Perspectives on emerging multidrug resistant organisms in the pediatric setting

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27th April 2018; 18th KPA Annual Scientific Conference
Venue: Pride Inn Hotel, Mombasa KENYA
# Bacteremia among Children Admitted to a Rural Hospital in Kenya

**Table 2. Bacterial Species Isolated from 1094 Patients with Bacteremia.**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>&lt;7 Days</th>
<th>7–59 Days</th>
<th>60–364 Days</th>
<th>≥1 Yr</th>
<th>Total (All Ages)</th>
<th>Rank of Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number of isolates (percent)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gram-positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>5 (4)</td>
<td>14 (12)</td>
<td>63 (20)</td>
<td>200 (34)</td>
<td>282</td>
<td>1</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>7 (5)</td>
<td>13 (12)</td>
<td>17 (5)</td>
<td>41 (7)</td>
<td>78</td>
<td>5</td>
</tr>
<tr>
<td>Group A streptococci</td>
<td>3 (2)</td>
<td>17 (15)</td>
<td>10 (3)</td>
<td>18 (3)</td>
<td>48</td>
<td>7</td>
</tr>
<tr>
<td>Group B streptococci</td>
<td>11 (9)</td>
<td>15 (13)</td>
<td>0</td>
<td>2 (&lt;1)</td>
<td>28</td>
<td>10</td>
</tr>
<tr>
<td>Other†</td>
<td>11 (9)</td>
<td>3 (3)</td>
<td>11 (4)</td>
<td>11 (2)</td>
<td>36</td>
<td>—</td>
</tr>
<tr>
<td><strong>Gram-negative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-typhoidal salmonella species</td>
<td>1 (&lt;1)</td>
<td>4 (4)</td>
<td>56 (18)</td>
<td>105 (18)</td>
<td>166</td>
<td>2</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>1 (&lt;1)</td>
<td>7 (6)</td>
<td>62 (20)</td>
<td>66 (11)</td>
<td>136</td>
<td>3</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>25 (19)</td>
<td>8 (7)</td>
<td>41 (13)</td>
<td>47 (8)</td>
<td>121</td>
<td>4</td>
</tr>
<tr>
<td>Acinetobacter species</td>
<td>16 (12)</td>
<td>9 (8)</td>
<td>16 (5)</td>
<td>30 (5)</td>
<td>71</td>
<td>6</td>
</tr>
<tr>
<td>Pseudomonas species</td>
<td>6 (5)</td>
<td>3 (3)</td>
<td>15 (5)</td>
<td>15 (3)</td>
<td>39</td>
<td>8</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td>13 (10)</td>
<td>7 (6)</td>
<td>7 (2)</td>
<td>9 (2)</td>
<td>36</td>
<td>9</td>
</tr>
<tr>
<td>Other‡</td>
<td>30 (23)</td>
<td>12 (11)</td>
<td>12 (4)</td>
<td>37 (6)</td>
<td>91</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>129</strong></td>
<td><strong>112</strong></td>
<td><strong>310</strong></td>
<td><strong>581</strong></td>
<td><strong>1132</strong></td>
<td></td>
</tr>
</tbody>
</table>

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NEJM Study – Bacterial infections & bacteremia a major problem in Kenya
Observations from this Kenyan study

Current figures underestimate actual incidence of bacterial sepsis:

- blood cultures are insensitive for detecting bacteremia
- Small volumes of inoculation and the use of antibiotics may compromise the sensitivity of blood cultures
- Recent antibiotic use reduced blood-culture yields by 62 to 73 percent in patients with severe or fatal disease.

