Updates in Osteomyelitis Management

Russell McCulloh, MD
Assistant Professor, Pediatrics and Internal Medicine
Divisions of Hospital Medicine and Infectious Diseases
Children's Mercy Hospital

UMKC School of Medicine

Children's Mercy KANSAS CITY

Disclosure

- I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity.
- I do not intend to discuss an unapproved/investigative use of a commercial product/device in this presentation.

UMKC School of Medicine

Children's Mercy KANSAS CITY

Disclosures

- No financial Conflicts of Interest to Disclose
- Research Support:
  - NIH1UG1HD090849 for pediatric clinical trials research
  - Gerber Foundation
  - Eva and Kenneth Smith Foundation
  - Kansas Health Foundation
  - Kansas City Area Life Sciences Institute
  - Courtney Turner Foundation

Objectives

This quick hit session will provide participants with updates on how to manage osteomyelitis in a hospital setting.

1. Review clinical findings suggestive of AHOM
2. Identify the most common pathogens and empiric antibiotic therapy options in pediatric acute hematogenous osteomyelitis (AHOM).
3. Updates regarding controversies surrounding the management of pediatric AHOM.
4. Updates on the existing evidence for managing AHOM.

Recent Publications (Not Reviews)

- New articles for acute hematogenous osteomyelitis since 2015 (PubMed): 17
- Of these, 2 are multi-site!

Background

- AHOM accounts for 1% of pediatric hospitalizations
- Limited evidence results in varied treatment approaches
- Oftentimes a topic of controversy

Why osteomyelitis?

- Uncertainty surrounds:
  - empiric antibiotic selection
  - use of prolonged intravenous versus oral antibiotics
  - optimizing patient follow-up
  - how to manage cases without positive cultures
  - differentiating complicated from uncomplicated AHOM

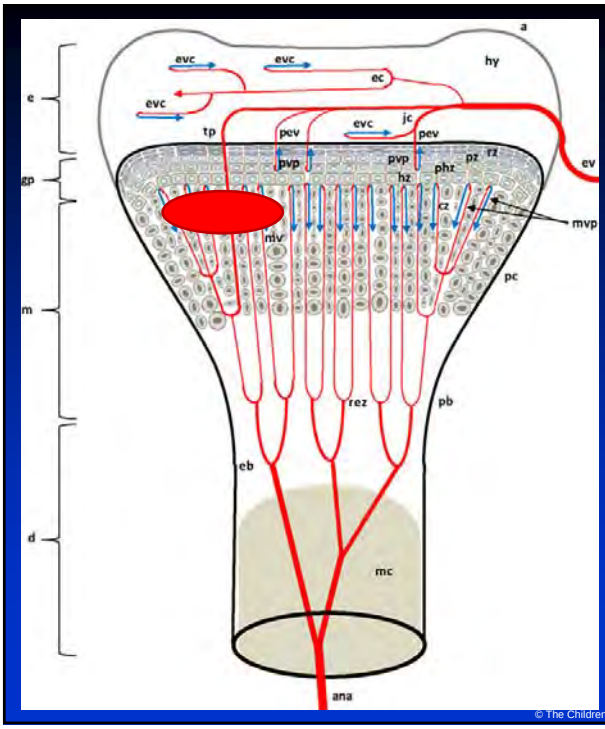
Outline

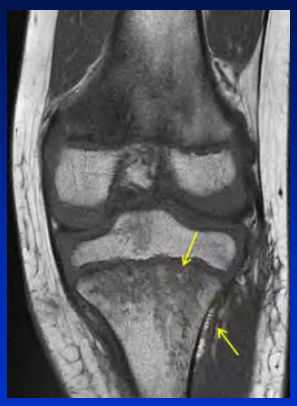
- Recognizing the patient suspected with AHOM
- Common pathogens and diagnosis
- Empiric therapy/antibiotic selection
- Oral vs. IV therapy
- Common exclusion criteria/complicated osteo
- PICC lines
- Discharge planning

AHOM Clinical Dx Pearls

- General features:
  - Fever (40-80%); focal pain (NOT infants 56-95%); decreased mobility (50-84%)
  - 2015 review of MSK infections (single site): 68% of pts with septic arthritis had concomitant osteomyelitis
- Preceding symptoms over several days-1week
- Culture-positive more likely to have: trauma; skin findings; higher WBC; shorter sx duration

Monsalve, et. al. .AJR Am J Roentgenol. 2015 Jun;204(6):1289-95.





Supporting Evidence:

Thévenin-Lemoine, et. al., 2016

MRI of acute osteomyelitis in long bones of children: Pathophysiology study.

