Infectious Diseases

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1. Longitude Prize 2014 (National Endowment for Science, Technology and the Arts)

A. Flight - How can we fly without damaging the environment?
B. Food - How can we ensure everyone has nutritious sustainable food?
C. Antibiotics - How can we prevent the rise of resistance to antibiotics?
D. Paralysis - How can we restore movement to those with paralysis?
E. Water - How can we ensure everyone has access to safe and clean water?
F. Dementia - How can we help people with dementia live independently for longer?

Antimicrobial Armageddon by 2050

Lord O'Neill Report December 2014
Predictions: KPMG and RAND
Total Antimicrobial Resistance cost 100 trillion $
Annual deaths exceeding cancer

Wellcome Trust areas for action
- Diversity and inclusion
- Drug resistant infections
- Vaccines

https://longitudeprize.org/

‘Cast back into the Dark Ages of Medicine’?
The Challenge of Antimicrobial Resistance.

“...most of the gains in life expectancy now deemed under threat preceded the antibiotics revolution...”

“...public health measures, rising living standards, and new medical knowledge ...”

“The problem for now is ...carbapenem-resistant gram-negative bacteria ....”

“palliative care” & “infections 2015-2017”
Opinions on end of life antibiotics


No … it depends … benefits vs adverse events.

Antimicrobials at the End of Life: An Opportunity to Improve Palliative Care and Infection Management. JAMA. 2015.

Infections and antibiotic use common* and so should be part of advance plans.
If only symptom relief – limit investigation.
If duration of life and clinical expectation of benefit – investigate.

Data on end of life antibiotics


*“evident symptom relief” in 37%, especially for suspected sepsis


Limited evidence – best for UTI


Policies on initiation 31%, Discontinuation 17%

 Relevant risk factors for resistance

Old age [1]

Residence in a setting with high antibiotic use [2]


The (rise and) fall of C. difficile

Clostridium difficile cases per quarter in England 2007-2016


Admission Total

<table>
<thead>
<tr>
<th></th>
<th>Delirium</th>
<th>43%</th>
<th>70%</th>
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</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>20%</td>
<td>46%</td>
<td></td>
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<tr>
<td>Bowel obstruction</td>
<td>16%</td>
<td>35%</td>
<td></td>
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</tbody>
</table>

(Texas and Brazil)

Bacterial infections in terminally ill hospice patients. J Pain Symptom Manage. 2000 (Australia)

36% prevalence with UTI (42%) and RTI (23%) dominant


39% infection.

* Hospital cases Community cases
Why did *C. difficile* decline?

A. Changing antibiotic use  
B. Handwashing  
C. Cleaning in hospitals  
D. Reduction in acid supressing drugs

![Bar chart showing the percentage of decline due to each factor]

Risk factors and control

"Uncontrollable"

- Age
- Long term care
- Comorbidities

Antibiotics

*Clostridium difficile* infection: risk with broad-spectrum antibiotics. NICE. Evidence summary (ESMPB1) March 2015.

Stronger risk in community

Highest risk: Cefepime, Ciprofloxacin, Fluoroquinolones

Most common *C. difficile* associated now: Co-amoxiclav

Interventions work?


Proton pump inhibitors

- May be a risk factor
- Any risk per patient on PPIs is very small (e.g. 1/4000) but very high levels of use may contribute to a lot of cases.

Other interventions

- Clean environment
- Clean hands
- Probiotics?

"Time"?

Meningococcal infection in England: Cases per year, 1998-2016.
What is your first line treatment for *C. difficile*

A. Metronidazole  
B. Vancomycin  
C. Fidaxomicin  
D. Other

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>71%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>28%</td>
</tr>
<tr>
<td>Fidaxomicin</td>
<td>0%</td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
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</tbody>
</table>

Updated guidance on the management of Clostridium difficile infection


Date of download: 1/26/2017

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From Decreased Diversity of the Fecal Microbiome in Recurrent Clostridium difficile—Associated Diarrhea

From Decreased Diversity of the Fecal Microbiome in Recurrent Clostridium difficile—Associated Diarrhea


Is there increased risk in the immunosuppressed?

A. Measles  
B. Tuberculosis  
C. Whooping cough  
D. Influenza

<table>
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<th>Disease</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Measles</td>
<td>20%</td>
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<tr>
<td>Tuberculosis</td>
<td>37%</td>
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<tr>
<td>Whooping cough</td>
<td>27%</td>
</tr>
<tr>
<td>Influenza</td>
<td>43%</td>
</tr>
</tbody>
</table>
Measles case: Primary Care

- Measles in unvaccinated adult
- 2 visits to GP
- GP immunocompromised, uncertain status
- One pregnant contact
- Child developed measles and isolated
- 6 staff members unvaccinated

Staff exposed to measles

- Excluded until confirmed immune
- If non immune excluded for incubation period
- Units with incidents – usually then vaccinate all their staff

Measles case 2: Hospital

- Health care worker
- 102 contacts
- 54 advised MMR
- 5 advised Human Normal Immunoglobulin

Influenza

- Influenza A
  - Haemagglutinin
  - Attachment of virus
  - Neuraminidase
  - Release and spread of virus

How effective is flu vaccine?

- Community
  - "Influenza like illness" 0%
  - Hospitalised (flu/pneumonia) 26%

Effectiveness of flu vaccine in the elderly

- Institution
  - "Influenza like illness" 23%
  - Hospitalised (flu/pneumonia) 43%


Effectiveness of flu vaccine in health care workers

- 60-80% effective in healthy adults against “swine flu” in 2009 (year 1)

- Reduces influenza in staff

- Reduces influenza in patients

Controlling outbreaks in institutions

Norovirus duration in institutions (median [range])

<table>
<thead>
<tr>
<th>Infection control used</th>
<th>No infection control used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital 17 days [6-37]</td>
<td>Hospital 25 days [9-92]</td>
</tr>
<tr>
<td>Overall 16 days [1-44]</td>
<td>Overall 14 days [2-92]</td>
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Who spreads and who suffers?

Coverage vs relative risk

- Uptake of immunisation compared to age adjusted relative risk of mortality from seasonal flu

Coverage vs relative risk

- Uptake of immunisation compared to age adjusted relative risk of mortality from seasonal flu

Influenza in an institution

- Model vs outcome

Norovirus duration in institutions

- Median [range] for different scenarios

Who spreads and who suffers?

**Spreads?**

- A. Children
- B. Teen / Young adult
- C. Adults
- D. Older adults

**Suffers?**

- A. Children
- B. Teen / Young adult
- C. Adults
- D. Older adults

Changes in invasive pneumococcal disease due to grouped PCV7 serotypes since introduction of PCV7 into national immunisation programmes.