Rheumatoid Arthritis: Diagnosis, Management and Monitoring Summary

Diagnosis: Early Rheumatoid Arthritis Investigation

Differentiate Inflammatory from Non-inflammatory Arthritis

Early recognition and intervention has been shown to improve outcome. The treatment approach varies depending on whether the symptoms arise from inflammation or joint damage, making the differentiation vital.

Feature	Inflammatory	Non-Inflammatory
Joint pain	With activity and at rest	With activity
Joint swelling	Soft tissue	Bony
Local erythema	Sometimes	Absent
Local warmth	Frequent	Absent
Morning stiffness	>30 minutes	<30 minutes
Systematic symptoms	Common, especially fatigue	Absent

Differentiate RA from Other Inflammatory Arthritides

RA Likely	Differential Diagnoses	Features Suggesting Alternative Diagnosis
• Morning stiffness > 30 minutes • Painful swelling of 3 or more joints • Symmetric involvement of hands and feet (especially metacarpophalangeal and metatarsophalangeal joints) • Duration of 4 or more weeks	• Crystal arthropathy • Psoriatic arthritis • Lupus • Reactive arthritis • Spondyloarthropathies • Polyarticular sepsis	• Mucosal ulcers, photosensitivity, psoriasis, skin rashes • Ocular inflammation – iritis/uveitis • Inflammatory bowel disease • Isolated distal interphalangeal joint inflammation • Raynaud's • Infectious diarrhea • Urethritis • Nephritis

Investigations

Referral to a specialist should not be based on the results of lab tests if there are no clinical features suggesting RA. There are no tests that can reliably make the diagnosis of RA. If there are clinical features then the following lab tests may be useful for monitoring and ruling out other types of arthritis.

Tests*	Diagnostic Value	Disease Activity Monitoring
C-Reactive Protein (CRP) or Erythrocyte Sedimentation Rate (ESR)	CRP is the preferred test. Indicate only inflammatory process - very low specificity.	May be useful in monitoring disease activity and response to treatment. Both can be useful, but CRP is more sensitive to short term fluctuations. ESR elevated in many but not all with active inflammation.
Rheumatoid Factor Latex Test (RF)	RF has low sensitivity and specificity for RA. Seropositive RA has a worse prognosis than seronegative RA.	No value - do not repeat
Antinuclear Antibody (ANA)	ANA is rarely positive in RA. Unless there are other clinical features indicating SLE or other connective tissue diseases, ordering ANA is not indicated.	No value - do not repeat
X-Rays	Diagnostic erosions rarely seen in disease of <3 months duration.	If clinically indicated, serial x-rays over years may show disease progression and indicate need for medication change.
Joint Aspiration	Joint aspiration indicated if infection or crystal arthropathy is suspected. Antibiotics may be started only after aspiration.	

** Anti-cyclic citrullinated protein antibodies (Anti-CCP) may have some value but can only be ordered by a specialist in BC. If ordered by a GP then the test is patient pay.*

Referral to Specialists

- Specialist intervention has been shown to improve RA outcomes. Referrals to specialists should indicate "**Urgent: new-onset RA**". Copy all relevant tests to specialist.
- Referral to Physiotherapist (PT) and/or Occupational Therapist (OT) with expertise in RA and indicate "**Urgent: new-onset RA**".

Management of Early RA

Before patient's specialist appointment initiate treatment as follows:

- Patient education: provide RA patient guide.
- Start NSAIDs and acetaminophen for pain management having recorded blood pressure and ordered baseline CBC, creatinine, electrolytes and chest x-ray.
- Can start with:
  - Hydroxychloroquine until diagnosis of RA is confirmed,

    OR
  - Sulfasalazine and methotrexate if confident about diagnosis and in using these medications. Combination DMARD therapy is the current standard of care.
- If symptoms are severe add low-dose prednisone (up to 10 mg/day).

