

Rheumatoid Arthritis

Your immune system is attacking the soft lining inside your joints.

THE STORY IN ONE SENTENCE

Your immune system is attacking the soft lining inside your joints.

“Rheumatoid arthritis happens when your body mistakes the slippery lining inside joints for an enemy and attacks it—special medicines can stop this attack and protect your joints.”

Normal anatomy — the body's job

Every joint where bones meet has a thin, soft lining called the synovium that makes slippery fluid so the bones can glide past each other without grinding. Your immune system patrols your body to attack germs and foreign invaders, but it leaves your own tissues alone because they carry the right markers. Keep that picture in your head, because all the weird findings in rheumatoid arthritis make sense only as a change from this normal setup.

BODY'S JOB

The synovium's job is to keep joints smooth and cushioned. It makes synovial fluid—a slippery liquid that works like oil in a hinge—so cartilage (the rubbery cap on the end of each bone) does not wear down when you move. Your immune system's job is to recognize 'self' markers on your cells and ignore them, while hunting down anything that looks foreign.

1. Bone ends meet inside a joint capsule, a tough bag that holds everything together.
2. The synovium lines the inside of that capsule and secretes (releases) synovial fluid into the joint space.
3. Synovial fluid lubricates the cartilage on the bone ends so they glide smoothly.
4. Your immune system—white blood cells, antibodies, and chemical signals—circulates in your blood and ignores the synovium because it carries 'self' markers.
5. Result: pain-free movement, no swelling, no stiffness.

What breaks

In rheumatoid arthritis, your immune system loses the ability to tell 'self' from 'foreign' and starts attacking the synovium as if it were a germ. White blood cells flood the joint, the synovium swells and thickens, and the inflamed tissue releases enzymes that eat away cartilage and bone. That one upstream break—autoimmune attack on the synovium—explains every downstream finding you see.

CLINICAL TERM

The immune system produces autoantibodies (rheumatoid factor and anti-CCP antibodies) that bind to proteins in the synovium. This triggers a cascade: T cells and B cells migrate into the joint, macrophages (immune cells that eat debris) and fibroblasts (cells that make scar tissue) multiply, and the synovium transforms into a thick, invasive tissue called pannus. The pannus secretes pro-inflammatory cytokines (TNF- α , IL-1, IL-6) and matrix metalloproteinases (enzymes that break down collagen and bone). Cartilage erodes, subchondral bone (the bone just under cartilage) develops erosions, and joint architecture is destroyed. Because autoantibodies circulate in the bloodstream, the attack is systemic and typically symmetric (both sides of the body).

How the body compensates

Early on, your body tries to dilute the inflammation by increasing blood flow to the joint (causing warmth and redness) and walling off the damage with scar tissue. Vital signs often stay normal even while joints are being destroyed, which is why rheumatoid arthritis can smolder for months before anyone realizes how much damage has happened. The danger is missing the point where compensation fails and life-threatening complications appear.

1. **Increased synovial fluid production:** The inflamed synovium makes extra fluid to try to flush out inflammatory chemicals—this causes the joint to swell like a water balloon.
2. **Angiogenesis (new blood vessel growth):** The pannus grows new tiny blood vessels to feed itself, which paradoxically brings in more immune cells and more inflammation.
3. **Muscle guarding and morning stiffness:** Muscles around the joint tighten overnight to splint and protect the inflamed area—gel phenomenon—leading to stiffness that takes over an hour to loosen up.
4. **Bone remodeling:** Osteoclasts (cells that break down bone) try to reshape eroded bone, but in RA they are overactive and cause more bone loss instead of repair.
5. **Systemic acute-phase response:** The liver cranks out C-reactive protein (CRP) and other acute-phase proteins to try to contain inflammation, which is why ESR and CRP are elevated in blood tests.

6. The crash points to watch for: Atlanto-axial instability (the top two neck bones, C1 and C2, slip because inflamed ligaments loosen—this can compress the spinal cord and cause paralysis or death), interstitial lung disease (scarring of lung tissue from chronic inflammation, leading to shortness of breath and low oxygen), vasculitis (inflammation of blood vessel walls that can cut off blood to fingers, toes, skin, or organs), serious infection (because the medicines that calm the immune system also raise infection risk), and Felty syndrome (RA plus an enlarged spleen plus low white blood cell count, which further raises infection risk).

