



Welcome!

Initial Therapy: Methotrexate

Jennifer Mandal, MD

April 11, 2022

As you arrive, please put your name, service unit, and preferred email into the chat.

Methotrexate

Jennifer Mandal, MD

RAE Initiative, UCSF Rheumatology

April 11, 2022

DISCLOSURES

AMA Designation Statement

The University of California, San Francisco School of Medicine (UCSF) is accredited by the Accreditation Council of Continuing Medical Education (ACCME) to provide continuing medical education for physicians. UCSF designates this live activity for a maximum of 1 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosure Statement

Planners Jennifer Mandal, MD, Leslie Dexheimer Gleason, RN, and Tabitha Foraker, MPH have stated they have no relationships to disclose. Speaker Jennifer Mandal, MD has stated she has no relationships to disclose.



Please remember to sign
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Type your name, service unit, and email into the
chat

DIGITAL STORY TELLING WORKSHOP

3-Day
In-Person Workshop

\$50.00 incentive each day,
breakfast and lunch
provided, and free lodging
for eligible participants

May 12, 13 &
14, 2022

8:30AM to
4:30PM

Gallup, NM



You are invited to make a Digital Story

In this workshop, you will learn to tell your story using your voice, pictures, video clips, music, etc. You will put all these together to make your video story about living with Rheumatoid Arthritis.

- Create your own 3-minute digital story
- Learn the basics of script development, digital imagery and video editing
- Record & use your voice with your pictures

We are excited to hear your story!

- How has Rheumatoid Arthritis impacted your life?
- What do you want others to understand about Rheumatoid Arthritis?
- What are ways to take care of yourself while living with Rheumatoid Arthritis? What keeps you strong?

