

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Rheumatoid Arthritis: Diagnosis and Management

Effective Date: May 1, 2006

Scope

The guideline summarizes current recommendations for diagnosis and treatment of Rheumatoid Arthritis (RA) for patients 16 years-of-age and older.

Introduction

Rheumatoid Arthritis (RA) is not a benign disease. RA is associated with decreased life expectancy. The risk of cardiovascular mortality is twice that of the general population. Affecting approximately 1% of the adult population, RA is associated with considerable disability. RA adversely impacts an individual's quality of life and results in increased financial burden both to the individual and society through medical costs and loss of productivity.

It is now well recognised that there is a “window of opportunity” early in the disease process to initiate treatment which will fundamentally change the course of the disease. Treatment must be started early to maximise the benefits of medications and prevent joint damage. The use of traditional medications in combination and the new biologic therapies has revolutionised the paradigm of RA treatment in recent years.¹

In this new era of RA treatment, specialist care has become increasingly important in managing complex regimens. Access to timely specialized care is not universally available. This guideline is intended to aid in initiating early recognition and intervention and managing patients with this chronic disease.

The approach to care of patients with RA should be considered as falling into two groups.

- Early RA (ERA) is defined as patients with symptoms of less than 3 months duration.
- Patients with established disease who have symptoms due to inflammation and/or joint damage.

The treatment approach varies depending on whether the symptoms arise from inflammation or joint damage making the differentiation vital.

Recommendations to improve quality of care

RECOMMENDATION 1 Differentiate inflammatory from non-inflammatory arthritis

FEATURE	INFLAMMATORY	NON-INFLAMMATORY
Joint pain	With activity and at rest	With activity
Joint swelling	Soft tissue	Bony
Joint deformity	Common	Common
Local erythema	Sometimes	Absent
Local warmth	Frequent	Absent
Morning stiffness	>30 minutes	<30 minutes
Systemic symptoms	Common, especially fatigue	Absent

RECOMMENDATION 2 Differentiate RA from other inflammatory arthritides

RA likely if

- Morning stiffness > 30 minutes
- Painful swelling of 3 or more joints
- Involvement of hands and feet (especially MCP and MTP joints)
- Duration of 4 or more weeks

Differential diagnoses include: crystal arthropathy, psoriatic arthritis, lupus, reactive arthritis, spondyloarthropathies.

N.B. Always consider infection

Features suggesting alternative diagnosis include

- Mucosal ulcers, photosensitivity, psoriasis, skin rashes
- Raynaud's
- Ocular inflammation
- Urethritis
- Inflammatory bowel disease
- Infectious diarrhea
- Nephritis
- Isolated distal interphalangeal (DIP) joints

It should be noted that extra-articular manifestations are an indication of more severe disease and thus have prognostic value. Established RA may have extra-articular manifestations including:

CUTANEOUS	OCULAR	PULMONARY	CARDIAC	NEUROLOGICAL	HEMATOLOGICAL
<ul style="list-style-type: none"> • Nodules • Vasculitis 	<ul style="list-style-type: none"> • Sicca • Episcleritis • Scleritis 	<ul style="list-style-type: none"> • Pleuritis • Nodules • Interstitial lung disease • Fibrosis 	<ul style="list-style-type: none"> • Pericarditis • Atherosclerosis • Myocardial infarction 	<ul style="list-style-type: none"> • Peripheral neuropathy • Cervical myelopathy 	<ul style="list-style-type: none"> • Leukopenia • Anemia of chronic disease • Lymphadenopathy

RECOMMENDATION 3 Testing

RA is a clinical diagnosis. There are no tests that are completely reliable in making the diagnosis. Tests are primarily used to monitor the disease or exclude other types of arthritis.

TESTS	DIAGNOSTIC VALUE	DISEASE ACTIVITY MONITORING	COST (as of 2005)
Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP)	Indicate only inflammatory process - very low specificity	Often useful. ESR elevated in many but not all with active inflammation. May be useful in monitoring disease activity and response to treatment.	ESR \$2.46 CRP \$24.94
Rheumatoid Factor (RF)	RF has low sensitivity and specificity for RA. Seropositive RA has a worse prognosis than seronegative RA.	No value	\$11.49
Antinuclear Antibody (ANA)	Positive in cases with severe RA, systemic lupus erythematosus (SLE) or other connective tissue disorders (CTD). Most patients with positive ANA do not have RA, SLE, or CTD. Negative ANA usually excludes SLE.	No value - do not repeat	\$33.40
X-Rays	Diagnostic erosions rarely seen in disease of <3 months duration.	Serial X-rays over years may show disease progression and indicate need for medication change.	Varies depending on body area.
Joint Aspiration	Joint aspiration indicated if infection or crystal arthropathy is suspected.		\$11.42