Domino effect

1. Autoantibodies (rheumatoid factor and anti-CCP) appear in your blood and bind to proteins in the synovium. — A genetic trigger (often HLA-DR4) plus an environmental spark (smoking, infection, or gut bacteria) causes B cells to make antibodies that mistake your own joint lining for an enemy.
2. White blood cells flood into matching joints on both sides of your body—wrists, knuckles, finger joints—and the synovium swells. — Autoantibodies tag the synovium, so T cells, macrophages, and other immune cells migrate in through the bloodstream and release inflammatory chemicals (TNF- α , IL-1, IL-6) that cause redness, warmth, and swelling.
3. You wake up with stiff, swollen fingers that take over an hour to loosen up (morning stiffness), and the joints feel warm and tender. — Overnight, inflammatory fluid and gel-like debris pool in the joint (gel phenomenon), and muscles tighten to protect the area—movement pumps the fluid out and loosens things up slowly.
4. You feel tired, weak, and may run a low-grade fever even when your joints do not hurt much. — Cytokines circulating in your bloodstream signal your brain to release fever chemicals (prostaglandins) and trigger your liver to shift energy toward fighting inflammation, leaving you exhausted and sometimes anemic.
5. Over weeks to months, the thick synovium (pannus) releases enzymes that eat away cartilage and carve pits (erosions) into the bone underneath. — Matrix metalloproteinases and other proteases from the pannus digest collagen and calcium, eroding the bone surface—X-rays show these erosions as tiny holes at the joint edges.
6. Your fingers start to curve sideways (ulnar deviation), bend into swan-neck or boutonniere shapes, or your wrist bones collapse. — Bone erosions, stretched ligaments, and damaged tendons can no longer hold the joint in line, so the bones slip and deform under the pull of muscles and gravity.

7. The inflammation spreads beyond joints: your lungs scar (interstitial lung disease), blood vessels inflame (vasculitis), firm bumps appear under your skin (rheumatoid nodules), or the top neck bones slip (atlanto-axial instability). — The same autoantibodies and cytokines in your blood attack tissue in your lungs, blood vessel walls, skin, and the ligaments holding your skull to your spine—these extra-articular (outside the joint) problems can be more dangerous than the joint damage itself.
8. If untreated, you face serious complications: spinal cord compression from neck instability, lung failure from scarring, heart attack from inflamed arteries, or overwhelming infection from immune-suppressing drugs. — Chronic systemic inflammation damages organs, and the medicines used to calm the immune attack (methotrexate, biologics, steroids) lower your defenses against infection—early aggressive treatment prevents these life-threatening dominoes.

Symptoms · what the patient feels, and why

- Small joints in the hands and feet are swollen, warm, and tender on both sides of the body: The immune system mistakenly attacks the synovium (the thin tissue lining the inside of the joint). This causes inflammation (swelling, heat, and pain) — like the joint is under attack from the inside. The body's own white blood cells flood in and release chemicals that make the area hot, puffy, and sore.
- Morning stiffness that lasts over an hour: Overnight, fluid and inflammatory chemicals pool in the joints because you are not moving. It takes time for movement to pump the swelling out and loosen the stiff tissue — like trying to bend a cardboard tube that got damp and rigid.
- You feel very tired all the time: The immune system is running on overdrive, making cytokines (chemical alarm signals) like TNF-alpha and interleukin-6. These signals drain energy and make the whole body feel worn out — like fighting off a flu that never ends.
- The DIP joints (the fingertip knuckles) are NOT swollen or sore: Rheumatoid arthritis prefers the lining of joints that move a lot, especially the PIP (middle knuckles) and MCP (base knuckles). For reasons not fully understood, the tiny DIP joints at the fingertips are usually spared — this pattern helps tell rheumatoid arthritis apart from osteoarthritis.
- Rheumatoid nodules (firm lumps under the skin, often near elbows): Immune cells form clumps of inflamed tissue under the skin, usually over pressure points like the elbow or the back of the hand. These nodules are made of collagen and immune cells piled together — like hard little knots of scar tissue.
- Low-grade fever: Cytokines (inflammatory messenger chemicals) tell the hypothalamus (the brain's thermostat) to turn up body heat, just like during an infection — because the body thinks it is under attack.

