



Welcome!

Other Conventional DMARDs

Jennifer Mandal, MD

April 18, 2022

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

DISCLOSURES

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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
in:

Type your name, service unit, and email into the
chat

Location Update: Farmington, NM

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

Farmington,
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



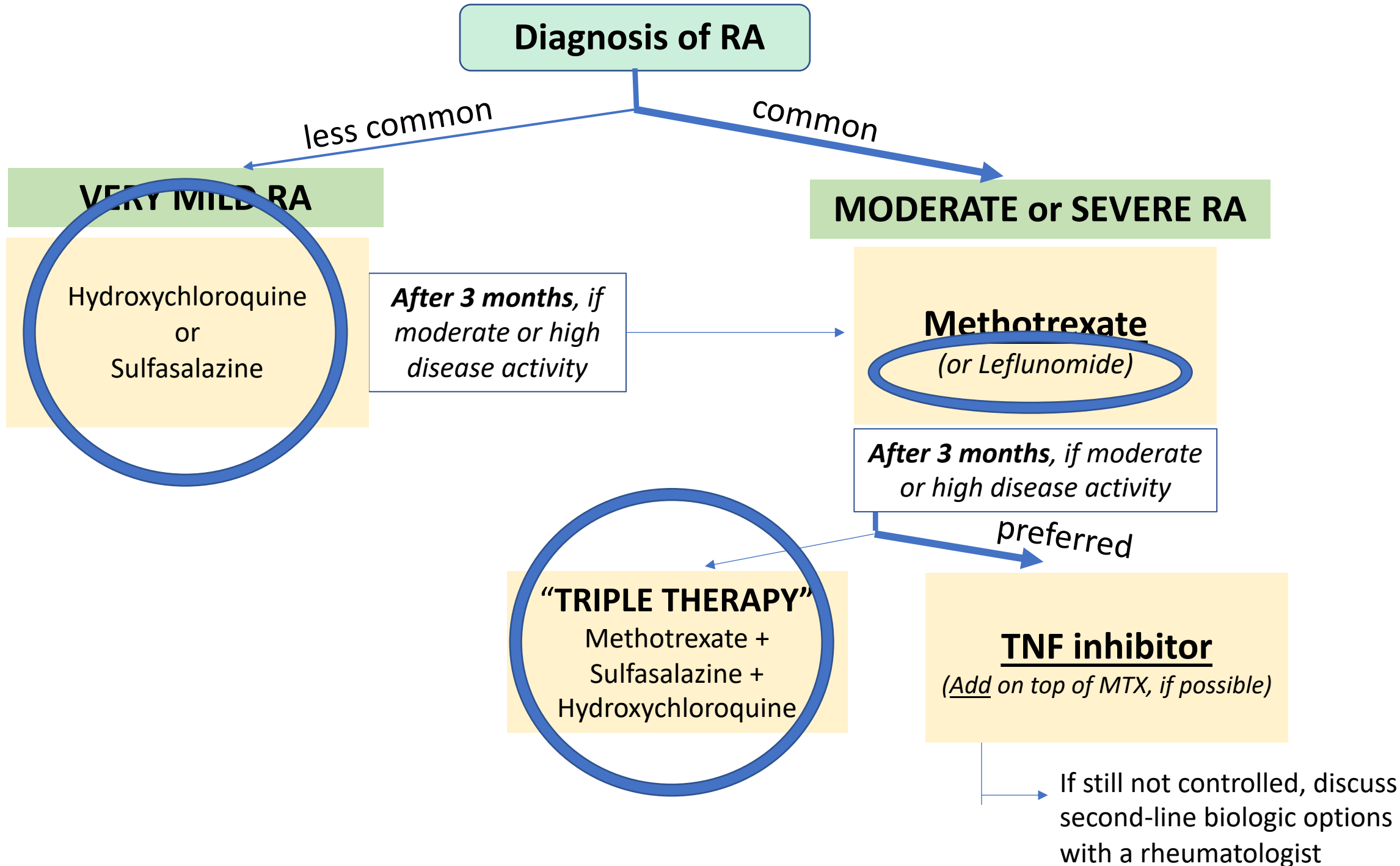
Other Conventional DMARDs for RA

Leflunomide · Hydroxychloroquine · Sulfasalazine

Jennifer Mandal, MD

RAE Initiative, UCSF Rheumatology

April 18, 2022





Hydroxychloroquine

Hydroxychloroquine (Plaquenil)

