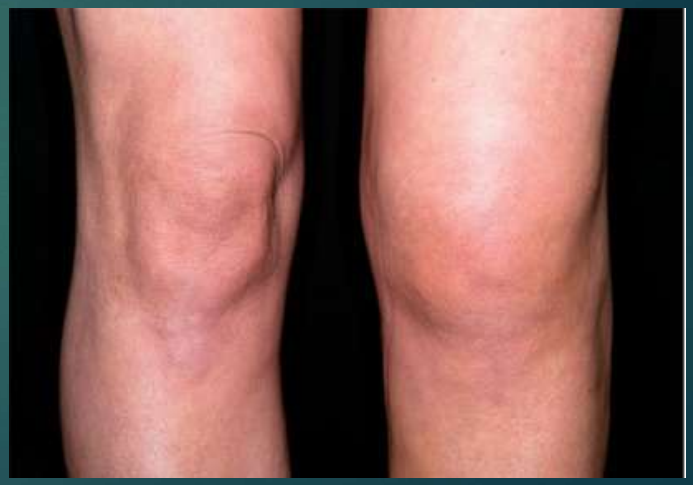
On average, skin symptoms occur ~9-10 years prior to musculoskeletal symptoms

Psoriatic Arthritis

- 5 different types
  - Symmetric arthritis (RA-like)
  - Asymmetric arthritis (small # of joints, large joints)
  - DIP predominant
  - Spondylitis
  - Arthritis mutilans (rare)







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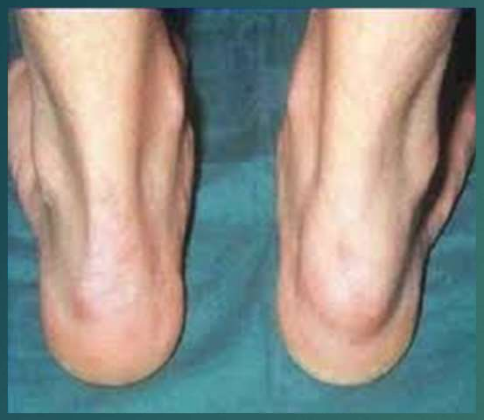
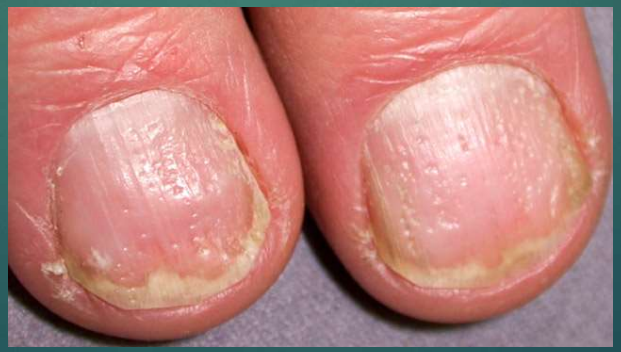
Psoriatic arthritis signs and symptoms



Iritis



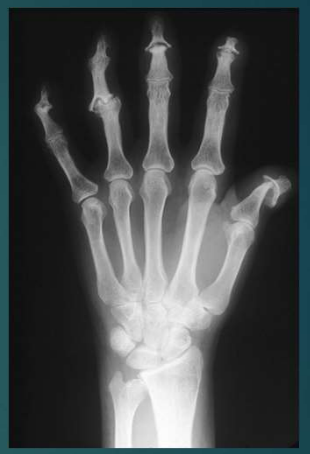
Psoriatic Arthritis Diagnosis

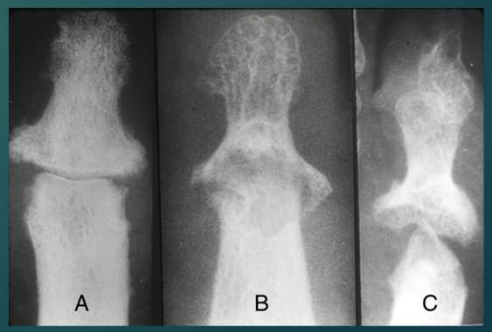
Labs:

- HLA-B27
  - More commonly seen in spondylotic form of PsA
- Negative RF/ACPA
- ESR and CRP

Imaging:

- X-rays
  - May show pencil-in-cup deformities at DIPs
  - Marginal erosions
  - Periostitis of long bones
  - Sacroiliitis





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Psoriatic Arthritis Treatment

Conventional DMARDs – SAME AS RA

	Hydroxychloroquine	Sulfasalazine	Methotrexate	Leflunomide	Azathioprine
MOA	EXACT MECHANISM IS UNKNOWN				
Route (standard dosing)	Oral 400 mg daily	Oral 1000 mg bid	Oral or Parental 7.5mg-25mg weekly	Oral 20 mg daily	Oral 50-150 mg daily
Potential Risks	Retinal toxicity Photosensitivity May worsen psoriasis	Hepatoxicity Hematological abnormalities Oligospermia	Hepatoxicity Pulmonary toxicity Hematological abnormalities Fetal toxicity	Hepatoxicity Pulmonary toxicity Hematological abnormalities Fetal toxicity	Pancreatitis AML Hematological abnormalitlies

Almost all above DMARDs have multiple possible side effects including but not limited to nausea, diarrhea, hair loss, headache, fatigue, increased risk of infection, hypersensitivity reactions, etc.

