

# Role of Operative or Interventional Radiology-Guided Cultures for Osteomyelitis

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abstract

**BACKGROUND AND OBJECTIVE:** Acute hematogenous osteomyelitis (AHO) is a severe infection in children. Drainage of purulent collections in bones provides specimens for culture as well as therapeutic benefit. Interventional radiology (IR)-guided procedures may serve as a less invasive means of culture in select patients. We examined the impact of IR and surgically obtained cultures in the diagnosis and management of AHO.

**METHODS:** A retrospective review of cases of AHO was performed from 2011 to 2014. Patients with chronic disease, orthopedic hardware, puncture wounds, or an infected contiguous focus were excluded.

**RESULTS:** A total of 250 cases met inclusion criteria. Blood cultures were positive in 107 of 231 cases (46.3%), and 123 of 150 patients had positive cultures (82%) obtained by orthopedic surgery. Of these 123 patients, 62 (50.4%) had organisms identified only through operating room (OR) cultures. Of the 66 patients who had cultures obtained by IR, 34 (51.5%) had positive IR cultures. For those with positive IR cultures, 18 (52.9%) had negative blood cultures. Among the 80 patients with negative blood culture and positive OR/IR culture, the results changed antibiotic therapy in 68 (85%) patients.

**CONCLUSIONS:** IR or OR culture was the only means of identifying a pathogen in 80 of 216 cases (37%), and in >80% changed medical management. IR can be used effectively to obtain bone cultures in children with AHO not requiring open surgical drainage. Further research is needed to better understand the optimal utilization of IR and OR culture in pediatric AHO.



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Dr McNeil designed and implemented the study, performed initial data analysis, and drafted and revised the manuscript; Ms Forbes implemented the study, performed data collection, and assisted with data analysis; Dr Vallejo assisted with design and implementation of the study and data collection and analysis; Drs Flores, Hultén, and Mason collected data and performed data analysis; Dr Kaplan performed data analysis; and all authors approved the final manuscript as submitted.

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**WHAT'S KNOWN ON THIS SUBJECT:** Interventional radiology (IR)-guided bone sampling is used to diagnose osteomyelitis in adults but has been little studied in children.

**WHAT THIS STUDY ADDS:** A microbiologic diagnosis can be achieved in >50% of IR-guided cases. Deep cultures alter antibiotic management in 85% of cases with negative blood cultures. Antibiotic pretreatment has minimal impact on culture yield in the first 72 hours of therapy.

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Osteomyelitis is one of the most common serious infections of childhood, and optimal antimicrobial therapy is essential for satisfactory clinical outcomes. Although the majority of cases are secondary to *Staphylococcus aureus*, the introduction of community-acquired methicillin-resistant *S aureus* (MRSA) in the 1990s and early 2000s complicated the management of these infections.<sup>1,2</sup> At a large tertiary care center, 62.9% of *S aureus* osteomyelitis was secondary to MRSA from 2001 to 2004.<sup>3</sup> Antibiotic choice is further complicated in that *S aureus* resistance to clindamycin is increasing in many regions. In a recent study from St Louis, the prevalence of clindamycin resistance among MRSA causing soft tissue infections was 13%.<sup>4</sup>

Deep cultures obtained from bone, subperiosteal abscesses, or adjacent purulent collections in children with osteomyelitis can provide both microbiologic diagnosis and therapeutic benefit. Cultures obtained from bone yield a pathogen in  $\leq 67\%$  of children with osteomyelitis.<sup>5</sup> More than 60% of patients with *S aureus* osteomyelitis have evidence of subperiosteal abscesses,<sup>3</sup> and in 1 series, 56.9% of children with acute osteomyelitis of all causes had some form of surgical intervention performed.<sup>6</sup> The desire for microbiologic diagnosis in children with mild disease, however, must be weighed in the context of the risk for adverse events from surgery or anesthesia, financial cost, and the availability of providers.<sup>7</sup> These factors must be considered, as some studies have shown similar outcomes for children with culture-positive versus culture-negative osteomyelitis.<sup>8,9</sup>

Interventional radiology (IR)-guided culture of musculoskeletal infections provides a less invasive means of potentially establishing a microbiologic diagnosis. The majority of the literature on this subject

focuses on adults with vertebral osteomyelitis/discitis for which the bone culture yield ranges from 30.2% to 53.3%.<sup>10-12</sup> However, data on this subject in a pediatric population are limited.

