Methicillin-Resistant *Staphylococcus aureus* (MRSA) in PWH: Increased Prevalence, Increased Mortality

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Farley has no relevant financial relationships with ineligible companies to disclose. (Updated 10/10/22)

Slide 2

Learning Objectives

At the end of this presentation, participants will be able to:

- Delineate the current and evolving epidemiology of MRSA globally
- Identify the clinical importance of MRSA colonization as a risk factor for disease
- Compare and contrast community-acquired and hospital-acquired MRSA infection
- Discuss current treatment approaches for hospital and community-acquired MRSA

Slide 3

The case of ME

- ME presents to your practice for specialty care for HIV.
  - He notes, "I think my foot is really bad. I didn't get to see my PCP as his office was full and so I can to see you since I had an appointment anyway."
  - JF: When did you last have the foot evaluated?
  - Patient: In the ER about 2-3 weeks ago.

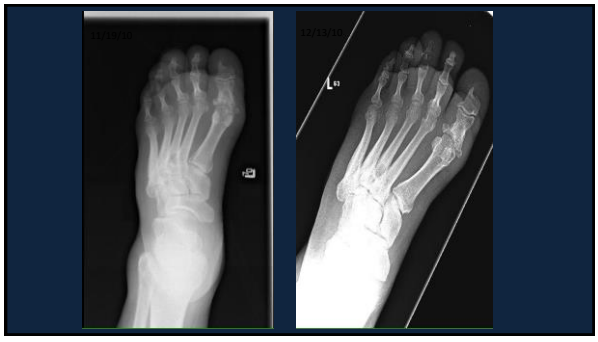
ME

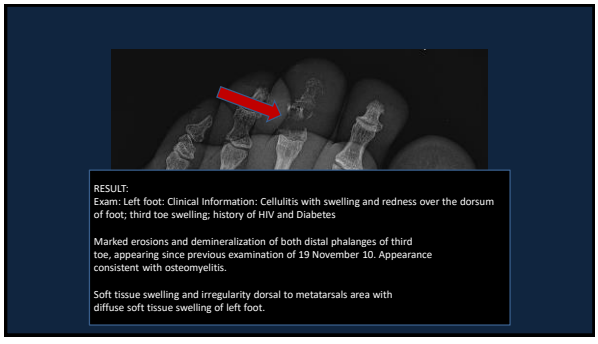
- 51 y/o CM
  - Works as a maintenance man
- PMH:
  - HIV, well controlled with CD4 count 578; Viral Load < 50 copies
  - DM (HgB A1C ranging between 6 and 7)
  - Hyperlipidemia (well controlled, LDL 74)
  - GERD
  - Renal Insufficiency (Creatinine 1.2; GFR > 60 ml/min)
  - HTN, stage I
  - Obesity, BMI of 30

ME – Physical Exam

- HPI:
  - Pain and swelling to foot began in November 2010
  - Presented to ER on 11/28/10
    - Started on IV clindamycin in ER
    - PO clindamycin and ciprofloxacin for home
      - Completed as directed
    - X-Ray revealed no osteomyelitis

v-up





DX: Osteomyelitis of 3rd toe

- PLAN:
- Admission Orders:
  - CBC with differential
  - ESR and CRP
  - CMP
  - PT/PTT
  - BC x 2
  - Place peripheral IV

Admission Surveillance and Clinical Cultures

Nares


NASAL SWAB SPECIMEN: 44-OE3040
COLLECTION DATE/TIME: 11/14/2012 14:00

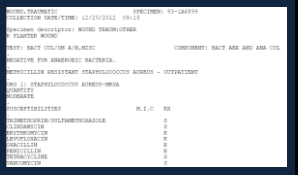
TEST: MRSA SURVEIL CULTURE COMPONENT: BACTERIAL SURV CULT

Positive

ORG 1:
Methicillin resistant staphylococcus aureus
Result finalized: 11/17/2012 13:59:49

Test performed by:
Johns Hopkins Medical Labs
600 N. Wolfe
601 North Wolfe Street
Baltimore, MD. 21287

Wound


WOUND,TRAUMATIC SPECIMEN: 93-1A4995
COLLECTION DATE/TIME: 12/20/2012 09:15

Specimen descriptor: WOUND TRAUM/OTHER
R PLANTER WOUND

TEST: BACT CUL/SM A/B,MISC COMPONENT: BACT AER AND ANA CUL

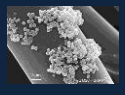
NEGATIVE FOR ANAEROBIC BACTERIA.

METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS - OUTPATIENT

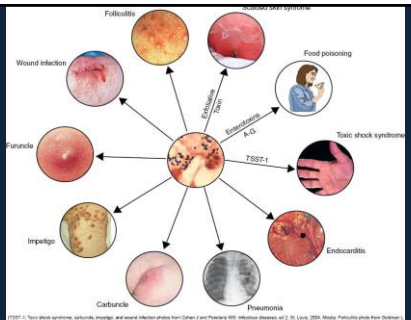
ORG 1: STAPHYLOCOCCUS AUREUS-MRSA
QUANTITY
MODERATE

SUSCEPTIBILITIES M.I.C RX
TRIMETHOPRIM/SULFAMETHOXAZOLE S
CLINDAMYCIN S
ERYTHROMYCIN R
LEVOFLOXACIN R
OXACILLIN R
PENICILLIN R
TETRACYCLINE S
VANCOMYCIN S

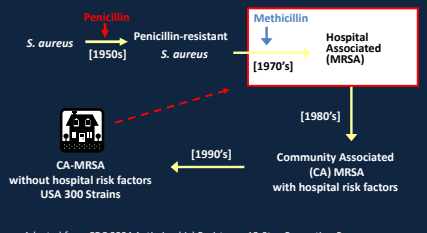
Staphylococcus aureus (*S. aureus*)



- Gram positive cocci in clusters
- Capable of colonizing or infecting the host
- Methicillin susceptible (MSSA) and Methicillin resistant *S. aureus* (MRSA)
- Transmission occurs by direct skin to skin contact (most common) or contact with a contaminated fomite or environmental surface



Evolution of Drug Resistance in *S. aureus*



Adapted from CDC 2004 Antimicrobial Resistance 12-Step Prevention Program

Prevalence of MRSA in Community Populations

- A secondary data analysis of the 2001-2002 NHANES Survey (n=9,622) determined:
  - prevalence of colonization with *S. aureus* is 31.6%
  - 0.84% of the general population harbor MRSA
    - Graham, et al. (2006). Annals of Internal Medicine, 144(5): 318-326.
- Among clinical isolates in Baltimore 2002-2003 (n=1720), 8% were CA-MRSA infections; 12% Minnesota; 20% Atlanta
  - Fridkin, et al. (2005). NEJM, 352(14): 1436-1444.

Studies of MRSA Colonization Prevalence by Body Site

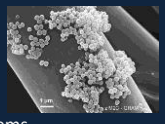
	Farley 2013*	Lee 2013	Popovich 2013
Sample (n)	498 Baltimore	294 Singapore	374 Chicago
Target pop	HIV positive patient in outpatient clinic	Newly admitted HIV positive	Newly admitted HIV positive
Nares (N)	9.2%	--	12%
Throat (T)	9.0%	11.1%	8%
Axillae (A)	1.8%	--	7%
Groin (G)	6.6%	--	11%
Perineum (P)	6.6%	9.3%	12%
Vaginal (V)	6.4%	--	--
Rectal (R)	6.8%	--	--
Pooled (N,A,P)	--	29.6%	--
Colonization Prevalence	15.6%	18.4%	20% (HIV)

Community Associated MRSA

- Began with individuals without known healthcare risk factors (mid 1990's) (MMWR, 1999)
- Currently identified in a variety of populations:
  - Prison/Jail inmates
  - Athletic teams (professional, college and high school)
  - Sexual transmission
  - Day care centers
  - Persons who use drugs
  - Recent hospitalizations
  - Persons with HIV/AIDS

5 C's of CA-MRSA

- Crowding
- Contact (skin to skin)
- Cleanliness (lack of)
- Contaminated surfaces or items
- Compromised skin



#6. Corrections; #7. Compromised Immunity

Adapted from CDC presentation entitled, "Community-Associated Methicillin-Resistant *Staphylococcus aureus*: Epidemiology and Public Health Management" .

Risk Factors for MRSA SSTI among Persons with HIV/AIDS

- Low CD4 cell count (1-5)
- High viral load (1-4)
- Recent hospital admission (2)
- Beta-lactam antibiotics (3,4)
  - (i.e. PCN, Cephalosporins, Carbapenems)
- Routine hands-on contact with customers at work (2)
- Lack of co-trimoxazole (Bactrim) prophylaxis (2,3)

1. Diep, et al (2008). Annals of Internal Medicine: 148: 249 – 257.
2. Lee, et al. (2005). Clinical Infectious Diseases; 40: 1529 – 1534.
3. Crum-Cianflone, et al. (2007). International Journal of STD & HIV; 18: 521 – 526.
4. Skiest, et al. (2006). HIV Medicine; 7: 361 – 368.
5. Lee, et al. (2013). AIDS Research and Human Retrovirus; [e-pub ahead of print]