- Joint damage or deformity (in advanced or untreated disease): Ongoing inflammation eats away the cartilage (the smooth cushion at the end of bones) and then the bone itself. Tendons and ligaments also weaken and stretch, letting joints drift into crooked shapes — like a hinge that rusts and bends out of place.
- Lung problems (shortness of breath, dry cough) or chest pain: Inflammation can spread beyond the joints and attack the pleura (the lining around the lungs) or cause interstitial lung disease (scarring of lung tissue). This makes it harder to breathe and can cause chest pain — a serious extra problem that needs checking.

Focused exam

- Both hands swollen at the same time in the knuckle joints (MCP) and middle finger joints (PIP): Rheumatoid arthritis attacks both sides of the body at once — this mirror-image pattern is its fingerprint. Your immune system is treating your own joint lining like an invader and fighting it on both sides.
- Joints are warm, tender, and swollen, worst early in the morning: Morning stiffness lasting over an hour tells you inflammation cells piled up in the joint lining overnight. This is rheumatoid arthritis, not wear-and-tear — wear-and-tear gets better with rest, not worse.
- Fingers stay stiff and hard to bend for more than 60 minutes after waking: Long morning stiffness means the synovium (the slippery lining inside the joint) is thick with immune attack cells. It takes time for movement and warmth to loosen the swelling.
- The last joint on each finger (DIP joint, closest to the fingernail) is NOT swollen or tender: Rheumatoid arthritis skips this joint — it attacks the knuckles (MCP) and middle joints (PIP) but leaves the fingertip joint alone. This pattern rules out osteoarthritis, which loves the fingertip joints.
- The person feels tired, has a low fever (around 100°F), and feels generally sick: Rheumatoid arthritis is a whole-body disease, not just a joint problem. Your immune system is running hot — releasing cytokines (alarm chemicals) that make you feel like you have the flu even when you don't.
- Neck pain or trouble turning the head — check for atlantoaxial instability (the top two neck bones sliding out of place): Rheumatoid arthritis can loosen the ligaments holding the top neck bones together. If those bones slip, they can squeeze the spinal cord and cause paralysis or death. Always check the neck.
- Shortness of breath or dry cough that does not go away: Rheumatoid arthritis can attack the pleura (lung lining) or cause interstitial lung disease (scarring deep in the lung tissue). Catching this early prevents permanent lung damage.

Diagnostics · every test answers a question

- Rheumatoid factor (RF) → Is the immune system making antibodies that attack the body's own tissue?
- Anti-CCP antibodies (anti-cyclic citrullinated peptide) → Is the immune system targeting a specific marker found in joint tissue?
- ESR (erythrocyte sedimentation rate) and CRP (C-reactive protein) → How much inflammation is running in the body right now?
- Complete blood count (CBC) → Is chronic inflammation affecting the bone marrow's ability to make blood cells?
- Hand and foot X-rays (anteroposterior and oblique views) → Has the disease already started eating away bone, or is it still early enough to prevent permanent damage?
- Ultrasound or MRI of the hands and wrists (if X-ray is normal but suspicion is high) → Can we see inflammation and early erosions before they show up on X-ray?
- Hepatitis B and C screening, tuberculosis testing (IGRA or PPD) before starting immunosuppression → Does the person have a hidden infection that could explode when we turn down the immune system?

Treatment logic

- Methotrexate (a DMARD, disease-modifying antirheumatic drug) with folic acid 1 mg daily → Methotrexate blocks dihydrofolate reductase (an enzyme cells need to copy DNA), which slows down the immune cells attacking the joints. This calms the synovium (joint lining), stops erosions from forming, and preserves joint structure. Folic acid prevents mouth sores and nausea without blocking methotrexate's benefit.
- Biologic DMARDs: TNF inhibitors (adalimumab, etanercept, infliximab, certolizumab, golimumab), IL-6 inhibitors (tocilizumab, sarilumab), T-cell costimulation blocker (abatacept), or B-cell depletion (rituximab) → Biologics block specific cytokines (alarm chemicals) or immune cells that drive the attack on joints. TNF inhibitors block tumor tissue death (necrosis) factor-alpha (the main inflammation messenger), IL-6 inhibitors block interleukin-6 (another key alarm signal), abatacept stops T cells from turning on, and rituximab wipes out B cells (the cells that make antibodies). These stop inflammation faster and harder than methotrexate alone.
- JAK inhibitors (tofacitinib, baricitinib, upadacitinib) → JAK inhibitors block Janus kinases (enzymes inside immune cells that relay inflammation signals). This turns down the cell's ability to respond to cytokines, reducing swelling and stiffness quickly.

