

MRSA

Barber M. J Clin Path 1961;14:385

- 18 MSSA strains passed 40-50x on Celbenin (methicillin) ditch plates
- 8 strains grew in high methicillin concentration
 - Retained coagulase and hemolytic activity, mouse virulence testing
 - Remained resistant after repeated passage in the absence of methicillin

MRSA

Barber M. J Clin Path 1961;14:385

- “Clearly Celbenicin-resistant staphylococci are a potential danger...It is unwise to assume that the staphylococcus has met its match.”

Mary Barber, 1961

Healthcare-Associated (HA) MRSA

- 1961 – 1st report in a U.K. hospital
- 1967 – 1st major report in US
 - Boston City Hospital incidence 1.4% among all *S. aureus* isolates
- Late '60's to late '70's – relatively infrequent in the US
- 1980 – present – Increase incidence of MRSA from 5 to >50% in hospitals

HA-MRSA

- Generally resistant to most abx – all beta-lactams, usually macrolides, clindamycin, quinolones, TCNs
- Commonly considered an infection of hospitalized, chronically ill patients

HA-MRSA

Risk Factors

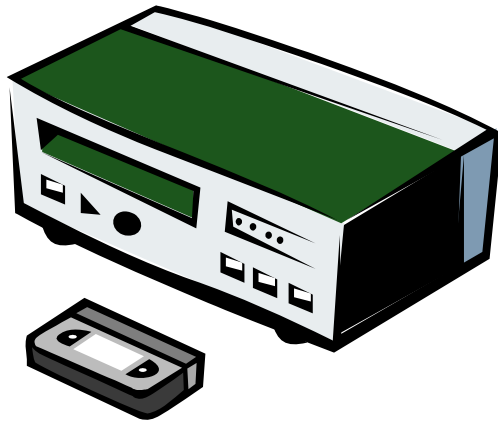
- Prolonged hospitalization, stay at nursing/rehab facilities
- ICU stay
- Prolonged abx therapy
- Surgical procedures
- Close proximity to infected/colonized patient

CA-MRSA

Surveillance Definition

- Infection or colonization in a person with no history of:
 - Surgery
 - Hospitalization/residence in a long-term facility a year before dx
 - Presence of a percutaneous device or indwelling catheter
 - Dialysis within the previous year
 - Hospitalization >48 h before MRSA culture
 - Previous MRSA infection or colonization

MRSA Genetics



Staphylococcal cassette
chromosome

- *MecA* is the gene in all MRSA
- Codes for a different PBP (2a)
- B-lactam cannot bind
- Located on the SCC
- Reservoir for other drug resistance

MRSA Genetics

MRSA

- SCC *MecA* I,II,III
- Hospital isolates
- 34-67 kb in size
- Other abx resistance genes

cMRSA

- SCC *MecA* IV, V
- Community isolates
- 20-27kb in size
- Only *MecA* gene

Genetics of MRSA

- SCC mec A gene complex used for molecular typing of MRSA
 - Type I and V lack other resistance genes
 - Type II and III (large complex) associated w/ multidrug resistance including beta-lactams
 - Type IV (small complex) associated with beta-lactam resistance only

Genetics of MRSA

- Pulsed-gel electrophoresis
- Various “USA” types
 - 100, 200, 500 usually associated with HA-MRSA
 - 300, 400, 1000 associated with CA-MRSA

Virulence Factors and Toxins

- Cell wall components: peptidoglycans, teichoic acid, protein A, clumping factor
- Enzymes: catalase, coagulase, beta-lactamase
- Toxins: hemolysins, superantigens, TSST, exotoxin, enterotoxin, PVL

Panton-Valentine Leukocidin Toxin

- 2 component pore-forming toxin
- Destroys human leukocytes and monocytes
- Induces severe inflammatory lesions, capillary dilation, chemotaxis, tissue necrosis

Panton-Valentine Leukocidin Toxin

- Gene present in 90% of CA-MRSA infections
 - 93% of strains in furunculosis; 55% cellulitis
- Uncommon in HA-MRSA; can occur in MSSA
- Usually associated with necrotizing pneumonia (70% mortality)

Table 1. Production of Panton-Valentine leukocidin by 171 *Staphylococcus aureus* strains associated with various clinical syndromes.

