the importance of image-guided percutaneous spinal biopsy [9].

Wu et al. observed that out of 41 (age range 3 to 82 years) histologically positive cases of OM, 14 (34%) cases were positive at culture. The proportion of positive culture results in confirmed cases of OM on the basis of histology was low. Patients who were on antimicrobial therapy in a 24 hour period of the biopsy, 24% had a positive culture, and the patients who were not on antibiotics had a 42% culture positivity rate. Larger prospective studies are required to investigate this finding further. They also advised or requested physicians to hold antibiotics for at least 24 hours before the biopsy [10].

Rankine et al. performed a retrospective study on 20 patients who had percutaneous spinal biopsies, with 8 out of 20 patients (40%) on antibiotics before the biopsy. An organism was isolated in 8 out of 20 cases (40%). Out of 8 patients on antibiotics, an organism was isolated in only 2 cases (25%). The result of the biopsy helped to modify the treatment in 7 of the 20 patients (35%). They also suggested that spinal biopsy should be done before starting antibiotic and a sample should be sent for both microbiology and histopathology [11].

Ng et al. reviewed the histopathological, cytological and microbiological results of patients who underwent bone and para-osseous biopsies between July 1977 and March 1996. The 502 biopsies were taken from 477 patients (age range for male patients was 5-86 years and for female patients was 2-86 years). Tumors were reported in 40% of the biopsies and infection in 16%. The latter study confirms the importance of bone biopsy in confirming diagnosis of infection and also detecting the presence of neoplasm, a differential diagnosis that needs to be born in mind when encountering pediatric patients suspected of infection. A bone biopsy can be taken from any site under the guidance of fluoroscopy or CT [12].

In conclusion, our extensive search of the literature has revealed one study evaluating the role of bone biopsy in children with the remainder of the studies being performed in an adult population. Based on the available evidence, we recommend that percutaneous bone biopsy under fluoroscopic or CT guidance is a reasonable, fast and cost-effective modality for diagnosis of OM and differentiating infection from neoplasm. It carries low complication rate but the ability of this test to isolate the infective organism in OM remains low. The above studies suggest that percutaneous bone biopsy shows high specificity but low sensitivity in microbiological diagnosis of OM but the combining results of microbiological examination with histological evaluation of the samples enhances the sensitivity. Literature also suggests that bone biopsy should be performed before initiating empirical antibiotic therapy in order to increase its yield for isolation of the infective organism.

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QUESTION 6: Is there any role for polymerase chain reaction (PCR) or molecular testing in pediatric musculoskeletal infection (PMSI)?

RECOMMENDATION: PCR may be a useful diagnostic adjunct with the potential to expedite a preliminary diagnosis of PMSI in comparison to the use of microbiological culture alone. Furthermore, PCR can enable pathogen identification in cases where the organism is indolent, fastidious or difficult to culture. However, data remains sparse and further research is needed to standardize molecular techniques, minimize contamination and explore emerging molecular methods that are primer-independent.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 2%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

The diagnosis of musculoskeletal infection is typically based on pertinent clinical findings, synovial fluid analysis and a positive gram stain or culture confirming the microbial identity of a pathogen [1]. Although culture results are used to identify the infecting organism and determine antimicrobial sensitivity, culture is often limited by sampling methodology, processing issues, early antibiotic administration, and/or the presence of hard to culture organisms [2–4]. PCR and other molecular techniques have been investigated to a limited

degree as diagnostic tools and are showing promise for improving PMSI diagnosis.

Evidence for the diagnostic use of PCR in PMSI is sparse. In a prospective study exploring the utility of PCR, Verdier et al. enrolled 171 pediatric patients with osteoarticular infection (OAI). From this cohort, 64 culture-positive specimens were identified, of which 9 cases were positive for *Kingella kingae*. When the 107 culture-negative specimens were tested with PCR, 15 additional cases of *Kingella kingae* were detected [5]. Similarly, Chometon et al. conducted a study of 131 patients with acute pediatric OAI in a single hospital and found that pathogen identification improved from 45% by culture alone to 66% with both culture and PCR testing [6].

Ferroni et al. performed a prospective study with 197 acute pediatric OAI cases in a single hospital and found that the use of PCR in addition to culture and histology increased bacterial diagnosis by 54%.

There is additional evidence for the utility of PCR aiding diagnosis of musculoskeletal infection from studies examining adult cases. However, the reported sensitivity of PCR varies widely in the literature from 43.8% to 92.5% and specificity ranges from 92.9% to 100% [7–9]. Despite this variation, investigators consistently conclude that the rapid availability of the results (<1 day) make PCR an adjunctive tool for guiding early treatment prior to the availability of culture results [7,8], especially in the setting of a negative culture [9]. It should be noted that these studies used different standards to compare to PCR performance; Bonilla et al. and Fenollar et al. used culture results as their gold standard, while Fihman et al. used clinician diagnostic judgment based on predetermined factors [7,9]. This significant inconsistency renders the results difficult to compare and interpret across studies.

PCR has also shown promise as a valuable tool for diagnosing tuberculosis affecting the bones and joints [10–12]. *Mycobacterium tuberculosis* is a particularly difficult organism to culture because false-negative results are relatively common. Therefore, a rapid, reliable diagnostic test is still needed. A study of 24 samples (21 patients) showed that PCR had 100% sensitivity and 87.5% specificity for identifying tuberculous disease affecting the bones and joints. However, two false-positive results were seen in patients who had previously been diagnosed with tuberculosis [10].

An infected joint can rapidly progress into a medical emergency. Rapid molecular diagnostic tools could play a crucial role in identifying and treating the infection promptly [13]. PCR is a sensitive, rapid and widely-available molecular methodology that can detect microbial pathogens in clinical samples. However, in order to obtain reliable and consistent results it is necessary to standardize PCR preparation protocols and take care to avoid contamination [1,13].

Further research is needed to investigate the role that PCR and other molecular methods can play in identifying a pathogen.

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QUESTION 7: How can we differentiate between sickle cell crisis and septic arthritis/osteomyelitis (OM)?

RECOMMENDATION: A combination of clinical, laboratory and imaging studies are all needed for differentiating between sickle cell crisis and infection. A positive aspiration for infection from the joint or periosteum confirms the presence of infection while sequential ultrasounds in the absence of sub-periosteal fluid collection favor sickle cell crisis. Tri-phasic bone scan in the first 24 hours can differentiate vaso-occlusive crisis (VOC) from acute infection. Contrast-enhanced magnetic resonance imaging (MRI) is fairly accurate in differentiating infection from infarction.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 87%, Disagree: 0%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

Differentiating bone and joint infection from osteonecrosis (ON) in sickle cell disease (SCD) can be very challenging. Clinical presentation is an important tool in distinguishing OM from VOC in SCD: sudden, often severe pain; no or low-grade fever of less than 100 F (<38 c); inflam-