

# Rheumatoid Arthritis (RA) Management

What You Need To Know About  
**Rheumatoid Arthritis**



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# Objectives

- **Define rheumatoid arthritis (RA) and discuss epidemiology and risk factors of RA**
- **Identify pathogenesis and clinical presentation of RA**
- **Review diagnostic criteria and RA disease activity**
- **Review the treatment algorithm for RA (pharmacologic & non-pharmacologic)**



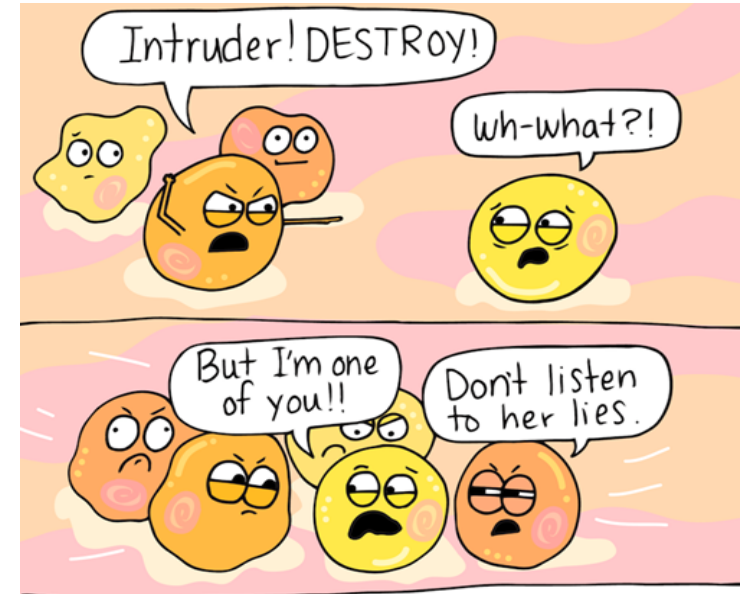
# NCQA Ratings and HEDIS Measures

- The National Committee for Quality Assurance (NCQA) is dedicated to improve the quality of health care by rating the established Healthcare Effectiveness Data and Information Set (HEDIS) measures
- The Disease-Modifying Anti-Rheumatic Drug Therapy for Rheumatoid Arthritis is a HEDIS measure which is under the effectiveness of care domain
- The measure is the percentage of members 18 years of age and older diagnosed with rheumatoid arthritis and who were dispensed at least one ambulatory prescription for a disease-modifying anti-rheumatic drug (DMARD)



# What is Rheumatoid Arthritis?

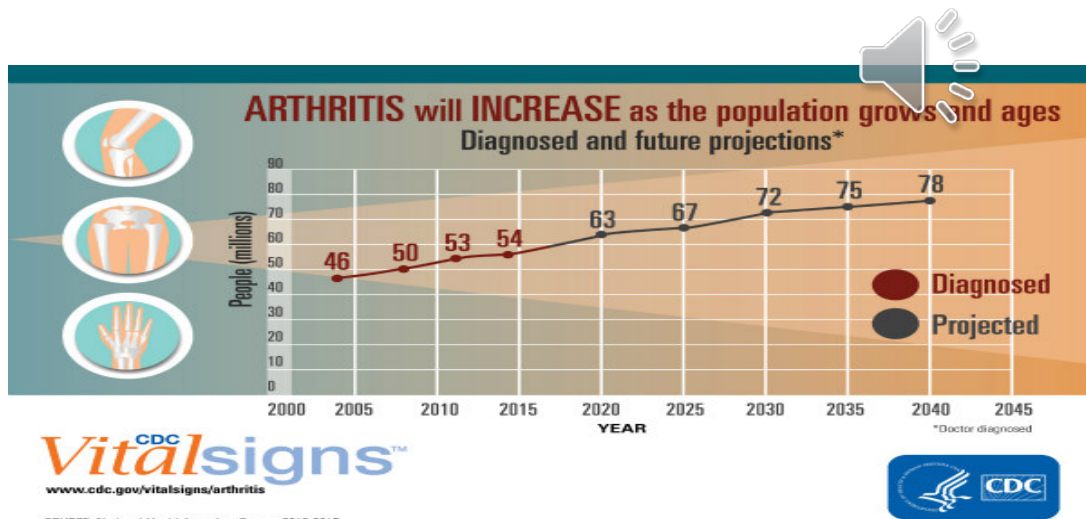
- The most common systemic autoimmune inflammatory disease characterized by symmetric, relapsing, or chronic destructive synovitis
  - **Synovitis = inflammation of the synovial membrane which lines joints**



Autoimmune disorders in a nutshell.  
•Beatrice the Biologist•

# Epidemiology

- Annual incidence of RA: 40 per 100,000 per year
- About 1.3 million U.S. adults are affected
- Women are affected two to three times more often than men



SOURCE: National Health Interview Survey, 2013-2015.