Type of infection	No. of strains tested	No. (%) of PVL-positive strains	<i>P</i> value
Pneumonia			
Hospital-acquired	13	0 (0)	— ^a
Community-acquired	27	23 (85)	<.001
Skin infection			
Superficial folliculitis	10	0 (0)	— ^b
Impetigo	4	0 (0)	NS
Finger pulp (felon)	15	2 (13)	NS
Cutaneous abscess	6	3 (50)	.03
Cellulitis	9	5 (55)	.01
Furunculosis	30	28 (93)	<.001
Other infection			
Infective endocarditis	21	0 (0)	— ^c
Osteomyelitis	13	3 (23)	NS
Urinary tract infection	5	0 (0)	NS
Enterocolitis	5	0 (0)	NS
Mediastinitis	5	0 (0)	NS
Toxic-shock syndrome	9	0 (0)	NS

^a Reference group for statistical analysis for pneumonia.

^b Reference group for statistical analysis for skin infections.

^c Reference group for statistical analysis for infective endocarditis.

CA-MRSA

- 1980's – Reports of infection in pts w/o “traditional” (HA) risk factors (e.g. IVDUs, children)
- 1990's – 4 deaths in kids w/o risk factors (MN, ND, MMWR 1999;48(32):707-710)
 - 2 respiratory, 2 disseminated
 - All initially Rx w/ a cephalosporin
 - Genetically different than HA strains

CA-MRSA

- Outbreaks – US, Canada, Europe, Finland, Saudi Arabia, India, Asia, Australia, New Zealand
- Often in clusters in young, healthy people who have close contact w/ each other
 - Athletic teams
 - Maternity wards
 - Correctional facilities
 - Day care
 - Military recruits
 - IVDU's
 - Native Americans
 - Pacific Islanders
 - Men who have sex with men

CA-MRSA

Rams Football Outbreak

- Kazkova SV et al. NEJM 2005;352:468-75
- Outbreak during the 2003 season
- 9% of players – skin/soft tissue infection
- Risk factors:
 - Lineman/linebacker position
 - Turf abrasion
 - Higher BMI (>30)
 - Abx use (10x > than general population)

CA-MRSA in Sports

- Sharing of towels and other items
- Lack of showers/handwashing
- Abrasions
- Failure to cover wounds
- Lack of disinfection of equipment
- Sharing of clothing
- Contaminated whirlpool
- Contaminated taping gel

MRSA SSTIs in Tattooed

MMWR 2006;55(24):677-8

- 6 separate communities in OH, KY, VT
- 34 primary and 10 secondary cases
- 15-42 y/o; no underlying disease in 33
- Incubation 4-22 days
- 20 large abscesses; cellulitis, pustules
- 4 bacteremic
- 13 unlicensed tattooists

MRSA SSTIs in Tattooed

MMWR 2006;55(24):677-8

- Lapses in infection control
 - Gloves worn in 4/6 clusters but not changed between clients
 - Inadequate hand hygiene
 - Inadequate skin antisepsis
 - Inadequate disinfection of equipment and surfaces
- 3 tattooists with recent incarceration
- Home made equipment: guitar string tattoo needles, ink-jet printer cartridges for dye

Personal Hygiene and MRSA

Turabelidze et al. EID 2006;12(3):422-7

- 2003 outbreak at MO women's prison
- USA 300 strain
- Case control study
- Significant association with low composite hygiene score
- Lower frequency of handwashing (<6x/d)
- Lower frequency of showering (<7/wk)

CA-MRSA ...Beyond Outbreaks

- Meta-analysis: 30-37% of all inpt MRSA (Saldago et al. CID 2003;36:131-9)
- LA – most common cause of CA SSTI in ER (Morgan et al. EID 2005;11:928-30)
- Houston, 2003 – 78% of CA *S. aureus* infection among hospitalized pediatric pts (Ochoa et al. EID 2005;11:966-8)
- Multicenter national study – 11 ERs: 60% of all SSTIs; 98% +PVL, Mec IV gene (Morgan et al. NEJM 2006;355:666-674)

MRSA Diseases in 3 Communities

Fridkin et al. NEJM 2005;352:2362

- Baltimore, Atlanta, Minnesota – total 1647 cases
- CA-MRSA: 8-20% of all MRSA isolates
- 6% invasive, 77% SSTI
- RR increased in blacks (Atlanta) and <2 years of age
- 73% placed on abx w/o *in vitro* activity
- 23% hospitalized for MRSA

CDC National Surveillance *S. aureus* Colonization Study

- 9622 participants
- 32% colonized with MSSA
- 0.84% colonized with MRSA – 2 million people
- Risk factors for colonization
 - Age <65, male, asthma, <high school ed
 - Being black or hispanic was protective

Colonization and Infection

- Could be harbinger of future infection
 - Among soldiers, risk of infection 38% if nares positive for CA-MRSA vs 3% for MSSA (Ellis et al. CID 2004;39:971-9)
 - Risk of infection after colonization with +PVL strains – 25% (Harbath et al. EID 2005;11:962-5)
- May decrease risk of mortality from bacteremia

Nose Picking and Nasal Carriage of *S. aureus*

Wertheim et al. ICHE 2006;27:863-7

- 238 pts at ENT clinic w/o nose complaints and 86 hospital employees
- Questionnaire on nose behavior; screened for *S. aureus*; Pt exam
- Nose pickers more likely than non-pickers to carry *S. aureus* (RR 1.5)
- “Overcoming the habit of nose picking may aid *S. aureus* decolonization strategies.”

