Antibiotic Resistance
A major global public health issue
Antibiotic Resistance

How does this happen?

Watch Antibiotic Resistance Evolve
**Antibiotic Resistance**

*Why should we care?*

According to the World Health Organisation, antimicrobial resistance poses the following threats:

1. Standard antibiotics are often ineffective when used to treat infections caused by resistant bacteria, resulting in prolonged illness and an increased risk of mortality

2. Resistance causes the effectiveness of treatment to be reduced, increases the amount of time that a person is infectious and increases the spread of resistant microorganisms to others

3. Infections which were previously easily managed may become untreatable and uncontrollable, as seen in the pre-antibiotic era

4. The costs of treating resistant infections (to healthcare, individuals and societies) is increased due to the need to use more expensive second-line treatments, longer treatment periods and a greater need for hospital care

5. Resistant infections are detrimental to the success of “modern medicine” treatments such as major surgery, chemotherapy and organ transplantation

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Antibiotic resistance is growing - new antibiotic approvals are declining

Incidence of selected antibiotic resistance (%)\(^1\)

<table>
<thead>
<tr>
<th>Year</th>
<th>MRSA</th>
<th>FQRP</th>
<th>VRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1985</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1990</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1995</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2000</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Number of new systemic antibiotics approved by the FDA\(^2\)

<table>
<thead>
<tr>
<th>Year</th>
<th>'83–'87</th>
<th>'88–'92</th>
<th>'93–'97</th>
<th>'98–'02</th>
<th>'03–'07</th>
<th>'09–'12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>18</td>
<td>16</td>
<td>14</td>
<td>12</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>1985</td>
<td>16</td>
<td>14</td>
<td>12</td>
<td>10</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>1990</td>
<td>14</td>
<td>12</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>1995</td>
<td>12</td>
<td>10</td>
<td>8</td>
<td>6</td>
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<td>2</td>
</tr>
<tr>
<td>2000</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^1\) Cooper & Shlaes (2011). Nature 472:32

FDA: Food and Drug Administration | FQRP: fluoroquinolone-resistant Pseudomonas aeruginosa | MRSA: methicillin-resistant Staphylococcus aureus | VRE: vancomycin-resistant enterococci
Antibiotic resistance and antibiotic stewardship
A global call to action

Major organisations recognize the need for action

Objectives and priority areas for action

There are five objectives that address priority areas for action on AMR.

1. **Awareness and understanding**: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training.

2. **Surveillance and research**: Strengthen the knowledge and evidence base about antimicrobial resistance through surveillance and research.

3. **Infection prevention and control**: Improve infection prevention and control measures across human health and animal care settings to prevent infection and the transmission of micro-organisms.

4. **Antimicrobial stewardship**: Optimise the use of antimicrobial medicines in human health, animal health and agriculture, including by maintaining and enhancing the regulation of animal and agriculture antimicrobials.

5. **Governance, collaboration and investment**: Establish and support clear governance, collaboration and investment arrangements for a sustainable approach to countering antimicrobial resistance.
Antibiotic Consumption in NZ

Human Consumption is High. Animal Consumption is Low

Antibiotic Consumption in NZ

Community Consumption is high. Hospital Consumption is Low

Diagram showing community and hospital antibiotic consumption in various countries, with New Zealand highlighted.
"These results suggest that improving antimicrobial stewardship in the community may provide greater overall benefits in combating antibacterial resistance than improving antimicrobial stewardship in hospitals."
Estimated Prescribing Rates
Antibiotic Prescribing for Respiratory Tract Infections

• Approximately 180 antibiotic prescriptions dispensed for every 100 children aged less than five years. In adults aged 25–29 years (the age group with the lowest level of antibiotic prescribing) there were more than 60 antibiotic prescriptions dispensed per 100 people.

• It has been reported that approximately 60% of all antibiotic prescribing in primary care in the United Kingdom is for patients with respiratory tract symptoms.