20 children dx'd with AHO with MRI of long bones

Red-Flag Symptoms

- Fever and gait disturbance
- Focal limb, back, or hip pain not explained by trauma
- Severe, focal back pain (particularly older children)
- Infants with irritability with movement of limb, or persistent history of inconsolability

Guides for evaluation

- WBC is not sensitive (elevated in only 35%)
- ESR/CRP almost always elevated (92% ESR; 98% CRP)
- Plain films insensitive in AHOM
  - 14 days for radiographic changes
- Preferred imaging: MRI
- 2 sets of blood cultures should be obtained in all children prior to initiating antibiotics

Effects of Antibiotic Pre-Treatment

- Zhorne, et. al. 2015
  - 1-year retrospective review of children 2mo-18yo with AHO
  - 67 children who underwent bone biopsy
    - 40 pre-treated with antibiotics
    - No difference in yield for bone bx if antibiotics given (OR 1.37, 95% CI: 0.49-3.86
      - Longer duration of abx prior to bx associated with lower yield from bx (p=0.04)
    - Bx only microbiological dx in 54% of non-bacteremic children

CASE 1

Case 1

- Previously healthy fully immunized 13 year old male presenting with knee pain
  - Knee pain for 2 days
  - Fever to 102 F at home
  - Minor trauma during sports, nothing specific
  - Knee pain is constant, but worsens with walking

Case 1

- On exam:
  - VS: T 38.1, HR 102, RR 21, BP 117/69
  - Point tenderness over right anterior proximal tibia
  - No palpable knee effusion
  - Mild swelling noted
  - Range of motion of knee normal

Case 1

- Labs:

Seg 63
Band 0
Lymph 22
Mono 13

ESR 20
CRP 11

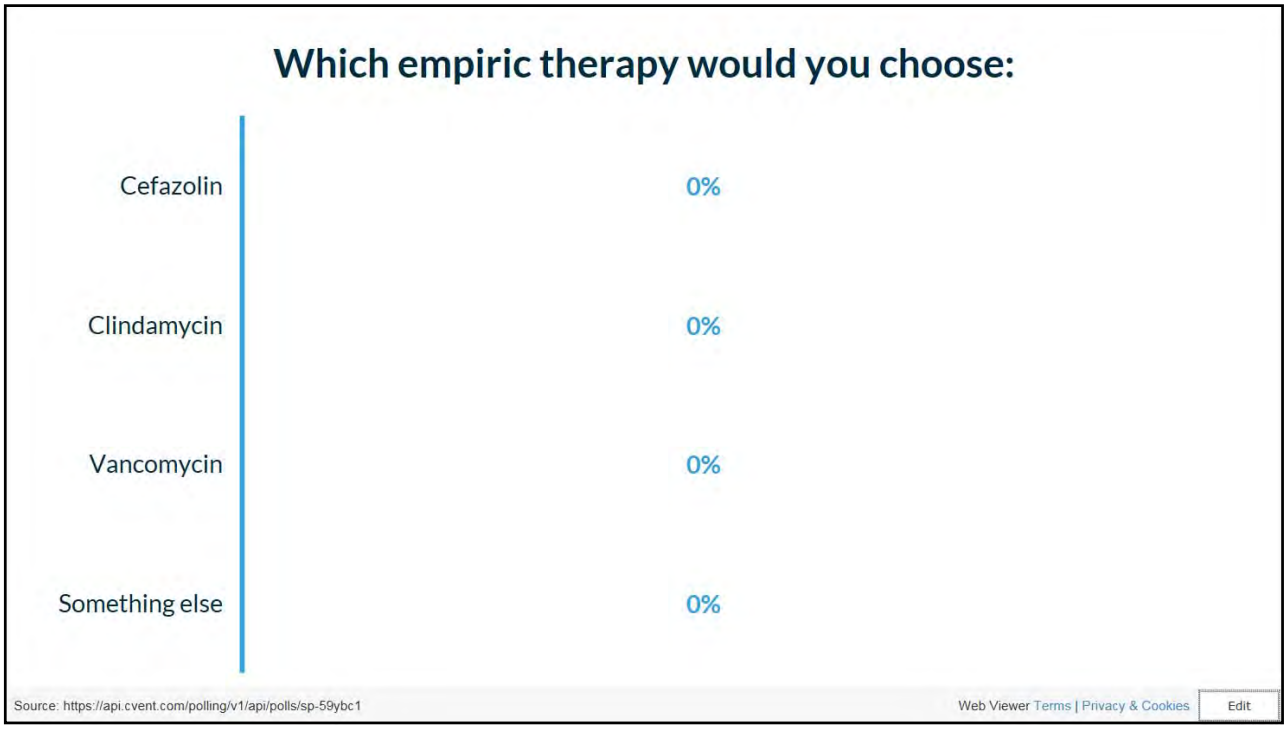
Blood culture pending

Case1

- Imaging:
  - Xray: *"Localized soft tissue swelling adjacent to the metaphysis. Otherwise normal."*
  - MRI result: *"Signal abnormality suggestive of osteomyelitis involving the right tibial tuberosity. There is a very small right knee joint effusion and synovitis which is nonspecific and can be reactive"*

What Would You Do?