RECOMMENDATION 4 Management of Early RA (ERA)

- Patient education: See *Rheumatoid Arthritis – A Guide for Adult Patients* (attached).
- Referral to PT and OT with expertise in RA and indicate “**Urgent: new-onset RA**”.
- Prior to starting medications do baseline CBC, creatinine, electrolytes, and blood pressure.
- Start NSAIDS for pain management.
- Specialist intervention has been shown to improve RA outcomes. Specialist referral should indicate “**Urgent: new-onset RA**”.
- Start hydroxychloroquine (See Appendix for DMARD information).
- Start sulfasalazine and methotrexate if confident about diagnosis and management and the patient is not pregnant. Combination DMARD therapy is the current standard of care.
- If symptoms severe while waiting for specialist assessment add low-dose prednisone (up to 10 mg/day).

RECOMMENDATION 5 Management of Established RA

Continuing joint inflammation will lead to joint damage. Most patients will require long-term DMARD therapy. The objective of treatment is to suppress all inflammation and prevent joint damage.

Follow-up by GP every 3-6 months and specialist every 6-12 months after disease is controlled.

At each visit:

- List and assess current drug therapy including dose and monitoring for side effects (see DMARD table in Appendix)
- Assess patient for active joint inflammation and disease activity
 - Review Recommendation 1
 - Consider investigations: ESR or CRP
- Focus exam to most troublesome joints
 - Differentiate inflammation versus damage
- Scan for general health concerns, co-morbidities, and extra-articular manifestations

If the assessment suggests ongoing active inflammation then:

- review adherence to medication regimen, consider adjusting dosages or substituting/adding alternative medications, consider referral to specialist, and consider referral to Physiotherapist (PT) and/or Occupational Therapist (OT) with expertise in RA.

If the assessment suggests joint damage then:

- consider referral to PT and/or OT
- consider referral to Orthopaedic Surgeon
- administer pain relieving modalities

Always consider that patients may have a combination of inflammation and damage.

For surgical procedures consider neck instability, increased risk of infection, and implications of medications especially steroids

RECOMMENDATION 6 Consider implications of chronic disease

As with all chronic diseases, optimal outcome is achieved through a multi-disciplinary approach coordinated by the Family Doctor. Consider or review:

- pain management
- psychosocial issues
- immunization (annual flu vaccine, pneumococcal vaccination)
- osteoporosis assessment and preventive measures
- RA is a risk factor for coronary artery disease. Consider dyslipidemia and minimize other risk factors.
- encourage Self-Management

Summary

Rheumatoid arthritis (RA) is not a benign disease and affects about 1% of the BC adult population. Early recognition and intervention clearly improves outcome. DMARDs, particularly when used early, change the disease process and have been proven to reduce damage and disability. Treatment is multi-disciplinary involving regular follow-up, medications, physiotherapy, self-management and other support.

References and Resources:

1. Guidelines for the Management of Rheumatoid Arthritis American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. *Arthritis & Rheumatism* 2002;46(2):328-346.
2. Getting a grip on arthritis best practice guidelines The Arthritis Society. (2004).
3. RA information and clinical resources available at www.rheuminfo.com
4. British Society of Rheumatology Guideline on Standards of Care for persons with Rheumatoid Arthritis. Kennedy T (Chair of the Guideline Working Group). *BSR Rheumatology* 2005 44(3):269-270. Available at <http://rheumatology.oxfordjournals.org/cgi/reprint/44/4/553>
5. Canadian consensus statement on early optimal therapy in early Rheumatoid Arthritis. Bykerk BP, Baron M, Boire M, et.al. Available at: <http://www.rheum.ca/Resources/pdf/ERA.pdf>
6. Rheumatoid Arthritis. Treatments. Matsumoto AK, Bathon J. Available at http://www.hopkins-arthritis.org/rheumatoid/rheum_treat.html.
7. Search for a Physiotherapist by name or workplace: Physiotherapy Association of British Columbia 604 736-5130. <http://www.bcphysio.org> or <http://www.bcphysio.org/app/index.cfm?fuseaction=public.home>
8. The Arthritis Society Toll free phone number: 1 800 321-1433

Sponsors

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This guideline is based on the scientific evidence at the time of the effective date.

