What’s worthwhile for MDRO screening and isolation in NZ?
A ‘complex problem’
Dr Michael Gardam
NZ IPC Nurses Conference 2015

• One size rarely fits all
• Simple rules
• Local conditions matter
• Engage with those who are touching the problem (front-line ownership)
• Resilience (safety nets)
What is a multidrug-resistant organism?
Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance


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Clin Microbiol Infect 2012; 18: 268–281
Definition

• MDRO = ‘acquired non-susceptibility to at least one agent in three or more antimicrobial categories’

• E.g. *Staph. aureus*

• MRSA = MDRO

• Otherwise ≥ 3 of →

*Clin Microbiol Infect* 2012; 18: 268–281
Definition

- In your location at a particular time:
  
  Clinically important +
  
  Uncommon +
  
  Resistant to standard empiric antibiotics.

**Staphylococcus aureus**

Isolates from all sources, 1 January 2013 to 31 December 2014. Method of testing: disk diffusion (Kirby-Bauer).

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<td>97% (6376)</td>
<td>91%</td>
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<td>Cotrimoxazole</td>
<td>99% (6189)</td>
<td>99%</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>98% (5589)</td>
<td>98%</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>91% (6422)</td>
<td>88%</td>
</tr>
<tr>
<td>Flucloxacin²</td>
<td>95% (6662)</td>
<td>90%</td>
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<td>Mupirocin</td>
<td>87% (489)</td>
<td>91%</td>
</tr>
<tr>
<td>Penicillin²</td>
<td>16% (5433)</td>
<td>14%</td>
</tr>
</tbody>
</table>
**MRSA - methicillin-resistant *S. aureus***

Figure 1. MRSA period-prevalence rates, 2005-2014

**VRE - vancomycin-resistant Enterococci***

Figure 1. Species and van genotype of VRE isolated in New Zealand, 2005-2014

**ESBL-producing Enterobacteriaceae***

Figure 1. ESBL-producing Enterobacteriaceae incidence rates, 2005-2014

**Carbapenem-resistant gram-negative bacilli***

Figure 1. Number of carbapenemase-producing Enterobacteriaceae isolates identified in New Zealand, by major β-lactamase class, each year from 2009 to 2014
What is the problem with MDROs?
MDROs

- More treatment failure.
- More expensive and toxic antibiotics.
- Ultimately untreatable?

The proportion of methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococcal (VRE) infections is increasing (1987–2003).

Note: Data refer to infections in intensive care unit (ICU) patients only.
Colonisation → infection

- 19 to 25% of ICU patients who are colonised with MDROs → infection with the same
- Recurrent UTI: Mrs RS
MDROs and hospitals
MDROs spread in hospitals

- Sewage
- Risk factors
29 patients without VRE bacteria on body

INTENSIVE CARE UNIT (Chicago, lots of VRE)

12 (41%) patients picked up VRE

Lancet 1996; 348(9042): 1615-9
316 patients without *S. aureus* bacteria on body

INTENSIVE CARE UNIT

45 (14%) patients picked up *S. aureus*
Do staff pick up bacteria from patients?

1. Patients with *Staphylococcus aureus* bacteria on skin

2. Nurses touch patient or his clothing or bed

3. Test nurses’ hands after leaving patient

17% of nurses have *Staphylococcus aureus* on hands
Do staff pick up bacteria from patients?

1. Patients with *Enterococcus* bacteria on skin
2. Nurses touch patient or his clothing or bed
3. Test nurses’ hands after leaving patient

75% of nurses have *Enterococcus* on hands
How long do germs live on hands?