Risk Factors for MRSA SSTI among Persons with HIV/AIDS (2)

- Known MRSA within the last 12 months (1-4)
- Methamphetamine use (2)
- Syphilis (3)
- A sex partner with an abscess (1-4)
- A buttock, genital or perineum abscess (1,3)
- Male to male sex (1-3)
- Previous Incarceration (4)
- Older age (5)

1. Diep, et al (2008). Annals of Internal Medicine; 148: 249 – 257.
2. Lee, et al. (2005). Clinical Infectious Diseases; 40: 1529 – 1534.
3. Crum-Cianflone, et al. (2007). International Journal of STD & HIV; 18: 521 – 526.
4. Skiest, et al. (2006). HIV Medicine; 7: 361 – 368.
5. Lee, et al. (2013). AIDS Research and Human Retrovirus; [e-pub ahead of print]

Meta Analysis: Risk for colonization and infection of MRSA among PWH

- 31 studies
  - 1410 MRSA events among 17,427 PWH
- Confirmed:
  - Previous hospitalization
  - Prior ABX treatment
  - CD4 count
  - CDC classification stage C
  - Skin lesions
  - IVD
  - MRSA Colonization

Risk factors for methicillin-resistant Staphylococcus aureus colonization and infection in patients with human immunodeficiency virus infection: A systematic review and meta-analysis

1. Hu, et al. (2021). International Journal of Medical Research; 50(1), 1-22.

INF-γ Deficiency

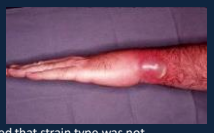
- *INF-γ CD4 count response muted in PWH*
  - *Lower IL-12 and IL-15 levels identified, which are key drivers of INF response*
  - *No defects in CD8 response noted*
- *Authors conclude that INF-γ CD4 count response is essential for prevention of initial and recurrent MRSA STTI*

MRSA Infections in HIV-Infected People Are Associated with Decreased MRSA-Specific Th1 Immunity

Utay, et al. (2016). PLOS Pathogens; 12(4).

Clinical Outcomes of CA-MRSA

- Recurrent Skin and Soft Tissue Infections (SSTI)
  - (most common)
- Otitis externa
- Bacteremia/Sepsis
- Penumonia
- Necrotizing fasciitis

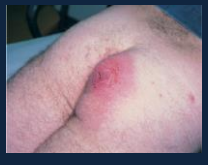


- A recent analysis at UCLA identified that strain type was not associated with treatment failure nor 30-day mortality in hospitalized patients with a hospital acquired infection
  - Ellis, et al (2012). Epidemiology and Infection. [e-pub ahead of print]

Treatment of CA-MRSA SSTI

Considerations:

- Very painful
- Disfiguring
- Associated with MRSA transmission to others
- Recurrence is common



Steps in Outpatient Treatment of CA-MRSA SSTI

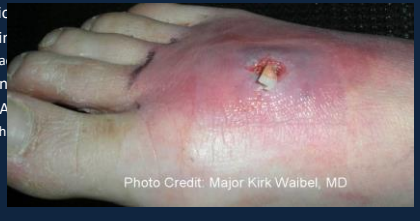
- Perform thorough HPI, systemic ROS and risk factor evaluation
- Consider differential diagnosis including cellulitis, abscess (boil), impetigo, and rule out potentially life threatening necrotizing fasciitis, if symptoms warrant
- For fluctuant abcesses, obtain aspirated pus/exudate from wound prior to performing incision and drainage (I/D) OR obtain a culture of the wound margins after I/D
  - send for gram stain and anaerobic/aerobic culture and sensitivity results

Steps in Outpatient Treatment of CA-MRSA SSTI

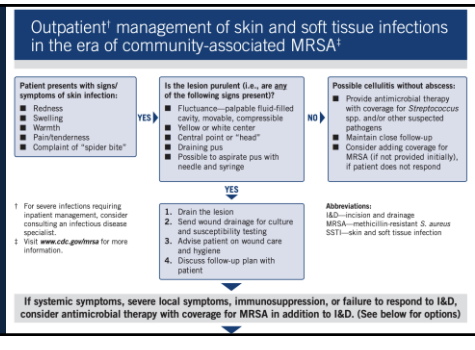
- Consider individual patient risk profile as well as community and hospital epidemiology of SSTI to determine appropriate empiric antimicrobial therapy
- Provide PO antimicrobial on an outpatient basis for 7 to 10 days
- Schedule patient for follow-up evaluation in 24-48 hours with appropriate provider
- Review antimicrobial sensitivities and follow-up with changes to therapy as appropriate