Psoriatic Arthritis Treatment

Biologic Treatment

TNF inhibitor	IL-12 and IL-23 inhibitors	IL-17A inhibitor	T-Cell inhibitor	IL-23A inhibitor
Injectable or Infusion	Injectable	Injectable	Injectable or Infusion	Injectable
Adalimumab (Humira) Etanercept (Enbrel) Infliximab(Remicade) Golimumab (Simponi) Certolizumab (Cimzia)	Ustekinumab (Stelara) Guselkumab (Tremfya) (IL-23)	Secukinumab (Cosentyx) Ixekizumab Taltz	Abatacept (Orencia)	Risankizumab-rzaa (Skyrizi)
Serious infections Malignancies TB or Hepatitis B reactivation Worsening MS Worsening CHF Lupus-like syndrome	Serious infections Malignancies TB reactivation RPLS	Serious infections TB reactivation IBD exacerbations	Serious infections Malignancies COPD worsening	Serious infections

Self injections → possible injection site reactions Infusions → possible infusion reactions

Psoriatic Arthritis Treatment

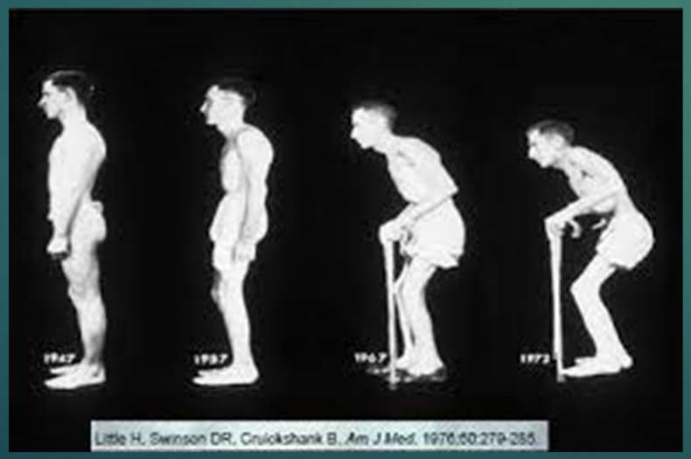
Targeted Synthetic DMARDs/ Small molecule Treatment

PDE4 inhibitor	JAX inhibitor
Oral	Oral
Ampremilast (Otezla)	Tofacitinib (Xeljanz) Upadacitinib (Rinvoq)
Weight loss Worsening of depression Nausea *No lab monitoring needed	Serious infections Malignancies Hepatoxicity Elevated cholesterol levels Bowel perforation Thrombosis Black Box Warning*

Ankylosing Spondylitis

Autoimmune inflammatory disease affecting axial spine and peripheral joints

- Prevalence: 0.1 – 1.4%
- 3:1 Men > women ?
- Hallmark: Inflammatory back pain/sacroiliitis
- Average age of onset: 20-40
- Associated with HLA-B27 gene



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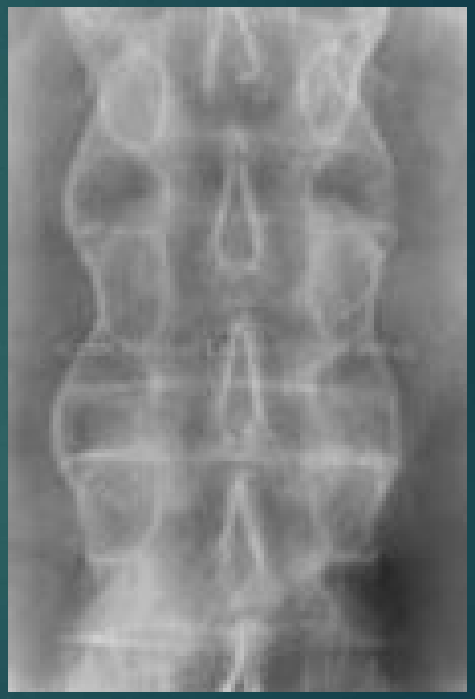
Ankylosing Spondylitis

Signs and symptoms

- Spinal and sacroiliac pain and stiffness
- Decreased ROM of axial spine, hips
- Fusion of spine (ankylosis); “bamboo spine”
- Peripheral joint pain and swelling
- Enthesitis
- Eye inflammation (iritis, etc.)
- Associated with Inflammatory Bowel Disease
- Inflammatory back pain: IPAIN