<table>
<thead>
<tr>
<th>Organism</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus (common cold)</td>
<td>38% at 1 hour</td>
</tr>
<tr>
<td>Rotavirus (diarrhoea)</td>
<td>16% at 1 hour</td>
</tr>
<tr>
<td><em>Shigella</em> (food poisoning)</td>
<td>More than 1 hour</td>
</tr>
<tr>
<td>Enterococci (gut bacteria)</td>
<td>More than 1 hour</td>
</tr>
</tbody>
</table>
Random hand testing
Burns unit nurses
• clean uniform and gown
• procedure

Remove gown

Put gown on researcher

Researcher
• 25-minute simulated patient care exercise

Bacteria from burns unit patient grown in
12 of 15 experiments.
Up to 3000 organisms.

Culture bedding and pajamas of simulated patient
Antibiotic-resistant bacteria on surfaces?

- Singapore, 800-bed hospital, where antibiotic-resistant bacteria are endemic

*J Med Micro 2013;62:766–772*

**Table 1. Environmental recovery of MDROs from sampled surfaces**

<table>
<thead>
<tr>
<th>Area</th>
<th>Surface</th>
<th>No. samples</th>
<th>MRSA Positive (%)</th>
<th>MRSA Organism density (c.f.u. cm⁻²)</th>
<th>CR A. baumannii Positive (%)</th>
<th>CR A. baumannii Organism density (c.f.u. cm⁻²)</th>
<th>VRE Positive (%)</th>
<th>VRE Organism density (c.f.u. cm⁻²)</th>
<th>Ceph-R Klebsiella spp.* Positive (%)</th>
<th>Ceph-R Klebsiella spp.* Organism density (c.f.u. cm⁻²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate patient</td>
<td>All sampled areas</td>
<td>50</td>
<td>82</td>
<td>0.42</td>
<td>40</td>
<td>0.47</td>
<td>4</td>
<td>0.29</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>environment</td>
<td>Bed frame</td>
<td>25</td>
<td>88</td>
<td>0.41</td>
<td>48</td>
<td>0.47</td>
<td>8</td>
<td>0.29</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Overbed table</td>
<td>25</td>
<td>76</td>
<td>0.44</td>
<td>32</td>
<td>0.46</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Commonly used</td>
<td>All sampled areas</td>
<td>13</td>
<td>62</td>
<td>0.83</td>
<td>15</td>
<td>0.31</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>equipment</td>
<td>Glucometer</td>
<td>2</td>
<td>50</td>
<td>1.54</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td></td>
<td>Stethoscope</td>
<td>6</td>
<td>67</td>
<td>0.64</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td></td>
<td>BP cuff</td>
<td>5</td>
<td>60</td>
<td>0.84</td>
<td>40</td>
<td>0.31</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Commonly touched</td>
<td>All sampled areas</td>
<td>19</td>
<td>63</td>
<td>0.59</td>
<td>10</td>
<td>0.11</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>surfaces</td>
<td>Bedside medical</td>
<td>6</td>
<td>100</td>
<td>0.37</td>
<td>17</td>
<td>0.11</td>
<td>–</td>
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<tr>
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<td>computer</td>
<td>–</td>
<td>–</td>
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<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Door handle</td>
<td>7</td>
<td>43</td>
<td>0.87</td>
<td>14</td>
<td>0.12</td>
<td>–</td>
<td>–</td>
<td>14</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>Telephone</td>
<td>6</td>
<td>50</td>
<td>0.76</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>All sites</td>
<td></td>
<td>82</td>
<td>74</td>
<td>0.51</td>
<td>29</td>
<td>0.42</td>
<td>2</td>
<td>0.29</td>
<td>1</td>
<td>0.29</td>
</tr>
</tbody>
</table>

*Ceph-R, third-generation cephalosporin resistant.*
Surface contamination

- Survival: days to months
- Becoming colonised in hospital linked to colonisation status of prior room occupant for MRSA, VRE, C. difficile, MDR-Acinetobacter baumanii and MDR-Pseudomonas aeruginosa
  
  *Arch Int Med 2006; 166: 1945*
  
  *Arch Int Med 2011; 171(6): 491-4*
  
  *ICHE 2011; 32: 201-6*
  
  *Clin Micro Infect 2011; 17: 201-8*

- Good cleaning reduces MDRO transmission.

