Control and Treatment of MRSA
Proportion of *S. aureus* Nosocomial Infections Resistant to Oxacillin (MRSA) Among Intensive Care Unit Patients, 1989-2003*

*Source: NNIS System*
Global MRSA Prevalence

- North America
  - Canada (Ottawa) 1%

- Europe
  - Netherlands 1.5%
  - Switzerland 4 to 68/10,000 adm (Up to 12%)
  - Poland 3-11%
  - UK 25% and Italy, France 30-50%

- Latin America
  - Brazil 70%

- Asia - Japan 60%

Antimicrobial Resistance: Key Prevention Strategies

Optimize Use
Prevent Transmission
Prevent Infection
Effective Diagnosis & Treatment

Susceptible Pathogen

Antimicrobial Resistance
Antimicrobial Use
Infection

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

1. Vaccinate
2. Get the catheters out
3. Target the pathogen
4. Access the experts
5. Practice antimicrobial control
6. Use local data
7. Treat infection, not contamination
8. Treat infection, not colonization
9. Know when to say “no” to vanco
10. Stop treatment when cured
11. Isolate the pathogen
12. Break the chain

Prevent Transmission
Use Antimicrobials Wisely
Diagnose & Treat Effectively
Prevent Infections
MRSA Transmission

- Clonal spread
  - Transmitted by direct person-to-person contact
  - Sites of colonization
    - Nares, axilla, skin
- Antibiotic selection
  - Methicillin resistance gene chromosomally-mediated
  - Mobilization of gene cassette in recent MRSA
  - Antibiotic selection
MRSA Transmission

- Transient hand carriage by personnel
  - Infected or colonized patient
  - Infected or colonized HCW
- Environment
  - Burn units
  - Dermatology wards
  - Fomites
"No doubt about it, Bob, you're infected with tiny fighter planes. What's worse — you're a carrier."
Decrease MRSA Transmission
Hand Hygiene Compliance

- 40% average compliance
- As low as 10%
- One study showed improvement to 60% with instant antisepsis
- Lowest compliance among physicians and nurses
- JCAHO Pt Safety monitor
Improved Patient Outcomes associated with Proper Hand Hygiene

Chlorinated lime hand antisepsis

Ignaz Philipp Semmelweis (1818-65)

Link to: Ignaz Semmelweis
MRSA Control Measures

- Acute Care Hospital
  - Microbiologic surveillance
  - Standard Precautions
  - Contact Precautions
  - Antisepsis
  - Standard housekeeping
  - Surveillance cultures
    - Standard vs. directed

Local assessment
Fact: Appropriate antimicrobial therapy saves lives.

Actions:

- culture the patient
- target empiric therapy to likely pathogens and local antibiogram
- target definitive therapy to known pathogens and antimicrobial susceptibility test results

Link to: IDSA guidelines for evaluating fever in critically ill adults
Use Antimicrobials Wisely

Step 6: Use local data

**Fact:** The prevalence of resistance can vary by locale, patient population, hospital unit, and length of stay.

**Actions:**

- ✓ know your local antibiogram
- ✓ know your patient population

[Link to: NCCLS Proposed Guidance for Antibiogram Development](#)
**Prevent Transmission**

**Step 11: Isolate the pathogen**

**Fact:** Patient-to-patient spread of pathogens can be prevented.

**Actions:**
- ✓ use standard infection control precautions
- ✓ contain infectious body fluids
  - (use approved airborne/droplet/contact isolation precautions)
- ✓ when in doubt, consult infection control experts

- Link to: A VRE prevention success story
- Link to: CDC isolation guidelines and recommendations
Surveillance Cultures

- Elimination of MRSA from Finland hospitals
  - 2 outbreaks MRSA 1991-2
  - 1991-2002
    - 202 persons with MRSA in medical district
  - Strict control measures for all 30 district hospitals
    - Contact precautions for colonized patients
    - Systematic screening for contacts of MRSA pts
    - Cohorts of MRSA+ and MRSA exposed pts
    - Continuous staff education

Kotilainen EID 2003
Surveillance Cultures

Cost-effectiveness

- NICUs of 2 tertiary care hospitals
- 11 month MRSA outbreak in hospital A vs. MRSA bacteremias in hospital B
  - Cost of control of outbreak in hospital A
    - $60,000 range
  - Attributable excess cost of MRSA bacteremias in hospital B
    - $1.3 million

Karchmer T et al. JHI 2002
Risk Factors for MRSA

- Invasive devices
- Time at risk
- ICU stay
- Coma
- Surgery

Law. Epidemiol Infect 1988; Ascensio. ICHE 1996
Crowcroft JHI. 1996; Crossley. JID. 1979
Fact:

Catheters and other invasive devices are the #1 exogenous cause of hospital-onset infections.
12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

Step 2: Get the catheters out

Biofilm on Intravenous Catheter Connector 24 hours after Insertion

Scanning Electron Micrograph

➤ Link to: Biofilms and device-associated infections
Prevent Infection

Step 2: Get the catheters out

Fact: Catheters and other invasive devices are the #1 exogenous cause of hospital-onset infections.

