DIAGNOSIS & MANAGEMENT OF RHEUMATOID ARTHRITIS: NAVAJO NATION

Initial visit checklist:

- ❑ LABWORK: RF, CCP, CBC, CMP, ESR, CRP, PPD or Quantiferon, HBV sAg/sAb/cAb, HCV Ab
- ❑ IMAGING: bilateral hand and foot xrays (to establish baseline and screen for alternate diagnoses)
- ❑ MEDS: consider scheduled NSAIDs vs. prednisone 5-10mg daily (temporary measure until patient is stable on DMARD therapy)
- ❑ Pneumovax/Prevnar, flu shot, Shingrix, HBV vaccine, COVID19 vaccine as early as possible.
- ❑ If TB screen positive (and active TB has been ruled out), start LTBI treatment at least 1 week before starting methotrexate
- ❑ Schedule follow-up to review labs/xrays and discuss DMARD initiation

DIAGNOSIS: 2010 ACR/EULAR CRITERIA

1. Synovitis must be present; no other diagnosis to explain it
2. RA diagnosed if **≥6 points** from the following:

JOINTS:
- 2-10 large joints (i.e. any joint except wrist/hand) …1 point.
- 1-3 small joints (wrists, any hand joint).....2 points
- 4-10 small joints.....3 points
- >10 joints, including ≥1 small joint.....5 points

SEROLOGY:
- RF or anti-CCP low-positive (above ULN).....2 points
- RF or anti-CCP high-titer (3x >ULN).....3 points

ESR **or** CRP ELEVATED.....1 point
SYMPTOM DURATION ≥6 weeks.....1 point

General principles of treatment:

- Choose initial DMARD based on disease severity, baseline labs, and comorbidities (MTX is most common first-line tx)
- Start DMARD ASAP to avoid progressive joint damage
- **Goal is remission or low disease activity** (RAPID-3 ≤2 or CDAI ≤10)
- Evaluate patient q3 months until this is achieved
- Vast majority of patients will require life-long medication

less common

VERY MILD RA
ALL of the following: <5 joints involved, no extra-articular disease, minimal limitation in joint function, RAPID-3 ≤2 or CDAI ≤10.

common

MODERATE or SEVERE RA
ANY of the following: >5 joints involved, extra-articular disease, erosions on baseline x- rays, function limited, RAPID-3 >2 or CDAI >10

1st line for most RA patients

HYDROXYCHLOROQUINE
200-400mg PO daily [max dose 5mg/kg]
* May reduce risk of diabetes and improve lipids
* Well-tolerated, safe in pregnancy
* Retinal exam at baseline and q1yr

OR

SULFASALAZINE
500mg BID x 1 week → 1000mg BID
* Better efficacy than hydroxychloroquine, but more likely to cause GI upset
* Monitor WBC q2 months

After 3 months, if moderate or high disease activity

METHOTREXATE
10mg PO qWEEK x 4 weeks, then check labs. If no side effects and labs stable then increase to **20mg PO qWEEK**. Recheck labs after 4 weeks.
If RA activity still mod-high after 3 months: switch to **25mg subcutaneous qWEEK**
MTX monitoring:
* CBC, liver panel, Cr q3months once the dose is stable
* Must take with **folic acid 1mg daily** (increase to 2mg daily if mild side effects)

If not tolerating MTX, might consider:

LEFLUNOMIDE
10mg PO daily x 6 weeks, then check labs. If tolerating, increase to **20mg PO daily**
* Diarrhea in 20%
* Labs and contraindications same as for MTX (see page 2); Avoid in women of childbearing age: risk of birth defects up to 2 years after cessation!

After 3 months, if moderate or high disease activity

preferred

"TRIPLE THERAPY"
Methotrexate + Sulfasalazine + Hydroxychloroquine
- Large pill burden makes adherence challenging
- Lower infectious risk compared to TNFi
- Can be considered in patients who strongly prefer pills over injections

TNF-INHIBITOR
Adalimumab (Humira) 40mg SC q2weeks
or Etanercept (Enbrel) 50mg SC qweek
or Certolizumab pegol (Cimzia) 200mg SC q2weeks
* Ideally, give TNFi AND weekly methotrexate
* Adalimumab and Etanercept are more readily available
* Certolizumab is specifically preferred in pregnancy

If still not controlled, discuss second-line biologic options with a rheumatologist

When to use prednisone in RA?

Prednisone 5-10mg daily may be considered initially (<3 months, while waiting for DMARD to take effect), but should be avoided as chronic therapy whenever possible, due to long term side effects.