- Which empiric therapy would you choose:
  - Cefazolin
  - Clindamycin
  - Vancomycin
  - Something else

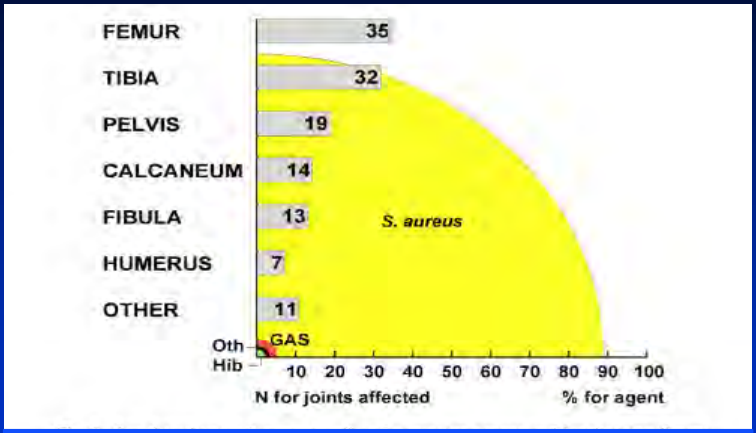


COMMON PATHOGENS

Common pathogens

- *S. aureus* is by far the most common etiology in all age groups
  - MRSA may comprise 50% or more of AHO due *S. aureus*
- The next most common are GAS, *S. pneumoniae*, or *K. kingae*
  - Study in France using RT-PCR to detect *K. kingae*, 45% were positive (most common in ages 6mos – 3yrs)
  - US study found *K. kingae* as causative agent in children with acute bacterial osteo 3% of time and acute bacterial arthritis 19% of time

Prevalence of organisms



Causative agents and localization of 131 cases of acute hematogenous osteomyelitis of children

Paakkonen M, Peltola H. Antibiotic treatment for acute haematogenous osteomyelitis of childhood: moving towards shorter courses and oral administration. Int J Antimicrob Agents 2011;38:273-80.

	OM (n = 298)	SA (n = 232)	OA (n = 78)	SpD (n = 33)	*P*
Microbiologic isolation (%)	98 (33)	104 (45)	48 (61)	2 (8)	<0.001
Total isolations*					
S. aureus (%)	78 (28)	52 (26)	28 (38)	1 (3.8)	0.005
K. kingae (%)	1 (0.7)	29 (15)	5 (7)		<0.001
S. pyogenes (%)	10 (3.5)	7 (3.5)	5 (7)		NS
Positive blood culture (%)	71/245 (29)	48/189 (25)	25/62 (40)	2/26 (8)	NS
S. aureus (%)	57 (80.3)†	24 (50)	18 (72)	1 (3.8)	
K. kingae (%)	1 (1.4)	2 (4.2)	-	-	
S. pyogenes (%)	8 (11.3)	6 (12.5)	3 (3.9)	-	
Positive synovial culture (%)	81/211 (38)	24/45 (53)			0.064
S. aureus (%)	-	42 (52)	12 (50)	-	
K. kingae (%)	-	19 (23.5)	2 (8.3)	-	
S. pyogenes (%)	-	8 (10)	1 (4)	-	
Positive synovial fluid PCR (%)	14/26 (55)	4/9 (44)			
K. kingae (%)	-	11/14 (79)	4/4 (100)	-	

*Other agents: *Streptococcus pneumoniae* (15), *Streptococcus agalactiae* (6), *Enterobacteriaceae* (10), *Haemophilus influenzae* (1), *Sphingomonas* (1).
†Of the total of positive isolates.
NS indicates not significant.

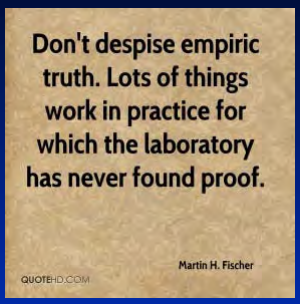
Epidemiology and Management of Acute, Uncomplicated Septic Arthritis and Osteomyelitis Spanish Multicenter Study.
Calvo, Cristina; MD, PhD; Nunez, Esmeralda; MD, PhD; Camacho, Maribel; Clemente, Danila; Fernandez-Cooke, Elisa; MD, PhD; Alcobendas, Rosa; Miqel, Lola; Soler-Palacin, Pere; MD, PhD; Ocon, Miren; Saavedra-Lozano, Jesus; MD, PhD

Pediatric Infectious Disease Journal. 35(12):1287-1292, December 2016.
DOI: 10.1097/INF.0000000000001309

Special Considerations: Epidemiology

- GBS and enteric GNRs in neonates
- Salmonella in children with hemoglobinopathies
- *P. aeruginosa* in children with puncture wounds of the foot
- *H. influenzae* now rare with success of HIB vaccine

- In almost half of children with acute osteomyelitis, a bacterial etiology is never established
  - Bone biopsy can help increase microbiological diagnosis



EMPIRIC THERAPY/ANTIBIOTIC SELECTION

Empiric Antibiotic Selection

- Always include treatment for *S. aureus*
  - Some experts recommend that if the rate of CA-MRSA is >10%, antibiotics directed against MRSA should be administered from the onset of treatment
  - Vancomycin recommended when MRSA clindamycin resistance >15%
  - Clindamycin is also effective
  - When local clindamycin resistance rates exceed 10-15%, clindamycin is not recommended for initial empiric treatment
- Vancomycin and clindamycin are effective against most GAS and *S. pneumoniae* but NOT *K. kingae*
- Penicillins and cephalosporins are effective against *K. kingae*

IDSA MRSA Guidelines – Vancomycin versus Clindamycin

"For children with acute hematogenous MRSA osteomyelitis and septic arthritis, IV vancomycin is recommended. If the patient is stable without ongoing bacteremia or intravascular infection, clindamycin can be used as empirical therapy if the clindamycin resistance rate is low (eg, <10%)."