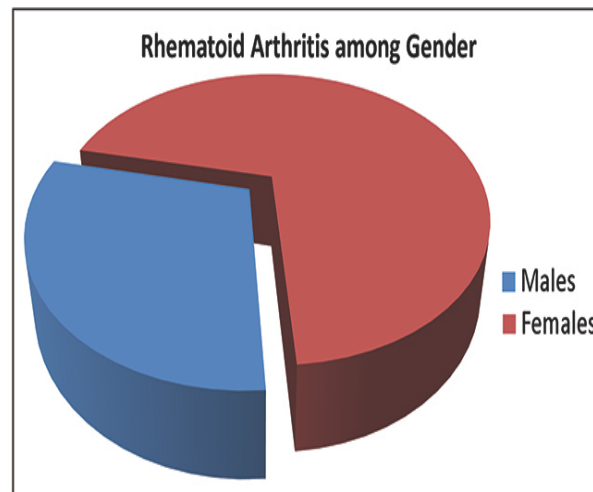
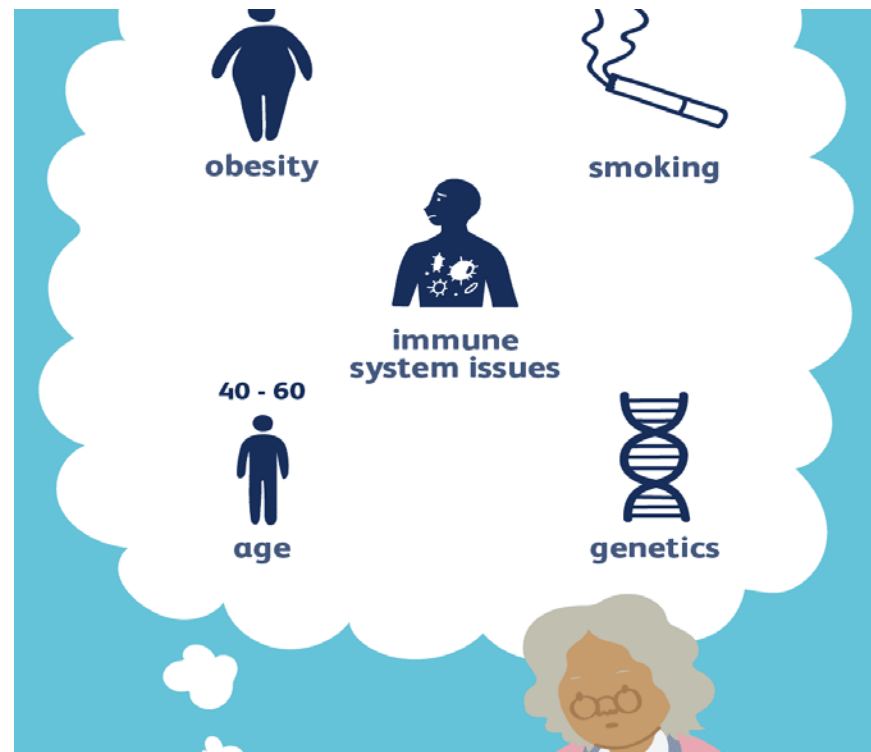


Figure-1: Distribution of rheumatoid arthritis with respect to gender.