- Anti-malarial
- First-line therapy for **very mild RA** (low disease activity, no extra-articular manifestations, no erosions), or can be used in combination w/ MTX+sulfasalazine (“triple therapy”) in more severe/refractory RA
- Also used in SLE, MCTD, Sjogrens

Hydroxychloroquine (Plaquenil)

- Unlike most other DMARDs, **HCQ is not immunosuppressive**
- Mechanisms of actions are poorly understood. Inhibitory effect on toll-like receptors (TLRs), many other proposed mechanisms
- **Can take months to have effect** (full effect typically by 6 months)
- Long terminal half-life (1-2 months)

Hydroxychloroquine: Dosing

- Once daily pill
- Calculate dose based on weight: **5mg/kg, then round down to nearest 100.** (Only comes in 200mg tablets. Ok to cut pills.)
 - Dose >5mg/kg is associated with increased risk of irreversible retinal toxicity
- Dose should be lowered in setting of severe renal impairment
 - HD: 200mg 3x/week after HD

Example:

70kg patient:


$$70\text{kg} \times 5\text{mg/kg} = 350\text{mg}$$

→ Round down to 300mg.


Dose = 300mg (1.5 pills) per day

Hydroxychloroquine: Adverse Effects

- **Retinal toxicity**
- GI upset (cramping, nausea)
- Skin hyperpigmentation
- Transient blurry vision
 - early; not associated with ↑ risk for retinal toxicity
- Neuromyotoxicity (rare)
 - painless proximal muscle weakness, CK normal or slightly elevated
- Cardiotoxicity (rare at dose <5mg/kg)
 - QTc prolongation, arrhythmias
 - Cardiomyopathy resulting in CHF



Not immunosuppressive



Safe in pregnancy & breastfeeding

What monitoring is recommended for a patient on hydroxychloroquine?

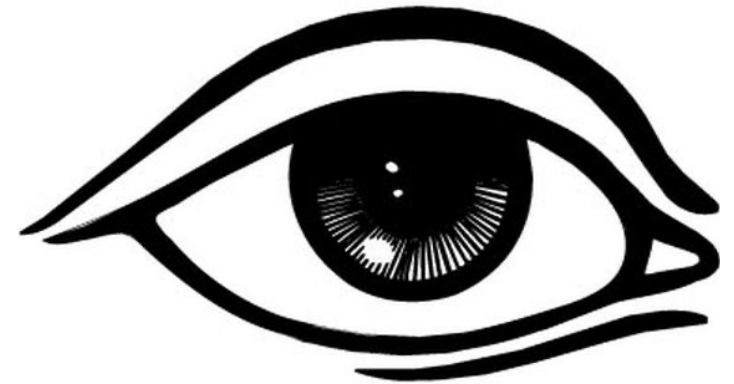
- A. Ophthalmology exam every 5 years
- B. Ophthalmology exam every year
- C. Ophthalmology exam every 5 years + CBC/CMP every year
- D. Ophthalmology exam every year + CBC/CMP every year

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Hydroxychloroquine: Retinal Toxicity

- Vision-threatening, irreversible retinal toxicity
- **Risk depends heavily on duration of HCQ use**
 - <2% risk in the first 5 years
 - But rises to 20% with >20 years of use
- Screening: Annual ophthalmology exam (visual acuity screening is not enough) while on HCQ
- Discontinue HCQ immediately if any sign of retinal toxicity



How to reduce the risk of hydroxychloroquine associated retinal toxicity:

- Make sure your patients are getting their annual ophthalmology exam (with dilation and full retinal exam)
- Limit dose to $<5\text{mg/kg}$
- Do not combine hydroxychloroquine with chloroquine
- If an ophthalmology exam reveals any retinal toxicity (even mild) stop hydroxychloroquine immediately and do not restart (list it as allergy/contraindicated in the patient's chart)

Hydroxychloroquine: Monitoring

- Annual retinal exam
- No routine lab monitoring required

The image features a central white diamond shape on a light gray background. The diamond is outlined by a thin white border. In the four corners of the image, there are overlapping geometric shapes: yellow diamonds in the top-left and bottom-right, and blue diamonds in the top-right and bottom-left. The text "Sulfasalazine" is centered within the white diamond.