66 percent of deaths of children between the ages of 3 months and 5 years occur outside hospitals

There's a large burden of undetected bacteremia with additional attributable mortality.
Community-acquired bloodstream infections in Africa: a systematic review and meta-analysis

22 studies - 58 296 patients with at least a blood culture:

- (13.5%) of adults and (8.2%) of children had bloodstream infections.
- (29.1%) non-malaria bloodstream infections were due to *Salmonella enterica* (58.4% of these non-typhoidal *Salmonella*),
- *Streptococcus pneumoniae* - most common isolate in children.
- Other isolates included *S. aureus* (9.5%) and *E. coli* (7.3%). *MTB* complex (30.7%) of 539 isolates in 7 studies that used mycobacterial culture techniques.
- HIV was associated with any BSI, esp with *S enterica* and *M tuberculosis* complex bacteraemia.
- Patients with BSIs had an in-hospital case fatality of 18.1%.
ESCAPE Pathogens remain a major concern

- Enterococcus
- Staph aureus
- Clostridium difficile/candida
- Acinetobacter
- Pseudomonas
- Enterobacteriaceae
Extended-spectrum β-lactamase (ESBL)

• MDR caused by ESBL production among Enterobacteriaceae is a growing global concern

• Extended-spectrum β-lactamases are enzymes that:
  1. hydrolyse oxyiminocephalosporins (e.g. cefotaxime, ceftriaxone and ceftazidime) and monobactams,
  2. do not inactivate the cephemycins (e.g. cefoxitin) and carbapenems,
  3. are inhibited by β-lactamase inhibitors such as clavulanic acid and tazobactam.

• The most frequently encountered ESBLs in clinical isolates are members of the SHV, TEM and CTX-M families.
**Extended-spectrum β-lactamase (ESBL)**

- E.coli and K. pneumoniae are 2 of the main ESBL-prod orgs
  - Enzymes belonging to the CTX-M family are most prevalent and are predominantly found in E. coli isolates.

- Patients with infections caused by ESBL-producing Enterobacteriaceae may experience poor outcome because of:
  - delays in initiating effective antimicrobial therapy
  - and/or availability of limited antibiotic options, resulting in high mortality

- New drugs were developed to counter emerging β-lactamase enzymes eg piperacillin, 3rd & 4th GC, clavulanate, tazobactam

- ESBLs emerged which hydrolyse them
  - Mostly also resistant to non β-lactams
  - Only carbapenems reliably effective
• 410 hospitalised children with lab confirmed KPBSI

• 339 (83 %) were caused by ESBL producing isolates.

• The median age (IQR) was 5.0 (2–16) months, 212 (51.7 %) were male,

• 20 % were HIV-infected
• 58.8 % were moderately or severely underweight.

• The infection was HA or HCA in 389 (95 %) children and community-acquired in 21 (5 %) children.
Significant risk factors for ESBL-KPBSI:

- Cephalosporin exposure in the 12 months prior to the KPBSI
- HIV infection
- IV infusions for > 3 days before the KPBSI

26.6% children died within 30 days, median age 4 (IQR 1–11) months.

The median (IQR) time between KPBSI and death was 3 (1–9) days.

Significant risk factors for death:

- HIV-infection,
- Skin erosions at the time of KPBSI,
- Being in PICU at the time of the KPBSI,
- Needing PICU admission after developing KPBSI
Annual incidence risk of *E. coli* bloodstream infection per 1000 hospital admissions at RCWMCH, 2005 – 2014.
**Escherichia coli** bloodstream infection at Red Cross War Memorial Children’s Hospital, Cape Town: 2005-2014

OO Malande MB ChB, MMed (Paed), Cert ID (SA) Paed¹,², J Nuttall MB ChB, DCH (SA), FCPaed (SA), MSc¹,², V Pillay MB ChB, MPH, DCH (SA)¹,², C Bamford MB ChB, DCH (SA), MPhil (Mat Child Health), FCPpath (Microbiol), MMed (Med Microbiol)³,⁴, B Eley MB ChB, FCPaed (SA), BSc Hons¹,²

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**Risk factors of death and / or admission to the intensive care unit**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Severe Infection N=67 (%)</th>
<th>No Severe Infection N=388 (%)</th>
<th>Crude Odds ratio (95% CI)</th>
<th>Adjusted Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 month of age</td>
<td>23 (34.3)</td>
<td>74 (19.1)</td>
<td>2.2 (1.3-3.9)</td>
<td>3.0 (1.4-6.3)</td>
</tr>
<tr>
<td>Hospitalization in the 12 months preceding <em>E. coli</em> BSI</td>
<td>42 (62.7)</td>
<td>158 (40.7)</td>
<td>2.4 (1.4-4.2)</td>
<td>3.3 (1.7-6.6)</td>
</tr>
<tr>
<td>BSI with no definable focus</td>
<td>39 (58.2)</td>
<td>48 (12.4)</td>
<td>9.9 (5.7-17.5)</td>
<td>8.2 (4.5-14.7)</td>
</tr>
</tbody>
</table>
Escherichia coli bloodstream infection at Red Cross War Memorial Children’s Hospital, Cape Town: 2005-2014