- Short-course oral corticosteroids (prednisone 5–10 mg daily for 2–4 weeks, then taper) during flares or as a bridge while waiting for DMARDs to work → Corticosteroids flood the body with cortisol-like signals that shut down the immune system's attack machinery fast. This quickly reduces swelling, pain, and stiffness, giving relief while slower DMARDs ramp up.
- NSAIDs (ibuprofen 400–800 mg three times daily, naproxen 500 mg twice daily) for symptom control → NSAIDs block cyclooxygenase (COX) enzymes, stopping the body from making prostaglandins (chemicals that cause pain and swelling). This reduces joint pain and stiffness so you can move and sleep.
- Vaccinate (inactivated flu, pneumococcal, hepatitis B, herpes zoster recombinant) before starting immunosuppression → Vaccines train your immune system to recognize and fight common germs before you take medicines that weaken it. This prevents life-threatening infections like pneumonia, flu, and shingles.
- Physical therapy and occupational therapy for joint protection, range-of-motion exercises, and assistive devices → Teaches you how to move and use joints in ways that reduce stress and preserve function. Strengthens muscles around joints to support them and prevent deformity.

Medications

Methotrexate · DMARD (disease-modifying antirheumatic drug) — a medicine that slows down the attack on joints instead of just covering up pain

Methotrexate blocks an enzyme called dihydrofolate reductase, which immune cells need to copy their DNA and multiply. When the enzyme is blocked, the fast-growing immune cells that attack the joints slow down and make fewer inflammatory signals like TNF-alpha and interleukin-1.

1. Methotrexate enters immune cells and blocks dihydrofolate reductase, the enzyme that recycles folate (a vitamin needed to build DNA).
2. Without enough folate, immune cells cannot copy their DNA quickly, so fewer new attack cells are made.
3. The drug also raises adenosine (a natural calming signal) outside cells, which tells immune cells to dial down inflammation.
4. Over weeks, fewer inflammatory chemicals like TNF-alpha and IL-1 are released, so the joint swelling, heat, and destruction slow down.

SAFETY WATCH

Take folic acid (usually 1 mg daily, 6 days a week) to lower the chance of mouth sores, nausea, and liver irritation. · Watch for liver damage — get liver blood tests (ALT, AST) every 8 to 12 weeks; tell your doctor if your skin or eyes turn yellow. · Watch for low blood counts — get a complete blood count every 8 to 12 weeks; call if you bruise easily, have tiny red dots on skin, or get repeated infections. · Watch for lung inflammation (rare but serious) — tell your doctor right away if you develop a new dry cough or trouble breathing. · Do not drink alcohol regularly; it raises the risk of liver damage. · Do not get pregnant while taking methotrexate or for 3 months after stopping (men or women) — the drug can cause severe birth defects. Use reliable birth control. · Avoid live vaccines (like nasal flu spray, shingles vaccine Zostavax, yellow fever) while on methotrexate; killed vaccines (flu shot, pneumonia, COVID, shingles vaccine Shingrix) are safe and recommended.

Hydroxychloroquine · DMARD (disease-modifying antirheumatic drug), originally an antimalarial medicine

Hydroxychloroquine gets concentrated inside immune cells and raises the pH (makes the inside less acidic) of little sacs called lysosomes and endosomes. This change makes it harder for immune cells to process antigens (foreign or self pieces) and activate, so fewer inflammatory signals are sent out.

1. Hydroxychloroquine enters immune cells and collects in acidic compartments (lysosomes and endosomes).
2. It raises the pH inside those compartments, which interferes with enzymes that break down and present antigens.
3. Fewer antigens are presented to T cells, so the T cells are less likely to activate and call in more inflammation.
4. The drug also blocks Toll-like receptors (alarm proteins on immune cells), lowering the release of cytokines like TNF-alpha and interleukin-6.
5. Over weeks to months, joint inflammation and pain decrease.

