Antibiotics *in vitro*:

Which properties do we need to consider for optimizing our therapeutic choice?

With the support of *Wallonie-Bruxelles-International*
In vitro evaluation of antibiotics: the antibiogram

- semi-quantitative evaluation

Disk loaded with antibiotic → Agar inoculated with bacteria → incubation at 37°C

- susceptible
- intermediate
- resistant
In vitro evaluation of antibiotics: the antibiogram

⇒ semi-quantitative evaluation

Disk loaded with antibiotic \[\rightarrow\] Agar inoculated with bacteria

But where is the limit?

susceptible \[\leftrightarrow\] intermediate \[\leftrightarrow\] resistant

incubation at 37°C
In vitro evaluation of antibiotics: MIC

Quantitative evaluation

1. Inoculation

Known amount of bacteria

<table>
<thead>
<tr>
<th>Antibiotic Concentration</th>
<th>Time (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0.25</td>
<td>0.25</td>
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<tr>
<td>0.5</td>
<td>0.5</td>
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<tr>
<td>1.0</td>
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<tr>
<td>2.0</td>
<td>2.0</td>
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<tr>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>8.0</td>
<td>8.0</td>
</tr>
<tr>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

Increasing antibiotic concentrations
In vitro evaluation of antibiotics: MIC

quantitative evaluation

2. incubation

0 µg/mL  0.25 µg/mL  0.5 µg/mL  1.0 µg/mL  2.0 µg/mL  4.0 µg/mL  8.0 µg/mL  16 µg/mL

MIC = minimal antibiotic concentration able to prevent bacterial growth
In vitro evaluation of antibiotics: MIC

⇒ quantitative evaluation

3. interpretation

The most active is the drug, the smallest is the MIC
Susceptibilities of bacteria populations: MIC$_{50}$ and MIC$_{90}$
Susceptibilities of bacteria populations: 
\( \text{MIC}_{50} \) and \( \text{MIC}_{90} \)

« susceptible » « intermediate » « resistant »
Susceptibilities of bacteria populations: MIC$_{50}$ and MIC$_{90}$

- **MIC$_{50}$**: 0.25 µg/ml
- **MIC$_{90}$**: 4 µg/ml

```
% strains

0.01 0.02 0.03 0.12 0.25 0.5 1 2 4 8 16

« susceptible » « intermediate » « resistant »

51% 93%
```
MIC distributions: unimodal populations

- $\text{MIC}_{50} = 0.25$ µg/ml
- $\text{MIC}_{90} = 4$ µg/ml
MIC distributions: unimodal populations

But is the same amount of antibiotic needed to eradicate these two bugs?
MIC distribution: bimodal populations

- MIC_{50} = 0.25
- MIC_{90} = 16

50% and 90% thresholds are indicated on the graph.
MIC distribution: bimodal populations

And to eradicate those ones?
MIC distribution: bimodal populations

50% at MIC$_{50}$: 0.25
90% at MIC$_{90}$: 16
bacteriostatic $<$ bactericidal activity

- **Bacteriostatic**: prevents bacterial growth
- **Bactericidal**: kills bacteria

**Telithromycin vs S. aureus**

**Moxifloxacin vs S. aureus**

Seral et al, AAC (2003) 47:228 3-2292
bacteriostatic $\Rightarrow$ bactericidal activity

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**Telithromycin vs S. aureus**

**Moxifloxacin vs S. aureus**

Seral et al, AAC (2003) 47:228-2292
bacteriostatic $\leftrightarrow$ bactericidal activity

- **Bacteriostatic**: prevents bacterial growth
  - Cooperation with host defences needed
  - Caution: immunosuppressed patients
    - Macrolides
    - Tetracyclines
    - Glycopeptides

- **Bactericidal**: kills bacteria
  - Able to eradicate infection by itself
  - Fluoroquinolones
  - Aminoglycosides
  - $\beta$-lactams
narrow => broad spectrum

- **Narrow spectrum**: active on a small number of bacterial species
  - Targetted treatment of documented infections

- **Broad spectrum**: active on a large number of bacterial species
  - Empiric treatment of non documented infections
  - Risk for selection of resistance

Some β-lactams, glycopeptides, macrolides, aminoglycosides, fluoroquinolones, tetracyclines, sulfamides, some β-lactams
Conclusions: how to choose an antibiotic on the basis of its microbiological properties?

1. Antibiotic with a spectrum as narrow as possible (depending on the suspected pathogens)

2. Bactericidal antibiotic preferred to bacteriostatic ones

3. Within a family, antibiotic with the lowest MIC of the most probable pathogens
But how shall we adapt the dosis to the MIC ?

Pharmacokinetics do describe this curve ...

Section 2