Sign Up Today

CONTACT: Marita Jones or Tina Tso

Call: (505) 368-6567

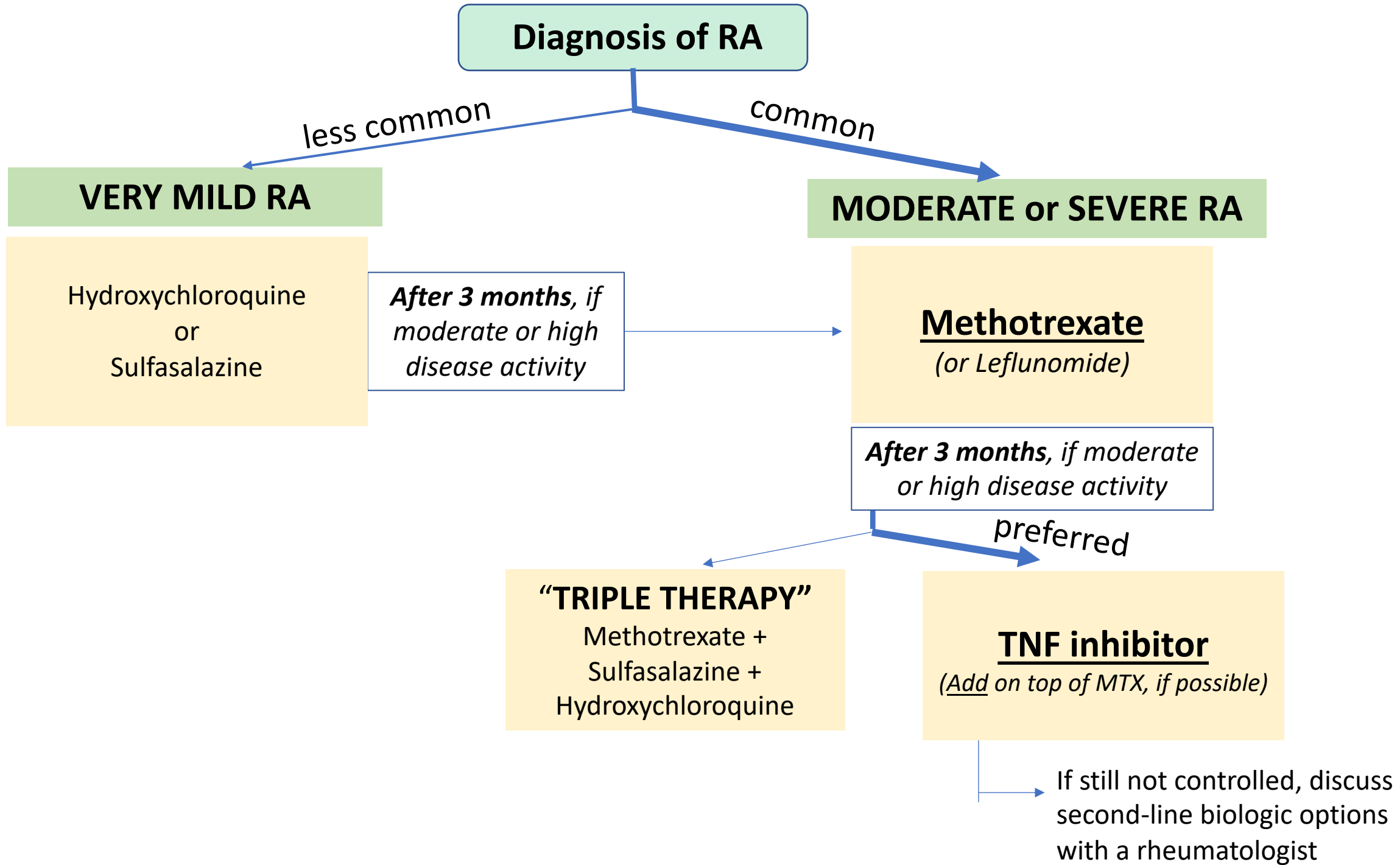
Email: marita.jones@hncpartners.org

Training by Healthy Native Communities Partnership, Inc.
PO Box 1019, Shiprock, NM 87420

Terminology: DMARDs

Disease Modifying Anti-Rheumatic Drugs

- “Conventional DMARDs”:
 - Methotrexate, Hydroxychloroquine, Sulfasalazine, Leflunomide
- “Biologic DMARDs”:
 - TNF inhibitors: etanercept/Enbrel (SQ), adalimumab/Humira (SQ), infliximab/Remicade (IV)
 - Others: abatacept (T cell costimulatory inhibitor), rituximab (anti-CD20), tocilizumab (IL-6 inhibitor), tofacitinib (JAK inhibitor)



Methotrexate

- MTX is the preferred first-line DMARD in patients with moderate-severe RA
- First used to treat RA in the 1950s, but didn't see widespread use until the 1980s
- MTX is a structural analogue of folic acid – it competitively inhibits folic acid metabolism (disrupting B and T cell proliferation) and increases extracellular concentrations of adenosine (anti-inflammatory effects)

Methotrexate

FDA-approved indications:

- RA
- Psoriasis

Off-label use:

- Inflammatory arthritis in SLE, MCTD
- Spondyloarthritis w/ peripheral joint involvement: Psoriatic arthritis, Reactive arthritis
- ANCA vasculitis, PAN, Takayasu arteritis
- Sarcoidosis
- Dermatomyositis/Polymyositis
- Scleroderma (skin/joints)
- Scleritis, Uveitis

Poll Question #1:

Which of the following is FALSE?

- A. The liquid formulation of MTX (for SQ injections) can be mixed with juice and taken orally
- B. Patients who don't have adequate disease response to 25mg of PO MTX should switch to 25mg of SQ MTX
- C. Typical starting dose of MTX is 7.5-10mg weekly
- D. Patients on MTX should take folic acid 1mg daily, except on the day of the week that they take their MTX

Poll Question #1: Answer

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Methotrexate Dosing

ONCE A WEEK (not daily)

Pills, oral liquid, or SQ

Starting dose for RA:

- Moderate disease: **7.5mg weekly** for 1 month → check labs → **15mg weekly**
- Severe disease: **10mg weekly** for 1 month → check labs → **20mg weekly**
- Max dose = 25mg weekly

Oral bioavailability varies greatly (20-95%).

