Inflammation that may elevate the blood WBC during the hospital treatment course, may not be caused by active infection (e.g., surgical trauma, necrotic tissue) in children with ABA.

Imaging studies generally are not needed to confirm response to therapy but may be indicated when clinical findings and laboratory studies are not demonstrating the expected resolution or normalization [158].

Rationale for recommendation

Physical examination provides essential information for clinical decision making. Measurement of serum CRP concentration is widely available in a timely manner, is relatively inexpensive, and can be an objective data point that supports clinical decision making. Pain, discomfort, and additional costs can occur from venipuncture.

The relatively rapid normalization of CRP has been interpreted as providing useful clinical guidance for early switch to oral therapy, discharge from the hospital, and avoidance of prolonged antibiotic therapy for uncomplicated disease. Although higher CRP peaks and prolonged time to normalization correlate in general with various aspects of the extent and severity of infection in children with ABA, no specific thresholds of CRP concentration have been well validated for specific pathogens or the various infected joints, with respect to the need to perform specific clinical/surgical interventions or, for the purposes of making decisions on duration of therapy.

As the infection is appropriately treated, fever abates and local signs of inflammation begin to resolve, there usually is a concurrent fall in serum CRP concentration. Persistent elevation of CRP from what is expected in a typical uncomplicated course, especially when associated with slower than expected clinical improvement, may prompt changes in management, including: 1) additional imaging to better define the extent of the infection and its complications; or 2) surgical intervention(s) that may optimize short- and long-term outcomes; and 3) reconsideration of the etiology of arthritis (e.g., infection vs autoimmune disorder).

The interpretation of persistent elevation of the CRP in the face of apparent clinical improvement is uncertain. This discordance can raise concerns about the need for more evaluation or intervention but acting on such data without regard to the clinical context of recovery could lead to unnecessary actions and procedures and their associated risks. Such discordance can be caused by intercurrent infection or other issues unrelated to ABA.

Within the limitations outlined above, the Guideline Panel suggests sequential monitoring of CRP as an adjunctive measure in children with ABA that can be taken into account with other clinical factors in management decision-making. There are no data to support a particular frequency of CRP monitoring during the course of ABA in children. Measurement every 2 to 3 days during the early therapeutic course, rather than daily, followed by weekly or other periodic measurement until a clear trend towards normalization is evident, is an acceptable approach [37].

Research needs

More detailed analyses of the clinical utility of serial serum CRP concentrations and other biomarkers of systemic inflammation, by pathogen and by joint involved would be useful. Identification of specific CRP or other biomarker cutoff values would be helpful for specific pathogens and for specific clinical situations, such as the need for additional surgery versus ongoing observation. It is likely that multicenter studies using iterative protocols will be required to gain insight into some of these questions [37].

XI. SHOULD HOSPITALIZED CHILDREN WITH PRESUMED OR CONFIRMED ABA WHO ARE RESPONDING WELL TO INITIAL INTRAVENOUS THERAPY, NO LONGER REQUIRING SKILLED NURSING CARE AND DEEMED READY FOR HOSPITAL DISCHARGE BE TRANSITIONED TO A) ORAL THERAPY OR B) OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY (OPAT)?

Recommendations:

1. For children with presumed or confirmed ABA who respond to initial intravenous antibiotic therapy, we recommend transition to an oral antibiotic regimen rather than OPAT when an appropriate, well-tolerated oral antibiotic option is available, and that antibiotic is active against the confirmed or presumed pathogen(s) (strong recommendation; *low certainty of evidence*). **Comment:** This recommendation places a high value on avoidance of harms and costs, as well as on considerations of patient's values and preferences, feasibility, acceptability, and equity.
2. For children with presumed or confirmed ABA who respond to initial parenteral antibiotic therapy but for whom oral antimicrobial therapy is not feasible, we suggest transition from the acute-care hospital to OPAT, rather than remaining in the hospital for the total duration of therapy (conditional recommendation, *very low certainty of evidence*). **Comment:** This recommendation places a high value on avoiding harms and costs associated with unnecessary and prolonged hospital stay. The decision to implement this recommendation and the selection of the type of OPAT (home, intermediate care facility, clinic) may be influenced by availability of local resources.

Background

ABA in children was once thought to require antimicrobial therapy for 21 to 28 days with at least 14 to 21 days via the intravenous route [270, 271]. Variations in approach have occurred