# Risk Factors

- Smoking
- Genetic predisposition
  - HLA-DRB1 gene
- family history
- Sex (female)
- Increasing age
- Obesity (overweight)



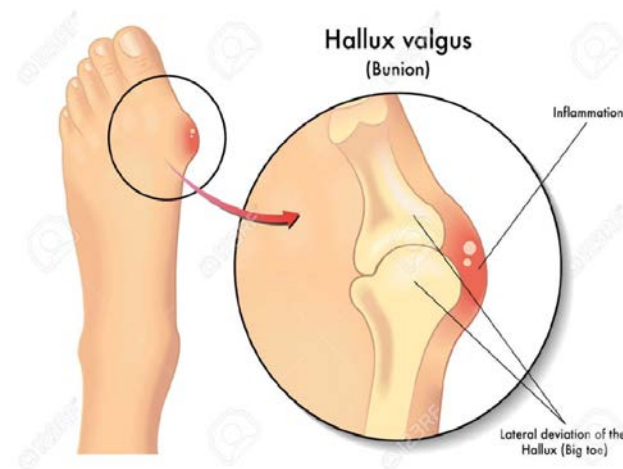


# Pathogenesis

- The initial triggering event is not clear
- T cells and B cells activated (in response to mutated citrullinated vimentin (MCV), structural protein in human)
- Antibodies to MCV complex with MCV to precipitate in joint
- Production of inflammatory cytokines (IL-6, TNF)
- Macrophages, lymphocytes, and plasma cells
- Metalloproteinases (MMP) from Macrophages to damage synovial tissue
- Rheumatoid factor from plasma cells

# Clinical Presentation

- Joint pain and stiffness (bilateral and symmetrical)
- Joint swelling and deformity (Hallux Valgus/Swan Neck Deformity)
- Tenderness
- Warmth
- Rheumatoid nodules





# Clinical Presentation



- Low grade fever
- Loss of appetite
- Fatigue and weakness

# Complications of RA

- Pulmonary – COPD, pulmonary fibrosis
- Cardiac – Pericarditis
- Eye – Inflammation of episclera
- Blood - Thrombocytosis



Medical  
Complications



# Diagnostic Criteria

- The American College of Rheumatology and European League Against Rheumatism 2010 Guideline (ACR/EULAR 2010 guideline)
- There are categories A to D
  - Category A: Joint Involvement
  - Category B: Serology
  - Category C: Acute Phase Reactants
  - Category D: Duration of Symptoms
- Patients must have a score of equal or greater than 6 out of 10



# ACR/EULAR Criteria

## Category A: Joint Involvement

- **Small Joint:** wrists, metacarpophalangeal joints, proximal interphalangeal joints, 2<sup>nd</sup> – 5<sup>th</sup> metatarsophalangeal joints, and thumb joints
- **Large joint:** shoulders, elbows, hips, knees, and ankles

Joint Involvement	Score
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

# ACR/EULAR Criteria

## Category B: Serology

- **RF** – rheumatoid factor
- **ACPA** – anti-citrullinated protein antibody
- **Low-positive**: defined as higher than the upper limit of normal (ULN) but not equal or less than three times of the ULN
- **High-positive**: defined as greater than three times of ULN

Serology	Score
Negative RF <u>AND</u> ACPA	0
Low-positive RF <u>OR</u> low-positive ACPA	2
High-positive RF <u>OR</u> high-positive ACPA	3

# ACR/EULAR Criteria

## Category C: Acute Phase Reactants

- **CRP** – C-reactive protein
- **ESR** – Erythrocyte sedimentation rate

Acute-Phase Reactants	Score
Normal CRP <u>AND</u> normal ESR	0
Abnormal CRP <u>OR</u> abnormal ESR	1

\*Adapted from ACR/EULAR 2010 Guideline

# ACR/EULAR Criteria

## Category D: Duration of Symptoms

- Patient self-report on duration of signs/symptoms

Duration of Symptoms	Score
< 6 weeks	0
≥ 6 weeks	1

\*Adapted from ACR/EULAR 2010 Guideline

# RA Disease Activity Instruments

**Table 3. Disease activity cutoffs for each American College of Rheumatology–recommended disease activity measure\***

Disease activity measure	Scale	Remission	Low/minimal	Moderate	High/severe
Patient-driven composite tools					
PAS	0–10	0.00–0.25	0.26–3.70	3.71 to <8.0	8.00–10.00
PAS-II	0–10	0.00–0.25	0.26–3.70	3.71 to <8.0	8.00–10.00
RAPID-3	0–10	0–1.0	>1.0 to 2.0	>2.0 to 4.0	>4.0 to 10
Patient and provider composite tool					
CDAI	0–76	≤2.8	>2.8 to 10.0	>10.0 to 22.0	>22.0
Patient, provider, and laboratory composite tools					
DAS28 (ESR or CRP)	0–9.4	<2.6	≥2.6 to <3.2	≥3.2 to ≤5.1	>5.1
SDAI	0–86	≤3.3	>3.3 to ≤11.0	>11.0 to ≤26	>26

\* PAS = Patient Activity Scale; RAPID-3 = Routine Assessment of Patient Index Data with 3 measures; CDAI = Clinical Disease Activity Index; DAS28 = Disease Activity Score with 28-joint counts; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; SDAI = Simplified Disease Activity Index.