  *Clin Infect Dis 2006; 42(11): 1552-60*
Identification and control of a gentamicin resistant, meticillin susceptible Staphylococcus aureus outbreak on a neonatal unit
Jonathan A Otter, Bethany Davies, Esse Menson, John L Klein, Timothy L Watts, Angela M Kearns, Bruno Pichon, Jonathan D Edgeworth and Gary L French
Journal of Infection Prevention 2014 15: 104 originally published online 11 February 2014
DOI: 10.1177/1757177413520057

The online version of this article can be found at:
http://bji.sagepub.com/content/15/3/104
Two conceptual solutions to hospital MDRO transmission
Conceptual paths

• Horizontal
  • Assume every patient has pathogenic organisms.
  • Hand hygiene, standard precautions, cleaning, antibiotic stewardship, chlorhexidine washes in ICU.
  • Why?: Minority of carriers known, most transmission from asymptomatic carriers, is a little MRSA more important than a lot of MSSA?

• Vertical
  • Target specific pathogenic organisms.
  • Surveillance/screening, isolation, decolonisation.
  • Why?: horizontal methods not perfect.
Do isolation precautions work?
Review #1 – JAC Jan 2014

- VRE transmission:
  - 2 studies show hand hygiene is effective.
  - 2 studies show isolation precautions *not* effective.
Review #2 – ICHE July 2014

- MRSA – more than 100 studies but poor quality, weak evidence, varied results and controversial conclusions – unable to prove that MRSA screening, isolation +/- decolonisation is effective.

- MDR-GNR – evidence even poorer.
Contact precautions ‘may help’ reduce patient-to-patient spread of MRSA within the hospital’

Isolate all MRSA-infected and colonised patients.

If transmission not controlled: one or more of increased surveillance, decolonisation, or universal gown and gloves.
Review #3 – SMW Sept 2014

- ARE, VRE, *C. difficile*, ESBLs in ICU
  - Mixed results for screening and isolation – difficult to know if it works.

*Enterococci, Clostridium difficile and ESBL-producing bacteria: epidemiology, clinical impact and prevention in ICU patients*

*Jan A. Sidler, Manuel Battegay, Sarah Tschudin-Sutter, Andreas F. Widmer, Maja Weissler*

Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Switzerland
Review #4 – ECDC Dec 2014

- ESBLs - poor studies – unable to be certain about anything.
- Probably effective:
  - Antibiotic restriction
  - Surveillance + isolation
  - IPC bundles (e.g., HH, isolation, cohorting, case notification, antiseptic bathing....)
Harm from isolation?

- Reduced healthcare worker visits – several studies
- Hassle and disruption
- Cost – construction and PPE
- Mixed results on:
  - patient falls
  - health-care errors
  - nurse efficiency
  - patient satisfaction.
Isolation - summary

- Poor evidence ≠ not effective
- Probably effective based on available studies
- I reckon isolation precautions are effective
- Guidelines say to do it!

→ use isolation precautions but
not instead of horizontal strategies.
→ prioritise isolation to highest risk patients,
organisms and locations.
Which MDRO patients to isolate?
Things to consider

**The hospital**
- How many isolation rooms?
- What’s your budget?
- How high is the risk of transmission and harm at a location?
  - ICU/Haem Onc > acute wards > rehab > mental health
  - (Beware: inconsistency → confusion)

**The patient**
- Known vs possible
- Active infection?
- IDUC or incontinent?

**The MDRO**
- How transmissible?
- Prevalence and impact
- Known to unknown ratio
- Outbreak?
Awaiting results of screening

- **MRSA**
  - Nelson – thousands of screens - almost all positives were previously known except:
    - 4 tertiary hospital-to-Nelson transfers
    - 4 new staff
  - Wellington – Tim Blackmore ‘1% of 4500 MRSA screens positive.’

