

# Pediatric Rheumatology

## Seven Things Clinicians and Patients Should Question

by

Canadian Rheumatology Association

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### 1 Do not order ANA as a screening test without specific signs or symptoms of a rheumatic condition.

Anti-nuclear antibody (ANA) should not be used as a screening test in patients without specific signs or symptoms of systemic lupus erythematosus or other systemic autoimmune rheumatic disease (e.g. inflammatory arthritis, malar rash, photosensitivity, etc.) since ANA positivity may occur in non-rheumatic conditions and in “healthy” populations (up to 20%). In consideration of juvenile idiopathic arthritis (JIA), a positive ANA indicates increased risk of uveitis, but is not a useful screening test for the diagnosis of JIA. Inappropriate ANA testing may be misleading, precipitate further unnecessary testing, and lead to patient anxiety.

### 2 Do not order labs for drug toxicity monitoring (i.e. CBC, liver enzymes, creatinine) more often than every 12 weeks for patients on a stable dose of non-biologic DMARDs.

Pediatric patients on stable doses of non-biologic disease modifying anti-rheumatic drugs (DMARDs) (e.g. methotrexate, sulfasalazine) without specific risk factors (e.g. obesity, diabetes mellitus, renal disease, alcohol use, concomitant use of hepatotoxic or myelosuppressive medications) are at a low overall risk of toxicity. More frequent blood draws pose an unnecessary burden to pediatric patients and the health-care system. Patients new to treatment, on escalating doses, or with abnormal baseline labs typically require more frequent monitoring.

### 3 Do not order HLA-B27 unless spondyloarthropathy is suspected based on clinical signs or symptoms.

Back pain is a common symptom relative to the incidence of spondyloarthropathy (SpA) in children. In addition, the prevalence of HLA-B27 is 2-8% in the general population, and individuals with a positive HLA-B27 have a low probability of developing SpA. As such, HLA-B27 testing is not useful as a single diagnostic test in a patient with low back pain without specific signs or symptoms of SpA (e.g., inflammatory back pain, peripheral arthritis, enthesitis, or acute anterior uveitis) or suggestive findings on MRI. Of note, patients with confirmed Juvenile Idiopathic Arthritis (JIA) may have HLA-B27 testing in order to classify their JIA subtype.

### 4 Do not order RF or anti-CCP in patients with arthralgia but no arthritis on exam.

In children, the vast majority of musculoskeletal (MSK) pain is non-inflammatory (97%) and is rarely secondary to a rheumatic disease. For patients with arthralgia (joint pain) but no arthritis on physical exam (defined as presence of joint effusion or  $\geq 2$  of warmth, tenderness, stress pain, reduced range of motion), testing rheumatoid factor (RF) or anti-cyclic citrullinated peptide (anti-CCP) is not clinically useful and has low diagnostic utility. For example, a positive RF may result from various infections. Performing such tests without clinical relevance may result in unnecessary additional testing and anxiety.

### 5 Do not order Lyme disease serology as an explanation for musculoskeletal symptoms without an exposure history and exam findings.

Lyme disease is most likely to occur if an individual resides in or visits an endemic area. The most common musculoskeletal (MSK) manifestation of Lyme disease is persistent or intermittent arthritis in at least one joint (typically the knee) which develops within weeks to months after a tick bite. Chronic diffuse arthralgias, myalgias or fibromyalgia alone are not criteria for MSK Lyme disease. Testing for Lyme disease should be limited to children with characteristic clinical signs and risk of exposure to Lyme to avoid false positive tests and unnecessary treatment.

**6 Do not use intra-articular corticosteroid injections as a treatment approach for a large number of joints or joints that have been injected multiple times.**

Pediatric patients with juvenile idiopathic arthritis (JIA) often benefit from treatment with intra-articular corticosteroid injections, especially when arthritis is impacting activities of daily living. However, in patients with polyarticular JIA ( $\geq 5$  affected joints) the probability of a short-lived or poor response to corticosteroid injections is increased when compared to those with oligoarticular JIA ( $\leq 4$  affected joints). Lack of concomitant initiation of a disease modifying anti-rheumatic drug (DMARD) in polyarticular disease is also a risk factor for suboptimal response to joint injections. In addition, repeating joint injections in the same joint (e.g.  $>2-3$  times/year) has a lower probability of achieving disease control compared to initiating a DMARD and may be a risk factor for the development of osteochondritis dissecans. Multiple or recurrent intra-articular corticosteroid injections may be considered as an adjunctive therapy while awaiting the effect of an escalation in systemic therapy.