We sought to evaluate the relative contribution of IR-guided and surgically obtained cultures in the microbiologic diagnosis and management of acute hematogenous osteomyelitis (AHO) in children. Secondary goals included determination of the contemporary microbiology of AHO at Texas Children's Hospital (TCH) and the potential impact that antibiotic pretreatment may have on IR or surgically-obtained culture yield.

## METHODS

Patients were identified from consultation records of the inpatient infectious diseases service of TCH Main Campus. TCH is a tertiary freestanding academic children's hospital with 639 licensed inpatient beds. All patients with osteomyelitis admitted to TCH are seen by the infectious diseases and orthopedic surgery services per institutional guidelines. The decision for surgical intervention is at the discretion of the attending orthopedist based on physical examination and radiologic findings; IR is typically consulted in cases in which orthopedic intervention is not deemed necessary. In such cases, the attending interventionalist decides whether biopsy/aspiration is technically feasible after review of available imaging data. Infectious diseases consultation records were reviewed from January 1, 2011, to December 31, 2014, for patients with AHO. Patients were considered eligible for inclusion if disease was acute in nature ( $< 28$  days of symptoms).<sup>13</sup> Patients with open or penetrating trauma, orthopedic hardware in place, osteomyelitis secondary to a contiguous focus,

or osteomyelitis secondary to a surgical procedure (such as sternal osteomyelitis after cardiac surgery) were excluded. The diagnosis of osteomyelitis was defined by the constellation of physical examination findings, radiology reports, and microbiologic studies. Medical records were reviewed from the time of hospital admission until discharge. This study was approved by the institutional review board of Baylor College of Medicine.

## Definitions

The isolation of coagulase-negative staphylococci,  $\alpha$ -streptococci (other than *S pneumoniae* or *S milleri* group), diphtherioids, and *Bacillus* spp. were regarded as culture contaminants. Fever was defined as a body temperature  $\geq 100.4^\circ\text{F}$ ; duration of fever was defined as the number of calendar days with fever. The presence of concomitant septic arthritis was defined by using a combination of classic clinical findings (joint swelling, erythema, tenderness, limited range of motion, etc), radiologic findings, and results of synovial fluid culture and cytology. Patients were considered to have attendant myositis or pyomyositis based on the MRI report. Myositis was considered abnormal enhancement within skeletal muscle in the absence of an abscess; pyomyositis refers to the presence of  $\geq 1$  abscess within skeletal muscle. Patients were regarded as having an IR culture performed regardless of whether core bone samples were collected or aspiration of subperiosteal abscesses or adjacent purulent collections was performed by the IR service. A change in antimicrobial therapy was considered if the results of culture data prompted the infectious disease clinician to change antimicrobial therapy to a narrower-spectrum agent or one specific to the organism isolated. For example, in patients whose cultures

grew clindamycin-susceptible MRSA, a change from vancomycin to clindamycin would be considered an appropriate narrowing of coverage. In patients with methicillin-susceptible *S aureus* (MSSA) or group A streptococcal (GAS) infection, a change from either vancomycin or clindamycin to a  $\beta$ -lactam agent would be considered appropriate, based on clinical data and expert opinion.<sup>14–18</sup> Furthermore, vancomycin cannot be continued at our institution beyond 48 hours when alternative antibiotics are effective without approval of the antibiotic stewardship program. Antibiotic pretreatment was regarded as  $\geq 1$  dose of intravenous antibiotics administered  $\geq 1$  h before the obtainment of operating room (OR) or IR-guided cultures.

### Microbiology, Antimicrobial Susceptibility, and Strain Typing

Organism identification and antimicrobial susceptibility were performed by the TCH clinical microbiology laboratory in the routine course of care. TCH uses the VersaTREK blood culture system (Thermo Fisher Scientific, Waltham, MA) which utilizes blood culture vials without resin. Polymerase chain reaction for *Kingella kingae* is not routinely performed at our institution. Bone and synovial fluid samples for culture were inoculated into blood culture bottles at the discretion of the attending orthopedist/interventionalist. The exact technique used for collection of samples by IR was at the preference of the individual interventionist. In general, however, the epicenter of the lesion was localized with ultrasound, fluoroscopy, or computed tomography (CT) (and compared with images obtained via MRI) and used to direct the aspirating or biopsy needle. *S aureus* isolates collected at TCH are included as part of an ongoing *S aureus* surveillance study.<sup>19</sup> Isolates are stored in horse blood in the Infectious Diseases

