Understanding transmission of invasive non-typhoidal *Salmonella*

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Salmonella taxonomy

<table>
<thead>
<tr>
<th>Species</th>
<th>S. enterica</th>
<th>S. bongori (V)</th>
<th>Subspecies</th>
<th>enterica (I)</th>
<th>salamae (II)</th>
<th>arizonae (IIIa)</th>
<th>diarizonae (IIIb)</th>
<th>houtenae (IV)</th>
<th>indica (VI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual habitat</td>
<td>Warm blooded animals</td>
<td>Cold-blooded animals and environment</td>
<td></td>
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</tbody>
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- >2600 serovars
- New serovars emerging
- Well-described host-specificity, but some serovars may be promiscuous
## Predominant invasive serovars

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>Typhimurium (1.6)</td>
<td>30%</td>
<td>11%</td>
<td>46%</td>
<td>4%</td>
</tr>
<tr>
<td>Enteritidis (1.8)</td>
<td>16%</td>
<td>20%</td>
<td>24%</td>
<td>19%</td>
</tr>
<tr>
<td>Heidelberg (7.0)</td>
<td>13%</td>
<td>12%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Dublin (33.3)</td>
<td>4%</td>
<td>4%</td>
<td>4%</td>
<td>-</td>
</tr>
<tr>
<td>Choleraesuis (55.2)</td>
<td>3%</td>
<td>-</td>
<td>&lt;1%</td>
<td>-</td>
</tr>
<tr>
<td>Schwarzengrund (10.8)</td>
<td>2%</td>
<td>-</td>
<td>&lt;1%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Newport (2.6)</td>
<td>-</td>
<td>5%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Virchow (4.4)</td>
<td>-</td>
<td>4%</td>
<td>1%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

*Vugia, 2004; **Laupland, 2010; ‡Unpublished data; ‡‡Langridge 2009
Mechanisms – 1

*Salmonella* and host adaptation

• Interaction with host through host-specific invasion: attachment, escape IR, survival in host macrophages & dendritic cells.

• Common core of virulence genes.

• *Salmonella* Pathogenicity Islands: genes encoding proteins responsible for host IR & virulence factors exploiting host processes.

• SPI1 -SPI5 common to all serovars.

• ~23 SPIs described.
Mechanisms (2)

- Person-to-person, including nosocomial disease – adaptation of “non-human serotypes” as human pathogens
  - *Salmonella* Typhimurium ST313 (Okoro *et al*; 2012)
  - New evidence that *Salmonella* Enteritidis has also become host adapted.
  - *Salmonella* Isangi – documented nosocomial outbreaks

Snapshot of dendrogram to illustrate PFGE banding patterns in invasive *Salmonella* Isangi isolates South Africa
Mechanisms (3)

• Environmental contamination – related to human-to-human transmission as well as foodborne disease:
  – Kenyan data suggest that in Africa different pathotypes circulate among humans versus domesticated animals: some environmental contamination (Kariuki et al; 2006).
  – Contamination of hospital environment in nosocomial transmission (Smith et al; 2014).
Foodborne disease – how host specific is this

- Reports of invasive *Salmonella* Enteritidis and *Salmonella* Typhimurium associated with foodborne outbreaks; molecular similarity to food animal isolates, including chicken, beef, pork.
- *Salmonella* Dublin - beef and dairy products: raw milk; raw calves’ liver
- *Salmonella* Newport - cattle & horse meat.
- *Salmonella* Choleraesuis - pork: localisation of disease in elderly.
- Rarer serotypes e.g. *Salmonella* Isangi – outbreak reports: pork, milk formula, chicken, eggs -

  Protein shakes widely used in RSA for AIDS patients pre-HAART?
Predisposing factors for invasive disease

- Extremes of age – the very old and the very young; role of HIV-exposure in HIV uninfected infants.
- Immunosuppression – HIV; malignancy; immunosuppressive therapy.
- Malnutrition
- Malaria
- Sickle cell disease
- Schistosomiasis
Other considerations

