



Five Things Physicians and Patients Should Question

1

Do not prescribe opioids for chronic pain management in patients with autoimmune disease.

Opioids are generally acceptable in pediatric medicine for short-term pain control associated with surgery or trauma. They are not recommended for treatment of chronic pain. Research has shown morphine and similar medications are not superior to ibuprofen and have significantly more adverse effects, e.g. opioid dependence and withdrawal symptoms. Adverse effects may occur after as few as 5 days of use. Use of opioids for medical purposes in adolescence also increases the risk for long-term use and misuse in adulthood. Opioids do not reduce inflammation from active arthritis and should be reserved for short-term use in cases of severe pain secondary to joint damage. Long-term pain control should be addressed with a multidisciplinary approach combining pharmacologic, behavioral, and exercise-based modalities.

2

Do not order antinuclear antibody (ANA) and other autoantibody testing on a child unless there is strong suspicion or specific signs of autoimmune disease.

The antinuclear antibody (ANA) has a high sensitivity for only one disease, systemic lupus erythematosus (SLE), but has very poor specificity for SLE and every other rheumatic disease. Therefore, it is not useful or indicated as a general screen of autoimmunity.

A positive ANA may occur secondary to polyclonal activation of the immune system following an infection, or it may be positive without any identifiable reason/disease in up to 32% of the population. Limiting patients on which to order ANA would reduce unnecessary physician visits and laboratory expenses as well as parental anxiety. "Lupus panels" and other similar panels should also not be ordered without concerns for specific autoimmune disease. Additionally, since the ANA may always be positive and may fluctuate in titer, it is not recommended to retest it unless there is some new clinical concern.

3

Do not test for Lyme disease as a cause of musculoskeletal symptoms without an exposure history or appropriate exam findings.

The musculoskeletal manifestations of Lyme disease include brief attacks of arthralgia with early disseminated Lyme and/or intermittent or persistent episodes of arthritis in one or a few large joints, with predilection for the knee, in late disease. Lyme testing in the absence of these features and without appropriate exposure from living in or traveling to a Lyme endemic area increases the likelihood of false positive results and may lead to unnecessary follow-up and therapy. Diffuse arthralgias, myalgias, or fibromyalgia alone are not criteria for musculoskeletal Lyme disease.

4

Do not send periodic fever syndrome genetic panels prior to infectious and oncologic work up or in a patient without clear evidence of recurrent fever.

Fever is a common complaint in the pediatric age group with infectious etiology as the most common followed by malignancy. Thorough history and physical exam in addition to diligent documentation of fever and accompanying symptoms can often help define underlying etiology, minimizing as well as targeting additional work-up. Of note, most children with a periodic fever syndrome do not have a genetic mutation, and the most common periodic fever syndrome – PFAPA (periodic fever, adenitis, pharyngitis, aphthous ulcer) – is not associated with a monogenic mutation.

5

Do not order rheumatoid factor (RF) alone, or as part of a “panel” or “cascade” in children to evaluate for rheumatologic disease such as juvenile idiopathic arthritis (JIA) due to musculoskeletal complaints. Do not let laboratory results guide referral.

JIA is a clinical diagnosis, and laboratory studies are used to prognosticate severity. Only 10-30% of children with JIA have a positive RF compared to the majority of adults with rheumatoid arthritis. The relevance of other antibodies such as anti-cyclic citrullinated peptide (anti-CCP) has not been established in the pediatric population. Additionally, RF is nonspecific and can be positive in other diseases, infections, or healthy individuals, and these labs are typically expensive. Patients may still have JIA despite a negative RF, and a positive test with no clinical disease causes significant parental anxiety and may result in additional unnecessary testing.

How This List Was Created

The American Academy of Pediatrics' Section on Rheumatology (SORh) consists of pediatric rheumatologists, pediatricians, and allied health care professionals who are actively involved in some aspect of the study of rheumatologic disease in children and adolescents. The SORh strives to inform pediatricians, parents, communities, and policy makers on rheumatic disease in children. The fellow members of the SORh were queried to develop a list of diagnostic and management decisions that have resulted in misuse of laboratory studies and resources. Through a series of votes, the fellow members developed the list into five statements to address the most common misconceptions seen when encountering pediatric autoimmune conditions. The fellows involved in this project are: Kathleen Collins, Brian Dizon, Suhas Ganguli, Miriah Gillispie, Marla Guzman, Michael B. Nelson, Onengiya Harry, Meiqian Ma, MaiLan Nguyen, Amir Orandi, Amanda Schlefman, Laura Tasan, and Erin Treemarcki. The list was shared with membership of the SORh Executive Committee for feedback and then finalized by collaboration. These five clinical issues are the result. Various expert committees and sections of the AAP reviewed and approved the list. The AAP Executive Committee granted final approval of the list.

The guidance in this list does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

Sources

- Eccleston C, Cooper T, Fisher E, Anderson B, Wilkinson N. Non-steroidal anti-inflammatory drugs (NSAIDs) for chronic non-cancer pain in children and adolescents. *Cochrane Database Syst Rev*. 2017;2(8).