Research Laboratory, and basic clinical data are collected. A similar surveillance study is carried out for invasive *S pneumoniae* isolates. Starting in 2012, invasive GAS isolates obtained at TCH are collected as a component of a third surveillance study. Available *S aureus* isolates were characterized by pulsed field electrophoresis,<sup>20</sup> pneumococcal isolates underwent serotype determination using the capsular swelling method,<sup>21</sup> and GAS isolates were analyzed by *emm* type.<sup>22</sup>

### Statistical Analyses

Dichotomous variables were analyzed using Fisher exact test and continuous variables with *t* test, Wilcoxon rank sum, and Kruskal–Wallis tests, with *P* values  $< .05$  considered statistically significant. Comparisons were made between patients who had blood cultures alone, those who had IR-guided cultures, and those who had OR cultures; patients who had both IR and OR procedures performed were included in the overall study but were excluded from these specific analyses. For comparisons of organism and culture yield across anatomic sites, cases were grouped into infection of long bones (femur, tibia, fibula, radius, ulna, and humerus), infection of pelvis, central skeleton (spine, mandible, sternum, clavicle, rib, and scapula), and other small/flat bones (small bones of hands/feet); patients with multifocal disease, which included  $> 1$  of these classes, were excluded from this analysis. All statistical analyses were performed with the assistance of Stata version 13 (Stata Corp, College Station, TX).

### RESULTS

From January 1, 2011, to December 31, 2014, 401 consultations for osteomyelitis were performed by the TCH main campus infectious diseases service. After review of

medical records, 250 patients met inclusion criteria (Table 1). Ninety-five patients (38%) had subperiosteal or intraosseous abscesses, 88 had concomitant septic arthritis (35.2%), 103 had myositis (41.2%), and 57 had pyomyositis (22.8%) based on MRI. Eleven children had an underlying hemoglobinopathy, 3 had a history of prematurity, and 2 had a history of malignancy in remission.

### Microbiology

Overall, a specific etiologic agent was identified in 76% of cases. The most common organism isolated was *Staphylococcus aureus* (62.8%) followed by GAS (6.8%), *Salmonella* spp. (2.7%), and *S pneumoniae* (0.8%, Fig 1). Among *S aureus*, 51 of 157 (32.5%) were MRSA; 9.8% and 19.8% of MRSA and MSSA isolates, respectively, were resistant to clindamycin. No cases of *K kingae* osteomyelitis were noted. Cases caused by MRSA were more often associated with subperiosteal abscesses, larger abscesses, a longer duration of fever and hospital stay, and higher admission C-reactive protein (CRP) than AHO due to other etiologies (Supplemental Table 5). Among the patients with *Salmonella* AHO, 3 of 7 cases had an underlying hemoglobinopathy. There was no difference in the microbiologic etiologies by anatomic site. There was no difference in age between patients who had culture-positive and culture-negative AHO.

Of the 157 *S aureus* isolates, 113 (72%) were available for pulsed-field gel electrophoresis. The most common pulsotype was USA300, accounting for 58 (51.3%). All 3 pneumococcal isolates were available for serotyping. One isolate each belonged to the following serotypes: 3, 15A, and 33F. Six of the 17 (35.3%) GAS isolates were available for *emm* typing; the most common *emm* type was *emm*89 ( $n = 3$ ), followed by *emm*1 ( $n = 2$ ) and *emm*6 ( $n = 1$ ).

**TABLE 1** General Features of Study Group

Characteristic	%
<i>n</i>	250
Age, years	7.7 (3.5–11.5)
Neonate	8 (3.2)
Male gender	154 (61.6)
Fever on presentation	129/172 (75)
Duration of fever after admission, d	3 (1–5)
MRI performed	235 (94)
Subperiosteal/intraosseous abscess	95 (38)
Pyomyositis	57 (22.8)
Contiguous septic arthritis	88 (35.2)
Synovial fluid culture positive	36/65 (55.4)
Synovial fluid WBC count, /mm <sup>3a</sup>	76547 (29 100–130 888)
Length of hospital stay, d	8 (5–12)
Anatomic site <sup>b</sup>	
Tibia/fibula	61 (24.4)
Pelvis	49 (19.6)
Femur	43 (17.2)
Foot/ankle	35 (14)
Humerus	24 (9.6)
Spine	17 (6.8)
Radius/ulna	13 (5.2)
Other <sup>c</sup>	20 (8)
Multiple anatomic sites <sup>d</sup>	26 (10.4)