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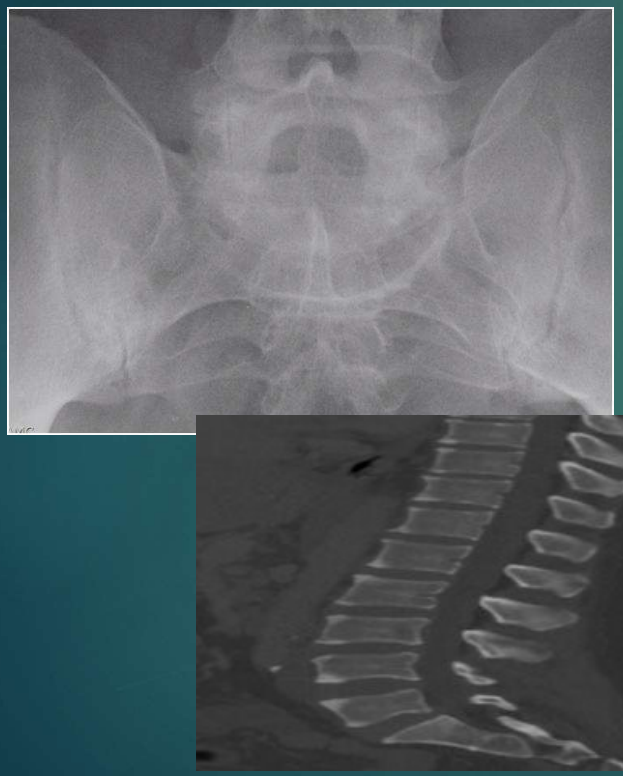
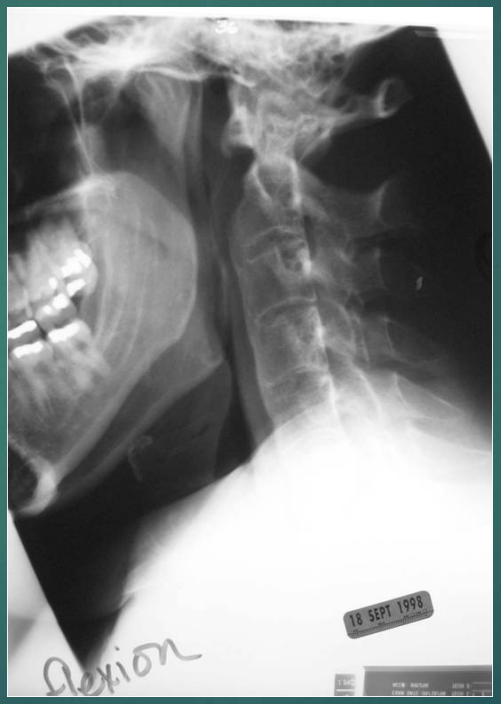
Imaging - Radiographs

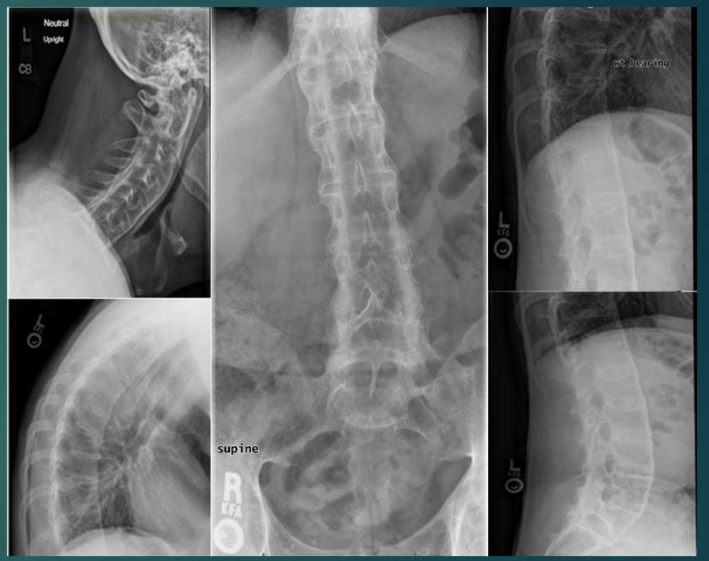
- SI joints
  - Initially will widen before they narrow
  - Subchondral erosions, sclerosis, and proliferation on the iliac side of the SI joints
  - At end-stage, fusion occurs
  - Symmetrical sacroiliitis in axial SpA
- Spine
  - Erosions or reactive sclerosis at corners of vertebral bodies ”shiny corner” sign
  - Syndesmophytes
  - Vertebral squaring
  - Interspinous ligament ossification – may cause “dagger sign”
  - Disc calcifications