- **VRE** - Nelson – only one pos, known (Akld)

- **CR-GNR**
  - Nelson – two positive, both recent hospitalisation in SE Asia.
Provisional positive lab results
How recent MDRO positive?

- **MRSA** – if no ongoing risk factors then low carriage at 1 to 2 years.
- **VRE** - 64% negative at 4 months.
- **Enteric GNR**
  - Mean duration 160 days for *Kleb. pneumoinoa*
  - 31% still detectable at 1 year
  - Median duration 98 days, ↑ by AB
  - Median time to clear 6.6 months
  - 24% still positive at 3-8 months and 10% still positive at 3 years

NMDHB
‘Cull’ alert at 3 years if no ongoing risk factors
Finite colonisation?!

- Screening known MRSA and VRE carriers during prolonged admissions
- Median clearance
  - MRSA 11% undetectable at 23 days
  - VRE 18% undetectable at 26.5 days
- Cost savings from removal from isolation = $140/day
- Cost of tests = $8.50/test.

*J Hosp Infect 2014; 88(4): 230-3*
Heavy ‘shedders’

- Hospitalised patients with *C. difficile*
  - Active colitis: skin or environmental contamination in 5 of 6 (83%)
  - Asymptomatic carriers: 3 of 18 (17%)

- *Staphylococcus aureus*
  - Infected patients shed more than carriers

- ESBLs
  - IDUC 6.1-fold more environmental contamination
  - Infected less likely (probably due to antibiotics)

*J Hosp Infect 2013; 85: 155-8*

*Joshua Freeman, Auckland – Antimicr Res IC 2014; 3: 5*
Heavy ‘shedders’

- But….
  - Infection one day, on antibiotics the next
  - IDUC one day, out the next (or the opposite)
  - How do you define a draining wound?
  - Who is non-hygienic?

- Too confusing and complex to differentiate?
- Rehab: consult with IPC Nurse about each case?
How transmissible?

- **Gram-negative rods**
  - *Klebsiella pneumoniae* 26-fold more likely to grow from hospital room surface swabs than *E. coli*
    
    Joshua Freeman, Auckland – Antimicr Res IC 2014; 3: 5
  
  - If share room with ESBL-positive patient, risk of transmission (standard precautions only) is 1%
    
    CID 2012; 55: 1505-11
  
  - Cross-transmission of non-ESBL MDR GNR was 4.8%, MRSA 9% and ESBL 11%.

- **VRE**
  
  - Hospital acquisition 1.2% to 41.4% (VRE endemic?)
    
    Swiss MedWkly 2014; 144: w14009

NMDHB
MRSA, VRE, GNR all =
(including *E. coli* = *Klebs*)
Local prevalence and impact

**Staphylococcus aureus**

Isolates from all sources, 1 January 2013 to 31 December 2014. Method of testing: disk diffusion (Kirby-Bauer).

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<td>14%</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>100% (503)</td>
<td>-</td>
</tr>
</tbody>
</table>

1. Flucloxacillin susceptibility predicts susceptibility to amoxicillin-clavulanate and all cephalosporins
2. Penicillin susceptibility predicts amoxicillin susceptibility.

NMDHB
Isolate all MRSA (no differentiate MR-MRSA)
Local prevalence and impact

Enterococcus spp.

All sources, 1 January 2013 to 31 December 2014. Method: disk diffusion (Kirby-Bauer).

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</thead>
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<tr>
<td>Amoxicillin¹</td>
<td>97% (1985)</td>
<td>95%</td>
</tr>
<tr>
<td>High-level gentamicin²</td>
<td>92% (13)</td>
<td>72%</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>99% (1824)</td>
<td>98%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>99.8% (1787)</td>
<td>98.2%</td>
</tr>
</tbody>
</table>

1. Amoxicillin susceptibility predicts penicillin and amoxicillin-clavulanate susceptibility
2. Only tested on blood isolates; predicts for synergistic effect when given with amoxicillin or vancomycin, not active against enterococci when used alone.

