Antibiotic resistance in invasive bacterial infections in low-resources settings

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Invasive bacterial infections
Bloodstream infection

Europe: 150 cases per 100,000 persons/year

African children: > 2000 cases per 100,000/year

Asia: ???

Laupland, Clin Microbiol Infect 2013
Bloodstream infections (BSI)

- Mortality is influenced by:
  - Type of bacterium
  - Host health status
  - Type and treatment of infection

Survival chances improve through:

1. supportive (intensive) care
2. early and correct antibiotic therapy
Antibiotic resistance world wide

Molton, Clin Infect Dis 2013
Distribution of 450 key pathogens from BSI (SHCH 2007-2010)

- **Enterobacter spp. (n = 14)**
- **Acinetobacter spp. (n = 21)**
- **Klebsiella spp. (n = 34)**
- **Streptococcus spp. (n = 35)**
- **S. aureus (n = 54)**
- **B. pseudomallei (n = 56)**
- **Salmonella spp. (n = 66)**
- **E. coli (n = 133)**

Vlieghe et al, Plos One 2013
126 *E. coli* bloodstream infections

- 60 cephalosporin susceptible *E. coli* BSI
- 66 cephalosporin resistant *E. coli* BSI

65 ESBL+ *E. coli* BSI

- 32 CTX-M-15
- 6 CTX-M-55
- 17 CTX-M-14
- 7 CTX-M-27

77% co-resistant to SMX-TMP, ciprofloxacin, gentamicin

Use carbapenems: $$$ and further resistance induction
ESBL-positive *E. coli* in Asia

Impact in low-resources settings?

Cohort study
1828 Tanzanian children with fever
13.9% BSI

40% Enterobacteriaceae
⇒ ESBL 18%

Risk factors for mortality

• Gram- sepsis
• HIV+
• Malnutrition
• Inappropriate AB

Figure 3
Impact of antimicrobial resistance on survival from laboratory-confirmed bloodstream infection.
Human-animal overlapping resistance

Source: WHO 2005
Frequency of Severe Malaria and Invasive Bacterial Infections among Children Admitted to a Rural Hospital in Burkina Faso

Jessica Maltha¹,2*, Issa Guiraud³, Bérenger Kaboré³, Palpouguini Lombo³, Benedikt Ley¹, Emmanuel Bottieau¹, Chris Van Geet²,⁴, Halidou Tinto³, Jan Jacobs¹

- 2012-2013
- All children temp ≥ 39°C +/- severe illness’ signs

- n = 711 → 63 bacteremia + 6 meningitis

- Top 4 pathogens (> 80%)
  - Non-typhoid *Salmonella*
  - *Salmonella* Typhi
  - *Streptococcus pneumoniae*
  - *Escherichia coli*

- 28% had recently used AB (cotrim, amoxy)
Salmonella susceptibility

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Non-typhoid Salmonella</th>
<th>Salmonella Typhi</th>
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<tbody>
<tr>
<td></td>
<td>n = 21</td>
<td>n = 12</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>19 (90.5)</td>
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</tr>
<tr>
<td>Chloramphenicol</td>
<td>19 (90.5)</td>
<td>10 (83.3)</td>
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<tr>
<td>TMP-SMX</td>
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<tr>
<td>MDR</td>
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<td>Nalidixic acid</td>
<td>1 (4.8)</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>NA</td>
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<tr>
<td>DCS</td>
<td>1 (4.8)</td>
<td>0</td>
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<tr>
<td>ESBL confirmed</td>
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<tr>
<td>Azithromycin</td>
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<tr>
<td>Gentamicin</td>
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<td>NA</td>
</tr>
<tr>
<td>Meropenem/Ertapenem</td>
<td>NA</td>
<td>NA</td>
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</tbody>
</table>
Deaths attributable to antimicrobial resistance every year by 2050

Antibiotic use (rational + irrational) is an important fuelling factor

Source: Review on Antimicrobial Resistance 2014
Antibiotics to compensate for lack of diagnostic means
Antibiotics to compensate for lack of hygiene/infection control

‘Only 1 dose of surgical prophylaxis? Nooo...!
Our patients and hospitals are too dirty.
In this place, we need to give more and longer antibiotics...
This is not Europe...!’
Antibiotics as the cheapest solution

Invasive pneumococcal or staphylococcal infections:

IV penicillin or cloxacillin is most rational choice (q4-q6)

Ceftriaxone 1-2 g q24 is cheaper and easier to access...
Selling AB per tablet
... also for animals
Antibiotics to compensate (need for) training

Last training: 20 y ago...
Good training, (too) many students
Antibiotics as a status symbol

Antibiotic Sales in India by Type

Source: GARP
Retail sales of carbapenem antibiotics to treat Gram-negative bacteria are increasing rapidly in India and Pakistan.
The vicious circle of resistance

Increasing resistance

use of broad spectrum AB
Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study

Timothy RWalsh, Janis Weeks, David M Livermore, Mark A Toleman

Summary

Background Not all patients infected with NDM-1-positive bacteria have a history of hospital admission in India, and extended-spectrum β-lactamases are known to be circulating in the Indian community. We therefore measured the

Rapid communications

Detection of mcr-1 encoding plasmid-mediated colistin-resistant Escherichia coli isolates from human bloodstream infection and imported chicken meat, Denmark 2015

H Hasman¹, AM Hammerum¹, F Hansen¹, RS Hendriksen², B Olesen³, Y Agersø², E Zankari², P Leekitcharoenphon², M Stegger⁴, RS Kaas², LM Cavaco², DS Hansen³, FM Aarestrup², RL Skov¹
TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS

- Public awareness
- Sanitation and hygiene
- Antibiotics in agriculture and the environment
- Vaccines and alternatives
- Surveillance
- Rapid diagnostics
- Human capital
- Drugs
- Global Innovation Fund
- International coalition for action

https://amr-review.org/
Work to do...

Access to/ restrict drugs

Education

Revise treatment guidelines

Infection control

Surveillance
Blood culture-based surveillance

Individual patient management

Standard treatment guidelines writing
Clinician’s learning curve on melioidosis management, SHCH

<table>
<thead>
<tr>
<th>Years</th>
<th>% Bacteremia</th>
<th>% Mortality</th>
<th>% Correct directed treatment</th>
<th>% Correct empiric treatment</th>
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<tr>
<td>2007</td>
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<td>2008</td>
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<td>2011</td>
<td>88</td>
<td>16</td>
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March 6-24 2017

CONTAINMENT OF ANTIBIOTIC RESISTANCE IN HOSPITALS IN LOW RESOURCES SETTINGS

TRUNCUS COMMUNIS (all participants)
AND
TRACK SPECIFIC MODULES (per track)

A  ANTIBIOTIC STEWARDSHIP
   MEDICAL DOCTORS
   PHARMACISTS

I  INFECTION PREVENTION & CONTROL
   NURSES
   MEDICAL DOCTORS

M  MICROBIOLOGICAL SURVEILLANCE
   MICROBIOLOGISTS
   LABORATORY TECHNICIANS

INTERACTIVE
GROUP WORK: HOSPITAL COMMITTEE
PERSONAL PROJECT: MY HOSPITAL

METHODS
PRACTICE
CARROUSSEL
LECTURES

MULTIDISCIPLINARY
