

MRSA INFECTIONS 2007 plus MISC. ID/DERM ITEMS

David S. Feingold, M.D.
Professor of Dermatology, Tufts University School of
Medicine

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Antibiotic Resistance (1)

- The modern age of medicine began with the discovery of antibiotics
- Initial success led some to envision the end of all infectious diseases

Antibiotic Resistance (2)

- An increasing problem since the inception of antimicrobial Rx
- Rx of infections now versus 50 years ago-worse!

Antibiotic Resistance (3)

“Sooner or later bacteria develop resistance to virtually any antimicrobial agent”

- Jacoby and Archer

Chief Concerns (1)

- Bacteria resistant to all chemotherapy will become prominent pathogens e.g. superbugs
- Hasn't happened

Chief Concerns (2)

- Pathogens for normal host will acquire a critical complement of resistance and virulence genes leading to widespread dissemination and serious infections in the community, e.g. *Str. pneumoniae*, *S. aureus* strain USA 300
- Has happened in spades

S. aureus strain USA 300 (1)

- Methicillin resistance (MRSA)
- S. aureus isolates resistant to all currently available beta-lactams
- MRSA first noted soon after methicillin introduced
- Slowly increased through 1980s primarily in health care facilities

S. aureus strain USA 300 (2)

- Mid 1990s – a major change
- MRSA began to be detected in the community
- Molecular typing of these CA-MRSA revealed a new strain(s)

S. aureus strain USA 300 (3)

- These strains have a gene cluster that gives them a selective advantage in growth survival over other S. aureus
- This has resulted in the “nightmare scenario” of the rapid replacement of staph flora with USA 300

S. aureus strain USA 300 (4)

- It has virulence factors resulting in often aggressive skin and soft-tissue infections. 85% of CA-MRSA infections present in the skin
- Panton-Valentine leukocidin is likely the major virulence factor
- PVL causes leukocyte destruction and tissue necrosis, and is associated with most cases of severe skin infections and necrotizing pneumonias

S. aureus strain USA 300 (5)

- Methicillin resistance is carried in small DNA cassettes (mec type IVa) that are easily transferred among staph
- Spread most common where close contact
- Outbreaks often clustered in households, day-care centers, military installations, prisons, athletic teams, etc

S. aureus strain USA 300 (6)

- CA-MRSA colonization is much more likely to progress to infection than MSSA colonization
- As opposed to MSSA, skin and fomite colonization with CA-MRSA is at least as important as nasal colonization
- Thus, elimination of carriage important to break the cycle, but not easy since must attack skin as well as nares

S. aureus strain USA 300 (7)

- How widespread is S. aureus USA 300?
- Landmark study of Moran et al in NEJM August 2006

S. aureus strain USA 300 (8)

- They examined 422 “purulent skin and soft-tissue infections” from 11 ERs during August 2004
- 422 cases, 320 grew S. aureus, MRSA from 59% (74%-15%)
- 97% were USA 300, 98% had PVL toxin gene

S. aureus strain USA 300 (9)

- In most, but not all, US cities CA-MRSA is most common pathogen cultured from the skin and soft-tissue infections
- Can be impetigo or cellulitis but characteristic is an abscess with a necrotic surface
- Necrotizing pneumonia, osteomyelitis, necrotizing fasciitis, myositis, severe sepsis, etc have all been seen with CA-MRSA

S. aureus strain USA 300 (10)

- No clinical feature distinguishes with certainty skin and soft-tissue infection with MRSA from MSSA
- Local knowledge! Not easy to obtain
- Suggested threshold to consider MRSA - >10%

Suggested Rx of PYODERMAS 2007 (1)

- Wound culture of pyodermas where feasible
- I and D if appropriate
- For localized impetigo topical antibiotics adequate
- When oral antibiotics are indicated, I now advise you to “Think beyond Keflex”

Suggested Rx of PYODERMAS 2007 (2)

- How should Moran data affect our management of pyodermas?
- Study patients in ERs had mostly abscesses. 85% were treated with I and D
- Outpatients with pyodermas are mostly impetigo, folliculitis, cellulitis. Some of these are GAS
- In my experience, about 1/3 of *S. aureus* isolates are MRSA

Suggested Rx of PYODERMAS 2007 (3)

- TM-SMX 100%
- Rifampin 100
- Linezolid 100
- Clindamycin 95
- Tetracycline 92
- Fluoroquinolones 60
- Erythromycin 6

Antibiotic considerations (1)

