a six-week course of antibiotics are administered to children with methicillin-resistant *Staphylococcus aureus* (MRSA) infection of the musculoskeletal system [11].

There is also no consensus or published studies about the optimal transition time from intravenous to oral antibiotic therapy in pediatric osteoarticular infection. There is, however, agreement in clinical practice that a transition from parenteral to oral antibiotics should occur when clinical signs and serum laboratory markers improve [12–14].

An extensive search of the literature revealed 33 retrospective observational studies related to management of pediatric musculoskeletal infections. The median length of antibiotic usage in these studies ranged from two to five weeks for SA patients and three to eight weeks for OM patients. Many of these studies had small sample sizes, short follow-up duration and heterogeneous patient populations, thus precluding meaningful comparison. In studies analyzing both SA and OM populations, a longer duration of antibiotics was consistently reported for OM patients [15–17].

There have been no high-level studies examining the appropriate length of antibiotic treatment for pediatric patients with SA vs. OM. In the absence of such concrete evidence, it remains unclear if the length of antibiotic treatment should be different for primary SA vs. OM. From the results of review of the available literature, it appears that uncomplicated cases of SA may be treated with a shorter duration of antibiotics than OM. This aligns with current guidelines from the European Society for Pediatric Infectious Diseases as well as the Australasian Society for Infectious Diseases, which both recommend an average of two to three weeks of antibiotics in SA and three to four weeks of antibiotics in OM [18,19]. Australian Therapeutic Guidelines suggest similar durations of three weeks in SA and three weeks minimum in OM [20,21]. However, length of antibiotic usage should be evaluated individually and guided by clinical response. There is a paucity of data on antibiotic duration in neonates, immunocompromised patients, patients with bone abscesses, those with chronic OM and infections caused by MRSA. The optimal length of therapy in these groups is yet to be defined. Thus, larger prospective randomized clinical trials of methodological rigor are required.

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QUESTION 5: Do steroids have a chondroprotective effect in children with septic arthritis (SA)?

RECOMMENDATION: Based on available pre-clinical and clinical studies it appears that the concurrent use of corticosteroids and antibiotics may have a protective role in the management of SA in the pediatric patient population.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 58%, Disagree: 20%, Abstain: 22% (Simple Majority, NO Consensus)

RATIONALE

SA can lead to severe joint disabilities in about 30% of affected children. These disabilities include restriction of bone growth, chondral destruction, stiffness, pathologic fracture, limb-length discrepancy, subluxation and chronic dislocation of the joint [1,2].

The processes leading to these sequelae are thought to be due more to inflammatory responses than direct damage caused by

microorganisms. Rapid proliferation of bacteria within the joint space activates a cascade of pro-inflammatory cytokines including, interleukin (IL)-1 beta, IL-6, IL-17 and tumor necrosis factor (TNF)-α [3]. These cytokines, in conjunction with the TNF receptor-ligand family receptor activator of nuclear factor kappa-B ligand (RANKL), are believed to play a critical role in the activation and proliferation of osteoclasts, leading to bone resorption. Specifically, the interaction between RANKL and its receptor, RANK, has been shown to be required for osteoclast differentiation. Expression dysregulation of these factors in SA can lead to significant osteolysis [4,5]. In addition, increased synovial fluid and joint effusion in SA can obstruct blood supply of the joint, leading to chondrocyte necrosis, even during the early hours of infection [6].

Glucocorticoids have an established role in suppressing the release of proinflammatory cytokines in almost all acute or chronic diseases [7]. They are used to control inflammatory conditions affecting the joint, such as rheumatoid arthritis and ankylosing spondylitis. Corticosteroids also reduce the production of proteolytic enzymes, such as elastase, collagenase and synovial matrix metallopeptidase-1 (MMP-1), thereby preventing the chondral degradation process [7,8]. Despite the use of corticosteroids in inflammatory conditions, they are avoided in patients who have infections due to their immunosuppressive effect and their potential to exacerbate infection. However, recent evidence suggests that the concurrent use of corticosteroids with antibiotics improved the care of patients with central nervous system infections, pneumonia, upper urinary tract infection and sepsis [9–12].

The chondroprotective effect of glucocorticoids was investigated by two separate studies in 1996. Stricker et al. and Sakiniene et al. investigated the chondroprotective effect of corticosteroids on the course of SA [13,14]. Both studies utilized animal models to investigate if the administration of glucocorticoids had any influence on the levels of circulating inflammatory mediators. Stricker et al. employed the rabbit model and Sakiniene et al. utilized a mouse model to demonstrate that the administration of glucocorticoids resulted in improvement in symptoms in the animals and a significant decrease in serum levels of inflammatory cytokines at two weeks.