(Khmelinskii, N., Regel, A., & Baraliakos, X. 2018

Imaging - Radiographs







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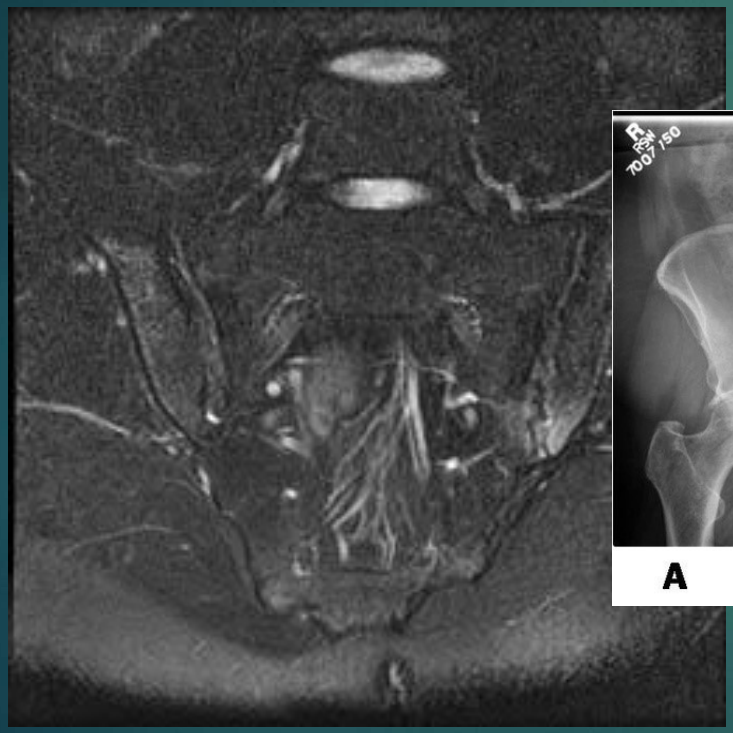
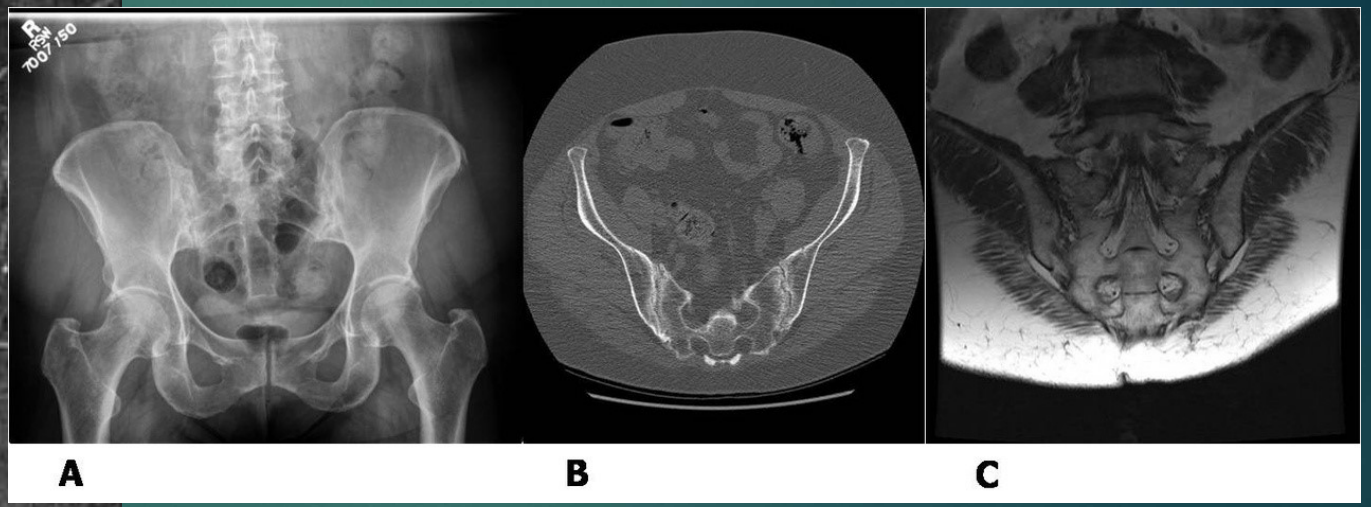
Imaging - MRI

- SI joints
  - Subchondral sclerosis
  - Erosions
  - Subchondral fat metaplasia/infiltration
  - Bony bridges/ankylosis
  - *Observe for false positives* (de Winter, et al 2018)
    - 23% of healthy individuals, 57% of post-partum women met ASAS + criteria,
    - Recreational runners, professional athletes, army recruits in training
- Spine
  - Spondylitis
  - Inflammation of the facet joints
  - Bone marrow lesions (osteitis)
  - Aseptic spondylodiscitis

Imaging - MRI





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Ankylosing Spondylitis Treatment

- Historically it has been noted that nothing slows disease progression
  - ??????????????????
- *NSAIDs
- Conventional DMARDs → do not treat spinal symptoms
- Biologic DMARDs
- Targeted synthetic DMARDs
- Corticosteroids
- Cortisone injections
- Exercise/PT**

Ankylosing Spondylitis Treatment

Biologic Treatment

TNF inhibitor	IL-17 inhibitor
Injectable or Infusion	Injectable
Adalimumab (Humira) Etanercept (Enbrel) Infliximab (Remicade) Golimumab (Simponi) Certolizumab (Cimzia)	Secukinumab (Cosentyx) Ixekizumab (Taltz)
Serious infections, Malignancies, TB or Hepatitis B reactivation, Worsening MS Worsening CHF Lupus-like syndrome	Serious infections TB reactivation IBD exacerbations

Small Molecule Treatment

JAX inhibitor
Oral
Tofacitinib (Xeljanz) Upadacitinib (Rinvoq)
Serious infections, Malignancies, Hepatoxicity, ↑ cholesterol levels Bowel perforation Thrombosis Black Box Warning*

Systemic lupus erythematous

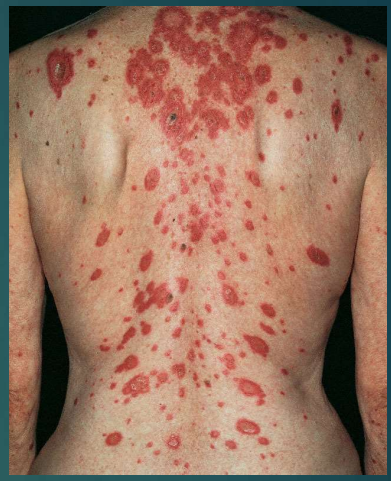
- Chronic inflammatory autoimmune condition that can affect many organ systems
  - Black Americans, Asians, Native Americans are 3x more likely to diagnosed
  - 1.5 Million Americans have lupus
  - 9 of 10 lupus patients are women
  - Most often diagnosed between ages of 15-40
  - 20% of those who have lupus have a parent or sibling with lupus
  - Often lupus patients suffer from other CTDs