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Other observations

• *E. coli* BSI mainly manifested without a definable clinical focus. Rarely: UTI/GIT disease

• 88% and 98% of the non-ESBL *E. coli* strains were susceptible to combinations of amp&gent, and piptaz/amik respectively. These antibiotic combinations are recommended as empiric therapy for CA and HA BSI, respectively.

• mortality was higher in patients with ESBL-ECBSI treated with piptaz/amik compared to a carbapenem as definitive therapy.
Other observations

• **Mortality was higher in patients with ESBL-ECBSI treated with piptaz/amik compared to a carbapenem as definitive therapy.**

• An RCT that determined whether piptaz was as effective as meropenem for treating BSI caused by *E. coli* or *K. pneumoniae* with non-susceptibility to third generation cephalosporins found mortality at 30 days after randomization, the study’s primary outcome measure was significantly higher in the piptaz group, indicating that piptaz should no longer be used as definitive therapy in this context.

• **Recent study - Risk factors for severe disease {admission to the ICU and / or death during the *E. coli* BSI} – age< 3 months and non-urinary BSI were sig associated with severe disease.**
  • Our analysis - age < 1 month and BSI without a definable focus of infection as predictors of severe disease.
Carbapenem Resistant Enterobacteriaceae (CRE)

Clinically relevant carbapenemases belong to three of these classes, namely:

- **Class A** β-lactamases such as Klebsiella pneumoniae carbapenemase (KPC) and Guiana extended-spectrum carbapenemase (GES)

- **class B** metallo-β-lactamases such as Verona integron-mediated metallo-β-lactamase (VIM), imipenemase (IMP) and New Delhi metallo-β-lactamase (NDM)

- **Class C** AmpC, FOX, CMY, LAT, ACC, DHA

- **class D** β-lactamases including oxacillinase (OXA) subtypes such as OXA-48

Bradford *CID* 2004  
Segal *South Afr J Epidemiol Infect* 2006  
Elliott *CID* 2006  
Brink *J Clin Micro* 2012
Carbapenem Resistant Enterobacteriaceae (CRE)

- Invasive infection caused by CRE, first documented in the late 1990s

- CREs have become a serious global public health problem.

- Resistance to carbapenems may result from several mechanisms, including:
  1. alteration of outer membrane permeability due to loss of porins,
  2. upregulation of efflux systems together with extended-spectrum β-lactamases (ESBLs),
  3. or commonly the production of carbapenemases.

Bradford CID 2004
Segal South Afr J Epidemiol Infect 2006
Elliott CID 2006
Brink J Clin Micro 2012
CRE risk factors

- previous admission to an intensive care unit (ICU),
- hospitalisation for >48 hours,
- Presence of an indwelling device,
- underlying chronic medical conditions,
- necrotizing enterocolitis and/or short-bowel syndrome,
- solid organ or stem cell transplantation,
- exposure to immunosuppressants,
- previous exposure to antibiotics, including third-generation cephalosporins, fluoroquinolones or carbapenems, and
- previous infection by a multidrug-resistant organism.
9 CRE infections were caused by *K. pneumoniae*, and one by both *K. pneumoniae* and *E. coli*.

The median age was 25 months (interquartile range (IQR) 5 - 60).

All 10 CRE infections were HA.

Median length of hospitalisation before CRE infection was 28.5 days (IQR 20 - 44).

8/10 children were exposed to carbapenems during the 12-month period prior to invasive CRE infection.

Six were treated with colistin and carbapenem combination therapy, of whom 2 died, including 1 of a non-CRE event.