**7 Do not order a periodic fever genetic panel in patients with a classic presentation of PFAPA syndrome without features concerning for other genetic periodic fever syndromes.**

Periodic fever, aphthous stomatitis, pharyngitis, adenitis (PFAPA) syndrome is a clinical diagnosis, and currently, no genetic mutations have been identified for this condition. Periodic fever genetic panel in patients with classic features of PFAPA—without any features of another periodic fever syndrome—rarely yields an alternate diagnosis and as such is costly and has no clinical benefit. However, genetic testing may be warranted if patients have atypical features at presentation, don't respond to treatment as expected, or develop concerning features over time.

## How the list was created

The Canadian Rheumatology Association (CRA) Pediatrics Committee established its Choosing Wisely Canada Top 7 recommendations in a multistage process combining consensus methodology and literature review. A Choosing Wisely working group was formed including pediatric rheumatologists from across the country from diverse clinical settings, an allied health professional, a parent and a patient. This group generated candidate recommendations using a series of Delphi surveys. Recommendations with high content agreement and perceived prevalence advanced to a survey of all CRA members who practice pediatric rheumatology. CRA members ranked these top items based on content agreement, impact and item ranking. A methodology subcommittee discussed the items in light of their relevance to pediatric rheumatology, potential impact on patients and the member survey results. The Top 7 items were selected to advance for literature review. The list was reviewed by all pediatric committee members and patient partners, and has been approved by the CRA Board of Directors.