Outpatient Treatment Plan

- Incisio
- Packin
  - Exa
- Woun
- Oral A
  - Wh



http://apps.med.buffalo.edu/procedures/abscess.asp?p=1



Options for empiric outpatient antimicrobial treatment of SSTIs when MRSA is a consideration*

Drug name	Considerations	Precautions**
Clindamycin	■ FDA-approved to treat serious infections due to *S. aureus* ■ D-zone test should be performed to identify inducible clindamycin resistance in erythromycin-resistant isolates	■ *Clostridium difficile*-associated disease, while uncommon, may occur more frequently in association with clindamycin compared to other agents.
Tetracyclines ■ Doxycycline ■ Minocycline	■ Doxycycline is FDA-approved to treat *S. aureus* skin infections.	■ Not recommended during pregnancy. ■ Not recommended for children under the age of 8. ■ Activity against group A streptococcus, a common cause of cellulitis, unknown.
Trimethoprim-Sulfamethoxazole	■ Not FDA-approved to treat any staphylococcal infection	■ May not provide coverage for group A streptococcus, a common cause of cellulitis. ■ Not recommended for women in the third trimester of pregnancy. ■ Not recommended for infants less than 2 months.
Rifampin	■ Use only in combination with other agents.	■ Drug-drug interactions are common.
Linezolid	■ Consultation with an infectious disease specialist is suggested. ■ FDA-approved to treat complicated skin infections, including those caused by MRSA.	■ Has been associated with myelosuppression, neuropathy and lactic acidosis during prolonged therapy.

■ MRSA is resistant to all currently available beta-lactam agents (penicillins and cephalosporins)
■ Fluoroquinolones (e.g., ciprofloxacin, levofloxacin) and macrolides (erythromycin, clarithromycin, azithromycine) are not optimal for treatment of MRSA SSTIs because resistance is common or may develop rapidly.

* Data from controlled clinical trials are needed to establish the comparative efficacy of these agents in treating MRSA SSTIs. Patients with signs and symptoms of severe illness should be treated as inpatients.
** Consult product labeling for a complete list of potential adverse effects associated with each agent.

Role of decolonization

Regimens intended to eliminate MRSA colonization should not be used in patients with active infections. Decolonization regimens may have a role in preventing recurrent infections, but more data are needed to establish their efficacy and to identify optimal regimens for use in community settings. After treating active infections and reinforcing hygiene and appropriate wound care, consider consultation with an infectious disease specialist regarding use of decolonization when there are recurrent infections in an individual patient or members of a household.

Published September 2007

CDC AMA IDSA

Patient Education Plan

- Wise use of antibiotics
- It is transmissible to your sexual contacts, household members, pets, and immunocompromised family members
- It is transmissible to your healthcare providers
  - Johnston, et al (2006). Infection Control/Hospital Epidemiology; 27(10): 1133 – 1136.
- Recurrence is common
- CDC Web Resource:
  - http://www.cdc.gov/mrsa/mrsa_initiative/skin_infection/index.html
  - http://www.cdc.gov/mrsa/mrsa_initiative/skin_infection/mrsa_provider_info.html

Recurrent SSTI

- To decolonize or not
  - First you must identify colonization
    - Anterior Nasal Swab provides highest yield
    - If positive, discuss possibility of recolonization even after treatment
- Mupiricin Ointment 1%
  - Apply intranasally BID x 5 days
- Chlorhexadine gluconate Showers
  - Use daily during Mupiricin therapy
- Do we need to treat family members?
  - Assess family spread and occurrence of boils within the family unit
- Multi-dimensional approach = best outcome
  - Simor AE, et al. (2007). Randomized controlled trial of chlorhexidine gluconate for washing, intranasal mupirocin, and rifampin and doxycycline versus no treatment for the eradication of methicillin-resistant Staphylococcus aureus colonization. CID 15;44(2):178-85.

Management of Recurrent Infections

- To decolonize or not…
  - Mixed data
  - Unanswered questions:
    - Individual vs household
    - Duration
    - Cost Benefit
    - Efficacy in high burden community
    - Sites of colonization

- Trimethoprim-sulfa DS po BID x 7 days in conjunction with I/D
- Chlorhexidine showers daily for duration of antimicrobials
- Mupiricin intranasal ointment BID – if nasally colonized
  - No data on decolonization of other sites

Q and A Session