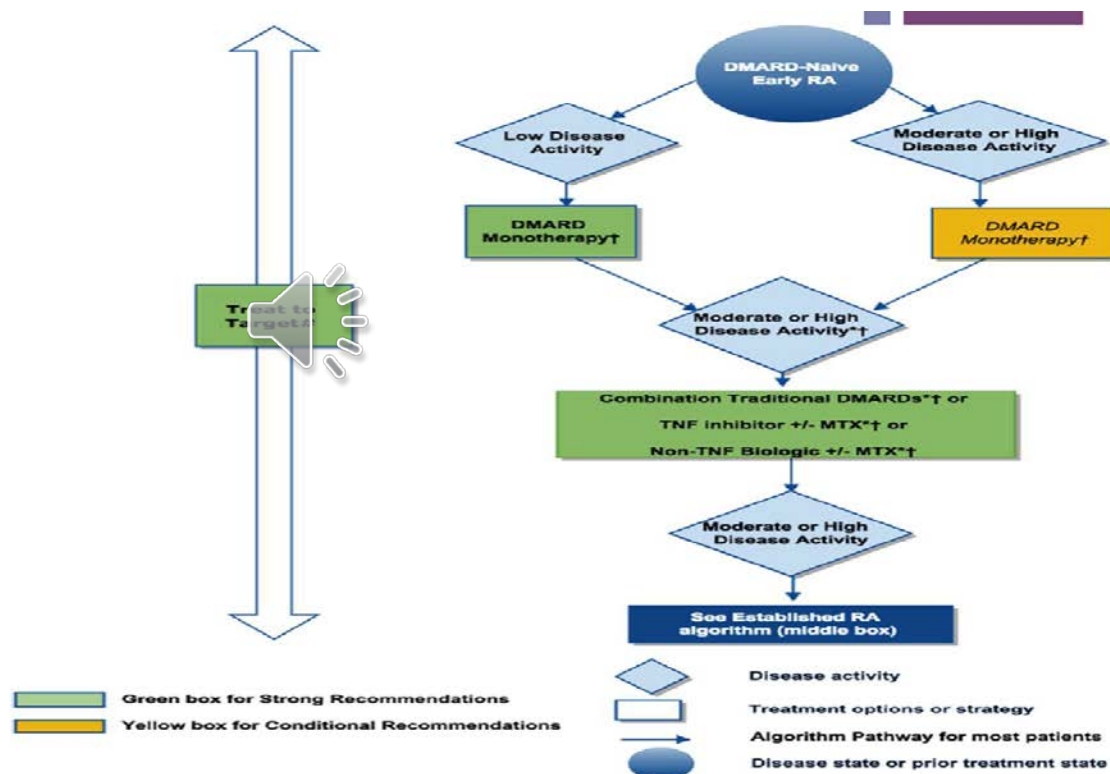
# Treatment Algorithm for RA



Tofacitinib?  
Biologics?  
DMARDs?