SAFETY WATCH

Get an eye exam by an ophthalmologist at the start and then every year — the drug can deposit in the retina (the light-sensing back of the eye) and cause vision loss if used for many years. · Tell your doctor if you notice blurry vision, trouble seeing colors, or flashing lights. · Watch for rare heart rhythm changes — tell your doctor if you feel a fast or skipping heartbeat.

Sulfasalazine · DMARD (disease-modifying antirheumatic drug), a combination of an antibiotic and an anti-inflammatory

Sulfasalazine is broken down in the gut into sulfapyridine and 5-aminosalicylic acid. The sulfapyridine part is thought to lower inflammation by blocking enzymes (like cyclooxygenase and lipoxygenase) that make inflammatory prostaglandins and leukotrienes, and by reducing immune cell activity.

1. Gut bacteria break sulfasalazine into sulfapyridine and 5-ASA.
2. Sulfapyridine enters the blood and reaches inflamed joints.
3. It blocks enzymes that make prostaglandins and leukotrienes (chemicals that cause swelling and pain).
4. It also slows the activity of immune cells in the joint lining, lowering cytokine release.
5. Over 1 to 3 months, joint pain and swelling decrease.

SAFETY WATCH

Watch for low blood counts — get a complete blood count and liver tests every month for the first 3 months, then every 3 months; tell your doctor if you bruise easily, get infections, or feel very tired. · Tell your doctor if you develop a rash, fever, or sore throat — these can be signs of a serious allergic reaction. · The drug can turn urine or skin slightly yellow-orange (harmless). · Men: sulfasalazine can lower sperm count temporarily; counts return to normal after stopping the drug. · Take the drug with food to reduce stomach upset.

Adalimumab, Etanercept, Infliximab, Golimumab, Certolizumab · Biologic DMARD — TNF inhibitor (a lab-made antibody or receptor that blocks tumor tissue death (necrosis) factor, a key inflammation signal)

These drugs grab onto TNF-alpha (a powerful inflammatory messenger made by immune cells) in the blood and joints before it can lock onto receptors on other cells. By blocking TNF-alpha, the chain reaction of inflammation — more immune cells swarming in, more enzymes chewing up cartilage and bone — is interrupted.

1. TNF inhibitors are injected under the skin or into a vein and enter the bloodstream.
2. They bind to free-floating TNF-alpha and to TNF-alpha sitting on the surface of immune cells.
3. This stops TNF-alpha from docking onto TNF receptors on cells in the joint lining and cartilage.
4. Without TNF-alpha signals, fewer immune cells are called to the joint, and fewer enzymes (like matrix metalloproteinases) are released to break down cartilage and bone.

5. Within weeks, swelling, pain, stiffness, and blood markers of inflammation (like CRP and ESR) drop.

SAFETY WATCH

Get tested for tuberculosis (TB) with a skin test or blood test (QuantiFERON or T-SPOT) before starting — TNF blockers can wake up hidden TB. If positive, treat TB first. · Get tested for hepatitis B — the virus can reactivate and damage the liver. · Avoid live vaccines (nasal flu spray, Zostavax shingles vaccine, yellow fever); get killed vaccines (flu shot, pneumonia, COVID, Shingrix shingles vaccine) before starting if possible. · Watch for serious infections — call your doctor if you have fever, chills, a cough that won't go away, or a wound that gets red and painful. Do not take the drug if you have an active infection. · Watch for new or worsening heart failure — tell your doctor if you have trouble breathing, sudden weight gain, or swollen ankles. · Rarely, these drugs raise the risk of certain cancers, especially lymphoma (cancer of lymph nodes) and skin cancer — wear sunscreen and see a doctor for any new lumps or changing moles. · Injection-site reactions (redness, itching) are common but usually mild.

Abatacept · Biologic DMARD — T-cell co-stimulation blocker

T cells (a type of white blood cell that directs the immune attack) need two signals to fully activate: one from recognizing an antigen and one from a helper molecule called CD28. Abatacept blocks the second signal by attaching to CD80 and CD86 (proteins on antigen-presenting cells that normally give the go-ahead). Without both signals, T cells stay quiet and do not call in more inflammation.

