Antibiotic Restriction Policies - Can they hold back the tide?
Dr. Mark Thomas, Auckland City Hospital, New Zealand
A Webber Training Teleclass

His courtiers flattered him by saying that “He was so great he could command the tides of the sea to go back”
Canute had his throne taken to the waters edge to demonstrate the impossibility of this claim.

Can antibiotic restriction policies hold back the waves of resistant bacteria?

Antibiotic use

Resistance to antibiotics

MRSA, ESBL, VRE, VRSA, etc.

Restriction policies
Antibiotic use

Resistance to antibiotics

Assumptions!
1. Antibiotic use leads to bacterial resistance
2. Antibiotic use has potential for reduction
3. Restriction policies will reduce antibiotic use
4. Reduced use will result in reduced resistance
5. Reduced use will not result in worse patient outcomes
6. Reduced use will not cost more

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Antibiotic use leads to bacterial resistance?

YES!!
Penicillin  S. aureus 90%

NO!! (not yet)
Penicillin  S. pyogenes 0%
T. pallidum  0%

Resistance to the antibiotic used:
VRSA in a patient treated with vancomycin

June 2002, Michigan USA
49 yr old diabetic, PVD, renal failure
MRSA bacteraemia – infected A-V graft
Treated with vancomycin and rifampicin
VRSA infection temporary dialysis catheter
VRE and Klebsiella oxytoca in foot ulcer


Resistance to other antibiotics:
risk of acquisition of VRE in relation to antimicrobial treatment

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</tr>
</thead>
<tbody>
<tr>
<td>Broad spectrum cephalosporins</td>
<td>2.36</td>
<td>3.44</td>
<td>5.0</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Metronidazole, clindamycin</td>
<td>2.02</td>
<td>2.64</td>
<td>3.38</td>
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<tr>
<td>Fluoroquinolones</td>
<td>1.5</td>
<td>2.33</td>
<td>3.61</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Vancomycin</td>
<td>0.7</td>
<td>1.4</td>
<td>2.6</td>
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Resistance to the antibiotic used:
fluoroquinolones and S. pneumoniae in Canada

Chen et al. NEJM '99;341:233-15-64yrs
≥ 65yrs

Antibiotic use:
does have potential for reduction!

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<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Human</td>
<td>80%</td>
<td>community</td>
</tr>
<tr>
<td></td>
<td>20-50%</td>
<td>hospital</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>unnecessary</td>
</tr>
<tr>
<td>Agricultural</td>
<td>80%</td>
<td>prophylactic</td>
</tr>
<tr>
<td></td>
<td>40-80%</td>
<td>treatment</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>highly questionable</td>
</tr>
</tbody>
</table>

Harbath et al. Antimicrobial Agents and Chemotherapy '92;68:1619-
BMJ '98;317:609-

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Community antibiotic use in France = 3x that in Netherlands in 1997

Community use correlates with hospital use

Hospital antibiotic use in France = 2.5x that in Norway in 2002

Restriction policies can reduce use:
Erythromycin and S. pyogenes in Finland.

3X increase in macrolide antibiotic use during 1980s

Erythromycin resistance in S. pyogenes:
1988, 1989 = 5%
1990 = 13%

High use regions had high resistance rates.

Education program to reduce macrolide use in Finland

Reduced use can result in reduced resistance:
50% reduction in erythromycin resistance in S. pyogenes in Finland

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Methods to reduce antibiotic use (in hospitals)

- Education and Guideline Formulation
- Formulary and Restriction Strategies
- Pharmacist, Physician or Computer administered
- Persuasive or Restrictive

Survey of 88 US hospitals

- 2/3 used a formulary to restrict antimicrobial choices
- 28% required ID approval for dispensing of restricted antimicrobials
- 21% required pharmacist approval for dispensing of restricted antimicrobials

A computer-based restriction program in an Australian Hospital

Royal Melbourne Hospital – 1999 - excessive use of cefotaxime and ceftriaxone
Web-based approval system
- prescriber login code
- patient identifiers
- select indication from drop-down list
  (or seek approval from ID registrar)
- no dispensing without approval number

Conclusion:

A computer based restriction policy can dramatically reduce prescribing of targeted antimicrobials.

But be aware of potential for increased prescribing of other agents!
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Another restriction policy that reduced antibiotic use
Carney Hospital, Boston, 1988-1998
Full-time pharmacist + ¼ time ID physician
Formulary
Review of all prescriptions for:
  3rd cephalosporins, aztreonam
  IV quinolones, imipenem
  7 day stop orders for all antibiotics
Exclusion of pharmaceutical company staff

Do reductions in antibiotic use result in reductions in bacterial resistance?
Yes, and No.

Restriction of cephalosporin use to control cephalosporin resistant Klebsiella in Queens NY.
Increase in ESBL +ve Klebsiella during 90s
Cephalosporin use severely restricted in 1996
JAMA ’98; 280: 1233–

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“Squeezing the balloon”

<table>
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<tr>
<th>1995</th>
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<tr>
<td>Cephalosporin consumption</td>
<td>5.6kg</td>
</tr>
<tr>
<td>Pts with ESBL Klebsiella</td>
<td>150</td>
</tr>
<tr>
<td>Imipenem consumption</td>
<td>0.2kg</td>
</tr>
<tr>
<td>Pts with I res Pseudomonas</td>
<td>67</td>
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</table>

Cochrane Review!
Interventions to improve antibiotic prescribing practices for hospital inpatients, July 2005

- 66 acceptable studies
- 42 USA, 24 elsewhere
- 29 educational, 27 restrictive, 7 mixed
- 57 1 hospital only, 9 2 or more hospitals
- 22 pharmacist, 17 ID physician, 11 team

10/14 studies that aimed to reduce consumption showed a significant effect (8-69% reduction in consumption)

4/5 studies showed a reduction in C. difficile diarrhoea
6/10 studies showed a reduction in antibiotic resistant GNB
2/4 studies showed a reduction in VRE or MRSA

5 studies monitored mortality
3 monitored readmission rates
with no consistent conclusions

While there are relatively few studies of the effect of restriction policies on the rates of antibiotic resistance (or other clinical outcomes) there is a large amount of data showing antibiotic use correlates with resistance rates.

Beta-lactam antimicrobial use and penicillin resistance in S. pneumoniae

Macrolide antimicrobial use and macrolide resistance in S. pneumoniae

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Overview

1. Antimicrobial use selects for colonisation and disease due to resistant organisms
2. Patients’ outcomes are worse when infected with resistant organisms
3. Cautious antimicrobial prescribing can reduce the selection of resistant organisms
4. There is some evidence that restriction policies are effective in slowing the evolution of resistance

A useful review

MacDougall C, Polk RE.
Antimicrobial stewardship programs in health care systems.