Asymptomatic Nasal Carriage of Mupirocin-Resistant
MRSA in a Pet Dog

Manian FA. CID 2003;36:e26-8

- Recurrent MRSA infx in DM pt and wife
- Several unsuccessful decontamination attempts – vanc ointment/chlorhexidine scrubs
- Dalmation only other family member
 - Nares colonization with identical PFGE chromosomal pattern as the pt and wife
 - Slept in bed w/ couple, licking their faces

MRSA in Companion Animals

Baptiste et al. EID 2005;11:1942-4

- MRSA isolate from 3 dogs with infections (joint, pleuropneumonia, wound)
- 1 dog w/ joint infx also + in nares and perineum
- All MRSA isolates + for Type IV Mec A
- Identical MRSA strain isolated from 3/11 (27%) vet staff
- Cats negative for MRSA; horses unrelated MRSA strains

Clinical Manifestations

Skin and Soft Tissue Infections

- Furuncles
- Folliculitis
- Impetigo
- Cellulitis
- Abscess
- Fasciitis/Ecthyma

MRSA vs. Spider Bite

- Think of MRSA when pt or other physician reports skin lesion looks like “spider bite”
- Spider bite usually does not become raised or drain pus
- Most pts don’t recall seeing a spider
- Misinformed physicians reinforce misdiagnosis