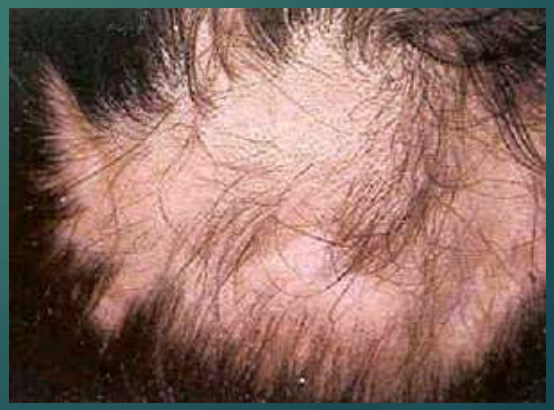
- Other forms of lupus
  - Discoid (skin lupus)
  - Subacute lupus
  - Drug-induced lupus

Symptoms

- Joint pain and swelling
- Rash
- Butterfly rash
- Mouth/nasal sores
- Alopecia
- Fatigue
- Fever
- Raynaud's phenomenon
- Photosensitivity
- Pleurisy

Each case of lupus is different





Diagnosis

Need 4 of 11 listed criteria

Table 1 – Criteria for the classification of systemic lupus erythematosus

Criteria	Comments
Discoid rash	Erythematous raised patches with adherent scaling and follicular plugging; atrophic scarring can be seen in older lesions
Photosensitivity	By patient history or physician observation
Oral ulcers	Oral or nasopharyngeal, usually painless, observed by physician
Arthritis	Nonerosive; 2 or more peripheral joints affected by tenderness, swelling, or an effusion
Serositis	Pleuritis defined as history of pleuritic pain or rub heard by a physician or a pleural effusion; pericarditis documented by ECG, rub, or pericardial effusion
Renal disorder	Cellular casts (red cell, hemoglobin, granular, tubular, or mixed) or persistent proteinuria > 0.5 g/d or > 3+ if quantification not performed
Neurological disorder	Seizures or psychosis (without other offending drug or metabolic derangement)
Hematological disorder	Hemolytic anemia (with reticulocytosis) or leukopenia (leukocyte count < 4000/μL on 2 or more occasions) or lymphopenia (lymphocyte count < 1500/μL) on 2 or more occasions or thrombocytopenia (platelet count < 100,000/μL) in the absence of drugs
Immunological disorder	Anti-DNA: antibody to native DNA or anti-Smith; or positive finding of antiphospholipid antibodies based on (1) abnormal level of IgG or IgM anticardiolipin antibodies, (2) a positive test result for lupus anticoagulant using a standard method, or (3) false positive serological test for syphilis known to be positive for 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test
Antinuclear antibody test	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point and in the absence of drugs known to be associated with "drug-induced" lupus
Malar rash	Fixed erythema, flat or raised, over the malar eminences, sparing the nasolabial folds

Adapted from Klippel JH, ed. *Primer on the Rheumatic Diseases*. 2001.[3]

Diagnosis

- + ANA DOES NOT NECESSARILY MEAN PATIENT HAS LUPUS!!!!!!
  - % of the US population has a +ANA with no CTD
  - risk of ANA positivity increases with age
  - other conditions can lead to a +ANA other than lupus
  - many lupus symptoms are vague and can be caused by other conditions

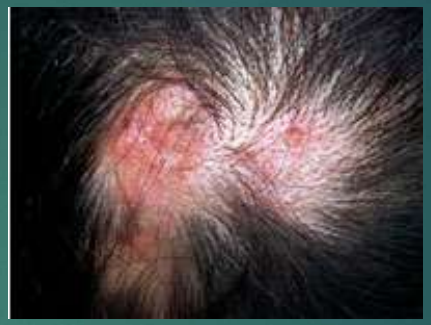
- Systemic lupus vs. discoid lupus (rash only) vs. subacute vs. drug-induced

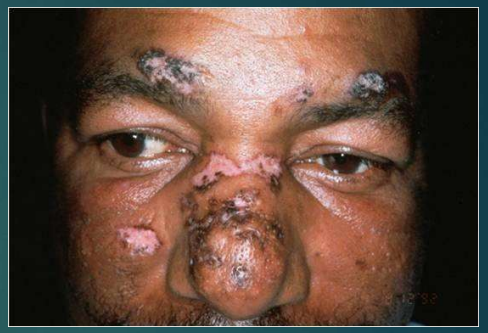
- Labs
  - +dsDNA is much more specific for lupus than ANA; +SM/RNP antibodies
  - Complement levels → decreased during lupus flares
  - ESR, CRP
  - ***Urinalysis*** → abnormality can be first indicator of kidney disease

- Biopsy
  - Skin and renal

Lupus Complications

- Lupus nephritis
- Scarring rashes
- Neuropathy
- Osteoporosis
- Atherosclerosis/CVD
- Neuropsychiatric lupus
  - headaches, movement disorders, seizures, transverse myelopathy, dementia, delirium, stroke, TIA, etc
- Anti-phospholipid syndrome
- Pregnancy complications
- Jaccoud's arthropathy





Drug-Induced Lupus

- Most common medications that cause drug-induced lupus include: **isoniazid, hydralazine,** and **procainamide**.