The other 4 children received colistin monotherapy. All these children died, including 2 from non-CRE events.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Specimen type</th>
<th>Carbapenem-resistant pathogens</th>
<th>Carbapenemase gene</th>
<th>MICs</th>
<th>Antibiotic susceptibility profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Peritoneal swab</td>
<td><em>K. pneumoniae</em></td>
<td>Negative</td>
<td>Meropenem: 1 µg/mL. Imipenem: 1 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Meropenem, imipenem, colistin</td>
</tr>
<tr>
<td>2</td>
<td>Peritoneal swab</td>
<td><em>E. coli</em></td>
<td><em>bla</em>$_{NDM}$</td>
<td>Meropenem: 2 µg/mL. Imipenem: 4 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Tigecycline, colistin</td>
</tr>
<tr>
<td>2</td>
<td>Peritoneal swab</td>
<td><em>K. pneumoniae</em></td>
<td><em>bla</em>$_{NDM}$</td>
<td>Meropenem: &lt;1 µg/mL. Imipenem: &lt;1 µg/mL. Ertapenem: 1 µg/mL.</td>
<td>Amikacin, imipenem, meropenem, tigecycline, colistin</td>
</tr>
<tr>
<td>3</td>
<td>Blood culture</td>
<td><em>K. pneumoniae</em></td>
<td><em>bla</em>$_{GES}$</td>
<td>Meropenem: &gt;32 µg/mL. Imipenem: &gt;32 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Amikacin, colistin</td>
</tr>
<tr>
<td>4</td>
<td>Blood culture</td>
<td><em>K. pneumoniae</em></td>
<td>Negative</td>
<td>Meropenem: 8 µg/mL. Imipenem: 2 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Ciprofloxacin, tigecycline, colistin</td>
</tr>
<tr>
<td>5</td>
<td>Blood culture</td>
<td><em>K. pneumoniae</em></td>
<td>Negative</td>
<td>Meropenem: 4 µg/mL. Imipenem: 1 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Imipenem, tigecycline, colistin</td>
</tr>
<tr>
<td>6</td>
<td>Blood culture</td>
<td><em>K. pneumoniae</em></td>
<td><em>bla</em>$_{NDM}$</td>
<td>Meropenem: &gt;16 µg/mL. Imipenem: &gt;16 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Colistin</td>
</tr>
<tr>
<td>7</td>
<td>Blood culture</td>
<td><em>K. pneumoniae</em></td>
<td>Negative</td>
<td>Meropenem: 2 µg/mL. Imipenem: 0.5 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Amikacin, imipenem, colistin</td>
</tr>
<tr>
<td>8</td>
<td>Pleural fluid</td>
<td><em>K. pneumoniae</em></td>
<td><em>bla</em>$_{NDM}$</td>
<td>Meropenem: &gt; 32 µg/mL. Imipenem: &gt;32 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Amikacin, colistin</td>
</tr>
<tr>
<td>9</td>
<td>Burn tissue swab</td>
<td><em>K. pneumoniae</em></td>
<td>Not done</td>
<td>Meropenem: &gt;16 µg/mL. Imipenem: &gt;32 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Colistin</td>
</tr>
<tr>
<td>10</td>
<td>Blood culture</td>
<td><em>K. pneumoniae</em></td>
<td>Not done</td>
<td>Meropenem: 0.5 µg/mL. Imipenem: 0.5 µg/mL. Ertapenem: &gt;8 µg/mL.</td>
<td>Ciprofloxacin, amikacin, imipenem, meropenem, gentamicin, colistin</td>
</tr>
</tbody>
</table>
Table 2. Potential factors contributing to CRE infection (N=10)