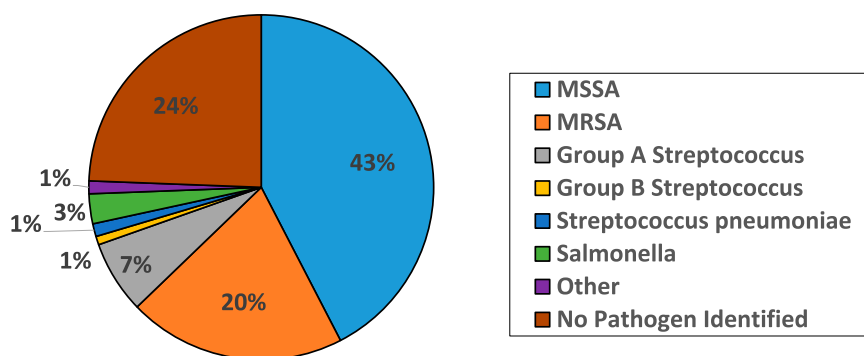
Values are expressed as median (interquartile range) or *n* (%).

<sup>a</sup> Sixteen patients with synovial fluid sent for cell count.

<sup>b</sup> Categories of anatomic sites are not mutually exclusive.

<sup>c</sup> Other sites included mandible (*n* = 3), clavicle (*n* = 2), patella (*n* = 1), rib (*n* = 4), scapula (*n* = 2), and wrist/hand (*n* = 8).

<sup>d</sup> Includes both contiguous and noncontiguous disease.

**FIGURE 1**

Etiologic agents of AHO: TCH, 2011 to 2014. Pathogens grouped as other include 1 case each of AHO due to *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *Streptococcus intermedius*, and *Bartonella henselae*.

### Utilization and Yield of Blood, OR, and IR Cultures

Blood cultures were obtained in the vast majority of patients on admission (231 of 250, 92.4%). Blood cultures were positive for a pathogen in 107 of 231 cases (46.3%), and the median time to positivity was 16.3 hours (interquartile range 12.5 to 19.5 hours). Four patients had blood

cultures that grew contaminant organisms (1.7%).

Cultures were obtained in the OR by the orthopedics service in 150 patients; 123 grew pathogens (82%). Four patients had positive Gram-stain and negative cultures (2.7%); 2 cultures grew contaminant organisms (1.3%). Among patients with positive OR cultures, 62 had organisms identified only through

OR culture (50.4%). Thirty-seven patients had histopathology sent from the bone specimen, of which 30 samples had tissue findings consistent with osteomyelitis (81.1%). In 9 of 37 cases, bone cultures were negative and histology specimens were consistent with AHO (24.3%); 3 of 37 cultures were positive and histology was not consistent with AHO (8.7%).

Sixty-six patients underwent procedures by IR to obtain material for culture (26.4%). Thirty-nine patients had core bone alone obtained for culture (59.1%), 18 underwent aspiration of purulent collections (27.2%), and 9 had core bone collected as well as purulent material aspirated (13.6%). In the majority of cases (52 of 66, 78.8%), culture material was taken directly from bone (as a core biopsy or an aspirate of a bone abscess); in 12 and 2 cases, culture material was taken from adjacent soft tissues or adjacent joints, respectively. IR cultures yielded a pathogen in 34 (51.5%) cases, and in 18 of 34 (52.9%) patients, this was the only source of pathogen identification. One additional patient had a positive Gram-stain but negative culture. Two IR cultures yielded contaminant organisms. The culture yield of core biopsy alone (15 of 39, 38.5%) and that of core + aspirate culture (4 of 9, 44.4%) were lower than aspirate culture alone (15 of 18, 83.3%, *P* = .006). The culture yield of specimens obtained directly from bone was lower (23 of 52, 44.2%) than that taken from adjacent soft tissues or septic joints (12 of 14, 85.7%, *P* = .007). Among patients who had IR cultures obtained, those with positive cultures were more likely to have CRP >3 mg/dL (29/34, 78.4%) than those with negative IR cultures (15/32, 46.8%, *P* = .001). Histopathology was performed on bone obtained from 36 of 66 patients who underwent an IR procedure; in 20 of the 36, histopathology