• Malaria - interaction with cells infected by *Plasmodium*.
• Sickle cell disease and malaria – role of abnormal iron metabolism and functional asplenia.
• Sickle cell disease - osteomyelitis.
• Predilection for damaged tissue.
• Genetic predisposition to disease – related to age, sex, race?
• Cystic fibrosis – CFTR association in typhoid fever – iNTS equivalent?
**Salmonella invasion**

Invasive *Salmonella* serovar

- SPI-1: Effector secretion
- SipA, SipB, SopB, SopD, SopE, SopE2

**Intestinal epithelium**

- Cytokine secretion: IL-1, IL-8, TNFα
- Basolateral invasion

**Macrophage**

- Phagocytosis
- Cytokine secretion: IL-1, IL-6, TNFα; IL-12, IL-8; IL-1β

**Translocation across epithelial barrier**

**M cell**

- Basolateral reseeding of epithelial cells

Adapted from Hurley et al, 2014
Host Immunity

- Host-specific *Salmonella* serovars – adapted to overcoming immunity in that host only
- Capitalise on immature / malfunctioning immune systems: failure of “host-specific barrier” in preventing disease.
- Neonates and very young – failure of protective immunity from mother.

Feasey *et al*; 2012
Nosocomial transmission


• Increased risk of invasion with MDR serotypes.

• At-risk patients: immune-suppressed.

• Host adaptation may favour certain serotypes or pathotypes – non-invasive outbreak in neonates in RSA (2012) due to *Salmonella* Typhimurium ST19.
Age-related incidence rates – invasive disease

*Vugia et al; 2004

**Laupland et al; 2010
Age-related incidence: Global Burden of iNTS

Ao et al, 2015 (EID in press)
Invasive *Salmonella* cases, South Africa; 2003 - 2014

![Graph showing the incidence rate and number of cases of invasive *Salmonella* cases in South Africa from 2003 to 2014.](image-url)

- **Number of cases**
- **Incidence rate per 100,000**

- **Year**
- **2003**
- **2004**
- **2005**
- **2006**
- **2007**
- **2008**
- **2009**
- **2010**
- **2011**
- **2012**
- **2013**
- **2014**

**Graph description:**
- The graph illustrates the incidence rate and number of cases of invasive *Salmonella* infections in South Africa from 2003 to 2014.
- The incidence rate is shown on the right y-axis, ranging from 0 to 2.5 per 100,000 population.
- The number of cases is shown on the left y-axis, ranging from 0 to 1200.
- The x-axis represents the years from 2003 to 2014.

**Key observations:**
- The incidence rate and number of cases show fluctuations over the years.
- The peak incidence rate and number of cases occurred around 2006.
- There is a general decline in the incidence rate and number of cases from 2006 onwards.

**Source:**
- National Institute for Communicable Diseases
- Division of the National Health Laboratory Service
iNTS in HIV-uninfected population 2003-2013 in South Africa

- 594/3242 (18.3%) cases
- Commonest serotypes *Salmonella* Enteritidis (210; 35.4%) *Salmonella* Typhimurium (188; 31.6%) *Salmonella Isangi* (32; 5.4%) *Salmonella Dublin* (24; 4.0%).
- Associated with HIV-exposure; prematurity and PEM in children.
- Older children & adults: malignancy; DM; corticosteroid therapy; renal disease.
- Focal infections: septic arthritis; abscess.
Implications for control

• Need to understand where and why: food (including food animals); environment (including nosocomial); patient (immune suppression & genetics); population (vaccine campaigns etc).
• Need more evidence of host adaptation and how and where this occurs.
• Need more understanding of the immunology and the role of diseases besides HIV for management and prevention campaigns.
• Panel discussion: 3 May 2015
Thank you!

A Sooka
AM Smith
CED staff
GERMS-SA