Actions:
- use catheters only when essential
- use the correct catheter
- use proper insertion & catheter-care protocols
- remove catheters when not essential

Link to: New IV Guideline
Link to: Urinary catheter infection prevention
Link to: Guidelines for the Prevention of Intravascular Catheter-related Infections
VISA (GISA)

- Intermediate resistance to vancomycin
  - MIC 8 μg/ml
  - Japan: ≤ 20% prevalence among noso MRSA
  - Cases in all continents
  - Continuum of strains with decreasing susceptibility to vancomycin

- Risk factors
  - Exposure to vancomycin
  - Prior MRSA infection
  - Renal failure

Hiramatsu 1997, CDC 1997-98
Vancomycin-Resistant *S. aureus*

- 3 VRSA isolates reported in US, 2002
- June 2002
  - Catheter exit infection
    - MRSA, vanco MIC 1024 µg/ml
    - Susc TMP/S, Clinda, tetracycline, minocycline, linezolid, quinu/dalfo
  - VRE vanA gene detected in the VRSA isolate
  - Rx TMP/S and removal of catheter

MMWR 2002;51(26):565        MMWR 2002;51(40):902
VRSA/VISA Control Measures

- Laboratory detection
  - Revised NCCLS standards
    - broth dilution, agar dilution, agar-gradient diffusion
  - Strains with MIC $> 4\mu g/ml$
    - Confirm genus and species; repeat vanco MIC
  - Report state health dept, CDC
- May be missed by automated systems
  - Add vancomycin screening plates
- Antimicrobials
- Prevent spread with Contact Precautions

CDC, 1997; 2003
VRSA/VISA Control Measures

- Prevent spread
  - Lab to notify infection control, attending MD
  - Initiate epidemiologic investigation
- Contact Precautions
  - Good antisepsis; gloves, gown
- Monitor compliance
- Surveillance cultures HCWs, pt roommates
- Consider: mupirocin for nasal eradication

CDC, 1997; 2003
Prevention is Primary!
**Fact:** Appropriate antimicrobial therapy saves lives.

**Actions:**

- culture the patient
- target **empiric therapy** to likely pathogens and local antibiogram
- target **definitive therapy** to known pathogens and antimicrobial susceptibility test results

➢ Link to: [IDSA guidelines for evaluating fever in critically ill adults](#)
Diagnose & Treat Infection Effectively

Step 3:
Target the pathogen

Appropriate antimicrobial therapy (correct regimen, timing, dosage, route, and duration) saves lives.

Step 4:
Access the experts

Infectious diseases expert input improves the outcome of serious infections.
Therapy of Hospital MRSA Infections

- **Vancomycin**
  - Good safety record
  - 10-15 mg/kg; trough levels 12-15
  - Monitor ototoxicity in elderly
  - No po or IM route
  - Resistance now reported
  - Tolerance more widespread problem
Linezolid

- Oxazolidinone; IV and po
- Broad Gram-positive activity
- Mechanism – protein synthesis inhibitor
  - Bacteriostatic
- Adverse effects
  - Marrow suppression, weak MAOI
  - Uveitis, peripheral neuropathy
  - Rare serotonin syndrome with concurrent SSRI
Daptomycin

- Cyclic lipopeptide
- Broad Gram-positive activity
- Bactericidal, including enterococci
- Unique mechanism – disrupts plasma membrane function
- Adverse effect – myopathy
Daptomycin Mode of Action

- Binds to Gram-positive bacterial cell membrane
  - Calcium-dependent insertion of lipid tail
- Rapidly depolarizes the cell membrane
  - Efflux of potassium
  - Destroys ion-concentration gradient
- Cell death
  - Multiple failures in biosystems, DNA, RNA, protein synthesis
Therapy of HA MRSA Infections

- Minocycline
  - Most active tetracycline to date
  - IV or po form
  - Used in Japan for MRSA and MRCNS
- TMP/S or Clinda if susceptible
Fluoroquinolones and MRSA

- In vitro and in vivo rapid emergence of FQ resistance in MRSA
- Duration of exposure and serial passages may yield conflicting results
- Cipro > Levo > Gati ≥ Moxi
- FQ use associated with clinical isolates of MRSA?

Community MRSA Infections

- Therapy skin & soft tissue infection
- Local drainage
- 2 drugs: clinda + TMP/S
- Chlorhexidine baths
- Mupirocin nasal eradication
- Treat affected family members
MRSA Nasal Eradication

Route and efficacy

- **Intranasal**
  - Mupirocin anterior nares BID X 7 days
    - 95%

- **Oral +/- intranasal**
  - RIF + TMP/SMX + Bacitracin (intranasal) X 5 days
    - 90%
  - RIF + TMP/SMX X 5 days
    - 50-75%
  - MIN + RIF X 14 days + MUP X 3 days
    - 90%
Diagnose & Treat Infection Effectively

Step 4: Access the experts

Fact: Infectious diseases expert input improves the outcome of serious infections.

Action:

✓ consult infectious diseases experts about patients with serious infections

Link to: SHEA / IDSA: Guidelines for the Prevention of Antimicrobial Resistance in Hospitals
Summary

- Major nosocomial pathogen
- Community onset cases increasing
- Controlled by antisepsis
- Contact vs. Standard Precautions
- Surveillance cultures in some settings
- New options for therapy
- Vancomycin resistance
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