If 20-25mg PO is not getting adequate response, try splitting the PO dose AM/PM, or switch to SQ.

Everyone on MTX should also take **folic acid 1mg daily** (can increase to 2-5mg daily if needed)

Poll Question #2:

Which of the following is TRUE?

- Methotrexate typically achieves full effect within 1-2 months
- Methotrexate should not be combined with NSAIDs due to decreased MTX metabolism
- Methotrexate can be used in combination with sulfasalazine
- Methotrexate should not be combined with TNF inhibitors (infliximab, adalimumab) due to increased risk of serious infections

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Expectations

- Can take 2-3 months to start seeing improvement.
~6 months for full effect.
- May need to combine with other medications (ex: sulfasalazine, hydroxychloroquine, or biologic DMARDs) to achieve adequate disease control
- When possible, MTX should be continued when adding a TNFi (especially adalimumab/Humira or infliximab/Remicade)
 - Decreases the risk of forming anti-TNFi antibodies



Poll Question #3:

Which of the following is TRUE?

- Non-alcoholic fatty liver disease (NAFLD) is an absolute contraindication to MTX
- MTX is contraindicated in pregnancy, but safe during breastfeeding
- Patients taking MTX should be counseled to limit alcohol consumption to 2 drinks/week
- Men who are planning to father a child should stop MTX 3 months prior to trying to conceive

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Avoid methotrexate if:

- Woman of childbearing age considering pregnancy or not using birth control. (Pregnancy Category X)
- Breastfeeding
- Pre-existing liver disease, hepatitis B or C
 - Mild NAFLD with normal liver enzymes is ok
- Heavy alcohol use
 - US guideline is ≤ 2 drinks/week, European guideline more lenient...
- CKD stage 4 or 5 (caution w/ stage 3)
- Consider alternatives if they also have lung disease



Potential side effects

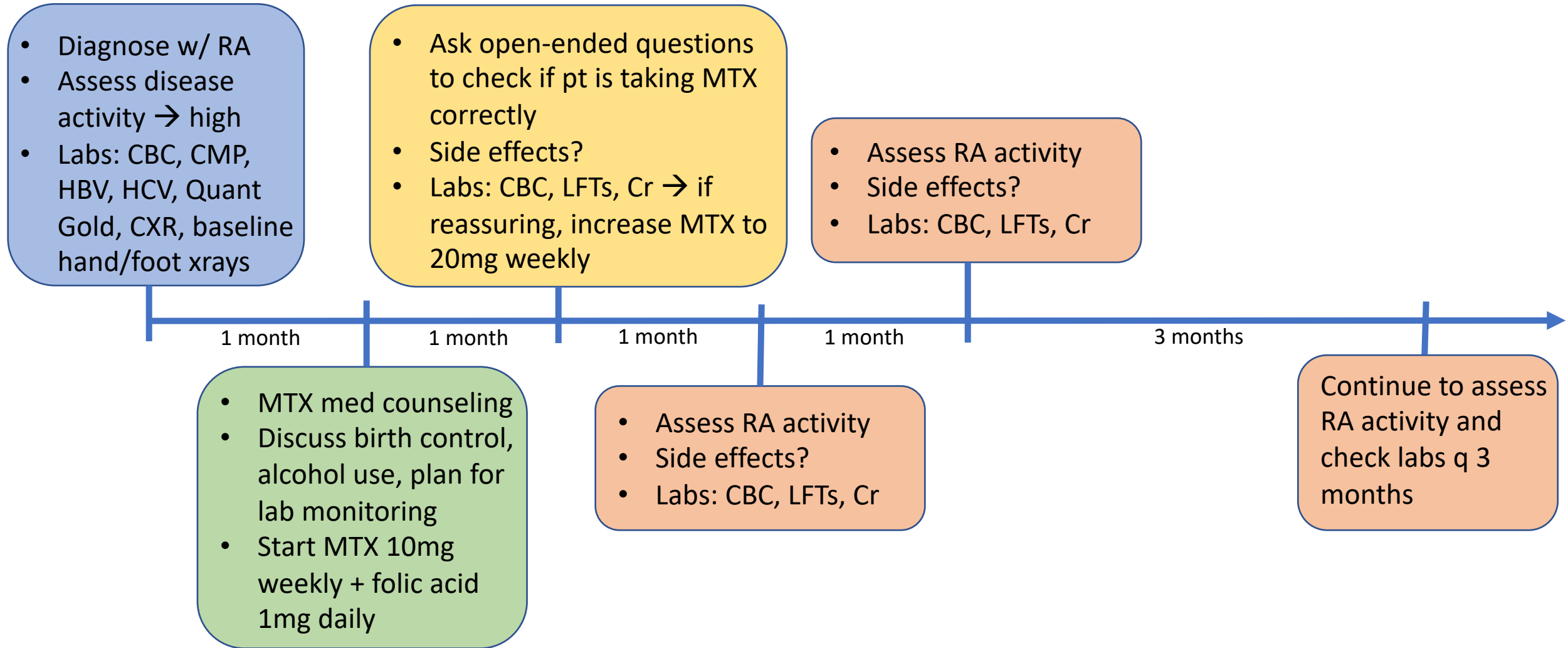
- GI upset (splitting the dose AM/PM can help)
- Oral ulcers
- Hepatotoxicity (transaminitis, cirrhosis)
- Infections
- Bone marrow suppression (cytopenias)
- Macrocytosis
- Brain fog
- Pneumonitis (very rare)