**TABLE 2** Comparison of Patients With Blood Culture Alone, IR Cultures, and OR Cultures

Characteristic	Blood Culture Alone	IR Culture	OR Culture <sup>a</sup>	P
n	35	59	143	
Age, y	7.2 (3.4–10.6)	7.8 (3.6–12)	7.3 (2.9–11.2)	.9
Fever on presentation	18 (51.4)	38/56 (67.8)	66/137 (48.1)	.04
Duration of fever after admission, d	2 (1–3)	2 (1–3)	4 (2–6)	.006
Positive blood culture	26 (74.2)	14/53 (26.3)	64/136 (47.1)	<.001
Subperiosteal/intraosseous abscess	6 (17.1)	8 (13.6)	77 (53.8)	<.001
Pyomyositis	4 (11.5)	11 (18.6)	38 (26.6)	.1
Contiguous septic arthritis	4 (11.5)	10 (16.9)	70 (48.9)	<.001
<i>S aureus</i> as causative pathogen	22 (62.9)	26 (44.1)	106 (74.1)	<.001
MRSA	1 (4.5)	3 (11.5)	46 (43.4)	<.001
No pathogen identified	7 (20)	26 (44.1)	4 (2.8)	<.001
Anatomic site				
Pelvis	6 (17.1)	23 (38.9)	14 (9.8)	<.001
Spine	3 (8.6)	7 (11.8)	1 (0.6)	.001
Femur	37 (20)	3 (5.1)	33 (23.1)	.005
Tibia/fibula	7 (20)	7 (11.9)	37 (25.9)	.08
Foot/ankle	5 (14.2)	9 (15.3)	19 (13.3)	.9
Humerus	1 (2.9)	2 (3.4)	20 (14)	.02
Radius/ulna	1 (2.9)	1 (1.7)	6 (4.2)	.8
Other	5 (14.3) <sup>b</sup>	6 (10.2) <sup>c</sup>	8 (5.6) <sup>d</sup>	.2
Multiple	3 (8.6)	10 (16.9)	11 (7.7)	.1
Length of hospital stay, d	8 (5–11)	6 (4–8)	9 (6–13)	.001

Values are expressed as median (interquartile range) or n (%).

<sup>a</sup> Excludes 7 patients who had both IR and OR cultures obtained.

<sup>b</sup> Hand/wrist (n = 3), rib (n = 2), clavicle (n = 1).

<sup>c</sup> Rib (n = 2), mandible (n = 2), patella (n = 1), clavicle (n = 1).

<sup>d</sup> Hand/wrist (n = 4), scapula (n = 2), mandible (n = 1), sternum (n = 1).

was consistent with osteomyelitis (55.6%). One additional patient had histology that consisted of necrotizing granulomas, and polymerase chain reaction from the tissue was positive for *Bartonella henselae*. Among the patients with histology available, 10 of 36 (27.8%) had histology consistent with AHO and negative culture; 3

patients had positive cultures and negative histology (8.3%). Overall, IR cultures and tissue sampling provided microbiologic diagnosis or confirmed the diagnosis of AHO in 45 of 66 cases (68.2%). Among patients who underwent IR-guided procedures, the following modalities were used for imaging: CT guidance (n = 14), ultrasound guidance (n =

14), fluoroscopy guidance (n = 17), and a combination of ultrasound and fluoroscopy (n = 21). No adverse events were directly attributable to IR cultures in this study.

Comparisons were made between children who had OR cultures, those who had IR cultures, and those who had blood cultures alone (Table 2). Patients who underwent OR cultures were more likely to have concomitant septic arthritis, bone abscesses, or infection confirmed to be caused by *S aureus*. Patients who underwent IR procedures were more likely to have disease of the pelvis or spine as well as a shorter length of hospital stay. There were no discordant pathogens between patients who had both positive blood cultures and positive IR/OR culture. When comparisons are made across anatomic site, it is apparent that although IR procedures are used more often in patients with infection of the pelvis and central skeleton, the yield of IR and OR cultures did not vary by anatomic site (Table 3).

