How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Objectives
- Describe different control measures to control the transmission of MDRO
- Discuss the role of hand hygiene compared to other preventive measures
- Present recent research findings of high-quality studies
- To highlight strengths and weaknesses of the current evidence base

Disclosures
- Advisory board: Destiny Pharma, DaVolterra, bioMérieux
- Financial support for MDRO research activities: B.Braun, Pfizer, UniGe/HUG, European Commission

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

-- Control of endemic MDRO --

Identify carriers ⇒ Screening ⇒ Isolation

Reduce antibiotic use ⇒ Restriction

Stop transmission ⇒ Hand hygiene

Eliminate carriage ⇒ Decolonization

Improve infection control

- Surveillance of multi-R bacteria
  - Passive: Clinical cultures
  - Active: Surveillance swabs
  - Optional: Genotyping

Third-generation cephalosporin-resistant *Escherichia coli*, blood and CSF, 2008

Prevalence of multiresistant pathogens in repatriates to the Netherlands

Spread of KPC-containing *Klebsiella pneumoniae* from Greece

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Possible explanations

**Study Design**

- **Transaction performance**
- **MRSA screening rates**
- **Baseline rates**
- **Patient Population**

**Results of the STAR*ICU Trial**

Strategies to Reduce Transmission of Antimicrobial Resistant Bacteria in Adult Intensive Care Units

W. Charles Huskins, MD, MSc
Mayo Clinic College of Medicine, Rochester, MN

Conducted by the Bacteriology and Mycology Study Group (BAMMSG)
19 US academic medical centers


**STAR*ICU: Study Design**

- **Baseline 4-6 Months**
- **Implementation 3 Months**
- **Intervention 6 Months**

- **Standard control**
  - Screening for MRSA & VRE: without result notification.
  - Hand hygiene & education.

- **Intensive control**
  - Screening for MRSA & VRE: with result notification.
  - Preemptive contact isolation until negative screening result.
  - No rapid test available.


Incidence Density of New Colonization / Infection Events in Intensive vs. Standard Control Strategy ICUs

- **MRSA or VRE**
  - **MRSA**
    - p = 0.39
  - **VRE**
    - p = 0.53

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Possible reasons for failure

- Central laboratory facility
  - No rapid testing available
- No intensive search & destroy
  - No uniform decontamination approach
  - No environmental control
  - No HCW screening

Possible reasons for failure (2)

- High rates of MRSA & VRE acquisition in both arms
  - Antibiotic misuse and overuse?
- Universal gloving policy:
  - In intervention ICUs, health care providers used clean gloves, gowns, and hand hygiene less frequently than required for contacts with patients assigned to barrier precautions

Improve infection control

- Surveillance
- Promote and improve hand hygiene

Implementation tools:

Key tools

- Guide to Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy
- Template Action Plan

Use of alcohol hand rubs

Johnson et al. Med J Australia 2005

1. System change
   - Alcohol-based handrub at point of care
   - Access to safe, continuous water supply, soap and towels
2. Training and Education
3. Observation and feedback
4. Reminders in the hospital
5. Hospital safety climate

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

ESBL bacteremia

Johnson et al. Med J Australia 2005

Hand Hygiene Culture Change Program (HHCCP)
Pilot Program
Oct 2002 – Sep 2004 (2 years)
6 sites (2379 beds)

Statewide roll-out
From Mar to July 2006 (1 year)
75 sites (6154 beds)

Significant reduction of MRSA bacteremia following hand hygiene promotion


MRSA Bacteraemia, England 1990-2010

(Courtesy G. Frélich)

Estimated average procurement of Alcohol Hand
Rub and Liquid Soap in mls per bed-day July
2004-December 2007 in 148 acute NHS Trusts

• 3-fold increase in combined use to 60 mls per pt-day

• Analysis shows highly significant association between each ml of AHR used and 1% drop in MRSA BSI