Take Home Points: Empiric Antibiotic Selection

- Clindamycin is a good choice for empiric coverage of *S. aureus* for AHOM in a stable patient if your local susceptibility patterns allow
- In a patient with bacteremia or abnormal vital signs, consider vancomycin for empiric coverage of *S. aureus**
- In a patient < 3 years of age with septic arthritis, consider addition of a beta lactam for coverage of *K. kingae*

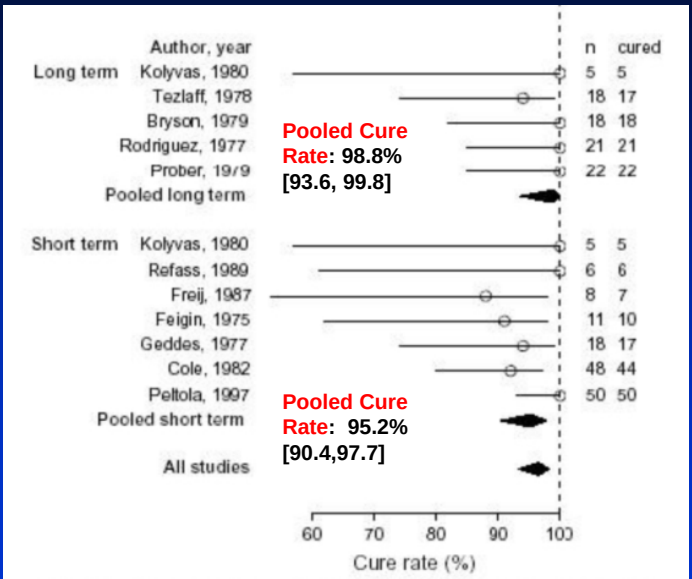
ORAL VS. IV THERAPY

Do oral antibiotics work as well as IV?

- LeSaux, BMC ID, 2002
  - Systematic review of short vs. long course parenteral antibiotic therapy for AHOM
  - Identified 11 eligible prospective studies
    - AHOM defined as:
      - +Staph aureus from bone or periosteum, or
      - clinical signs of osteomyelitis with + blood culture, or
      - clinical signs and compatible radiologic study
    - Exposure: <7 days of IV therapy vs. ≥7 days of IV therapy
    - Outcome: Clinical cure rate at 6 months

Do oral antibiotics work as well as IV?

LeSaux, BMC ID, 2002



No significant difference in the cure rate between the two groups
(z-test p value 0.838)

Do oral antibiotics work as well as IV?

- Zaou
  - Re
  - Ex
    - >
    - A
      c
  - Ex
    - I
  - Ou
    - I

elitis

- Comorbid conditions whose presence suggests complicated or difficult- to-treat osteomyelitis
  - Congenital and acquired immunodeficiencies
  - Sickle cell disease
  - Trauma
  - Osteomyelitis associated with immobilization or pressure ulcers (eg, spina bifida, quadriplegia, paraplegia, mechanical ventilation, and postoperative infections)
  - Osteomyelitis of the head, face, and orbits
- Conditions that predispose to inadequate absorption of oral medications
- Prior admissions that might increase the risk of subsequent complicated osteomyelitis
  - Cellulitis
  - Sacroiliitis
  - Arthropathy
  - Myositis
  - Congenital or acquired diseases of bone
  - Placement of orthopedic devices or prosthesis.
  - Pyogenic arthritis
    - Synovitis
    - Chronic sinusitis
  - Fasciitis
    - Postoperative wounds

Do oral antibiotics work as well as IV?

TABLE 1 Demographic and Clinical Characteristics

Characteristics	Intravenous Therapy (*N* = 1021)	Oral Therapy (*N* = 948)
Age, *n* (%)		
0–1 y	86 (8)	77 (8)
1–5 y	343 (34)	322 (34)
>5 y	592 (58)	549 (58)
Length of hospital stay, median (interquartile range), d	5 (3–6)	4 (3–6)
Gender, *n* (%)		
Male	629 (62)	583 (62)
Race, *n* (%)		
White	725 (71)	676 (71)
Black	186 (18)	150 (16)
Other	66 (6)	80 (8)
Missing	44 (4)	42 (4)
Site, *n* (%)		
Shoulder	23 (2)	25 (3)
Upper arm	48 (5)	39 (4)
Forearm	31 (3)	34 (4)
Hand	38 (4)	38 (4)
Pelvic/thigh	315 (31)	287 (30)
Lower leg	247 (24)	245 (26)
Ankle/foot	182 (18)	178 (19)
Multiple sites	25 (2)	25 (3)
Unspecified	112 (11)	77 (8)