Galinkin J, Koh J, Committee on Drugs, Section on Anesthesiology and Pain Medicine, American Academy of Pediatrics. Recognition and management of iatrogenically induced opioid dependence and withdrawal in children. Galinkin J, Koh JL; Committee on Drugs; Section on Anesthesiology and Pain Medicine; American Academy of Pediatrics. *Pediatrics*. 2014;133(1):152-155.

Gmuca S, Sherry D. Fibromyalgia: Treating Pain in the Juvenile Patient. *Paediatr Drugs*. 2017;19(4):325-338.

Miech R, Johnston L, O'Malley P, Keyes K, Heard K. Prescription Opioids in Adolescence and Future Opioid Misuse. Miech R, Johnston L, O'Malley PM, Keyes KM, Heard K. *Pediatrics*. 2015;136(5):e1169-e1177.

Poonai N, Dattoo N, Ali S, et al. Oral morphine versus ibuprofen administered at home for postoperative orthopedic pain in children: A randomized controlled trial. *CMAJ*. 2017;10(189(40)):E1252-E1258.
- Cabral DA, Petty RE, Fung M, Malleson PN. Persistent Antinuclear Antibodies in Children Without Identifiable Inflammatory Rheumatic or Autoimmune Disease. *Pediatrics*. 1992;89(3):441-444.

Deane PMG, Liard G, Siegel DM, Baum J. The Outcome of Children Referred to a Pediatric Rheumatology Clinic With a Positive Antinuclear Antibody Test but Without an Autoimmune Disease. *Pediatrics*. 1995;95(6):892-895.

Hilario MOE, Len CA, Roja SC, Terreri MT, Almeida G, Andrade LEC. Frequency of Antinuclear Antibodies in Healthy Children and Adolescents. *Clinical Pediatrics*. 2004;43:637-642.

Malleson PN, Sailer M, Mackinnon MJ. Usefulness of antinuclear antibody testing to screen for rheumatic disease. *Arch Dis Child*. 1997;77:299-304.
- Lantos P, Lipsett S, Nigrovic L. False positive lyme disease IgM immunoblots in children. *J Pediatr*. 2016(174):267-269.

Lipsett S, Nigrovic L. Diagnosis of Lyme disease in the pediatric acute care setting. *Curr Opin Pediatr*. 2016;28(3):287-293.

Markowicz M, Kivaranovic D, Stanek G. Testing patients with non-specific symptoms for antibodies against borrelia burgdorferi sensu lato does not provide useful clinical information about their aetiology. *Clin Microbiol Infect*. 2015;21(1098):1103.

Moore A, Nelson C, Molins C, Mead P, Schriefer M. Current guidelines, common clinical pitfalls, and future directions for laboratory diagnosis of Lyme disease, United States. *Emerg Infect Dis*. 2016(22):7.

Sigal L. Musculoskeletal features of Lyme disease: understanding the pathogenesis of clinical findings helps make appropriate therapeutic choices. *J Clin Rheumatol*. 2011;17(5):256-265
- Antoon J, Peritz D, Parsons M, Skinner A, Lohr J. Etiology and resource use of fever of unknown origin in hospitalized children. *Hosp Pediatr*. 2018;8(3):135-140.

Antoon J, Potisek N, Lohr J. Pediatric fever of unknown origin. *Pediatr Rev*. 2015;36(9):380-390.

Chusid M. Fever of unknown origin in childhood. *Pediatr Clin North Am*. 2017;64(1):205-230.

Gattorno M, Sormani M, D'Osualdo A, et al. A diagnostic score for molecular analysis of hereditary autoinflammatory syndromes with periodic fever in children. *Arthritis Rheum*. 2008;58(6):1823-1832.

Tchernitchko D, Moutereau S, Legendre M, et al. Mefv analysis is of particularly weak diagnostic value for recurrent fevers in western European Caucasian patients. *Arthritis Rheum*. 2005;52(11):3603-3605
- Groot N, Heijstek M, Wulffraat N, Agarwal M, Sawhney S. Laboratory tests in pediatric rheumatology. *Indian J Pediatr* 2010;77(9):1011-6.

Dalrymple A. Laboratory evaluation in pediatric autoimmune disease. *Pediatr Rev* 2015;36(11):496.

Ingegnoli F, Castelli R, Gualtierotti R. Rheumatoid Factors: Clinical Applications. *Hindawi* 2013;35(6):727-34.

Smolen, Josef S, Aletaha, Daniel, McInnes, Iain B. Rheumatoid arthritis. *The Lancet* 2016;338(10055):2023-2038.

Wong, Kai O, Bond, Kenneth Homik, Joanne Ellsworth, Janet E. Karkhaneh, Mohammad Ha, Christine Dryden DM. Antinuclear Antibody, Rheumatoid Factor, and Cyclic-Citrullinated Peptide Tests for Evaluating Musculoskeletal Complaints in Children. 2012.

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