Clinical Manifestations

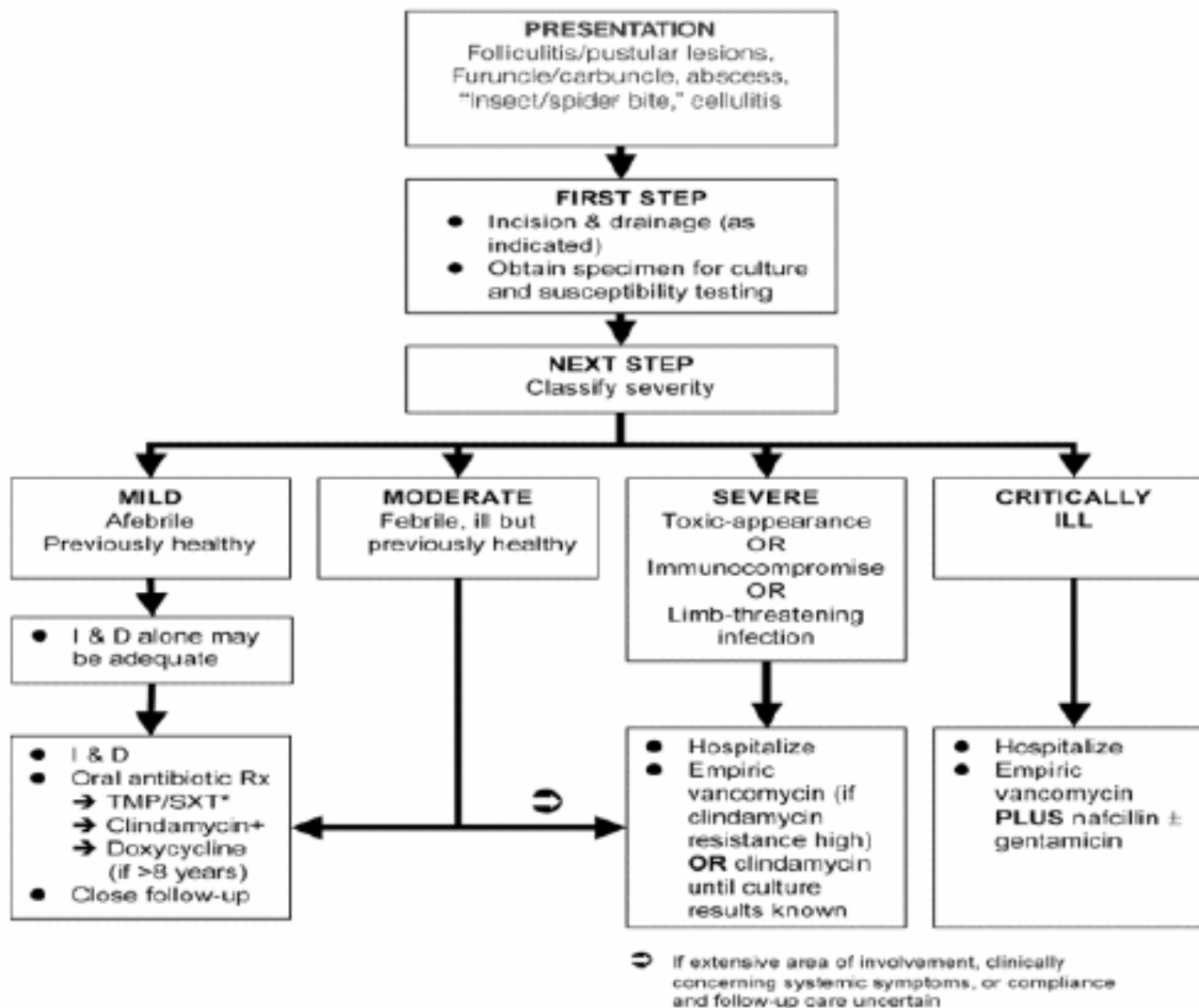
CA-MRSA

- Necrotizing pneumonia
- Severe sepsis
- Waterhouse-Fredrickson
- Septic thrombophlebitis
- Bone/joint infections
- Pyomyositis

Treatment of CA-MRSA Infection SSTI

- Incision and drainage for abscesses
 - May be adequate sole therapy in some cases
- Obtain cultures for sensitivities
- Occasionally needs skin grafting
- Systemic abx for more serious infxns, extensive SSTI, systemic signs of illness, associated co-morbidities

cMRSA Therapy



CA-MRSA

Antibiotic Selection

- Based on *in vitro* susceptibility testing
- Most isolates susceptible to SXT/TMP, doxycycline, clindamycin (D-test if emycin resistant)
- Virtually all isolates susceptible to vancomycin, rifampin
- Linezolid, daptomycin, quinopristin/dalfo
- Not optimal – macrolides, quinolones

cMRSA Therapy - Clindamycin?

- Yes, if pt is a child, mild to moderately ill, to be managed as an inpt or an outpt
- No, if pt is a child, critically ill, to be managed as an inpt
- Probably not if pt is an adult, mild to moderately ill, to be managed as an inpt or an outpt without a “D-test” from the lab
- No, if pt is an adult, critically ill, to be managed as an inpt

CA-MRSA

Decolonization

- No data to support efficacy in preventing disease transmission in the community (CDC)
- “Real world” – Screen pts with:
 - Recurrent infections
 - Multiple household members with MRSA infection
 - Comorbidities
 - Impending major surgery, esp. prosthetic implant

Decolonization Regimens

- Topical Nasal Agents
 - Mupirocin bid-tid for 5-10 days
- Antiseptic body washes
 - Chlorhexidine, others for 5-10 days
- Oral abx
 - TMP/SMX + Rifampin, others for 5-10 days

5 “C”s of CA-MRSA

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

Prevention in the Community

- Hand washing/disinfection
- Gloves when touching potentially infectious wounds ... Wash hands too
- Cover wounds
- Dispose soiled used dressings/bandages in plastic bag to throw into trash
- Shower daily with antibacterial soap, before close contact with others

Prevention in the Community

- Limit physical contact with others if wound drainage cannot be contained
- Avoid sharing personal items (razors, towels, clothing, etc.)
- Towels, clothing, soiled linens laundered in hot water and detergent or in warm water and bleach
 - Dry in hot dryer
- Clean/disinfect surfaces, objects with Lysol or bleach solution (1:10)

Prevention at the Gym

- Avoid punctures, abrasions, scratches
- Wash/disinfect hand
- Don't share towels, razors, bar soap, etc.
- Use long sleeves and long pants
- Use towel or clothing to avoid direct exposure to exercise machines
- Shower after workout
- Wipe surfaces before/after use

CA-MRSA

Hospital Transmission

- Post-partum women, NY
 - Saiman et al. CID 2003;37:1313-9
- NICU, TX
 - Healy et al. CID 2004;39:1460-6
- Orthopedic post-prosthetic joint, GA
 - Kourbatova et al. AJIC 2005;33:385-91

Healthcare Setting Control

- Private room or cohort
- Gloves when entering room
- Gown when entering room
- Limit movement and transport of patient
- Screening cultures of pts in selected settings
- Screening cultures of HCWs in selected settings
- ? vaccine

Conclusion

- Consider MRSA in dx of SSTI, severe infx, pneumonia
- “Spider bite” may be MRSA
- C&S of drainage, blood
- I&D as appropriate for SSTIs
- Empiric abx in severe infections, cellulitis, systemic illness
- Good hygiene
- Strict infection control in health care settings