- TM-SMX: high incidence of allergic reactions, a poor anti-GAS drug
- Clindamycin: Sensitivity testing can be deceptive
- Rifampin: secreted onto mucosal surfaces, do not use alone
- Doxy or minocycline: a good choice
- Linezolid: Save if possible for hospital use to treat life-threatening infections

Topical agents (1)

- Mupirocin resist, increasing rapidly
- ~ 40% of CNSA resist
 - ~ 20% of MRSA resist
 - ~ 5% of MSSA resist
- One can no longer count on mupirocin

Topical agents (2)

- Bacitracin and neomycin – no good studies, ACD.
- Retapamulin/Altabox

Retapamulin/Altabax (1)

- New topical ointment developed by GSK
- Approved 4/07 for Rx of impetigo
- A semi-synthetic pleuromulin – a family produced by mushrooms
- Several used in veterinary medicine
- Effective vs gram positives

Retapamulin/Altabax (2)

- No cross resistance to presently used antibiotics, including mupirocin
- Effective vs MRSA
- Little ACD – so far
- Little resist – so far

Retapamulin/Altabax (3)

- Works by binding to 50 S ribosomal subunit
- Suggested use – only infection, not prophylaxis
- Minimal absorption
- \$ 41 – 5 gm
\$ 70 – 10 gm
\$ 85 – 15 gm

Topical Agents (3)

- Difficulty of clearing CA-MRSA carriage
- Mupirocin and retapamulin can't be used on large skin areas or fomites
- Options: alcohol-based hand sanitizers, alcohol-free scrubs containing benzalkonium chloride or chlorhexidine products, triclosan soaps
- Parenteral antibiotics do not get to skin adequately

Antibiotic considerations (2)

- The good news in the CA-MRSA story has been that good treatment options have been available
- The bad news is that almost certainly, this isn't going to last. CA-MRSA has now crossed over into the health-care settings where it causes the same type of infections as it does in the community
- A study from a Boston ambulatory health clinic published this year found high frequencies of clinda and TCN resistance in USA 300/MRSA

- Without doubt, development of antibiotic resistance is proportional to the amount of antibiotics used
- Dermatologists have big users/offenders of antibiotics, primarily for acne and rosacea
- How can we become better citizens?

SPAUD (1)

- Scientific Panel of Antibiotic Use in Dermatology (SPAUD) published its suggestions this year
- Wherever possible, the duration of chronic oral antibiotic therapy for acne or rosacea should be limited as much as clinically feasible

SPAUD (2)

- To me, that translates to:
 - 1) Aggressive topical Rx
 - 2) Increased Accutane use, esp. in men
 - 3) Increased reliance on anti-androgen Rx in women.
- Antibiotic monotherapy, especially prolonged use, is not recommended in the treatment of acne vulgaris
- Prolonged topical or oral antibiotic therapy for acne is best accompanied by use of BP to optimize efficiency and mitigate emergence of less sensitive *P. acne* strains

SPAUD (3)

- In rosacea, effectiveness of oral tetracycline is probably related to anti-inflammatory effects more than antibiotic activity
- Anti-inflammatory effect of doxy requires a much smaller dose than the antibiotic effect, so low dose doxy is part of my standard regimen for rosacea

TETRACYCLINES (1)

- Tetracycline itself is inferior to doxy and minocycline
- Generic doxy and minocycline now are about the same price
- Minocycline has better pharmacodynamics but a less good side-effect profile

TETRACYCLINES (2)

- New preparation – Oracea
 - 40 mg doxy
 - 30 mg immediate release
 - 10 mg delayed release
- Only “antibiotic” approved to treat rosacea
- Effective for inflammatory lesions of rosacea
- No antibiotic action or effect on microbial flora
- Fewer side-effects

TETRACYCLINES (3)

- Is Oracea needed?
- Doxycycline hyclate 20mg tablets bid does everything Oracea does at ½ cost
- This has been part of my standard rosacea regimen for some time

TETRACYCLINES (4)

- Solodyn is a new extended release once daily minocycline preparation
- It is antimicrobial and marketed to treat acne vulgaris
- Is it needed? You decide.
- Cost is more than 10 x cost of generic minocycline
- Half-life of minocycline averages 15 hours
- To treat acne with minocycline I recommend 100mg once daily

HOW WE CAN BE GOOD CITIZENS

- Change our ways in acne/rosacea Rx
- Short, focused antibiotics when needed for skin infections

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