TABLE 1

Characteristics	Intravenous Therapy (*N* = 1021)	Oral Therapy (*N* = 948)
Organism, *n* (%)[a]		
Group A streptococcus	35 (3)	34 (4)
Streptococci, other	11 (1)	15 (2)
S aureus	351 (34)	291 (31)
Staphylococcus, other	51 (5)	33 (3)
Methicillin-resistant *S aureus*	83 (8)	62 (7)
Escherichia coli	2 (<1)	2 (<1)
Pneumococcus	12 (1)	9 (1)
Other Gram-negative organisms	9 (1)	5 (1)
>1 organism	89 (9)	73 (8)
Surgical procedure	377 (37)	314 (33)
Parental antibiotics received, *n* (%)		
Cefazolin	603 (59)	508 (54)
Oxacillin/nafcillin	345 (34)	243 (26)
Vancomycin	188 (18)	83 (9)
Clindamycin	309 (30)	321 (34)
Trimethoprim-sulfamethoxazole	5 (<1)	6 (1)
Linezolid	2 (<1)	2 (<1)
Other[b]	355 (35)	216 (23)
Case mix index, median (interquartile range)[c]	1.67 (1.67–1.67)	1.67 (1.67–1.67)

Do oral antibiotics work as well as IV?

- Zaoutis, *Pediatrics*, 2009
  - Results: Readmissions
    - 5% in prolonged IV therapy
    - 4% in early transition group
    - 3.4% catheter associated complications

What would you do?

- When would you consider transition to oral antimicrobial therapy?
  - When CRP normalized and patient is afebrile
  - Following 3-4 days of IV therapy
  - At time of discharge
  - When seen in follow up by PCP
  - When ID tells me to
  - My answer is still never

When would you consider transition to oral antimicrobial therapy?

When CRP normalized and patient is afebrile	0%
Following 3-4 days of IV therapy	0%
At time of discharge	0%
When seen in follow up by PCP	0%
When ID tells me to	0%
My answer is still never	0%

Source: https://api.cvent.com/polling/v1/api/polls/sps5j9en

Web Viewer Terms | Privacy & Cookies Edit

Timing of transition to oral

- LeSaux, *BMC ID*, 2002
  - Using cut off of 7 days, found no difference between long and short-term IV antibiotics courses
- Unkila-Kallio, *Pediatrics*, 1994
  - Prospective study of 44 patients with culture positive AHOM studying trends of CRP/ESR/WBC
  - CRP peaked at day 2, normalized by 1 week
  - ESR peaked at day 3-5,normalized by 3 weeks

Timing of transition to oral

- Arnold, *Pediatrics*, 2012
  - Single center, retrospective review
    - 194 patients with culture positive AHOM and ABA
    - Transitioned to oral therapy with CRP declining to <2-3 and evidence of clinical response
  - Outcome: Complication rates
    - prolonged therapy, re-hospitalization, relapse, long term complications (joint, AVN, limb-length)

Timing of transition to oral

- Arnold, *Pediatrics*, 2012
  - Findings:
    - 21% (40) had complications
      - 87.5% (35) had "prolonged therapy"; associated with a higher CRP at time of diagnosis and lower CRP at end of IV course
      - 1 had microbiologic failure after oral stepdown therapy

Time	Uncomplicated	Complicated
Admit	8.7 (±7.4)	10.5 (±7.2)
Max	11.7 (±8.8)	15.7 (±8.1)
Transition to PO	2.1 (± 1.9)	1.5 (±1.4)

Bacteremia and oral antibiotics

- Pääkönen, et. al. 2015
  - Review of 265 patients with AHO and/or septic arthritis, 157 with bacteremia
    - 130 bacteremic with *S. aureus* (most MSSA)
  - All patients had IV antibiotics 2-4 days then transitioned to PO
  - No differences in length of therapy, treatment failure for bacteremic vs non-bacteremic children

All Oral Therapy?

- Roul-Levy, et. al. 2016
- Retrospective analysis of 45 children 1-11 yo with AHO without complications
  - CRP >50mg/L; fever>38.5C; septic shock; periosteal abscess at admission; multifocal infection; immunodepression; Sickle Cell Disease
- 26 pts IV→PO; 19 with amox-clav only

	IV Group (n = 26)	Oral Group (n = 19)	Total (N = 45)	*P*
Duration of treatment, d	42.5 (34.5–51.5)	43 (28.5–46)	43 (33–48)	0.1409
General complications, n (%)	2 (8)	0	2 (4)	0.5010
Radiographic complications, n (%)	1 (4)	1 (5)	2 (4)	1
Treatment failure, n (%)	3 (12)	1 (5)	5 (9)	0.6270

Take Home Points: Transition to Oral Antibiotics

- Oral antibiotics are efficacious in treating **acute, uncomplicated** osteomyelitis
- Early transition to oral antibiotics demonstrates success similar to that of long term IV therapy
- Early transition to oral therapy, even in cases of bacteremia, may be equally efficacious in uncomplicated AHO

