Three epidemics of multidrug resistant invasive Salmonella disease in Blantyre, Malawi

Nick Feasey, Gordon Dougan, Melita Gordon, Robert Heyderman

3rd May 2105
Malawi Liverpool Wellcome Trust Clinical Research Programme at Queen Elizabeth Central Hospital
Longitudinal bacteraemia surveillance since 1998
Relationship between MDR and incidence of NTS serovars

[Graph showing the relationship between MDR and incidence of NTS serovars from 1998 to 2004.

Legend:
- Red bars: S. Enteritidis isolates
- Blue bars: S. Typhimurium isolates
- Red line: % S. Enteritidis MDR
- Blue line: % S. Typhimurium MDR]
Risk factors for iNTS disease

- Bimodal age distribution
- Adults with severe HIV
- Children with
  - HIV
  - Malaria
  - Malnutrition
Susceptible host or novel pathogen?

Msefula, Kingsley Gen Res 2009
Okoro et al Nat Gen 2012
Novel MDR plasmid associated with ST313
Prior to the epidemic of S. Typhimurium ST313, there was an epidemic of S. Enteritidis
Novel clades of S. Enteritidis restricted to sub-Saharan Africa with MDR-plasmids

Global epidemic

South/East Africa

West Africa

MS in preparation
NTS remains a prominent pathogen, but MDR S. Typhi has now emerged

- All 3 epidemics preceded by the emergence of MDR
- Reports of ESBL STm and SEn
- FQR STm
- 1 phenotypic DCS & no ESBL amongst S. Typhi

Feasey et al EID 2014 & Feasey et al MS in prep
H58-S. Typhi, but with chromosomal MDR locus

Key (Malawian isolates only):

Clade/Haplotype: 1/H55 2/H50 3/H42 4/H54 5/H58

Year: Pre-2010 2010-2011 2012-2013

Scale bar

S. Paratyphi A

Feasey et al PLoS NTDs 2015
## Clinical features and complications of iNTS disease

<table>
<thead>
<tr>
<th></th>
<th>2001</th>
<th>2009-11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruited</td>
<td>100</td>
<td>63</td>
</tr>
<tr>
<td>Inpatient mortality</td>
<td>47%</td>
<td>11%</td>
</tr>
<tr>
<td>1 year mortality</td>
<td>77%</td>
<td>38%</td>
</tr>
<tr>
<td>HIV positive</td>
<td>99%</td>
<td>98%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>43% (19/44)</td>
<td>5% (3/56)</td>
</tr>
<tr>
<td>Multiple recurrences</td>
<td>11% (5/44)</td>
<td>2% (1/56)</td>
</tr>
</tbody>
</table>
Clinical features and complications of S. Typhi

<table>
<thead>
<tr>
<th></th>
<th>Adults (n= 77)</th>
<th>Children (n=330)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16% HIV infected</td>
<td>HIV data pending</td>
</tr>
<tr>
<td></td>
<td>5% severe/complicated</td>
<td>21% complicated</td>
</tr>
<tr>
<td></td>
<td>1% perforation</td>
<td>2% perforation</td>
</tr>
<tr>
<td></td>
<td>4% mortality</td>
<td>2% mortality</td>
</tr>
</tbody>
</table>
Does iNTS disease still matter?

- Decline has leveled off
- Still a major pathogen
- iNTS disease likely to be responsible for approximately double the number of deaths caused by Typhoid fever in Blantyre, 2014
Conclusions

- 3 epidemics of Salmonella bloodstream infection since 1999
- Epidemics of iNTS disease associated with novel clades
- Recent emergence of H58-S. Typhi

- Risk factors for iNTS disease and Typhoid fever differ
- BUT all 3 epidemics associated with emergence of MDR
- In-turn driving increased use of cephalosporins and fluoroquinolones

- Reservoirs of pathovars associated with iNTS disease unknown
Acknowledgements

Sam Kariuki
Calman MacLennan
Robert Onsare
Franscois X Weill
Simon Le Hello
Karen Keddy
Anthony Smith
Michael McClelland
Prereak Desai
Xiangyu Deng
Christopher Parry
John Cheesbrough
Neil French
Jan Jacobs
Josephina Campos
Jose A Chabalgoity
Katie Hopkins
Tom J Humphrey
Tristan Cogan
Sharon Tennant
Kristen Bornstein
Myron Levine
Lizeth Lacharme-Lora

Theresa Feltwell
Simon Harris
Rob Kingsley
Del Pickard
Nick Thomson