Sulfasalazine

Sulfasalazine


- Used in RA since the 1980s
- Can be used as an alternative to HCQ in mild RA (low disease activity), or in combination with MTX+HCQ (“triple therapy”) in more severe/refractory disease

Sulfasalazine: Dosing & Monitoring

- Pre-treatment testing: CBC, LFTs, Cr
 - Consider testing for G6PD deficiency (increased risk of hemolytic anemia)
- Typically start with 500mg daily → then increase dose by 500mg weekly (w/ lab checks) until target dose of 2g/daily (divided BID) is achieved
- Monitoring: Check labs (CBC, LFTs, Cr) ~1 week after each dose increase. Once on a stable dose, can check labs q 3 months

Sulfasalazine: Adverse Effects

- GI upset
- Hepatotoxicity
- Leukopenia (usually mild, but life-threatening agranulocytosis can rarely occur, typically within first 3 months of starting tx)
- Hemolytic anemia (usually in setting of G6PD deficiency)
- Men: reversible oligospermia (Avoid in men who are trying to conceive.)



Safe in pregnancy & breastfeeding

What is “Triple Therapy” for RA?

- A. Methotrexate + Leflunomide + Hydroxychloroquine
- B. Methotrexate + Hydroxychloroquine + Sulfasalazine
- C. Methotrexate + Sulfasalazine + Prednisone
- D. Methotrexate + Hydroxychloroquine + Prednisone

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RA “Triple Therapy”: MTX + HCQ + Sulfasalazine

- For patients who have inadequate response to MTX alone, options for escalating therapy include:
 - 1) Adding a biologic DMARD such as TNFi (preferred)
 - 2) Starting triple therapy (PO)

Complex oral regimen with heavy pill burden...

1-2 pills of HCQ once daily
2-6 pills of sulfasalazine daily (divided BID)
1 folic acid pill daily
6-10 methotrexate pills (or SQ injection) once a week



34 – 73 pills per week,
just for RA!

RA “Triple Therapy”: MTX + HCQ + Sulfasalazine

Reasons to choose Triple Therapy over a Biologic DMARD:

- Patient strongly prefers pills over injections (ex: needle phobia)
 - Note: JAK inhibitors are another potential option for patients who will only take pills
- Cost: Triple therapy is MUCH less expensive than TNFi (and other biologics).
Depends on insurance coverage.
- “Don’t Rock the Boat”: Patient has been stable on triple therapy for a long time and doesn’t want/need to change.



Leflunomide

Quick Pearls: Leflunomide

- Oral conventional DMARD
- Sometimes used as an alternative to MTX (ex: pt in whom daily dosing is strongly preferred)
- Very similar side effect profile to MTX (GI upset, hepatotoxicity, teratogenic), same lab monitoring guidelines
 - CBC, Cr, LFTs: monthly until stable dose, then q3 months
- Typical dose = 20mg daily (can decrease to 10mg daily if side effects)

A 41 year old woman with RA on leflunomide discovers that she is 8 weeks pregnant. She wishes to continue the pregnancy. In addition to stopping leflunomide, what is the most appropriate next step:

- A. Start methotrexate
- B. Counsel her that termination of the pregnancy is recommended due to high risk of maternal mortality
- C. Start cholestyramine
- D. Refer to high risk OB for serial fetal echocardiograms throughout the pregnancy

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Quick Pearls: Leflunomide

- **EXTREMELY LONG HALF-LIFE:** Can linger in the body for **up to 2 years** after discontinuation!
 - **Avoid in women of childbearing age!**
 - In case of serious adverse event or accidental pregnancy, there is a (very unpleasant) accelerated drug elimination protocol: cholestyramine 8g PO TID for 11 days



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