<table>
<thead>
<tr>
<th>Factor</th>
<th>n (%)</th>
<th>Corresponding cases as shown in Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer in from another hospital</td>
<td>2 (20)</td>
<td>1, 10</td>
</tr>
<tr>
<td>Colonisation with CRE within 6 months of invasive CRE infection</td>
<td>3 (30)</td>
<td>2, 6, 10</td>
</tr>
<tr>
<td>HIV infection</td>
<td>1 (10)</td>
<td>10</td>
</tr>
<tr>
<td>Parenteral nutrition at the time of CRE infection</td>
<td>2 (20)</td>
<td>1, 2</td>
</tr>
<tr>
<td>Exposure to carbapenems during the preceding 12 months</td>
<td>8 (80)</td>
<td>1, 2, 3, 4, 5, 8, 9, 10</td>
</tr>
<tr>
<td>Exposure to cephalosporins during the preceding 12 months</td>
<td>5 (50)</td>
<td>2, 3, 4, 5, 6</td>
</tr>
<tr>
<td>Exposure to fluoroquinolones during the preceding 12 months</td>
<td>5 (50)</td>
<td>3, 4, 5, 6, 9</td>
</tr>
<tr>
<td>Age &lt;1 year</td>
<td>4 (40)</td>
<td>2, 3, 4, 10</td>
</tr>
<tr>
<td>ICU admission within the month preceding CRE infection</td>
<td>8 (80)</td>
<td>1, 2, 3, 5, 6, 7, 9, 10</td>
</tr>
<tr>
<td>Surgical procedures/operations within the month preceding CRE infection</td>
<td>6 (60)</td>
<td>1, 2, 4, 6, 7, 8</td>
</tr>
<tr>
<td>Central intravenous catheterisation within the month preceding CRE infection</td>
<td>4 (40)</td>
<td>2, 3, 5, 6</td>
</tr>
<tr>
<td>Hospitalisation for a period of &gt;14 days within the 6 months preceding CRE infection</td>
<td>8 (80)</td>
<td>1, 2, 3, 5, 7, 8, 9, 10</td>
</tr>
<tr>
<td>Two or more hospital admissions within the 12 months preceding CRE infection</td>
<td>3 (30)</td>
<td>3, 5, 8</td>
</tr>
<tr>
<td>Immunosuppressive therapy, including glucocorticostoid therapy, for ≥3 months at the time of CRE infection</td>
<td>3 (30)</td>
<td>4, 5, 8</td>
</tr>
</tbody>
</table>
Observations from our recent CRE study

• Inadequate infection control practice maybe contributing to CRE emergence

• Colonisation of MDR pathogens/CRE may persist for lengthy periods.

• Persistent carriage is an important reservoir for their spread.

• Asymptomatic faecal carriage among hospitalised children may be widespread.

• Combination therapy is superior in patients with severe infections.
  • Colistin plus a carbapenem/tigecycline/aminoglycoside, or colistin plus a carbapenem plus tigecycline.

• When combining colistin with a carbapenem, an additive effect may be achieved if the carbapenem MIC is ≤ 4 μg/mL and possibly if ≤ 8 μg/mL.
Colistin Resistance: Plasmids

• mcr-1 & mcr-2 genes readily passed between E coli strains & Klebsiella & P. aeruginosa strains

• 29/6/17 mcr-3 gene discovered in a sample from a pig in China on a plasmid containing 18 additional resistance genes from an E coli

• Now also reported outside Asia in cattle from Spain & Denmark in S. enterica

• mcr-4 now identified in a 2013 pig sample from Italy & Spain & Belgium

Yin W mBio8:e00543-17
https://doi.org/10.1128/mBio.00543-17
Ways to overcome this problem
Bundles of care

• Hand hygiene

• Maximal barrier precautions on insertion

• Chlorhexidine skin antisepsis

• Optimal selection of catheter site

• Daily review of necessity of CVC

IHI Improvement Map:
Antibiotic Stewardship

• Decrease use

• Drug – narrowest spectrum?

• Dose: PK/PD principles (T>MIC, AUIC, Peak to MIC ratio), weight, ARC, Vd

• Duration: short as possible

• Delivery route: oral/IV

• De-escalation
: PK/PD

Peak to MIC ratio
AUIC >120
For efficacy
T > MIC

Serum Antibiotic Concentration (mcg/mL)

Dose

Time (hours)
Use Antibiotics Correctly:
Targeting of Higher MICs with Infusion & Increasing Dose

MIC, µg/mL

Target Attainment %

0 20 40 60 80 100

0.06 0.12 0.25 0.5 1 2 4 8 16

500mg tds over 1h
500mg tds over 4-h

*Probability of attaining 35% T > MIC based on Monte Carlo simulation. In vivo

Bhavnani AAC 2005
Continuous Infusion vs Intermittent in Severe Sepsis (BLISS)

• N=140: CI had:
  