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The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances.

Appendix: Disease Modifying Arthritis Drugs (DMARDs)

- Note that all DMARDs take several weeks to work
- Review medications if considering pregnancy as many are teratogenic
- Dose is oral unless specified

DRUG	DOSE	COMMON SIDE EFFECTS	SERIOUS ADVERSE EFFECTS	MONITORING	APPROX. MONTHLY COST (AS OF NOV. 2005)
Hydroxychloroquine (Plaquenil®, & generics)	Up to 6.5 mg/kg lean body weight	<ul style="list-style-type: none"> • nausea • cramps • diarrhea • rash 	<ul style="list-style-type: none"> • blindness • myopathy 	ocular exam specific to hydroxychloroquine risk Q 6-12 mo	\$25 - \$50
Sulfasalazine (Salazopyrin®)	1000 mg BID/TID	<ul style="list-style-type: none"> • skin rash • nausea • headache • photo sensitivity 	<ul style="list-style-type: none"> • bone marrow toxicity 	CBC and AST monthly for first 3 mos	\$10 - \$20
Cyclosporine** (Neoral® Sandimmune®, & generics)	2.5-4.5 mg/kg/day	<ul style="list-style-type: none"> • hirsutism • gum hyperplasia • numerous drug interactions 	<ul style="list-style-type: none"> • renal toxicity • hypertension • cytopenia 	serum creatinine and blood pressure Q 2 weeks for first 3 mo, then Q 2 mo if dose ≤ 2.5mg/kg/day or Q 4 weeks if > 2.5mg/kg/day	Solution: \$200-\$500 Caps: \$350 - \$750
Leflunomide** (Arava®)	10-20 mg/day	<ul style="list-style-type: none"> • diarrhea • rash • abdominal pain • bloating 	<ul style="list-style-type: none"> • infections • hepatitis • alopecia • hypertension • weight loss 	Before start of therapy check: hepatitis serology, AST, ALT, CBC & BP. Check CBC, AST and ALT Q mo first 6 mos, & Q 8 wks thereafter. CBC Q 2 wks for first 6 mos, & Q 8 wks thereafter. Check BP monthly for 3 mos.	\$300 - \$350
Methotrexate	7.5 – 25 mg/week PO, IM, or SC	<ul style="list-style-type: none"> • nausea • oral ulcers 	<ul style="list-style-type: none"> • bone marrow suppression • hepatitis • infections • pneumonitis 	Hepatitis B and C serology before treatment. Monthly CBC, AST, ALT, & creatinine for 3 mos then every 6-8 wks. Creatinine & liver enzymes Q 1-2 mo.	\$10 - \$40
Minocycline (Minocin®)	100 mg BID	<ul style="list-style-type: none"> • photo sensitivity 	<ul style="list-style-type: none"> • hyperpigmentation • SLE 		\$60 - \$75
Gold sodium thiomalate (Myochrysine® & generics)	10-50 mg IM Q 1-4 wks	<ul style="list-style-type: none"> • rash • pruritis • stomatitis 	<ul style="list-style-type: none"> • bone marrow suppression • proteinuria 	CBC and urinalysis every 2 wks for first 3 mos then monthly	\$10 - \$50
Azathioprine (Imuran®, generics)	2-2.5 mg/kg daily	<ul style="list-style-type: none"> • nausea • vomiting • diarrhea • rash 	<ul style="list-style-type: none"> • hepatitis • drug fever • bone marrow suppression • infection • malignancy 	CBC and AST every 2 wks for first 3 mos & then Q 3 mos	\$20 - \$60
Adalimumab** (Humira®)	40 mg Q 2 weeks SC	<ul style="list-style-type: none"> • injection site reaction 	<ul style="list-style-type: none"> • infections 	Tuberculin skin test, ANA, chest x-ray prior to initiating therapy	\$1,250 - \$1,500
Anakinra** (Kineret®)	100 mg SC/day	<ul style="list-style-type: none"> • injection site reactions (70%) 	<ul style="list-style-type: none"> • infections 	Tuberculin skin test, ANA, chest x-ray prior to initiating therapy	\$1,300 - \$1,400
Etanercept** (Enbrel®)	25 mg SC twice per wk	<ul style="list-style-type: none"> • injection site reactions 	<ul style="list-style-type: none"> • infections 	Tuberculin skin test, ANA, chest x-ray prior to initiating therapy	\$1400 - \$1600
Infliximab** (Remicade®)	3mg/Kg Q 8 wks IV infusion	<ul style="list-style-type: none"> • infusion reactions 	<ul style="list-style-type: none"> • infections 	Tuberculin skin test, ANA, chest x-ray prior to initiating therapy	\$1000 - \$2000

** Drug is covered by the provincial drug program only with prior Special Authority approval from PharmaCare. Special Authority criteria and forms are available on the PharmaCare Web site at <http://www.health.gov.bc.ca/pharmer/sa/criteria/formsindex.html>

Rheumatoid Arthritis

A GUIDE FOR ADULT PATIENTS

Effective Date: May 1, 2006

What is Rheumatoid Arthritis?