Extensive search of the literature revealed four clinical studies that relate to this subject (Table 1). These studies consist of two double-blinded randomized control trials, one non-randomized clinical trial and one retrospective study [15–18]. The findings of the studies are summarized in Table 1. All studies demonstrate improvements in clinical symptoms, length of hospital stay, reduced use of antibiotics or faster return to normal of serum inflammatory markers, such as C-reactive protein (CRP). In 2015 a meta-analysis was published regarding the use of corticosteroids in SA that included three of the aforementioned studies [19]. The finding of the meta-analysis was that the use of corticosteroids combined with antibiotics resulted in an improvement in the outcome of management of SA in children.

Despite the availability of evidence to support the use of corticosteroids in pediatric patients with SA, some concerns still remain. These concerns are:

1. The studies do not specifically seek adverse effects associated with the administration of corticosteroids.
2. Long term follow-up on patients receiving steroids is not available.
3. Total participant number of these studies is low.
4. Optimum dose, duration and route of prescription of corticosteroids is not clear yet.

TABLE 1. Summary of studies

Author (Year)	Study Design	Participants	Treatment Protocol	Results (Follow-up)
Odio et al. (2003) [15]	Randomised clinical trial	100 children	4 days of dexamethasone + AB	Significant decrease of joint dysfunction (12m) Quicker normalization of CRP Earlier symptoms relief Decreased IV antibiotics days
Harel et al. (2011) [16]	Randomised clinical trial	49 children	4 days of dexamethasone + AB	Significant decrease of joint dysfunction (12m) Became afebrile earlier Quicker normalization of CRP Decreased IV antibiotics days Decreased hospitalization
Arti et al. (2014) [17]	Non-randomized clinical trial	60 children	4 days of dexamethasone + AB	Decreased hospitalization Better final ROM Decreased local sign of inflammation Higher ESR reduction rate
Fogel et al. (2015) [18]	Retrospective	116 children	Few days of dexamethasone + AB	Rapid clinical improvement Quicker normalization of CRP Decreased IV antibiotics days Decreased hospitalization

The aforementioned concerns are important enough to justify the need for larger scale prospective studies with a longer follow-up that examine the benefits as well as the potential adverse effects of corticosteroids administered to pediatric patients with SA.

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QUESTION 6: What is the optimal management of septic arthritis/osteomyelitis (SA/OM) caused by methicillin-resistant *Staphylococcus aureus* (MRSA)?

RECOMMENDATION: Patients with MRSA infection should be started on an antibiotic regimen, such as vancomycin, intravenously followed by linezolid, which is effective against this organism. Early consideration for surgical treatment and close monitoring is essential in pediatric patients with musculoskeletal MRSA infection to reduce the high prevalence of complications and late sequelae that are often seen.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 85%, Disagree: 11%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE:

In past decade, the prevalence of MRSA in SA and acute OM has dramatically risen between 3- to 10-fold [1–3]. Compared to methicillin-susceptible *Staphylococcus aureus* (MSSA) infections, patients with MRSA have more extensive areas of soft tissue destruction, more rapid spread of infection and experience higher mortality rates [2–4]. The course of treatment of these patients is also protracted with a longer length of hospital stay, need for surgical intervention and an increased risk of complications, such as persistent bacteremia, deep vein thrombosis, pulmonary embolus, pathologic fractures and other long-term sequelae [1,2,5–10].

The severity of MRSA infections may be related to virulence factors, such as Panton-Valentine Leukocidin (PVL) found in many MRSA strains [11,12]. MRSA strains may also contain specific virulence factors that are linked to increased soft tissue destruction, such as α-hemolysin and α-type phenol-soluble modulin [3].

Pediatric patients with MRSA infections are more systematically unwell with higher temperatures and increased tachycardia. In addition, they present with even higher leukocytosis (or absolute neutrophil count), greater elevations in erythrocyte sedimentation rate and C-reactive protein but lower hematocrit values [5,7,10,13].

Commencing appropriate empiric antibiotics in these patients is paramount to improve outcomes. Children with suspected MRSA SA or OM should be started on intravenous vancomycin or clindamycin. Daptomycin or Linezolid are alternatives for the treatment of MRSA infections in children. The duration of therapy should be individualized based on the response to treatment. A minimum course of three to four weeks for SA and four to six weeks of antibiotics for OM is recommended [4,14].

Cultures should ideally be obtained before initiating antibiotics in patients with musculoskeletal infection, especially if MRSA is suspected. Aspiration of the affected joint and obtaining blood cultures helps isolate the infective organism and should be part of the initial work up of these patients [14,15]. New diagnostic methods, such as real time polymerase chain reaction (PCR), may be useful in the rapid identification of MRSA or other infective organisms [5].