  • Higher clinical cure (56 vs 34%, p = 0.011)
  
  • Higher median ventilator-free days (22 vs 14 days p<0.043)
  
  • Higher PK/PD target attainment 100% fT[MIC] on day 1 (97 vs 70%, p<0.001) & day 3 (97 vs 68%, p<0.001)
  
• No difference in 14 or 30-day survival

Abdul-Aziz Intensive Care Med 2015
De-escalation

• De-escalate whenever possible

• Conversion to monotherapy or narrow spectrum once culture available

• Always re-evaluate:
  • No culture pre empiric therapy
  • Duration of antibiotics > 7 days
  • Duration > 14 days
  • Redundant/double cover
  • Patients on > 4 antibiotics

Decrease Use as Growth Promoters

- In the USA in 2011 13.6 million kilograms of antibiotics were used as growth promoters representing 80% of all antibiotics sold.

- 72% of these are medically important for humans

- 38.5 million Kg used in China for swine and poultry alone

- Association with acquisition of resistant bacteria by humans is becoming increasingly clear

FDA Summary report 2013: Antimicrobials sold or distributed
For use in food producing animals
Wei Chemosphere 2011
Decrease Use: Vaccines: IPD pre & Post PCV-7

A

PCV7 serotypes

90
80
70
60
50
40
30
20
10
0

Cases/100,000 population

1998 1999 2000 2001 2002 2003 2004

Baseline Year

PCV7 introduced

Nonvaccine serotypes

Children aged <5 years

B

PCV7 serotypes

40
35
30
25
20
15
10
5
0

Cases/100,000 population

1998 1999 2000 2001 2002 2003 2004

Baseline Year

PCV7 introduced

Nonvaccine serotypes

Adults aged >65 years

Hicks JID 2007
Pneumococccoccal Vaccine & Antibiotic Use: Paediatrics

- RDBCT assessed efficacy of PCV7 vs placebo in children from California

- PCV 7 reduced OM visits by 7.0% after ≥1 dose

- Vaccine prevented 35 antibiotic prescriptions /100 vaccinated children- a potential reduction of 1.4 million prescriptions annually in US

Fireman Pediatr Infect Dis J 2003
Consequence of Decreased Use: Reduced Pneumococcal Resistance in SA

Figure 3. Incidence of Disease Caused by Non-Susceptible Pneumococcal Isolates Among All Ages by Year and Antimicrobial Agent. South Africa, 2005-2012

Von Gottberg A, et al. NEJM 2014
Influenza Vaccine

• Influenza vaccination reduced acute respiratory illnesses, febrile episodes, ILI & healthcare visits in neonates born to vaccinated mothers by 37.7%, 50.3%, 53.5% & 41.8%, respectively

• Reduced antibiotic prescriptions by 45.4%

Maltezou Clin Infect Dis 2013
Duration: Short-Course Therapy is Equivalent to Longer Therapy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment, Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia¹-³</td>
<td>3-5</td>
</tr>
<tr>
<td>Nosocomial pneumonia⁶,⁷</td>
<td>≤8</td>
</tr>
<tr>
<td>Pyelonephritis¹⁰</td>
<td>5-7</td>
</tr>
<tr>
<td>Intraabdominal infection¹¹</td>
<td>4</td>
</tr>
<tr>
<td>Acute exacerbation of chronic bronchitis and COPD¹²</td>
<td>≤5</td>
</tr>
<tr>
<td>Acute bacterial sinusitis¹³</td>
<td>5</td>
</tr>
<tr>
<td>Cellulitis¹⁴</td>
<td>5-6</td>
</tr>
<tr>
<td>Chronic osteomyelitis¹⁵</td>
<td>42</td>
</tr>
</tbody>
</table>

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Duration of Therapy

• Direct therapy to clinical response/CRP/PCT

• Sepsis after 2-3 days usually source control; possibly inappropriate ABs in HA infection

• 7 days on average, 10 days pseudomonas

• Discontinue if: Non infectious aetiology
  : Clinical resolution

CRP: C-reactive protein; PCT: procalcitonin; SIRS: systemic inflammatory response syndrome; AB: antibiotic; HA: hospital acquired

Thank you