### Impact of Culture Results on Antibiotic Choice

When patients who had deep cultures obtained via both IR and surgical services are considered together, a pathogen was identified in 80 patients with negative blood culture (OR culture n = 62, IR culture n = 18)

**TABLE 3** Comparisons of Clinical Features and Culture Yield by Anatomic Site

	Long Bone	Pelvis	Central Skeleton	Other Small Bone	P
n	130	45	22	41	
Age, y	7.1 (2.3–10.5)	10.1 (5.3–13.4)	8.9 (3.5–13.7)	6.9 (3.8–10)	.03
Subperiosteal abscess	71 (54.6)	11 (24.4)	2 (9.2)	8 (19.5)	<.001
Septic arthritis	53 (40.8)	14 (31.1)	4 (18.2)	12 (29.3)	.15
Length of stay, d	8.5 (6–13)	7 (5–10)	8 (6–14)	5 (4–8)	.001
Causative organism					
<i>S aureus</i>	87 (66.9)	30 (66.6)	11 (50)	19 (46.3)	.06
MRSA	33 (25.4)	6 (13.3)	2 (9.1)	5 (12.2)	.09
No organism identified	24 (18.5)	12 (26.7)	7 (31.8)	9 (21.9)	.3
Blood culture positive	64/129 (49.6)	21/41 (51.2)	9/21 (42.8)	10/32 (31.3)	.2
IR culture performed	18 (13.8)	25 (55.6)	13 (59.1)	6 (14.6)	<.001
IR culture positive	8/18 (44.4)	15/25 (60)	7/13 (53.8)	2/6 (33.3)	.5
OR culture performed	100 (76.9)	16 (35.6)	4 (18.2)	19 (46.3)	<.001
OR culture positive	82/100 (82)	14/16 (87.5)	3/4 (75)	14/19 (73.7)	.6

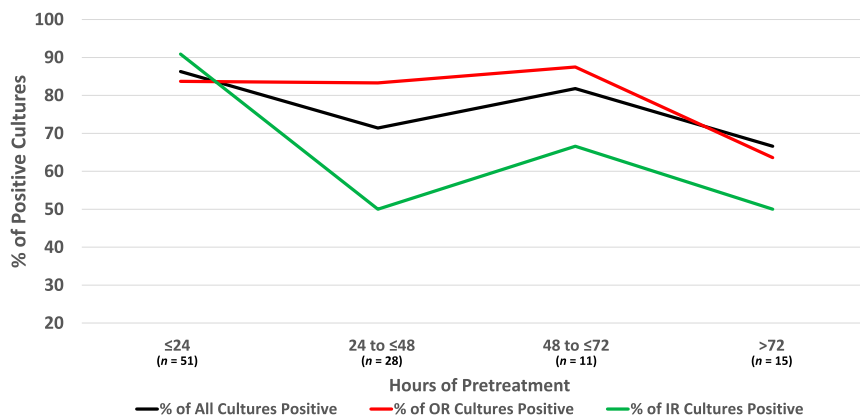
Values are expressed as median (interquartile range) or n (%).

and thus the deep culture was the only means of identifying a specific pathogen. In 68 of these cases, the OR/IR culture prompted a change in antibiotic therapy (85%); in 13 of these cases (19.1%), the empirical therapy was ineffective against the pathogen isolated.

Overall, the most commonly used initial antimicrobial agents were vancomycin (138 of 241, 57.3%) and clindamycin (96 of 241, 39.8%). Nafcillin was used with or without the 2 above agents in 48 of 241 (19.9%) patients. Among patients initiated on vancomycin, 11.6% remained on vancomycin for final therapy, with 29.7% being changed to clindamycin, 26.1% to a first-generation cephalosporin, and 22.5% to nafcillin. Among those initiated on clindamycin, 48.9% remained on clindamycin; 26% were changed to a first-generation cephalosporin.