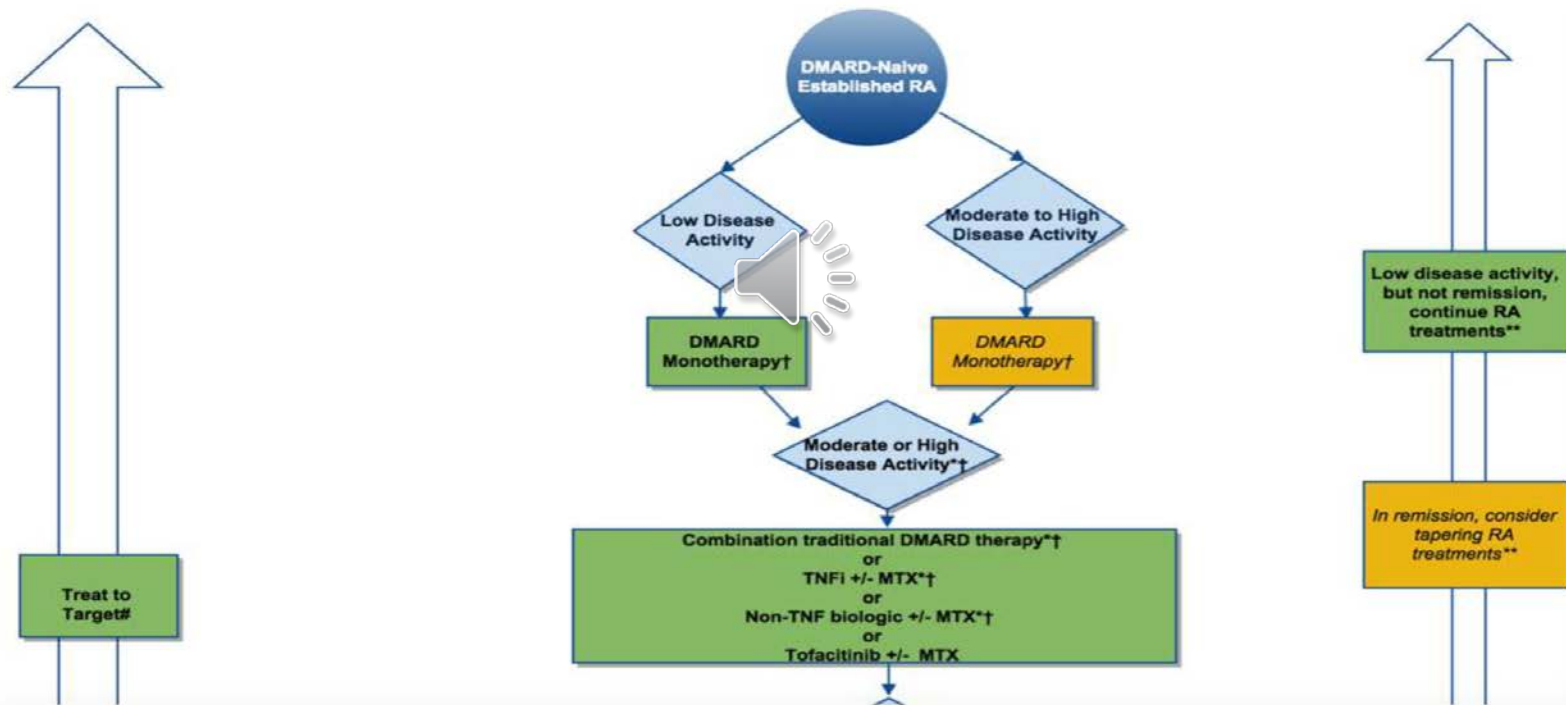
# Early RA

- Treatment Algorithm for Early RA: < 6 months

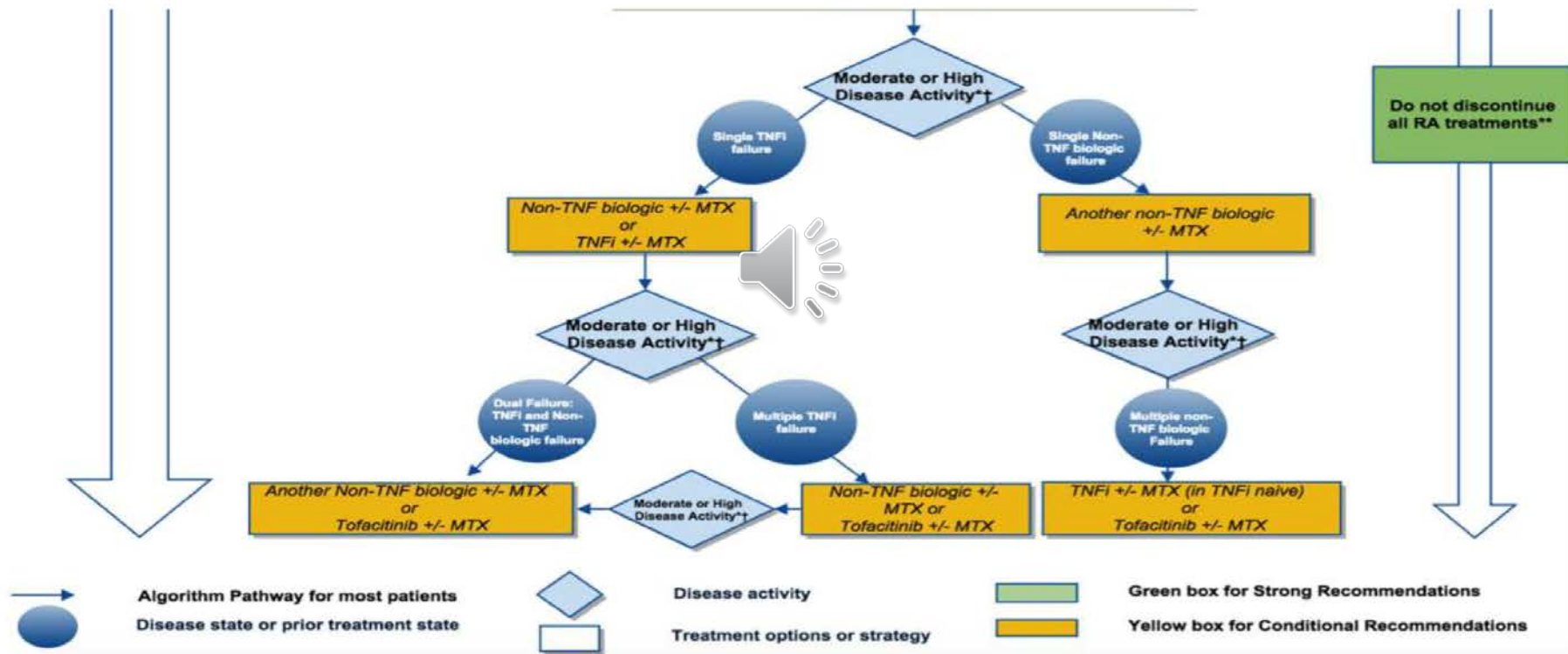


\*Adapted from ACR 2015 Guideline

# Treatment Algorithm for Established RA: $\geq 6$ months



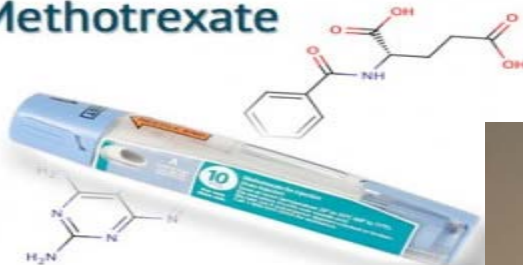
# Treatment Algorithm for Established RA: $\geq 6$ months (Continues)



# Medications (DMARDs)



Methotrexate



Updated SureClick<sup>®</sup> Autoinjector



# Traditional DMARDs

Drug names	Dosing	Adverse reactions	Clinical pearls
Methotrexate (Otrexup, Rasuvo, Trexall, Xatmep)	7.5 – 20 mg once weekly (PO, SC, IM)	Stomatitis, Myelosuppression, Hepatotoxicity, N/V/D	<ul style="list-style-type: none"> <li>• Lots of black box warnings!!</li> <li>• Pregnancy X</li> <li>• Give with folic acid</li> </ul>
Leflunomide (Arava)	100 mg PO daily x 3 days followed by 20 mg daily	Hepatotoxicity, Myelosuppression, HTN, Rash, N/D	<ul style="list-style-type: none"> <li>• Pregnancy X</li> <li>• Monitor BP</li> </ul>