Arthritis is a term used to describe conditions that involve pain and inflammation in the joints. There are over 100 different types of arthritis. Rheumatoid Arthritis (RA) is the most common type of inflammatory arthritis. When a joint is inflamed it is painful, swollen, hot and stiff. This inflammation is in the lining of the joints, and if it is not controlled, it will cause permanent damage to the bone and cartilage. RA affects ~1% of the adult population and affects women more than men. RA can start at any age but most commonly occurs in the 30-50 age group.

What is the cause of Rheumatoid Arthritis?

The cause of RA is not yet known but there is continuing research. It seems most likely that a virus triggers the person's immune system to react in an abnormal way. This produces inflammation in the lining of the joints. We don't know why this causes continuing joint inflammation. We do know that there is an inherited gene that makes some people more likely to get RA. Not everyone with this gene will get RA.

How do I know if I have Rheumatoid Arthritis?

When RA starts it may be sudden or gradual. The pain or stiffness with swelling in joints is usually worse in the morning. Any joint may be involved but it commonly starts in the fingers, wrists and feet. RA usually involves many joints but at onset there may be only one or two joints affected. Your doctor will look for clues that might suggest the joint inflammation could be another type of arthritis. Blood tests help give clues but there is no blood test to completely diagnosis RA. It often takes months to confirm a diagnosis of RA.

What treatments are available?

Modern medications can control most of the joint inflammation. There is no cure at this time but the impact of RA can be minimized. It is important to start medications early. Your doctor will discuss these with you and probably will refer you to an arthritis specialist or rheumatologist. It is important to remember that the small risks associated with medications are worth taking to prevent permanent joint damage.

Regular exercise is important. With painful joints you may need to see a physical therapist. You will learn how to exercise inflamed joints safely and how to stay fit. An occupational therapist can advise you how to reduce stress to your joints while continuing your daily activities.

Lifestyle issues are also important. These include a healthy diet, weight control, reducing stress, stopping smoking and proper rest.

What can I do?

Learn more about the disease and work towards meeting self-management and lifestyle goals. Take an active role, as a partner with your physician, in treating your RA. Talk to your family doctor if you have concerns about: nutrition, exercise, support groups, stress and depression, sexual/reproductive health, financial and employment issues (pension and housing), and child care support.

Resources for people affected by rheumatoid arthritis:

- The Arthritis Society Web site: www.arthritis.ca
- Arthritis Information Line (toll free): 1 800 321-1433
- Arthritis Foundation: www.arthritis.org
- Arthritis Consumer Experts: www.arthritisconsumerexperts.org
- Find a Physical Therapist: www.bcphysio.org or 1 888 736-5645
- Dial-A-Dietitian Nutrition Information Society: www.dialdietitian.org or 1 800 667-3438
- Search for an occupational therapist in BC by name, professional interest or workplace: www.bcsot.org
- B.C. Chronic Disease Management Web site provides patient information and resources on common chronic illnesses: <http://www.health.gov.bc.ca/cdm/patients/index.html>
- BC NurseLine for advice and information any time of day or night at:
604 215-4700 (Greater Vancouver)
1 866 215-4700 (toll free) if outside the lower Mainland
1 866 TTY-4700 deaf and hearing-impaired (toll-free province-wide)
- To see patient guides for other chronic conditions and the physician's guideline for rheumatoid arthritis, visit the Guidelines and Protocols Web Site at www.health.gov.bc.ca/msp/protoguides/gps/
- *BC HealthGuide Handbook* available at www.bchealthguide.org
- Buy from a bookstore or borrow from the library *The Arthritis Helpbook: A Tested Self-Management Program for Coping with Arthritis and Fibromyalgia* by Kate Lorig and James Fries, published by Da Capo Press. Several editions are available, with information on the 2006 edition at: http://www.perseusbooks.com/perseus/book_detail_redirect.do?imprintCid=DC&isbn=0738210382