### Impact of Antibiotic Pretreatment on OR- or IR-Guided Culture Yield

Complete information on preceding antimicrobial treatment was available for 205 patients with IR or OR culture performed. There was no statistically significant difference in rates of culture positivity among those who were pretreated and those who were not (68 of 91, 74.8% vs 84 of 114, 73.7%,  $P = .9$ ). When patients with bone abscesses were excluded from this analysis, there remained similar rates of culture positivity between pretreated (33 of 49, 67.3%) and nonpretreated (44 of 70, 62.8%) patients. Among patients who were pretreated, those with positive cultures had a shorter median duration of pretreatment than those with negative cultures, although this did not achieve statistical significance (28.9 vs 40.4 hours,  $P = .1$ ). Culture yield was 86.3% in patients treated  $\leq 24$  hours compared with 66.6% in those treated  $>72$  hours ( $P$  for trend .1). When patients with IR culture and antibiotic pretreatment were



**FIGURE 2**

Impact of duration of antibiotic pretreatment on culture yield. Lines represent the percentage of cultures positive for a pathogen.

considered separately, culture yield decreased with a longer duration of intravenous antibiotics ( $P = .04$ ) (Fig 2). Similar results were seen in both the overall and subgroup analyses when patients with Gram-negative pathogens were excluded.

### DISCUSSION

Osteomyelitis is one of the most common serious infections in the pediatric population, with the potential for substantial morbidity including the development of chronic infection, venous thrombosis, growth arrest, and pathologic fracture.<sup>23,24</sup> National evidence-based guidelines are needed to provide a framework for diagnosis and treatment of osteoarticular infections in children, as have been instituted at some single centers.<sup>25</sup> Appropriate antimicrobial therapy is essential for good clinical outcome and minimization of long-term complications. Although blood cultures yield a pathogen in approximately half of patients,<sup>5</sup> the need for obtaining additional invasive specimens for culture is uncertain in many cases.

The incidence of invasive community-acquired MRSA infections among children in the United States increased from 2005 to 2010.<sup>26</sup> In a study using diagnostic

coding data, the estimated incidence of MRSA osteoarticular infections was 2.38 per 1000 admissions in 2012.<sup>2</sup> Previous studies at our own institution from 2001 to 2004 had observed that  $>60\%$  of *S aureus* osteomyelitis was secondary to MRSA<sup>3</sup>; other centers have also noted a predominance of MRSA among osteoarticular infections.<sup>25</sup> By contrast, in the current study, MRSA only accounted for 31.7% of staphylococcal AHO (20% of all-cause AHO). This is consistent with recent work illustrating a declining incidence of both community-acquired and hospital-acquired MRSA among adults.<sup>27,28</sup> The reasons for this shift in microbiology are unclear and warrant further examination to inform empirical antibiotic choice in the future. This transition in etiology is significant, as MSSA had higher rates of clindamycin resistance than MRSA (19.8% vs 9.8%), emphasizing the importance of obtaining culture data. The predominant *S aureus* pulsed-field gel electrophoresis type was USA300, consistent with previous studies of *S aureus* musculoskeletal infection.<sup>29</sup> Among GAS strains available for *emm* typing, *emm89* and *emm1* predominated, consistent with previous studies of invasive GAS disease.<sup>22</sup> Although only 3 pneumococcal isolates were found in this study, 2 of the 3 belonged to serotypes not included in the

13-valent pneumococcal conjugate vaccine. Given that molecular methods for detection were not routinely used at our institution, it is possible that some of the culture-negative cases were secondary to *K kingae*, which is difficult to cultivate in traditional culture. As *K kingae* is typically a pathogen of toddler-age children, it is notable, however, that there was no difference in median age between patients with culture-positive versus culture-negative infections. Furthermore, the prevalence of *K kingae* seems to vary geographically, perhaps accounting in part for our findings.<sup>6,30-33</sup> Continued surveillance of the microbiology of AHO is needed to inform empirical therapy in the future.

IR-guided procedures have been shown to be helpful in the microbiologic diagnosis of osteomyelitis in adults. The yield of microbiologic specimens obtained by CT-guided biopsy has been as high as 90% in a series of adults with infectious discitis.<sup>34</sup> In adults in whom there is a high suspicion of vertebral osteomyelitis, imaging-guided percutaneous needle biopsy yielded a pathogen in 30.4% of cases but decreased to 5% in cases when malignancy was the initial working diagnosis in 1 study.<sup>11</sup> Imaging-guided aspiration/biopsy is being recognized as the standard of care in the diagnosis of vertebral osteomyelitis in adults and is currently endorsed by national guidelines.<sup>35</sup>