• 4,693,000 pop
• >60% pop getting AB prescription = 2,815,800 prescriptions total
• 60% AB prescriptions for RTI’s = 1,689,480

Can POCT Help?
CRP Testing on the cobas b 101
Guiding appropriate antibiotic use in Primary Care
C-reactive protein
A marker of infection, inflammation and tissue injury

- CRP is an acute phase response (APR) protein
- CRP is a marker of infection, inflammation and tissue injury
- CRP is not specific for any disease in particular and should only be used as part of a panel of clinical assessments
CRP testing assesses the nature (bacterial or viral) and severity of an infection

- Typical values in healthy individuals are below 10 mg/L\(^1\)
  - unaffected by age, gender, variations in plasma proteins or conditions such as anemia\(^2,3\)
- Levels above 10 mg/L are considered to be clinically significant\(^4\)

Major guidelines recommend CRP testing as part of diagnostic workup or treatment monitoring

- Acute respiratory infection diagnosis
- Management of pneumonia in adults
- Diagnosis and management of inflammatory bowel disease, irritable bowel syndrome
- Diagnosis of periprosthetic hip and knee joint infections
- Management and classification of rheumatoid arthritis
- Management of feverish illness in children <5 yrs, suspected neutropenic sepsis, early onset neonatal infection, paediatric bacterial meningitis and meningococcal septicemia


All online references accessed May 2017
Respiratory tract infections (RTI) in primary care

A challenging presentation

RTIs are one of the most common acute conditions seen in primary care

About 80% of patients with RTIs are treated with antibiotics

However RTIs seldom require antibiotics
• often self-limiting
• many are viral

Diagnostic uncertainty leads to inappropriate antibiotic prescribing

Excessive antibiotic use contributes to antibiotic resistance

RTI: respiratory tract infection
Clinical value of CRP in respiratory infections
Support diagnosis and guide therapy

**Reliable risk assessment & diagnosis**¹⁻³
- decrease diagnostic *uncertainty* and *differentiate* seriously illness from non serious illness

**Guiding treatment decisions in primary care**¹,²
- support *appropriate antibiotic* use and reassure patients when antibiotics are *unnecessary*

**Monitoring the effectiveness of therapy**³,⁴
- assess response to antibiotic treatment and guide *follow-up investigations*

   Accessed May 2017
Clinical Value of CRP testing at the Point of Care
Guiding Appropriate Antibiotic Use in Primary Care

This simple point-of-care CRP test on the cobas b 101 can provide physicians an assessment of the nature (bacterial or viral) and severity of an infection within four minutes\(^1\)-\(^3\) and aid in timely and effective antibiotic treatment, thereby helping to avoid antibiotic resistance\(^4\)-\(^7\).

\(^2\) Usefulness of consecutive C-reactive protein measurements in follow-up of severe community-acquired pneumonia. http://erj.ersjournals.com/content/32/3/726
\(^3\) Clinical Pharmacist, Vol 8, No 10, online | DOI: 10.1211/CP.2016.20201688 (Link)
\(^7\) National Targets Reduce Unnecessary Antibiotic Use in Outpatient Settings. An Infographic from The Pew Charitable Trusts, May 2016.
Available at: http://www.pewtrusts.org/~/media/assets/2016/05/national_goals_antibiotics
Why POC CRP?

Fast, reliable results to guide treatment

POC CRP testing at the **site of patient care** delivers **rapid test results** that can **enable appropriate treatment decisions** at the initial consultation


Laboratory CRP testing is **rarely used** to assess **acute infections** in **primary care** due to the **time** needed to obtain results (1 – 2 days)

NICE algorithm for management of RTI in primary care

POC CRP in conjunction with proper clinical examination

Adults presenting to primary care with symptoms of LRTI → Clinical assessment

- Pneumonia not diagnosed or unclear if antibiotics should be prescribed → POC CRP test
  - < 20 mg/L → Do not routinely offer antibiotic therapy
  - 20 – 100 mg/L → Consider a delayed antibiotic prescription (for use at a later date if symptoms worsen)
  - > 100 mg/L → Offer antibiotic therapy

- Pneumonia diagnosed → Follow NICE pathway for pneumonia

LRTI: lower respiratory tract infection | NICE: National Institute for Health and Clinical Excellence | POC: point-of-care
POC CRP testing changes prescribing decisions in primary care
One study demonstrated that antibiotic prescription decision changed in 27% of patients with RTI\(^1\)

Pre-test decision
(based on routine history taking and physical examination)

<table>
<thead>
<tr>
<th>Pre-test decision (based on routine history taking and physical examination)</th>
<th>Patients in whom a POC CRP test was conducted n=735</th>
</tr>
</thead>
<tbody>
<tr>
<td>POC CRP test</td>
<td>Would prescribe antibiotics n=234 (32%)</td>
</tr>
<tr>
<td>POC CRP test</td>
<td>Would not prescribe antibiotics n=201 (68%)</td>
</tr>
</tbody>
</table>

Post-test decision
(after POC CRP value available)