Consider seeing early RA patients monthly to monitor response to treatment and possible side effects of medications. Contact specialist if concerned. Biologic medications for treatment of RA will be initiated only by specialists. Details of initiation, dosing and monitoring are based on recommendations made by specialists in each case.

Management of Established RA

The objective of treatment is to suppress all inflammation and prevent joint damage. Most patients will require long-term DMARD therapy. Consider follow-up every 3-6 months and specialist follow-up every 6-12 months after inflammation is suppressed.

At each visit:

- Assess current drug therapy including dose and monitoring for side effects,
- Examine joints for active inflammation,
- When baseline CRP or ESR is elevated, serial assessment may be helpful,
- Review general health concerns and co-morbidities.

If the assessment suggests ongoing active inflammation, then consider or review:

- Adherence to medication regimen,
- Dosage of current medications and dosages of substitutions/additions of alternative medications,
- Referral back to specialist,
- Referral back to PT and/or OT.

If the assessment suggests joint damage, then consider or review:

- Pain relieving modalities,
- Re-referral to PT and/or OT,
- Referral for surgical opinion.

Consider or Review Implications of Chronic Disease

- Implications of chronic pain,
- Psychosocial issues,
- Immunizations (flu vaccine, pneumococcal polysaccharide vaccine (PPSV)),
- Osteoporosis assessment and preventive measures,
- Patients with RA have an increased risk of cardiovascular disease (CVD). CVD risk factors (e.g., cholesterol levels, blood pressure) should also be carefully screened and managed in this patient population,
- Encourage self-management for RA symptoms,
- Smoking cessation,
- Weight management.

Appendix A: Non-Biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

- Note that all DMARDs take 6-8 weeks to work
- Consider drug interactions
- Review medications if considering pregnancy as many are teratogenic
- Dose is oral unless specified