1. Abatacept is infused into a vein or injected under the skin and enters the bloodstream.
2. It binds to CD80 and CD86 on antigen-presenting cells (like dendritic cells and macrophages).
3. This blocks the co-stimulation signal that T cells need to fully activate.
4. Fewer T cells turn on, so fewer cytokines (like interferon-gamma and TNF-alpha) are released.
5. Over weeks, the immune attack on joints winds down, and swelling and pain decrease.

SAFETY WATCH

Get tested for tuberculosis (TB skin test or blood test) and hepatitis B before starting. · Avoid live vaccines; get killed vaccines before starting if possible. · Watch for infections — call your doctor if you have fever, cough, painful urination, or a red, warm wound. · Tell your doctor if you have COPD (chronic lung disease) — abatacept may raise the risk of breathing problems and infections in these patients. · Infusion reactions (headache, nausea, dizziness during or right after the IV) can happen but are usually mild.

Tocilizumab, Sarilumab · Biologic DMARD — IL-6 receptor blocker (blocks interleukin-6, another key inflammation messenger)

Interleukin-6 (IL-6) is a cytokine that tells the liver to make acute-phase proteins (like CRP), tells bone cells to break down bone, and keeps inflammation going. Tocilizumab and sarilumab block the IL-6 receptor on cells, so IL-6 cannot deliver its inflammation signals.

1. The drug is infused into a vein or injected under the skin and enters the bloodstream.
2. It binds to IL-6 receptors on the surface of cells, blocking IL-6 from docking.
3. Without IL-6 signals, the liver makes less CRP and other inflammatory proteins, immune cells calm down, and bone breakdown slows.
4. Over weeks, joint swelling, pain, stiffness, and blood markers of inflammation (CRP, ESR) drop.

SAFETY WATCH

Get tested for tuberculosis and hepatitis B before starting. · Avoid live vaccines; get killed vaccines before starting if possible. · Watch for infections — these drugs lower white blood cell counts (especially neutrophils), so call your doctor if you have fever, chills, or signs of infection. · Watch for liver damage — get liver tests (ALT, AST) regularly; tell your doctor if your skin or eyes turn yellow. · Watch for changes in cholesterol — the drug can raise LDL and total cholesterol; your doctor may check lipid levels and consider a statin if needed. · Watch for bowel perforation (a hole in the intestine, very rare but serious) — get immediate help if you have sudden severe belly pain, especially if you have a history of diverticulitis or bowel disease. · Infusion reactions (headache, high blood pressure during the IV) can happen but are usually manageable.

Rituximab · Biologic DMARD — B-cell depleting antibody

B cells are white blood cells that make antibodies, including the autoantibodies (like rheumatoid factor and anti-CCP) that attack the joints in rheumatoid arthritis. Rituximab is an antibody that locks onto CD20, a protein on the surface of B cells, marking them for destruction by the immune system. Wiping out B cells lowers autoantibody levels and calms the immune attack.

1. Rituximab is infused into a vein and enters the bloodstream.
2. It binds to CD20 on the surface of B cells (but not stem cells or plasma cells that have already lost CD20).
3. The marked B cells are destroyed by the immune system's cleanup crews (antibody-dependent cell-mediated cytotoxicity and complement).
4. B-cell numbers drop for months, lowering the production of autoantibodies and inflammatory cytokines.

5. Over weeks to months, joint inflammation and pain decrease.

SAFETY WATCH

Get tested for hepatitis B before starting — the virus can reactivate and cause severe liver damage or even liver failure. If positive, you may need antiviral medicine. · You will receive premedication (acetaminophen, an antihistamine, and sometimes a steroid) before each infusion to lower the chance of an infusion reaction (fever, chills, rash, low blood pressure). · Watch for serious infections — B-cell depletion raises the risk of bacterial, viral, and fungal infections. Call your doctor if you have fever, cough, painful urination, or unusual fatigue. · Very rarely, rituximab can cause progressive multifocal leukoencephalopathy (PML), a brain infection caused by JC virus — get immediate help if you have confusion, trouble speaking, vision changes, or weakness on one side. · Avoid live vaccines; check antibody levels (immunoglobulin levels) periodically because some people develop low antibodies over time.

Tofacitinib, Baricitinib, Upadacitinib · JAK inhibitor (Janus kinase inhibitor) — a small-molecule pill that blocks enzymes inside immune cells

Many inflammatory cytokines (like IL-6, interferon, and others) send their signals into cells by activating enzymes called Janus kinases (JAK1, JAK2, JAK3, TYK2). JAK inhibitors block these enzymes, so the cytokine signals cannot turn on the genes that keep inflammation going. This dials down the immune attack on joints.