Stone S et al. BMA 2012

% MRSA in S. aureus and MRSA incidence per 100 admissions or
1000 days of hospitalisation
Univ. hospitals of Paris area (n=39) 1993-2007

Jarlier V et al. Arch Intern Med 2010; 170: 552-559

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
Alcohol-Handrub Policy Predicts Low Hospital MRSA Rate

- Linear regression modelling of general infection control policies to predict local MRSA rate
- Adjusted for antibiotic consumption, case-mix, hospital size and teaching status:
  - Alcohol-based hand rubs (mean difference -10.3% MRSA rate; p=0.005)


Study Design

MOSAR surgery study
Prospective, controlled, multicentre, intervention
March 2008 to July 2010

Baseline Phase
6-7 months

Enhanced Standard Control (ESC) — 4 hosp

Active detection, Contact prec & Decolonisation (ACD) — 4 hosp

Combined Intervention (MIX) — 2 hosp

Washout Phase
12 months
6 months

Collection of data regarding MRSA rates and secondary outcomes

Methods

Setting and Participants
33 surgical wards
10 hospitals
9 countries
Serbia
France
Spain
Italy
Greece
Scotland
Israel
Germany
Switzerland

Results

Overall Hand Hygiene Compliance

Baseline
Intervention
Washout

Hand hygiene compliance (%)

Study month

Observed compliance rate — Predicted compliance rate

Results

MRSA Screening on Admission

Baseline Phase
Intervention Phase
Washout Phase

Percent screened on admission

Study month

Enhanced Standard Control
Active detection, Contact precautions & Decolonisation
Combined arm

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Results

MRSA Clinical Culture Isolation Rate

<table>
<thead>
<tr>
<th>Variable</th>
<th>aIRR*</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Phase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trend</td>
<td>0.97</td>
<td>0.89-1.06</td>
<td>0.55</td>
</tr>
<tr>
<td>Intervention Phase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enhanced Standard Control</td>
<td>1.44</td>
<td>0.96-2.15</td>
<td>0.076</td>
</tr>
<tr>
<td>Comparing study arms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enhanced Standard Control</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA screening</td>
<td>0.61</td>
<td>0.37-1.00</td>
<td>0.048</td>
</tr>
<tr>
<td>Combined</td>
<td>1.13</td>
<td>0.71-1.78</td>
<td>0.90</td>
</tr>
<tr>
<td>Change in trend</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enhanced Standard Control</td>
<td>0.99</td>
<td>0.91-1.09</td>
<td>0.88</td>
</tr>
<tr>
<td>Comparing study arms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enhanced Standard Control</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA screening</td>
<td>0.95</td>
<td>0.90-1.01</td>
<td>0.076</td>
</tr>
<tr>
<td>Combined</td>
<td>0.88</td>
<td>0.82-0.95</td>
<td>0.001</td>
</tr>
<tr>
<td>Washout Phase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in level</td>
<td>1.90</td>
<td>0.91-3.95</td>
<td>0.087</td>
</tr>
<tr>
<td>Change in trend</td>
<td>1.02</td>
<td>0.91-1.15</td>
<td>0.74</td>
</tr>
</tbody>
</table>

*aIRR = Adjusted incidence rate ratio

MRSA Clinical Culture Isolation Rate

Change in trend in MRSA Wards
- Screening and decolonisation arm
  aIRR 0.85, 95% CI 0.74-0.97, p=0.02
- Combined arm
  aIRR 0.82, 95% CI 0.71-0.95, p=0.01

Discussion

Conclusions
1. Compared to enhanced standard control measures with hand hygiene promotion, MRSA screening was more effective at initially reducing MRSA clinical culture isolation rates in surgical units.
2. Combining both strategies resulted in more marked reduction in MRSA rates over time.
3. The effect of screening and decolonisation on MRSA rates was more pronounced in clean surgery wards.
4. These findings are generalisable to a variety of healthcare settings.