CASE 2

Case 2

- 7yo female admitted with fever and L groin pain
  - Groin pain for 2 days
  - Fever to 102 F at home
  - Minor trauma during sports, nothing specific
  - Pain is constant, and she cries with attempts at walking
  - PMH: 2 prior episodes of MRSA skin infections
    (both required I&D followed by TMP- SMX)

Case 2

- MRI of hip: *"signal abnormality of the left femoral neck consistent with osteomyelitis"*
- On admission started IV vancomycin

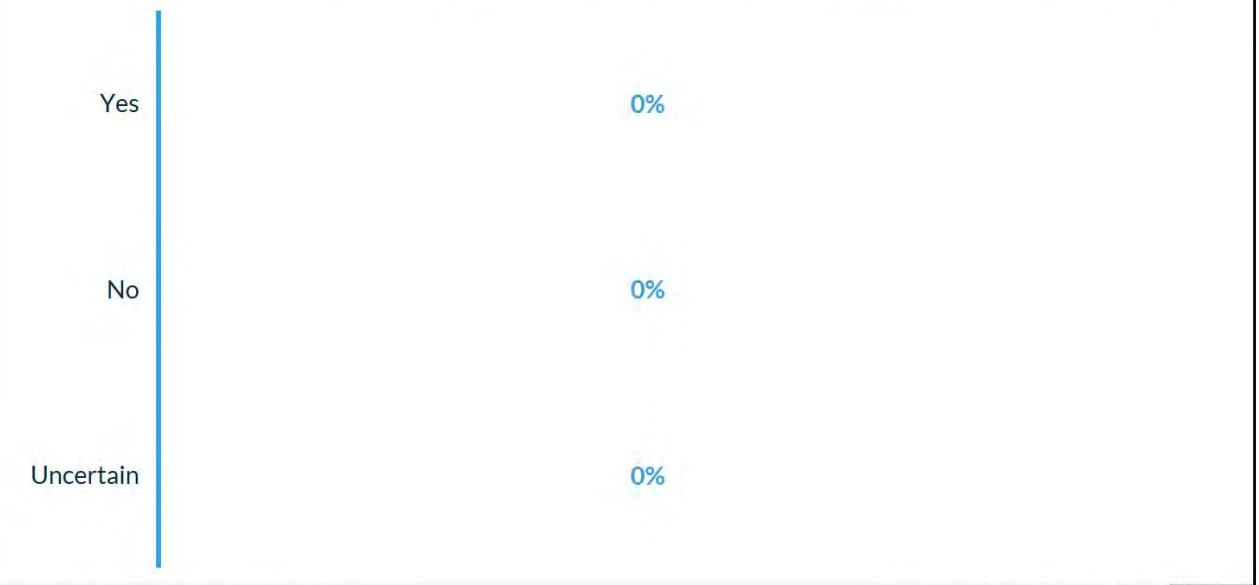
Case 2

- Patient remains febrile and irritable
- Initial blood cultures positive for MRSA
- Repeat blood cultures positive for 4 days
- Repeat MRI: *"Left proximal femoral neck osteomyelitis; left hip synovitis, effusion; medial compartment myositis and fasciitis"*

What would you do?

- Would you transition this patient to oral therapy prior to discharge?
  - Yes
  - No
  - Uncertain
- Why or why not?

Would you transition this patient to oral therapy prior to discharge?



COMMON EXCLUSION CRITERIA/COMPLICATED AHOM

Common Exclusion Criteria

- Patients <1 month and >18 years
- Sub acute or chronic osteomyelitis (sxs >14 days)
- Comorbid conditions (e.g., immunodeficiency, sickle cell disease, trauma, etc…)
- Osteomyelitis of head/face/orbits
- Previous admission for conditions increasing risk for complicated osteomyelitis (e.g., cellulitis, pyogenic arthritis, trauma, fractures, placement of orthopedic devices, etc…)
- Pretreatment with antibiotics
- Culture negative (no positive culture from either blood, bone or joint fluid)

Data Free Zone

- Complicated osteo
- Surgical interventions
- Hardware
- Not a long bone
- Culture negative
- Neonates

Severity Score for AHO

- Athey, et. al. 2016
- Prospective observational cohort of AHO at single center, 2012-2014 (148 children)
- Clinical, radiologic, and lab data used to calculate severity of illness (SOI) score (from within first 4 days)
- Validated by correlating with LOS and APR-DRG and ROM scores

Estimating Severity of Illness

CRP initial†:	CRP 48 hours:
<10 = 0	<5 = 0
10-15 = 1	5-10 = 1
>15 = 2	>10 = 2
CRP 96 hours:	Band Count‡:
<5 = 0	<1.5 = 0
5-10 = 1	≥1.5 = 1
>10 = 2	
Febrile Days on Antibiotics:	ICU Admission:
<2 = 0	No = 0
≥2 = 1	Yes = 1
Disseminated Disease:	
No = 0	
Yes = 1	

FIGURE 3. Modified severity of illness score with peripheral band count; †mg/dL; ‡thousand cells/mL. CRP indicates C-reactive protein; ICU, intensive care unit.