## Sources

- 1 Kavanaugh A, Tomar R, Reveille J, Solomon DH, Homburger HA. Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens. *American College of Pathologists. Arch Pathol Lab Med* 2000;124:71-81. PMID: [10629135](#).  
Solomon DH, Kavanaugh AJ, Schur PH. American College of Rheumatology Ad Hoc Committee on Immunologic Testing Guidelines. Evidence-based guidelines for the use of immunologic tests: antinuclear antibody testing. *Arthritis Rheum* 2002;47:434-44. PMID: [12209492](#).  
Tozzoli R, Bizzaro N, Tonutti E, et al. Guidelines for the laboratory use of autoantibody tests in the diagnosis and monitoring of autoimmune rheumatic diseases. *Am J Clin Pathol* 2002;117:316-24. PMID: [11863229](#).
- 2 Karlsson Sundbaum J, Eriksson N, Hallberg P, Lehto N, Wadelius M, Baecklund E. Methotrexate treatment in rheumatoid arthritis and elevated liver enzymes: A long-term follow-up of predictors, surveillance, and outcome in clinical practice. *Int J Rheum Dis*. 2019 Jul;22(7):1226-1232. PMID: [31012257](#).  
Ledingham J, Gullick N, Irving K, et al. BSR and BHPR Standards, Guidelines and Audit Working Group. *Rheumatology (Oxford)*. 2017 Jun 1;56(6):865-868. PMID: [28339817](#).  
Zajc Avramovic M, Dolžan V, Toplak N, Accetto M, Lusa L, Avin T. Relationship Between Polymorphisms in Methotrexate Pathway Genes and Outcome of Methotrexate Treatment in a Cohort of 119 Patients with Juvenile Idiopathic Arthritis. *J Rheumatol*. 2017 Aug;44(8):1216-1223. PMID: [28572465](#).
- 3 Gran JT, Husby G. HLA-B27 and spondyloarthritis: value for early diagnosis? *J Med Genet*. 1995;32(7):497-501. PMID: [7562959](#).  
Reveille JD. Epidemiology of spondyloarthritis in North America. *Am J Med Sci*. 2011;341(4):284-6. PMID: [21430444](#).  
Reveille JD, Hirsch R, Dillon CF, Carroll MD, Weisman MH. The prevalence of HLA-B27 in the US: data from the US National Health and Nutrition Examination Survey, 2009. *Arthritis Rheum*. 2012;64(5):1407-11. PMID: [22139851](#).
- 4 Hermosillo-Villafraña, J.A., et al., Role of rheumatoid factor isotypes and anti-citrullinated peptide antibodies in the differential diagnosis of non-selected patients with inflammatory arthralgia. *Reumatol Clin*. 2021. 17(1): p. 12-15. PMID: [31399351](#).  
Wang, Y., et al., Meta-analysis: diagnostic accuracy of anti-cyclic citrullinated peptide antibody for juvenile idiopathic arthritis. *J Immunol Res*. 2015. 2015: p. 915276. PMID: [25789331](#).  
Wong, K.O., et al., Antinuclear Antibody, Rheumatoid Factor, and Cyclic-Citrullinated Peptide Tests for Evaluating Musculoskeletal Complaints in Children. Comparative Effectiveness Review No. 50 (Prepared by the University of Alberta Evidence-based Practice Center under Contract No. HHS A 290 2007 10021 I). 2012, Agency for Healthcare Research and Quality: Rockville (MD). PMID: [22514802](#).
- 5 Government of Canada, [Surveillance of Lyme Disease](#). [Internet].  
Lantos PM, Rumbaugh J, Bockenstedt LK, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease. *Arthritis Rheum*. 2021;73(1):12-20. PMID: [33251700](#).  
Lipsett SC, Nigrovic LE. Diagnosis of Lyme disease in the pediatric acute care setting. *Curr Opin Pediatr*. 2016;28(3):287-293. PMID: [27138805](#).
- 6 Heidt C, Grueberger N, Grisch D, Righini-Grunder F, Rueger M, Ramseier L. The assessment of steroid injections as a potential risk factor for osteochondral lesions in children with juvenile idiopathic arthritis. *Cartilage*. 2020 Sep;1947603520961173. PMID: [32985233](#).  
Lanni S, Bertamino M, Consolaro A, et al. Outcome and predicting factors of single and multiple intra-articular corticosteroid injections in children with juvenile idiopathic arthritis. *Rheumatology (Oxford)*. 2011 Sep;50(9):1627-1634. PMID: [21561981](#).  
Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Care Res (Hoboken)*. 2019 Jun;71(6):717-734. PMID: [31021516](#).
- 7 Berkun Y, Levy R, Hurwitz A, et al. The familial Mediterranean fever gene as a modifier of periodic fever, aphthous stomatitis, pharyngitis, and adenopathy syndrome. *Semin Arthritis Rheum*. 2011 Apr;40(5):467-72. PMID: [20828792](#).  
Dagan E, Gershoni-Baruch R, Khatib I, Mori A, Brik R. MEFV, TNF1 $\alpha$ , CARD15 and NLRP3 mutation analysis in PFAPA. *Rheumatol Int*. 2010 Mar;30(5):633-6. PMID: [19579027](#).  
Gattorno M, Caorsi R, Meini A, et al. Differentiating PFAPA syndrome from monogenic periodic fevers. *Pediatrics*. 2009 Oct;124(4):e721-8. PMID: [19786432](#).

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### **About The Canadian Rheumatology Association**

The Canadian Rheumatology Association (CRA) is a proud partner of the Choosing Wisely Canada campaign. Representing close to 600 rheumatologists across Canada, the mission of the CRA is to promote the pursuit of excellence in arthritis care, education and research. The CRA strives to provide the best services and support to its membership to provide the best quality of care possible to patients. This includes an amazing lineup of topics and speakers for the Annual Scientific Meeting, a website full of information, programs to attract more medical students into rheumatology, awards to recognize its members, guidelines development, research funding opportunities and excellent working partnerships with other organizations.



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### **About Choosing Wisely Canada**

Choosing Wisely Canada is the national voice for reducing unnecessary tests and treatments in health care. One of its important functions is to help clinicians and patients engage in conversations that lead to smart and effective care choices.

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