Improve infection control
- Surveillance
- Promote and improve hand hygiene
- Use cohorting and isolation precautions (gowns, gloves, signs)

ISOLATION & COHORTING FOR MRSA
Systematic review with 6 high-quality studies
- Isolation wards
  - 1 effective, 1 ineffective, 1 transient
- Single room isolation
  - 1 transient hospital wide
- Cohorting
  - 1 effective hospital wide
- Cohorting & Single Room
  - 1 effective in paediatric ICU

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Control of ESBL-Klebsiella spp

- Modes of patient-to-patient transmission include transmission via colonisation of the inanimate environment, the hands of healthcare personnel, and of medical equipment

**ALL THESE MODES CAN BE DECREASED BY ISOLATION**

1. Falagas ME, Journal of Hospital Infection 2009;73: 345

CDC recommendation

- In acute care settings, implement contact precautions for all patients known to be colonized/infected with MDROs including ESBL-producing bacteria

- This was a grade 1B recommendation: Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale

Gloves and gowns block 90% of resistant bacteria

<table>
<thead>
<tr>
<th>Organism</th>
<th>HCW Room Entries</th>
<th>Hand + Before (%)</th>
<th>Gown and/or Glove + After %</th>
<th>Hands + After Removal</th>
<th>Effectiveness of PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. baumannii</td>
<td>202</td>
<td>1.5%</td>
<td>38.7%</td>
<td>4.5%</td>
<td>88%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>133</td>
<td>0%</td>
<td>8.2%</td>
<td>0.7%</td>
<td>90%</td>
</tr>
<tr>
<td>VRE</td>
<td>94</td>
<td>0%</td>
<td>9%</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>MRSA</td>
<td>81</td>
<td>2%</td>
<td>19%</td>
<td>2.6%</td>
<td>85%</td>
</tr>
</tbody>
</table>


Improve infection control

- Surveillance
- Promote and improve hand hygiene
- Use cohorting and isolation precautions (gowns, gloves, signs)
- Environmental control

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Acinetobacter Outbreak

- **Index patient**
  - Severe burn injuries, transfer from Bali (Oct 2002)
  - Multi-Resistant Acinetobacter at admission

- **Outbreak**
  - Spread to 2 patients
  - 6 months later: 6 new cases
  - Closure of the burn unit

- **Environment**
  - Widespread contamination: 16/161 (10%) positive swabs

  ▶ Environmental cleaning & disinfection
  ▶ Complete replacement of all disposable material


Foodborne Nosocomial Outbreak of SHV1 and CTX-M-15-producing Klebsiella pneumoniae: Epidemiology and Control

- Outbreak of ESBL K. pneumoniae in 2008 (clonal)
- 156 patients colonised
  - 22% infected
- 35% of the hospital kitchen-screened surfaces or foodstuff were colonised
- 6 (14%) of 44 food handlers found to be fecal carriers
- HCWs negative


Improve infection control

- Surveillance
- Promote and improve hand hygiene
- Use cohorting and isolation precautions (gowns, gloves, signs)
- Environmental control
- Decolonization


Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Need for a randomized, controlled study*

Colistin sulfate (50mg 4x/d)
+ Neomycin sulfate (250mg 4x/day)

Nitrofurantoin (100mg 3x/d)

10 days PLACEBO

10 days PLACEBO

Sample size: 27 patients in each group**

Targeted versus Universal Decolonization to Prevent ICU Infection
Group 1: Screen/Isolate
Group 2: Screen/Decolonize (Mupi/CHX)
Group 3: Universal Decolonization (Mupi/CHX)

Evolution of rectal ESBL - E carriage

Evolution of rectal ESBL - E carriage

Targeted versus Universal Decolonization to Prevent ICU Infection
Group 1: Screen/Isolate
Group 2: Screen/Decolonize (Mupi/CHX)
Group 3: Universal Decolonization (Mupi/CHX)

Sample size: 27 patients in each group**

Targeted versus Universal Decolonization to Prevent ICU Infection
Group 1: Screen/Isolate
Group 2: Screen/Decolonize (Mupi/CHX)
Group 3: Universal Decolonization (Mupi/CHX)