TABLE 5. Severity of Illness Score Correlation With Surrogate Markers of Disease Severity

	Corr	*P*
LOS	0.6960	< 0.0001
TLOS	0.6287	< 0.0001
MSDRG Case Mix Index	0.6031	< 0.0001
APR-DRG-CMI	0.7188	< 0.0001
SOI	0.6744	< 0.0001
ROM	0.5967	< 0.0001

Pearson correlation between severity of illness scores and markers of disease severity.

APR-DRG indicates All Patient Refined Diagnosis Related Groups; LOS, length of stay; MSDRG, Medicare Severity Diagnosis Related Groups; ROM, risk of mortality; SOI, severity of illness; TLOS, total length of stay (LOS + readmissions).

Estimating Illness Severity

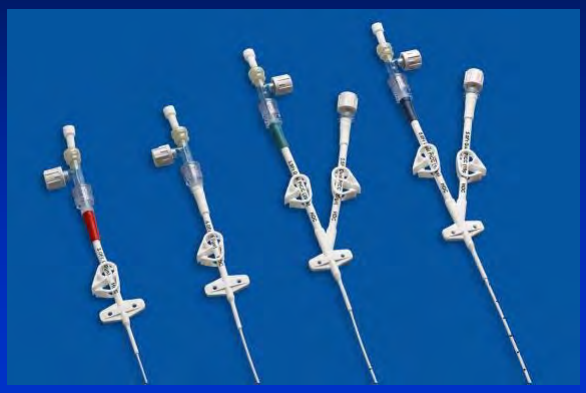
- Chiappini, et. al., 2017
- Retrospective review of 121 cases AHO 2010-2015
- Risk factors for complications:
  - Fever
  - Upper limb involvement
  - WBC >12,000
  - CRP >10 mg/L
  - *S. aureus* infection

Case 2 Update

- Patient required 1 trip to the OR for debridement
- Subsequently fever resolved, blood cultures cleared, and CRP trended down
- Clinically, patient significantly improved prior to discharge

Take Home Points: Complicated Osteo

- It's a headache when patients don't read the book….
- Involvement of ID specialists to help guide decisions
  - Prolonged IV therapy may be necessary in some cases…
  - But they may be able to transition to oral later in course
- Need for predicting severe cases
  - Role for multi-site studies?



PICC LINES

PICC Cautionary Tales

- Catheter-associated complications requiring medical attention occur in ~30% (17-41%) of children with PICC lines at home
  - Rate of complications: 13.9-19.3/1000 PICC days
- Risk factors for complications:
  - osteomyelitis*
  - increased number of daily doses*
  - double-lumen PICCs*
  - increased duration of therapy
  - younger age*
  - lower median household income*

*not consistently found in all studies

PICC Therapy in Osteo

- Ruebner et al, *Pediatrics,* 2006
  - 75 patients who received >2 weeks of IV therapy
  - 41% had ≥ 1 CVC-associated complication
    - 17 (23%) had malfunction or displacement
    - 8 (11%) had catheter associated blood stream infection
    - 8 (11%) had fever with negative blood cultures
    - 4 (5%) had local skin infection

Take Home Points: PICC Lines

- Complications are not uncommon.
  - Mechanical complications are most common type of PICC complication.
- It is important to assess the risks and benefits when placing a PICC.

Discharge Planning and Follow Up

- Responsible physician identified prior to discharge
- Close monitoring required
  - Recommends up to a year
- Follow clinical exam and CRP trends
  - If CRP levels rise, concern for complication
- Debate about basing continuation of therapy until normalization of ESR
- X-rays sufficient for detecting sequelae in most circumstances

Take Home Points: Discharge Planning

- Close follow up after discharge is key regardless of antibiotic plan
  - Assure that PCP is comfortable with plan
  - Consider follow up with ID
    - Especially in kids sent home on IV therapy

Summary

- Know thy enemy. (local susceptibility patterns)
- Evidence shows us transition to oral is safe and effective in uncomplicated cases.
- There is no consensus on management of complicated osteomyelitis or culture negative cases.
- PICC lines are interventions and not without risk.
- Reliable follow up is key.