Generic Name	Trade Name (dosage form and strength)	Usual Adult Dose	Cost per 30 days	PharmaCare Coverage	Adverse Effects	Monitoring
hydroxychloroquine sulfate	Plaquenil®, G (tablet: 200 mg)	200-400 mg PO daily (Max: 6.5 mg/kg lean body weight)	$8-17 (G) $20-40	Regular Coverage	nausea, diarrhea, anorexia, skin rash Serious: retinopathy, retinal deposition, myopathy	• Ophthalmologic exam: Q 6-12 months
sulfasalazine	Salazopyrin EN®, G (Enteric-coated tablet: 500 mg)	(Use enteric-coated tablets) Initial: 500 mg PO daily to bid; increase weekly to 1000 mg PO bid (Max: 1000 mg PO tid)	$44-66 (G) $52-78	Regular Coverage	nausea, headache, skin rash Serious: bone marrow toxicity	• CBCs with differentials, LFTs monthly x 3 months, then Q 3 months
methotrexate	Methotrexate (injections: 2.5, 10, 25 mg/mL; tablets: 2.5, 10 mg)	Initial: 7.5 mg PO/SC weekly; increased by 2.5-5 mg Q 1-4 weeks (max: 25 mg/week) Maintenance: 7.5-25 mg PO/SC weekly	$8-27 (tabs); $7-25 (injection)	Regular Coverage (tablet); Special Authority (injection)	nausea, vomiting, oral ulcers, flu-like symptoms Serious: bone marrow toxicity (avoid TMP-SMX), hepatitis, infection, pneumonitis	• LFT at baseline • Hepatitis B & C serology at baseline • CBC, LFTs, albumin, creatinine monthly x 6 months, then Q 2 months thereafter. • Give folic acid 5 mg PO once weekly. Folic acid may improve patient's ability to tolerate methotrexate therapy.[5-6]
leflunomide	Arava®, G (tablets: 10, 20 mg)	10-20 mg PO daily (Max: 20 mg PO daily)	$120 (G) $353	Special Authority	nausea, vomiting, diarrhea Serious: hypertension, alopecia, weight loss, hepatic toxicity, bone marrow toxicity, pneumonitis	• Hepatitis B & C serology: baseline • ALT, AST, CBCs (differentials and platelets): baseline & monthly during first 6 months. If stable, repeat Q 6-8 weeks (or monthly if also on methotrexate) • Blood pressure monthly x 3 months
gold sodium thiomalate	Myochrysine®, G (Injections: 10, 25, 50 mg/mL)	Initial: 10 mg IM first week, 25 mg IM second week, then 25-50 mg weekly x 20 weeks, then decrease to maintenance Maintenance: 50 mg IM Q 2-4 weeks	$15-30 (G) $23-46	Regular Coverage	rash, pruritus, stomatitis Serious: bone marrow toxicity, proteinuria, vasodilatation with hypotension	• CBC with differentials and platelets • Urinalysis weekly x 4 weeks, then Q 2 weeks x 20 weeks, then Q 3 weeks x 50 weeks, then Q 4-8 injections
azathioprine	Imuran®, G (tablet: 50 mg)	Initial: 1 mg/kg/day PO (once daily or divided BID) x 6-8 weeks, increase by 0.5 mg/kg Q 4 weeks until optimal response (max: 2.5 mg/kg/day)	$11-27 (G); $32-80	Regular Coverage	nausea, vomiting, diarrhea Serious: hepatitis, drug fever, infection, bone marrow toxicity	• CBC with differentials and platelets, LFTs Q 1-3 months, more frequently with dosage modifications
cyclosporine	Neoral®, G (capsules: 25, 50, 100 mg; solution: 100 mg/mL)	Initial: 2.5 mg/kg/day PO (divided BID); increased by 0.5-0.75 mg/kg/day after 4 weeks & 8 weeks if insufficient response (Maximum: 5 mg/kg/day) Discontinue if no benefit by 16 weeks Maintenance: 2.5-5 mg/kg/day (divided BID)	$223-535 (capsules); $198-475 (solution)	Special Authority	hirsutism, gum hyperplasia, nausea Serious: hypertension, renal toxicity, viral infection	• Blood pressure monthly (more frequently after dosage change) • CBCs with differentials & platelets, LFTs, magnesium, serum creatinine: baseline and Q 2-4 weeks • drug blood levels when drug interactions or altered bioavailability are suspected
minocycline	Minocin®, G (capsules: 50 mg, 100 mg)	100 mg PO bid	$38 (G)	Regular Coverage	gastrointestinal symptoms, dizziness, skin rash, photosensitivity Serious: hyperpigmentation, SLE	

Abbreviations

ALT alanine aminotransferase; **AST** aspartate aminotransferase; **bid** twice daily; **CBCs** complete blood counts; **G** generics; **IM** intramuscularly; **max** maximum; **LFTs** liver function tests; **mg** milligrams; **PO** by mouth; **Q** every; **SC** subcutaneously; **SLE** systemic lupus erythematosus; **tid** three times daily

Note: For complete details, please review product monographs at http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp and regularly review current Health Canada advisories, warnings and recalls at http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

Pricing is approximate as per PharmaCare Formulary Search 2012/10/05 and does not include dispensing fee.

PharmaCare Coverage Definitions

G: generic(s) are available.

Regular Coverage: also known as regular benefit; does not require Special Authority. Regular benefits may be fully or partially covered*.

Limited Coverage: requires Special Authority for coverage. Limited coverage benefits approved by Special Authority may be fully or partially covered*.

No Coverage: also known as non-benefit, does not fit the above categories.

* Note: Information on which products PharmaCare covers can be obtained using the BC PharmaCare Formulary Search (http://www.health.bc.ca/pharmacare/benefitslookup/). In all cases, coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See http://www.health.gov.bc.ca/pharmacare/plans/index.html and http://www.health.gov.bc.ca/pharmacare/policy.html for further information.

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