1. The pill is swallowed, absorbed in the gut, and enters the bloodstream.
2. The drug enters immune cells and binds to JAK enzymes (the specific JAKs blocked depend on the drug — tofacitinib blocks JAK1 and JAK3, baricitinib blocks JAK1 and JAK2, upadacitinib mainly blocks JAK1).
3. When cytokines like IL-6 or interferon land on their receptors, the blocked JAK enzymes cannot pass the signal along.
4. Fewer inflammatory genes are turned on, so fewer cytokines, chemokines, and antibodies are made.
5. Within weeks, joint swelling, pain, and stiffness decrease.

SAFETY WATCH

JAK inhibitors carry a boxed warning (the FDA's strongest warning) for serious infections (including tuberculosis, fungal infections, and shingles), cancer (especially lymphoma and lung cancer in people who smoke or used to smoke), blood clots (deep vein clot formation (thrombosis), pulmonary embolism (a clot lodging in a lung artery)), and major heart problems (heart attack, stroke) — especially in people over 50 with heart disease or risk factors. · Get tested for tuberculosis and hepatitis B before starting. · Avoid live vaccines; get the shingles vaccine (Shingrix, a killed vaccine) before starting if possible. · Tell your doctor if you smoke or have a history of heart disease, blood clots, cancer, or chronic lung disease — the risk-benefit balance may be different. · Watch for signs of blood clots: sudden leg pain or swelling, chest pain, shortness of breath, or sudden weakness or numbness on one side. · Watch for signs of infection: fever, cough, painful urination, or a wound that gets red and painful. · Get regular blood tests (complete blood count, liver tests, lipid panel) — JAK inhibitors can lower white blood cells and platelets, raise cholesterol, and (rarely) hurt the liver. · Do not use JAK inhibitors if you are pregnant or breastfeeding.

Prednisone, Methylprednisolone · Corticosteroid (a man-made version of cortisol, the body's natural stress and anti-inflammation hormone)

Steroids enter cells and bind to receptors in the cytoplasm. The steroid-receptor pair moves into the nucleus and changes which genes are turned on or off. This lowers the production of many inflammatory chemicals (cytokines, prostaglandins, leukotrienes) and tells immune cells to calm down. The effect is fast and powerful.

1. The steroid pill or injection enters the bloodstream.
2. It crosses into cells and binds to glucocorticoid receptors.
3. The complex moves into the nucleus and blocks the production of inflammatory genes (like those for IL-1, IL-6, TNF-alpha).
4. It also boosts anti-inflammatory genes.
5. Within hours to days, swelling, pain, and stiffness drop.

SAFETY WATCH

Short-term use (days to a few weeks) is generally safe but can raise blood sugar, blood pressure, and cause stomach upset, mood changes, trouble sleeping, and increased appetite. · Long-term use (months or longer) can cause weight gain (especially around the face and belly), thinning bones (osteoporosis) and fractures, cataracts, glaucoma, high blood pressure, diabetes, thin fragile skin, muscle weakness, and increased risk of infections. · Never stop steroids suddenly after using them for more than a few weeks — the dose must be tapered down slowly to let your adrenal glands (which make natural cortisol) wake back up. · Take the lowest dose for the shortest time needed. If you need steroids for more than a few weeks, talk to your doctor about bone protection (calcium, vitamin D, sometimes a bisphosphonate). · Take the pill with food to lower stomach irritation. Watch for black or tarry stools (sign of stomach bleeding).

Ibuprofen, Naproxen, Celecoxib, Diclofenac · NSAID (nonsteroidal anti-inflammatory drug) — a pain and inflammation reliever that does not change the course of the disease

NSAIDs block enzymes called cyclooxygenase-1 and cyclooxygenase-2 (COX-1 and COX-2), which make prostaglandins. Prostaglandins are chemicals that cause pain, fever, swelling, and (in the stomach) protect the lining. Blocking them lowers pain and inflammation but also raises the risk of stomach ulcers and bleeding.