- Other medications known to cause drug-induced lupus include:
  - Anti-seizure medications
  - Minocycline
  - Capoten
  - Penicillamine
  - Chlorpromazine
  - Sulfasalazine
  - Methyldopa
  - Estrogens

- Symptoms tend to occur after taking the drug for at least 3 to 6 months

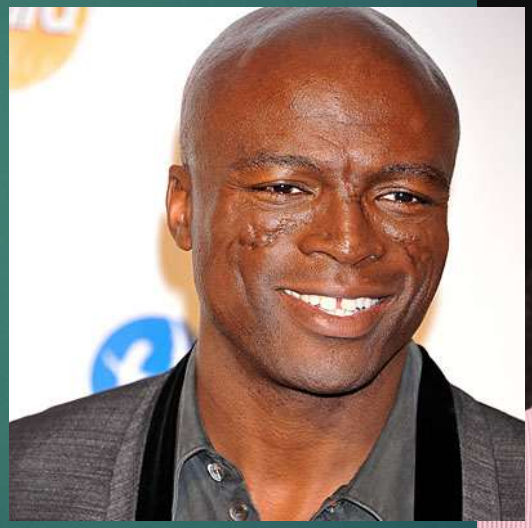
Lupus Treatment

- Plaquenil (hydroxychloroquine) → GOLD STANDARD
  - EVERY LUPUS PATIENT SHOULD BE ON THIS MEDICATION
  - Decreases risk of renal damage
  - Can treat joint symptoms, skin symptoms, fatigue, etc.

- Benlysta (belimumab) (2011) – Monthly infusion
  - – 1st FDA-approved medication for lupus in over 50 years
- Cellcept (mycophenolate mofetil)
- Saphnelo (anifrolumab) (2021) – Monthly infusion
- Joint symptoms - same as rheumatoid arthritis conventional DMARDs
- Skin symptoms – Plaquenil (hydroxychloroquine), azathioprine, dapsone
- Corticosteroids (especially for flare control)

Lupus Treatment

- Lupus nephritis – biopsy required
  - Cyclophosphamide
  - Mycophenolate mofetil
  - Tacrolimus
  - Lupkynis
  - Corticosteroids
  - Benlysta
  - Rituxan
  - Dialysis
  - Renal Transplant



- Symptom relief
  - NSAIDs, Corticosteroids, Joint injections, Analgesics

How has COVID-19 changed our treatment of Rheumatic Diseases?

Osteoporosis

Definition: T-score ≤ -2.5; low bone density

- T-score: number of standard deviations a patient's BMD measurement is above or below the young/normal mean BMD

Risks of osteoporosis

- 1.5 million osteoporosis fractures occur each year in the US
- 90% of hip and spinal fractures are related to osteoporosis
- Individuals now 50 years old have a lifetime risk of any fracture in hip, spine, or distal forearm of 40% in Caucasian women and 13% in Caucasian men

Symptoms: NONE other than related fractures

Complications:

Hip fractures → 20% die in 1 year, 20% require nursing home care, 50% never fully recover
Compression fractures and often kyphosis

Klippel, J.H. (2008) *Primer on the Rheumatic Diseases.* New York. Springer Science + Media

Osteoporosis

Bone is continually undergoing a process of remodeling

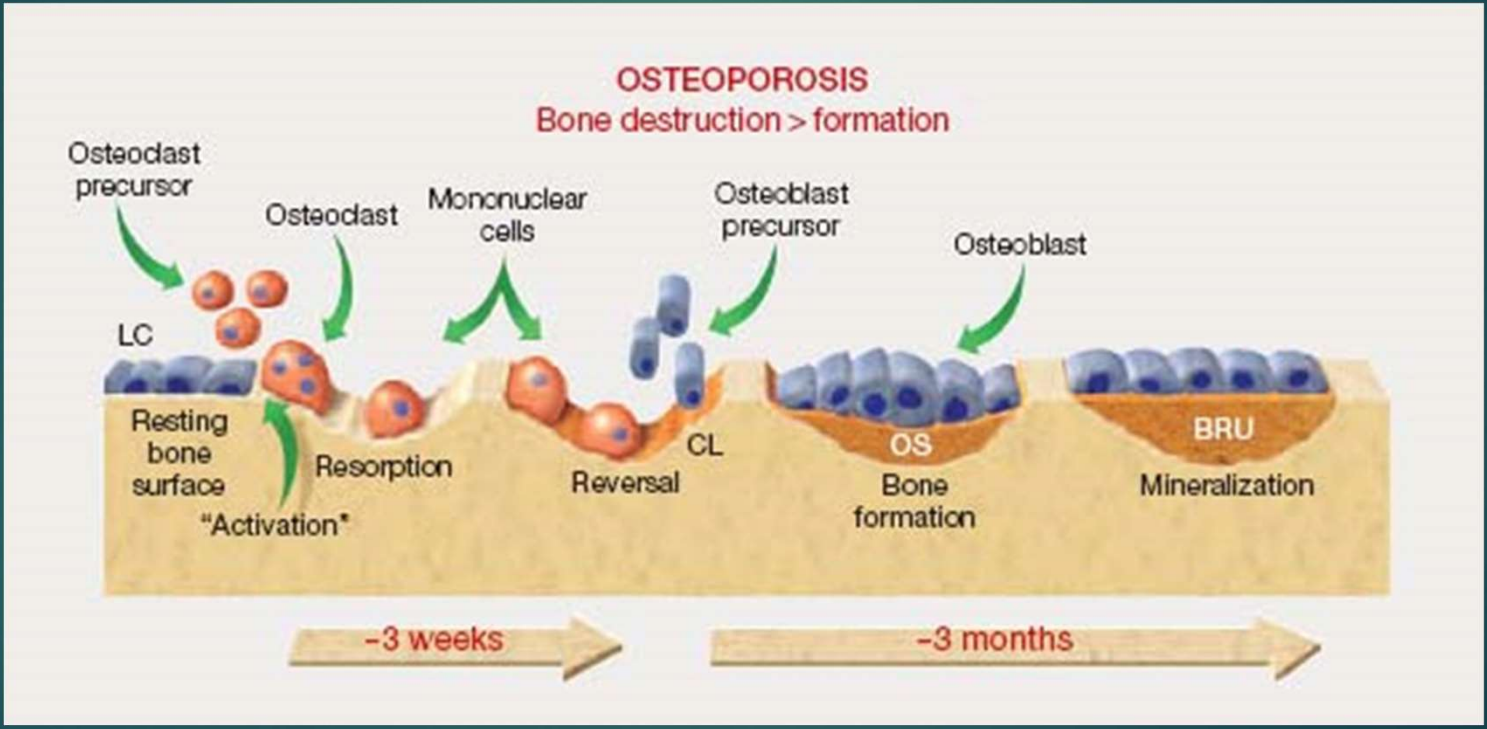
In utero + childhood + puberty → Bone formation > bone resorption
Adulthood → Bone formation = bone resorption
After menopause → Bone formation < bone resorption