NMDHB
Isolate VRE, not ARE. (Maybe if ARE outbreak)
Local prevalence and impact

**Pseudomonas aeruginosa**

Mucoid and non-mucoid strains from all sources, 1 January 2013 to 31 December 2014. Method: disk diffusion (Kirby-Bauer).

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</thead>
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<tr>
<td>Cefepime</td>
<td>99% (1626)</td>
<td>98%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>94% (1881)</td>
<td>93%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>91% (1624)</td>
<td>95%</td>
</tr>
<tr>
<td>Meropenem</td>
<td>-</td>
<td>95%</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>99% (1623)</td>
<td>98%</td>
</tr>
</tbody>
</table>

1. Insufficient data – tested locally only on resistant isolates

NMDHB
Isolate carbapenem-res *Ps. Aeruginosa* (Maybe others if outbreak)
Known to unknown ratio

- Nelson Hospital – screened all inpatients in January 2014 (n=107)
  - 6 MDR-GNR (4 E. coli, 1 Kleb)
  - 1 VRE
- None detected on clinical samples
- 6 of 7 not known to be MDRO-positive before screening.

NMDHB
No isolate ESBLs (but alert for AB choice and other DHBs).
(Maybe isolate ESBLs if outbreak)
Identification and control of a gentamicin resistant, meticillin susceptible *Staphylococcus aureus* outbreak on a neonatal unit

Jonathan A Otter, Bethany Davies, Esse Menson, John L Klein, Timothy L Watts, Angela M Kearns, Bruno Pichon, Jonathan D Edgeworth and Gary L French

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DOI: 10.1177/1757177413520057

The online version of this article can be found at:

http://bji.sagepub.com/content/15/3/104
Screening for MDROs
Screening – why?

- Because clinical samples only detect infected cases
  - Most CF/bronchiectasis carriers of *Pseudomonas aeruginosa* in sputum detected by clinical samples.
  - 15 to 81% MRSA carriers detected by clinical samples.
  - Minority of VRE and ESBL carriers detected by clinical samples.
- Detecting carriers enables isolation (most transmission from asymptomatic carriers) and good empiric antibiotic choice if develop infection.
Screening – why not?

- Time
  - Collecting swabs
  - Explaining positive results
- Cost.

Thanks to Dr Andrew Burns
Risk factors for MDROs

- Age
- Co-morbidities – esp. dialysis
- Surgery and invasive devices
- IDUC
- Rest home
- Prior broad-spectrum antibiotics…. Non-specific!
Risk factors for MDROs

- Overseas hospitals – especially long inpatient stay, high MDRO prevalence
- Overseas travel to developing country
  - Calgary to India: 60% come back carrying ESBLs
  - Australia to Asia: ≈ 40%
- Prior colonization with MDRO (how long since?)
- Positive family member (but do they know?)
So who to screen?

- ICU or Haem/Onc unit
  - May want to know all carriers – high risk infection and cross-infection
  - So swab all? Or.....

- Acute wards
  - Overseas hospital in last 6 months
  - Transfer from anywhere there is an outbreak MDRO
  - Others?
Sister we need a sample of his faeces, urine and semen.

Doctor how about you just send his underpants to the lab?
How to screen?

- **MRSA**
  - Nasal 93%
  - Nares + infected wound ≈ 100%
  - Others – groin/perineum (39%), axillae (25%)

- **VRE**
  - Stool ≈ peri-anal
  - *Enterobacteriaceae* (*E. coli, Klebsiella* etc.)
    - Stool ≈ peri-anal
  - *Pseudomonas, Acinotobacter* spp. etc.
    - Stool, throat, wounds/ulcers, IDUC urine......
Thank you
Richard.everts@nbph.org.nz