1. The NSAID is swallowed, absorbed in the gut, and enters the bloodstream.
2. It reaches inflamed tissues and blocks COX enzymes.
3. Fewer prostaglandins are made, so pain signals and swelling decrease.
4. Within hours, pain and stiffness improve.

SAFETY WATCH

Take the lowest dose for the shortest time needed. · Take with food to lower stomach upset. · NSAIDs can cause stomach ulcers and bleeding — watch for black or tarry stools, vomiting blood, or severe stomach pain. If you have a history of ulcers or are over 65, your doctor may prescribe a proton pump inhibitor (like omeprazole) to protect your stomach. · NSAIDs can raise blood pressure and cause fluid retention (swelling in the legs) — check your blood pressure regularly. · NSAIDs can harm the kidneys, especially in people with kidney disease, heart failure, or who take diuretics or ACE inhibitors — your doctor may check kidney function with blood tests. · NSAIDs (except aspirin) raise the risk of heart attack and stroke, especially with long-term use and high doses. · Avoid NSAIDs if you are pregnant (especially in the third trimester) — they can harm the baby's heart and kidneys.

Red flags

- Severe joint pain that suddenly gets much worse — may mean infection in the joint (septic arthritis) on top of rheumatoid arthritis
- New shortness of breath, persistent dry cough, or chest pain — may mean lung involvement (pleuritis or interstitial lung disease)
- Fever above 101°F (38.3°C) — may mean infection, especially if on immune-suppressing medicines
- Sudden vision changes or severe eye pain — may mean scleritis (inflammation of the white of the eye), which can damage vision
- Visible joint deformity or inability to use the hand or foot — means the disease is advancing and needs urgent treatment adjustment

Nursing priorities

1. Check both hands and feet for symmetrical joint swelling, warmth, and tenderness, and document which specific joints are affected — Symmetrical small-joint inflammation is the hallmark of rheumatoid arthritis and tracking the pattern helps measure if treatment is working or disease is spreading to new joints
2. Assess cervical spine stability by asking the patient to gently tuck chin to chest and report any electric-shock feelings down the spine or new arm weakness — Chronic inflammation weakens the ligaments holding the atlas (first neck bone) in place, allowing it to slide forward and compress the spinal cord, causing quadriplegia (paralysis of all four limbs)
3. Review the medication list to confirm the patient takes folic acid (1 mg daily) on the days they do not take methotrexate — Methotrexate blocks folic acid (a B vitamin) which causes mouth sores, liver damage, and low blood counts, and folic acid supplementation prevents these side effects without reducing the drug's effectiveness
4. Teach proper joint protection techniques like using larger joints to carry loads, avoiding tight grip positions, and using assistive devices for jars and buttons — Repetitive stress on inflamed joints accelerates cartilage destruction and causes permanent deformities like ulnar drift (fingers bending toward the pinky side), which cannot be reversed
5. Monitor for signs of infection including fever over 100.4 degrees Fahrenheit, new cough, burning with urination, or a single hot swollen joint — DMARDs (disease-modifying medicines) and biologics suppress the immune system so common infections become life-threatening sepsis faster, and a single infected joint can destroy cartilage in hours
6. Educate the patient that NSAIDs like ibuprofen only mask pain but do not stop joint damage, while DMARDs and biologics actually slow disease progression — Starting a DMARD within three months of symptom onset prevents irreversible erosions (bone holes) seen on X-rays, but patients often delay because NSAIDs temporarily make them feel better

7. Screen for depression and offer referrals to occupational therapy and support groups — Chronic pain, fatigue, and loss of hand function cause major depressive disorder in 40 percent of rheumatoid arthritis patients, and depression worsens pain perception and medication adherence
8. Schedule baseline tuberculosis testing (QuantiFERON or PPD skin test) and hepatitis B screening before starting biologic therapy — Biologics reactivate latent tuberculosis (sleeping TB bacteria in old lung scars) causing disseminated disease, and hepatitis B reactivation causes fulminant liver failure, both of which are preventable with preventive (prophylactic) treatment

Sources

- American College of Rheumatology (ACR) 2021 Guideline for the Treatment of Rheumatoid Arthritis
- European League Against Rheumatism (EULAR) 2022 Recommendations
- UpToDate Clinical Overview of Rheumatoid Arthritis
- Cochrane Review: DMARDs for Rheumatoid Arthritis

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