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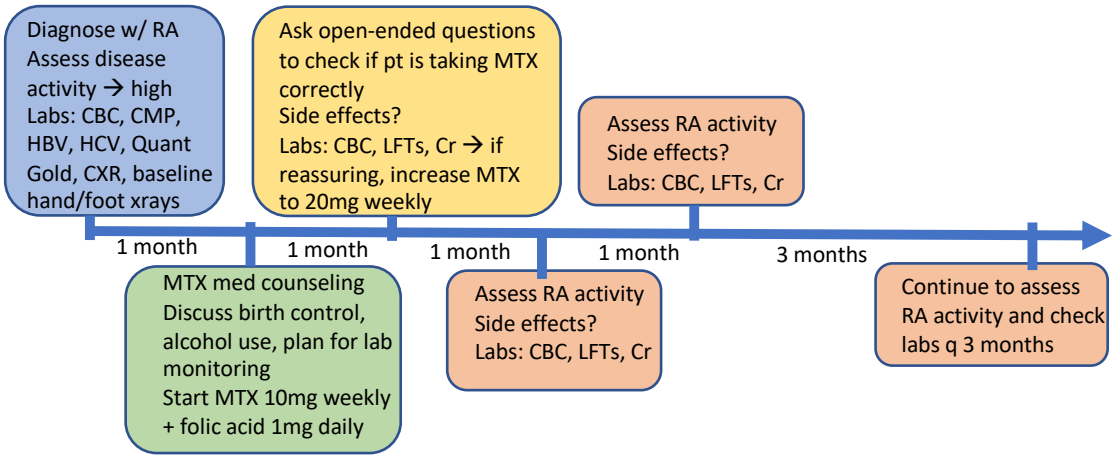
Conventional DMARD Safety & Monitoring:

Methotrexate:
Contraindicated in: pregnancy, breastfeeding, chronic liver disease, heavy alcohol use, CKD stage 4/5
Caution in: CKD 3 (decrease dose)
Side effects: GI upset, oral ulcers, transaminitis (if AST/ALT <2x ULN: ok to monitor; >2x ULN: reduce dose or discontinue), infections, cytopenias, macrocytosis, pneumonitis (very rare)
Pearls: Dosed once WEEKLY. Splitting the oral dose (half in AM, half in PM) or switching to SQ formulation can improve absorption/efficacy. Always prescribe along with folic acid 1-5mg daily. In case of overdose: IV leucovorin.
Monitoring: CBC, Cr, LFTs q 3 months

Hydroxychloroquine:
Caution in: advanced renal impairment (decrease dose)
Side effects: Retinal toxicity (risk increases with duration of therapy), GI upset, skin hyperpigmentation. Rare myopathy, rare cardiotoxicity (avoid with known QT prolongation).
Pearls: Not immunosuppressive. Safe in pregnancy/breastfeeding.
Monitoring: Annual retinal exam (q6 months after >10 years on therapy). No lab monitoring required.

Sulfasalazine:
Side effects: GI upset, hepatotoxicity, leukopenia, hemolytic anemia (higher risk in G6PD deficiency)

Typical Timeline for Starting Methotrexate:



Pregnancy & Breastfeeding:

Safe	Contraindicated	Insufficient/Limited Data
Hydroxychloroquine, Sulfasalazine, TNFi (certolizumab has most data)	Methotrexate, Leflunomide	Abatacept, IL-6 inhibitors, Rituximab, JAK inhibitors

Overview of Biologic DMARDs for RA:

Generic	Trade	Class	Administration	Frequency	Pearls
Etanercept Adalimumab Golimumab Certolizumab Infliximab	Enbrel Humira Simponi Cimzia Remicade	TNF inhibitor	SQ SQ SQ SQ IV	Weekly Q 14 days Monthly Monthly Q 4-8 weeks	Typically used as first-line biologic therapy. Often try 2 different TNFi before moving on to another class. Avoid in class III/IV CHF, SLE-overlap, demyelinating disease.
Abatacept	Orencia	Costim blocker	SQ/IV	Weekly/monthly	Pro: Fewer infectious complications. Con: Longer time to efficacy
Tocilizumab Sarilumab	Actemra Kevzara	IL-6 inhibitor	SQ/IV SQ/IV	Weekly/monthly Weekly/monthly	Pro: Well-tolerated Con: Can cause hyperlipidemia, intestinal perforation
Rituximab	Rituxan	Anti-CD20	IV	2 IV doses every 6 months	Pros: May help RA-ILD, q6 month dosing can help with compliance, lowest risk of activating TB. Cons: B cell depletion = high risk of severe COVID, poor response to vaccines.
Tofacitinib Baricitinib Upadacitinib	Xeljanz Olumient Rinvoq	JAK inhibitor	PO PO PO	Daily or BID Daily Daily	Pro: Oral Con: high rate of zoster, increased risk of CVE/VTE in at-risk patients