Rheumatoid Arthritis

ACR 2021 treatment guideline · methotrexate is the anchor, treat to target, and screen before every biologic

Erosions are *irreversible*

RECOGNIZE IT *the pattern matters more than any single test*

THE PATTERN

Symmetric, small-joint, inflammatory. MCPs, PIPs and wrists, **sparing the DIPs**, which is what separates it from osteoarthritis and psoriatic arthritis. **Morning stiffness over an hour**, improving with use. Six weeks or more of symptoms.

THE SEROLOGY

Anti-CCP is the more specific (roughly 95%) and predicts erosive disease; **rheumatoid factor is less specific** and appears in hepatitis C, Sjogren, endocarditis and healthy older people. **Seronegative RA is real**, so a negative pair does not exclude it.

DO NOT WAIT FOR X-RAYS

Erosions and joint space narrowing are **late** findings, so a normal film early is expected and reassures you about nothing. **Ultrasound or MRI detects synovitis and erosions far earlier.** The window for preventing damage is the first months.

TREAT TO TARGET *the core principle of the 2021 guideline*

Step	What to do
Start methotrexate strong recommendation	**Methotrexate monotherapy is first-line** in moderate to high disease activity in a DMARD-naive patient, preferred over other conventional DMARDs, over biologics and over JAK inhibitors. It remains the **anchor drug**, including as the backbone when a biologic is later added. **Oral is conditionally preferred to start**; switch to subcutaneous for GI intolerance or inadequate response, which improves bioavailability
Always co-prescribe folic acid	Reduces stomatitis, GI upset, cytopenias and transaminitis **without reducing efficacy**. Omitting it is the commonest avoidable reason a patient stops methotrexate
Set a target and measure it	Aim for **remission or, failing that, low disease activity**, using a composite score at each visit rather than a global impression. **Reassess at about 3 months and escalate if the target is not met**: drifting on an ineffective dose is how joints are lost
Use steroids as a bridge only	Effective and fast, but the guideline pushes toward **the shortest course and lowest dose possible**, because the harms accumulate silently: bone loss, glucose, infection, cataract. **Steroids are not a treatment plan**
Escalate	Add a **biologic (TNF inhibitor or a non-TNF agent) or a JAK inhibitor** when methotrexate is inadequate. Triple conventional therapy remains a reasonable alternative

Measure with a named score, not an impression: DAS28, CDAI or SDAI at each visit, so escalation decisions are defensible and comparable over time. **In sustained remission, taper rather than stop.** The guideline favors gradually reducing therapy while continuing at least one agent, because **complete withdrawal carries a high flare rate**, and a flare can undo control that took months to achieve. **Taper the steroid first, then the biologic, and keep methotrexate longest.**

THE DRUG CLASSES *what to reach for, and what each one costs you*

Class	Agents	Where it fits
Conventional DMARDs *csDMARD*	**Methotrexate**, leflunomide, sulfasalazine, hydroxychloroquine	**Methotrexate first in almost everyone.** Hydroxychloroquine and sulfasalazine are weaker alone but combine with methotrexate as **triple therapy**, which performs comparably to adding a biologic and costs far less
TNF inhibitors *bDMARD*	Etanercept, adalimumab, infliximab, certolizumab, golimumab	Usually the **first biologic**. **Keep methotrexate alongside** where tolerated: it improves response and reduces anti-drug antibodies. Avoid in advanced heart failure and demyelinating disease
Non-TNF biologics	**Abatacept** (T-cell co-stimulation), **tocilizumab** (IL-6), **rituximab** (anti-CD20)	For inadequate response to a TNF inhibitor. **Tocilizumab normalizes CRP regardless of disease control**, so the CRP can no longer be used to detect infection or track activity. **Rituximab suits seropositive disease** and is preferred where there is a history of malignancy or demyelination
JAK inhibitors *tsDMARD*	Tofacitinib, baricitinib, upadacitinib	Oral and rapidly effective, but carry the **class boxed warning** below. **Also raise herpes zoster risk substantially**, so vaccinate beforehand with the recombinant vaccine

BEFORE ANY BIOLOGIC OR JAK INHIBITOR *this checklist prevents the disasters*

Screen	Why
Latent tuberculosis	TB skin test or interferon-gamma release assay, plus a chest radiograph. **TNF inhibitors reactivate latent TB**, often extrapulmonary and disseminated. **Treat latent TB before starting**, not alongside
Hepatitis B and C	**HBsAg and anti-HBc.** Immunosuppression can cause **hepatitis B reactivation with fulminant liver failure**, which antiviral prophylaxis prevents
Vaccination status	Bring vaccines up to date **before** starting, ideally including pneumococcal, influenza, COVID-19 and recombinant zoster. **Live vaccines are contraindicated** once on biologics
Heart failure and demyelination	**TNF inhibitors are contraindicated in advanced heart failure** and are avoided with demyelinating disease, which they can unmask or worsen
Cardiovascular and malignancy risk JAK inhibitors	A safety trial of tofacitinib against TNF inhibitors in patients **over 50 with at least one cardiovascular risk factor** found **more major cardiovascular events and more malignancies**, and this carried into a class boxed warning covering MACE, malignancy, **thrombosis** and mortality. **Prefer a TNF inhibitor in that population**, and reserve JAK inhibitors for lower-risk patients or after biologic failure

MONITORING, EXTRA-ARTICULAR & PEARLS

- **Methotrexate monitoring:** CBC, transaminases and creatinine roughly every **2 to 3 months** once stable. **It is contraindicated in pregnancy and is an abortifacient**, so confirm contraception in both sexes and stop well before conception. **Avoid in significant renal impairment** and counsel about alcohol. **Never give trimethoprim-sulfamethoxazole with it**: both are antifolates and the combination causes severe pancytopenia.
- **Leflunomide needs a cholestyramine washout** before pregnancy or in toxicity, because it has an enterohepatic circulation and persists for many months.
- **The extra-articular disease is what shortens life. Accelerated cardiovascular disease** is the leading cause of death, so treat lipids and blood pressure actively. Also **ILD**, which methotrexate rarely causes but is far more often driven by the RA itself, plus Sjogren, nodules, anemia and secondary amyloidosis.
- **Ask about the neck before any intubation or surgery. Atlantoaxial subluxation** from long-standing RA can cause cord compression on neck extension. Longstanding erosive disease plus neck pain or any myelopathic sign needs **flexion-extension imaging before manipulation of the airway**.

References: 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis (Arthritis Care Res) · 2010 ACR/EULAR classification criteria · ORAL Surveillance and the resulting FDA class boxed warning for JAK inhibitors.

Educational aid; verify against current guidance, local formulary and patient factors.

roundsrx.com
roundsrx Infographic Series · #164