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Important issues to consider

• Very high MRSA on-admission prevalence
• High BSI rates in the universal decolonization arm (including 2 BMT units, by chance!)
• Surprisingly low rate of previously unknown MRSA carriers at admission
• Nasal screening only
• Slow screening method (no PCR tests)
• Chlorhex-R and HH issues: not addressed

Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial

- Reduction in MDRO acquisition by CBW plus hand hygiene program
  - Mainly caused by reduction in MRSA acquisition
- Screening and isolation of identified carriers did not have an incremental effect

Infection Control

- Promote adherence to alcohol-based hand hygiene & basic infection control
- Improve systems to recognize and detect patients colonized with MDROs
- Implement barrier precautions in high-risk situations and during outbreaks
- Don’t forget the environment
- Adapt preventive measures to your local setting and epidemiology

Independent risk factors associated with persistent MRSA colonization

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mupirocin/chlorhexidine resistance</td>
<td>3.4 (1.5-7.8)</td>
</tr>
<tr>
<td>Age (per 1 year increment)</td>
<td>1.04 (1.02-1.1)</td>
</tr>
<tr>
<td>Prior hospitalisation (2 years)</td>
<td>2.4 (1.1-5.7)</td>
</tr>
<tr>
<td>Wound/pressure sore</td>
<td>5.7 (1.8-17.6)</td>
</tr>
<tr>
<td>MRSA-inactive antibiotics</td>
<td>3.1 (1.3-7.2)</td>
</tr>
<tr>
<td>Central venous catheter</td>
<td>5.7 (1.4-23.9)</td>
</tr>
</tbody>
</table>

Lee & Harbarth, Clin Infect Dis 2011;52(12):1422–1430

Interventions

• Hand Hygiene compliance improved from 52% to 69% to 77% from phase 1 to 3

Infection Control

- Promote adherence to alcohol-based hand hygiene & basic infection control
- Improve systems to recognize and detect patients colonized with MDROs
- Implement barrier precautions in high-risk situations and during outbreaks
- Don’t forget the environment
- Adapt preventive measures to your local setting and epidemiology

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com
How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
Sponsored by the WHO Clean Care is SAFER Care

Participate in the WHO 5 May 2014 Global Surveys!

- A Global Prevalence Survey on Multidrug-Resistant Organisms (MDROs) – to assess and raise awareness of the burden of the five key health case-associated MDROs that have been identified at the global level
- WHO Global Prevalence Survey on use of SURGICAL ANTIBIOTIC PROPHYLAXIS - to assess surgical antibiotic prophylaxis prescribing in a wide range of acute health-care facilities

➤ Find out how to participate at:
  - English http://www.who.int/gpsc/5may/global-surveys/en/
  - French http://www.who.int/gpsc/5may/global-surveys/fr/
  - Spanish http://www.who.int/gpsc/5may/global-surveys/es/

Thank you for your attention!

2014 WHO Teleclass Schedule

January 29
Innovation and implementation of strategic approaches to reduce catheter-related bacteraemia: The results of a European multicentre study (PROHIBIT)
Dr. Walter Zingg, Switzerland

March 7
How to prevent the spread of multiresistant bacteria
Dr. Stephan Harbarth, Switzerland

April 9
Highlights on SSI prevention: The new CDC guidelines and more
Dr. Joseph Solomkin, USA

May 5
Special lecture for International Hand Hygiene Day
Prof. Didier Pittet, Switzerland

September 3
New WHO global campaign to eliminate unsafe therapeutic injections
Dr. Benedetta Allegranzi, Switzerland

October 8
Public reporting and disclosure of HIV rates: Positive impact or confusion?
Dr. Maryanna Medcalf, USA

November 5
Global application of behaviour change models and infection control strategies
Dr. Michael Borg, Malta

Hosted by Dr. Sergey Eremin, World Health Organization
A Webber Training Teleclass
www.webbertraining.com