Previous series in children have largely focused on the overall diagnostic yield of CT-guided musculoskeletal biopsy, including cases in which malignancy is highly suspect.<sup>36-38</sup> In 30% to 46% of patients in such series, imaging-guided biopsy revealed the diagnosis of osteomyelitis. In the series by Ballah et al,<sup>37</sup> among the children diagnosed with osteomyelitis through CT-guided biopsy, only 25% had positive cultures. Hoffer

et al<sup>39</sup> reported 3 patients with classic clinical features of chronic vertebral osteomyelitis who underwent CT-guided biopsy with culture, and in all 3 cases a pathogen was identified. The current study is the largest to evaluate the potential yield of IR-guided invasive cultures in the microbiologic diagnosis of osteomyelitis in children. The overall yield of IR cultures was 51.5%, and in 52.9% of these patients, IR was the only means of identifying a pathogen. A strength of our study is that typical contaminant organisms (such as *Corynebacterium* spp.) were not regarded as true pathogens, unlike in some previous studies.<sup>11,34</sup> This exclusion allows for a more accurate picture of the diagnostic utility of IR and surgical procedures in AHO. IR cultures were most often used in patients with disease of the pelvis, suggesting that these procedures may be particularly useful in patients with infection at sites that are difficult to access surgically. Further work is needed, however, to define the patients for whom IR cultures would have the highest yield.

In 80 of 250 patients (32%) in this study, IR/OR cultures served as the only means of identifying a pathogen. IR/OR cultures alone led to a change in antibiotic prescribing in >80% of these patients and thus made a significant impact on medical management. Beyond the potential impact that IR/OR culture result could have for the individual patient, these cultures may also play a role in antibiotic stewardship by allowing confident deescalation from broad-spectrum antibiotics.

A continuing controversy in the management of osteomyelitis is the need to withhold antibiotics while waiting to obtain bone culture. A study of vertebral osteomyelitis in adults found that antibiotic pretreatment did not increase the risk of negative cultures.<sup>10</sup> Recent guidelines from the Infectious Diseases Society of America,

however, recommend withholding antimicrobial agents in adult patients with suspected vertebral osteomyelitis who are neurologically and hemodynamically stable until bone cultures can be obtained.<sup>35</sup> In our study, receipt of any intravenous antibiotic before OR or IR culture was not associated with more negative cultures; there was, however, a trend toward a longer duration of pretreatment in those children who had negative cultures. This is consistent with another recent pediatric study which revealed a longer duration of pretreatment in children with negative bone biopsy cultures (79 hours vs 40 hours).<sup>5</sup> When all patients were considered, culture yield began to diminish after 72 hours of intravenous antibiotics but may be shorter in the patients who had IR cultures. This may reflect the fact that patients with IR cultures less often had abscesses and were perhaps more likely to sterilize bone with a shorter duration of antibiotics.

There are notable limitations to our findings. First, this is a retrospective single-center study, and as such, the results may not be generalizable to all sites. Moreover, the patients undergoing IR culture were a heterogeneous group in terms of techniques used, and this may have impacted our findings. The study is underpowered to detect adverse events related to anesthesia or IR/OR culture. In addition, the limited number of pediatric orthopedists and interventional radiologists restricts the implementation of surgical/IR guided culture in AHO in all centers. Furthermore, the small number of neonates included in the study suggests that our findings may not be generalizable to young children. Finally, our study does not address the absolute need to obtain deep cultures in patients with minor disease or who are clinically improving on empirical therapy. As long-term follow-up was not performed, we cannot address

the risk of long-term sequelae in children who do or do not have IR/OR cultures obtained. It is clear from the data, however, that deep culture results frequently alter antibiotic management and play a significant role in therapy.

## CONCLUSIONS

We have examined the contemporary microbiology and management of AHO at a major children's hospital. IR-guided culture procedures can be performed safely and effectively in

select patients with AHO, particularly those with disease of the pelvis. Invasive cultures obtained by either IR or surgical services are the only means of identifying a pathogen in 32% of cases, and this information leads to a change in antibiotic choice in >80%. Antibiotic pretreatment appears unlikely to significantly impact bone culture yield in the first 72 hours of therapy. Large multicenter studies are needed to validate these findings and better justify their implementation.

## ABBREVIATIONS

AHO: acute hematogenous osteomyelitis  
CRP: C-reactive protein  
CT: computed tomography  
GAS: group A streptococcal  
IR: interventional radiology  
MRSA: methicillin-resistant *S aureus*  
MSSA: methicillin-susceptible *S aureus*  
OR: operating room  
TCH: Texas Children's Hospital

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