Risks:

- Genetic factors
- Nutrition factors – low calcium or vitamin D
- Hormonal factors – menopause, hypogonadism, hyperparathyroidism
- Environmental factors – smoking, alcoholism, gastrectomy
- Advanced age
- Medications (thyroid replacement, steroids, chemo, chronic us of PPIs?)
- Low weight
- Caucasian or Asian

Osteoporosis

Bone break down > bone formation



Osteoporosis

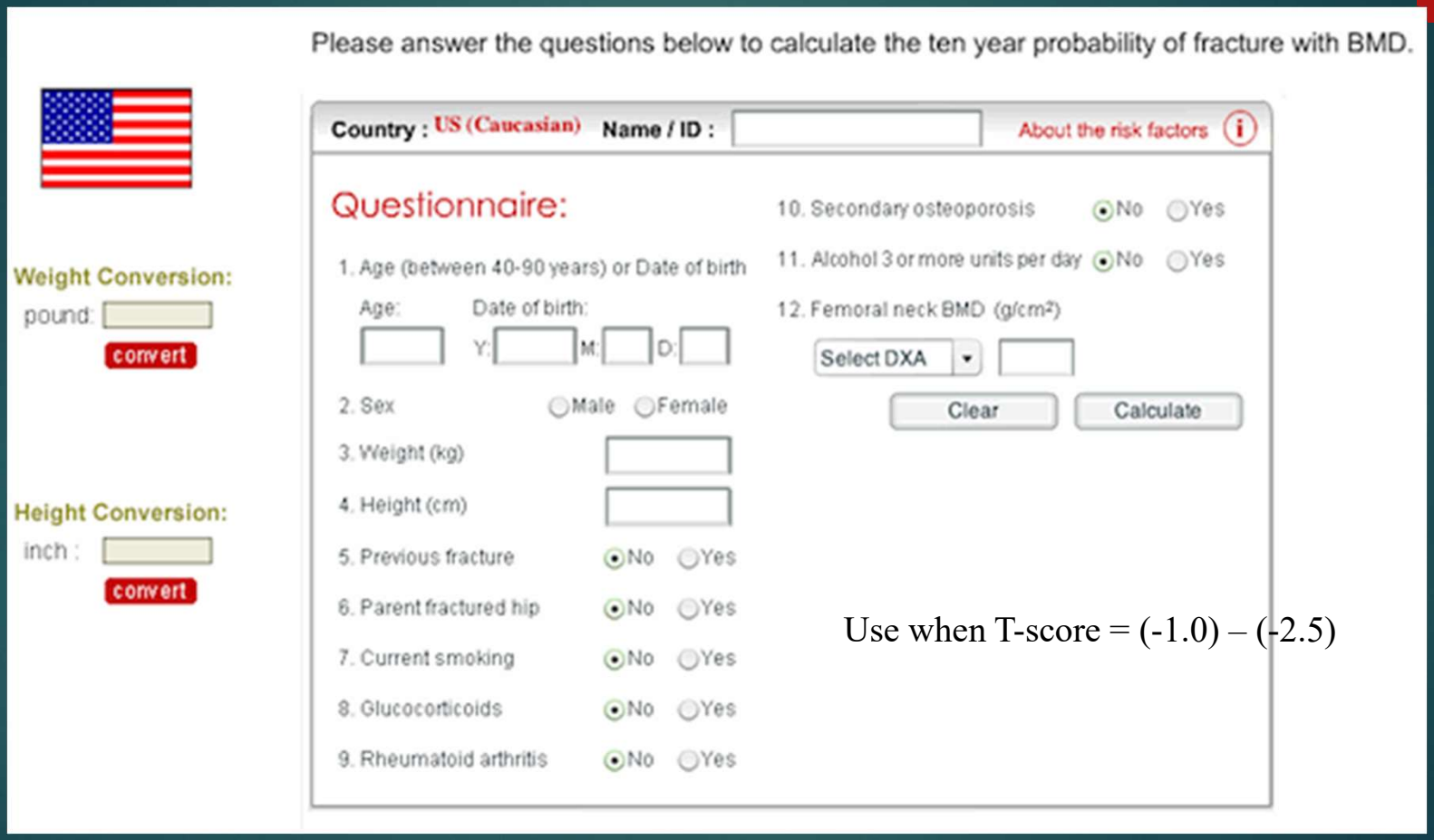
T-score ≤ (-2.5) = Osteoporosis
T-score (-1.0) – (-2.5) = Osteopenia
Normal = > (1.0)