Hydroxychloroquine (Plaquenil)	400 – 600 mg PO daily (monotherapy), 200 mg PO BID (with MTX)	Ocular toxicity, Insomnia, Rash, skin pigmentation, N/V/D	<ul style="list-style-type: none"> <li>• ophthalmologic exam every 3 months</li> <li>• Wear sunglasses and caution in driving</li> </ul>
Sulfasalazine (Azulfidine)	500 – 1000 mg daily with meals (initial) and increase by 500 mg weekly until maintenance dose of 2 g in 2-3 divided doses	Yellow-orange discoloration (Urine/Skin), Photosensitivity, Myelosuppression, transaminitis, N/D	<ul style="list-style-type: none"> <li>• Color change of urine and skin</li> <li>• Wear sunscreen and sunglasses</li> </ul>

# Biologic DMARDs (TNF-I)

- **Etanercept (Enbrel)** – 50 mg SC once weekly
- **Adalimumab (Humira)** – 40 mg SC every 2 weeks
- **Infliximab (Remicade)** – 3 mg/kg IV over  $\geq 2$  hrs at 0, 2, and 6 weeks.
- **Certolizumab pegol (Cimzia)** – 400 mg SC at 0, 2, and 4 weeks initially and 200 mg SC every other week or 400 mg every 4 weeks for maintenance.
- **Golimumab (Simponi Aria)** – 50 mg SC once a month or 2 mg/kg IV over 30 min at 0 and 4, then every 8 weeks.