References

- Peltola H, Paakkonen M, Kallio P, Kallio MJ. Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood: prospective, randomized trial on 131 culture-positive cases. *The Pediatric infectious disease journal.* Dec 2010;29(12):1123-1128.
- Peltola H, Unkila-Kallio L, Kallio MJ. Simplified treatment of acute staphylococcal osteomyelitis of childhood. The Finnish Study Group. *Pediatrics.* Jun 1997;99(6):846-850.
- Zaoutis T, Localio AR, Leckerman K, Saddlemire S, Bertoch D, Keren R. Prolonged intravenous therapy versus early transition to oral antimicrobial therapy for acute osteomyelitis in children. *Pediatrics.* Feb 2009;123(2):636-642.
- Le Saux N, Howard A, Barrowman NJ, Gaboury I, Sampson M, Moher D. Shorter courses of parenteral antibiotic therapy do not appear to influence response rates for children with acute hematogenous osteomyelitis: a systematic review. *BMC infectious diseases.* Aug 14 2002;2:16.
- Arnold JC, Cannavino CR, Ross MK, et al. Acute bacterial osteoarticular infections: eight-year analysis of C-reactive protein for oral step-down therapy. *Pediatrics.* Oct 2012;130(4):e821-828.
- Kaplan SL. Osteomyelitis in children. *Infectious disease clinics of North America.* Dec 2005;19(4):787-797, vii.
- Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: executive summary. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Feb 1 2011;52(3):285-292.
- Ruebner R, Keren R, Coffin S, Chu J, Horn D, Zaoutis TE. Complications of central venous catheters used for the treatment of acute hematogenous osteomyelitis. *Pediatrics.* Apr 2006;117(4):1210-1215.
- Chometon S, Benito Y, Chaker M, et al. Specific real-time polymerase chain reaction places Kingella kingae as the most common cause of osteoarticular infections in young children. *Pediatric Infectious Disease Journal.* May 2007;26(5):377-381.
- Barrier A, Williams DJ, Connelly M, Creech CB. Frequency of Peripherally Inserted Central Catheter Complications in Children. *Pediatric Infectious Disease Journal.* May 2012;31(5):519-521.
- Saphyakhajon P, Joshi AY, Huskins WC, Henry NK, Boyce TG. Empiric antibiotic therapy for acute osteoarticular infections with suspected methicillin-resistant Staphylococcus aureus or Kingella. *The Pediatric infectious disease journal.* Aug 2008;27(8):765-767.
- Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* Feb 1 2011;52(3):e18-55.
- Unkila-Kallio L, Kallio MJ, Eskola J, Peltola H. Serum C-reactive protein, erythrocyte sedimentation rate, and white blood cell count in acute hematogenous osteomyelitis of children. *Pediatrics.* Jan 1994;93(1):59-62.
- Le J, San Agustin M, Hernandez EA, Tran TT, Adler-Shohet FC. Complications associated with outpatient parenteral antibiotic therapy in children. *Clinical pediatrics.* Nov 2010;49(11):1038-1043.
- Paakkonen M, Peltola H. Antibiotic treatment for acute haematogenous osteomyelitis of childhood: moving towards shorter courses and oral administration. Int J Antimicrob Agents 2011;38:273-80.

More References

- Peltola H, Paakkonen M, Kallio P, Kallio MJ. Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood: prospective, randomized trial on 131 culture-positive cases. *The Pediatric infectious disease journal.* Dec 2010;29(12):1123-1128.
- Peltola H, Unkila-Kallio L, Kallio MJ. Simplified treatment of acute staphylococcal osteomyelitis of childhood. The Finnish Study Group. *Pediatrics.* Jun 1997;99(6):846-850.
- Chiappini E, Camposampiero C, Lazzeri S, Indolfi G, De Martino M, Galli L. Epidemiology and Management of Acute Haematogenous Osteomyelitis in a Tertiary Paediatric Center. Int J Environ Res Public Health. 2017 May 4;14(5). pii: E477.
- Athey AG1, Mignemi ME, Gheen WT, Lindsay EA, Jo CH, Copley LA. Validation and Modification of a Severity of Illness Score for Children With Acute Hematogenous Osteomyelitis. J Pediatr Orthop. 2016 Oct 12.
- Monsalve J, Kan JH, Schallert EK, Bisset GS, Zhang W, Rosenfeld SB. Septic arthritis in children: frequency of coexisting unsuspected osteomyelitis and implications on imaging work-up and management. AJR Am J Roentgenol. 2015 Jun;204(6):1289-95. doi: 10.2214/AJR.14.12891.
- Zhorne DJ, Altobelli ME, Cruz AT. Impact of antibiotic pretreatment on bone biopsy yield for children with acute hematogenous osteomyelitis. Hosp Pediatr. 2015 Jun;5(6):337-41. doi: 10.1542/hpeds.2014-0114.
- Ratnayake K, Davis AJ, Brown L, Young TP. Pediatric acute osteomyelitis in the postvaccine, methicillin-resistant Staphylococcus aureus era. Am J Emerg Med. 2015 Oct;33(10):1420-4. doi: 10.1016/j.ajem.2015.07.011. Epub 2015 Jul 17.
- Calvo C, Núñez E, Camacho M, Clemente D, Fernández-Cooke E, Alcobendas R, Mayol L, Soler-Palacin P, Oscoz M, Saavedra-Lozano J; Collaborative Group. Epidemiology and Management of Acute, Uncomplicated Septic Arthritis and Osteomyelitis: Spanish Multicenter Study. Pediatr Infect Dis J. 2016 Dec;35(12):1288-1293.
- Thévenin-Lemoine C1, Vial J2, Labbé JL3, Lepage B4, Ilharreborde B5, Accadbled F6; SOFOP. MRI of acute osteomyelitis in long bones of children: Pathophysiology study. Orthop Traumatol Surg Res. 2016 Nov;102(7):831-837. doi: 10.1016/j.otsr.2016.06.014. Epub 2016 Sep 15.