FRAX score:
Developed by WHO to evaluate fracture risk in individuals
Calculates: 1.) 10-year probability of major osteoporotic fracture
2.) 10-year probability of a hip fracture

Secondary causes of osteoporosis

▪ Hyperparathyroidism ▪ Kidney Disease ▪ Vitamin D deficiency ▪ Hyperthyroidism (overactive thyroid)	▪ Liver disease ▪ Intestinal disease ▪ Long term corticosteroid use

FRAX Score



Use when T-score = (-1.0) – (-2.5)

Osteoporosis Diagnosis

DEXA Scan – Who gets one?? Depends on who you ask.

- NOF vs ISCD vs AACE vs USPSTF vs AAFP vs NIH vs NAMS vs ACPM vs ACOG
  - Women > 65
  - Younger individuals at risk
  - Individuals with certain fractures

How often should DEXA be completed?

Vertebral fracture assessment - can detect vertebral deformities at time of DEXA

Trabecular bone score - measure of microarchitecture at time of DEXA

Osteoporosis Diagnosis

Evaluate for osteoporosis risks factors including medication risk factors

Labs

- CBC
- CMP
- Alkaline Phosphatase
- Vitamin D 25 OH level
- 24 hour urine calcium and creatinine
- PTH
- TSH, T4
- Testosterone and gonadotropin in men 50-69

Osteoporosis Treatment

- Calcium supplementation
  - 1200 mg/day for >50
  - 1000 mg/day for <50
  - Increase diet calcium
  - Calcium citrate for patients on PPIs
- Vitamin D supplementation
  - 800-2000 units per day
- Exercise recommendations
- Smoking cessation
- Alcohol reduction:
  - women – no more than 2/day
  - men – no more than 3/day

Osteoporosis Treatment

NOF's *Clinician's Guide* recommends that FDA-approved medical therapies be considered in postmenopausal women and men age 50 years and older with a:
a. Hip or vertebral (clinical or morphometric) fracture
b. T-score ≤ -2.5 at the spine or hip
c. Ten-year fracture probability by FRAX® ≥ 3% for hip fracture or ≥ 20% for major osteoporotic fracture.

- Bisphosphonates – Fosamax (alendronate), Actonel (risedronate), Boniva (ibandronate)
  Reclast (zoledronic acid) – IV once/year
  - inhibit osteoclast bone resorption, reduce osteoclast activity, increase osteoclast apoptosis
  - risks: renal toxicity, atypical femur fractures, osteonecrosis

- Prolia (denosumab) – subcutaneous injection q6months
  - RANK ligand inhibitor: inhibits osteoclast formation, function, survival
  - risks: serious infections, atypical femur fractures, osteonecrosis, hypocalcemia

Osteoporosis Treatment

- Forteo (teriparatide) – once daily subcutaneous injection x 2 years
  - recombinant form of human parathyroid hormone → osteoblast activity > ⇧osteoclast activity
  - risks: hypercalcemia, osteosarcoma???

- Tymlos (abaloparatide) – once daily subcutaenous injection x 2 years
  - human parathyroid hormone related peptide→ osteoblast activity > ⇧ osteoclast activity
  - risks: hypercalcemia, osteosarcoma??

- Evenity (romosozumab) - sclerostin inhibitor
  - increased bone production and decreased bone resorption
  - once monthly in-office injection x 12 months
  - risks: increased risk of cardiovascular events/death, osteonecrosis of jaw, atypical femur fx

- Evista (raloxifene) – one tablet daily
  - selective estrogen receptor modulator
  - risks: increases risk of cardiovascular events (venothrombosis, death due to stroke)
  - reduces risk of invasive breast carcinoma

Take Home Points

- Irreversible joint damage can occur if RA or PsA are not treated early and adequately
- MTX is the gold standard treatment in RA. However, we now have a plethora of medications to choose from and a treat-to-target approach should be used in each individual with RA
- When evaluating for PsA do not forget to evaluate for enthesitis, to ask about eye symptoms, and to look everywhere for psoriasis
- In a young patient with inflammatory back pain, evaluation for AS should be completed.
- +ANA is not adequate to make diagnosis of lupus. Every lupus patient is different.
- For those that suffer hip fractures: 20% die in 1 year, 20% require nursing home care, 50% never fully recover. We MUST treat osteoporosis better.

References

1. ACR Image Library, copyrighted 2022.
2. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken)*. 2021;73(7):924-939. doi:10.1002/acr.24596
3. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States- Part I. Arthritis & Rheum. 2008: 58(1):15-25.
4. Khmelinskii N, Regel A, Baraliakos X. The Role of Imaging in Diagnosing Axial Spondyloarthritis. *Front Med (Lausanne)*. 2018;5:106. Published 2018 Apr 17. doi:10.3389/fmed.2018.00106
5. Klippel, J.H. (2008) *Primer on the Rheumatic Diseases.* New York. Springer Science + Media.
6. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States- Part II. Arthritis & Rheum. 2008: 58(1):26-35.

Questions??

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