<table>
<thead>
<tr>
<th>Post-test decision (after POC CRP value available)</th>
<th>Change in antibiotic prescribing in 200 (27%) patients after POC CRP test results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Would prescribe antibiotics n=120 (16%)</td>
<td>Would not prescribe antibiotics n=114 (15%)</td>
</tr>
<tr>
<td>Would prescribe antibiotics n=86 (12%)</td>
<td>Would not prescribe antibiotics n=415 (56%)</td>
</tr>
</tbody>
</table>

POC: point-of-care | RTI: respiratory tract infection | SD: standard deviation
\(^1\) Minnaard et al (2016). Fam Pract 33:408–413
Best Practice (BPAC) New Zealand

Is point-of-care CRP testing useful in guiding antibiotic prescribing in patients with respiratory tract infections?¹

Evidence suggests that with appropriate training, point-of-care CRP testing in patients with a RTI can reduce unnecessary antibiotic prescribing in two specific clinical scenarios:

1. Identifying patients with symptoms of a lower RTI who are unlikely to have pneumonia, i.e. where an antibiotic is not appropriate

2. Providing patients with an upper RTI who are convinced they “need” an antibiotic with reassurance that a prescription for an antibiotic is unlikely to be beneficial

The Power of Point of Care Testing
cobas b 101 for HbA1c, lipids and CRP testing
cobas b 101 CRP Test

Specifications

**Multiple POC tests**
CRP, HbA1c, Lipid Panel

**Ease of use**
No sample preparation, direct dosing for capillary blood (12µL)

**Rapid test turnaround time**
CRP: ≤ 4 min

**Robust results**
CRP CV: 1.7% - 3.3%

**Measuring Range**
3.0 – 400 mg/L

**Installed user base**
>15,000 instruments in >41 countries

**Consumable Handling**
Discs can be stored at room temperature, therefore no need to warm up

**Connectivity to middleware**
Connects to cobas IT 1000, GP software, other DMSs

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CRP, C-reactive protein; CV, coefficient of variation; DMS, document management system; GP, general practitioner; HbA1c, glycated hemoglobin; POC, point-of-care
CRP Testing on the cobas b 101

Test Disc

Test Method - Latex Agglutination
Analytical performance of CRP testing on the cobas b 101
Fulfils the acceptance criteria for repeatability and precision

Precision of cobas CRP Test

Precision was determined using controls in a CLSI EP5-A3 protocol.

Precision was measured with 3 lots of cobas CRP Test using 5 different serum samples at the medical decision points and 2 cobas CRP Control solution levels over 21 days with 2 runs per day and duplicate measurements per run and specimen.

The tables shows the results obtained for a representative lot.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean mg/L</th>
<th>SD mg/L</th>
<th>CV %</th>
<th>Mean mg/L</th>
<th>SD mg/L</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample healthy</td>
<td>5.1</td>
<td>0.13</td>
<td>2.5</td>
<td>5.1</td>
<td>0.17</td>
<td>3.3</td>
</tr>
<tr>
<td>Sample cut off</td>
<td>10.0</td>
<td>0.23</td>
<td>2.3</td>
<td>10.0</td>
<td>0.24</td>
<td>2.4</td>
</tr>
<tr>
<td>Sample decision</td>
<td>39.9</td>
<td>0.93</td>
<td>2.3</td>
<td>39.9</td>
<td>0.98</td>
<td>2.5</td>
</tr>
<tr>
<td>Sample acute</td>
<td>93.4</td>
<td>1.62</td>
<td>1.7</td>
<td>93.4</td>
<td>1.84</td>
<td>2.0</td>
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<tr>
<td>Sample Acute high</td>
<td>351</td>
<td>7.99</td>
<td>2.3</td>
<td>351</td>
<td>8.42</td>
<td>2.4</td>
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<tr>
<td>Control level 1</td>
<td>9.7</td>
<td>0.29</td>
<td>2.9</td>
<td>9.7</td>
<td>0.30</td>
<td>3.1</td>
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<tr>
<td>Control level 2</td>
<td>39.2</td>
<td>0.79</td>
<td>2.0</td>
<td>39.2</td>
<td>1.09</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Source: Package Insert of the cobas b 101 CRP Test
Analytical performance of CRP testing on the cobas b 101
Fulfils the acceptance criteria for method comparison vs. reference system

Method comparison

The graph shows a comparison for serum samples with cobas CRP Test on the cobas b 101 instrument (y) and CRP-latex X2 “Seiken” NX reagent on the cobas c 501 analyzer (x).

The regression was calculated with the weighted Deming method which is the official regression method defined in the acceptance criteria for the Method comparison.

Source: Package Insert of the cobas b 101 CRP Test