Safety Pearl:
MTX is renally cleared, thus any impairment of GFR will result in ↑ serum levels of MTX and higher risk of toxicities

Medication Monitoring

- Before starting MTX:
 - CBC
 - CMP
 - Pre-immunosuppression labs: HBV Surface Ag/Surface Ab/Core Ab, HCV, Quant Gold/PPD
 - CXR
- Once on MTX:
 - CBC, LFTs, Cr every month for the first 3 months, then q3 months if stable dose

Typical MTX Timeline



Poll Question #4:

A 78F with h/o diabetes and mild dementia was newly diagnosed with RA and prescribed 15mg (6x 2.5mg tablets) once weekly. The pharmacy dispensed a 3-month supply of pills. 7 days later, she presents to the ER with severe nausea, diarrhea, bleeding oral ulcers, leukopenia (WBC 1.9), thrombocytopenia (platelets 70K), and transaminitis (AST 510, ALT 720). She is admitted to the hospital. What therapeutic intervention is most appropriate?

- A. Empiric broad-spectrum antibiotics
- B. IV leucovorin
- C. IV methylprednisolone
- D. IVIG

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MTX overdose

- Causes:
 - Misunderstanding of med instructions (i.e. taking dose daily instead of weekly)
 - Decreased GFR leading to increased serum levels of MTX
- Treatment:
 - Admit to hospital
 - Stop MTX
 - IV leucovorin (folinic acid) 5-10mg every 12 hours until recovery (improvement in cytopenias to safe range, improvement in transaminitis to <2x ULN, resolution of GI symptoms)

Prevention is better than cure

- Dispense only a 1-month supply of MTX, especially for new starts
- Provide easy-to-read instructions w/ a specific day of the week, e.g. “Take 4 pills every Sunday for rheumatoid arthritis”
- Emphasize that MTX should not be taken as-needed for symptom control
- At first follow-up appointment, ask open-ended questions (“How are you taking your methotrexate?”)
- Monitor Cr: If GFR <50, downtitrate or consider stopping MTX, if GFR<30, stop MTX

Case Presentation

Samantha Austin, NP

CME Credit Link