# Biologic DMARDs (non-TNF)

- **Rituximab (Rituxan)** – 1000 mg IV on days 1 and 15
- **Anakinra (Kineret)** – 100 mg SC once a day
- **Abatacept (Orencia)** – 500 – 1000 mg IV at 0,2, and 4 weeks, then every 4 weeks or 125 mg SC weekly
- **Tocilizumab (Actemra)** – 4 mg/kg IV over 60 min every 4 weeks or 162 mg SC every week (for  $\geq 100$ kg) and every other week (for  $< 100$  kg)
- **Sarilumab (Kevzara)** – 200 mg SC every 2 weeks



# Biologic DMARDs (TNFI & non-TNF)

- Must screen patient for TB prior to initiate therapy
- Treat latent or active TB for 1 month prior to starting or resuming biologics
- Avoid live vaccines while on therapy
- Give appropriate vaccinations (inactivated)
  - Pneumococcal
  - Influenza (IM)
  - Hepatitis B (if risk factors exist: healthcare personnel, drug abuse, multiple sex partners)

# Synthetic small molecule

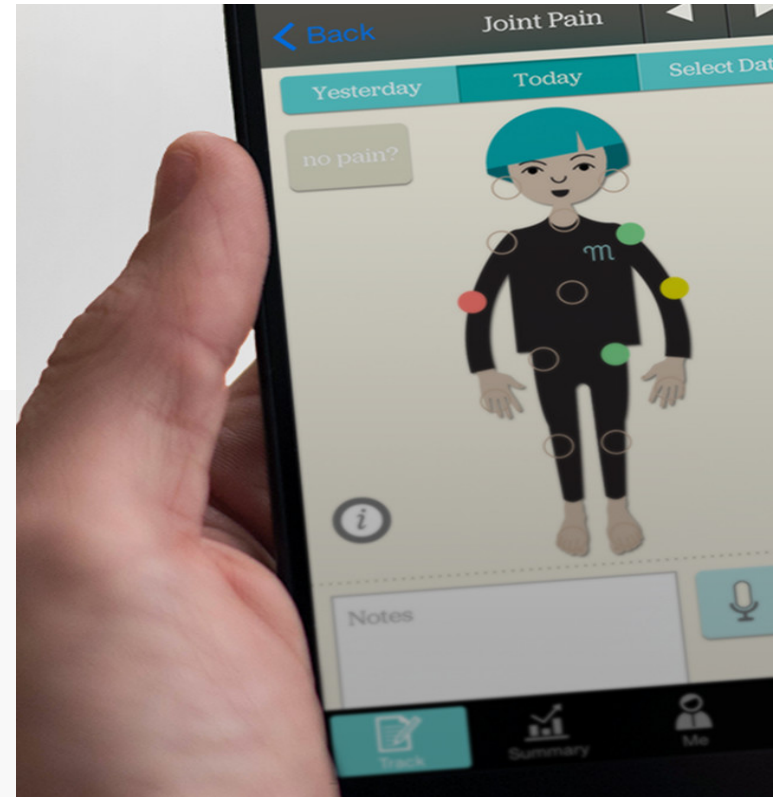
- **Tofacitinib (Xeljanz, Xeljanz XR)** – 5 mg by mouth twice a day for immediate release and 11 mg by mouth once a day for extended release.
- Adverse reactions – Serious infections including TB, fungal, viral, or other opportunistic infections, Lipid abnormalities, Bradycardia, Malignancy
- Patient education – avoid live vaccines during therapy and check TB prior to therapy

# Other Treatments

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroids
- Thermotherapy
- Electromagnetic and ultrasound therapies
- Patient education programs like nurse-led patient education program, mindfulness-based stress reduction, and coaching program for healthy physical activity.

# Interesting/Useful App

- MyRA
  - Track joint pain daily
  - Track medications
  - Track activity limits
  - Summary report



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