Transmission of invasive non-Typhoidal *Salmonella*:

Household study from Burkina Faso supports human-to-human transmission

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iNTS in Burkina Faso – previous studies

iNTS primary cause of childhood bacteremia in Nanoro
- 10% of cultures positive, around 30% of positive blood cultures iNTS
- Population based incidence: 4,138 (95%CI: 3,740-4,572) per 100,000 per PYO
- Serotype distribution: Typhimurium 70%, Enteritidis 30%, others sporadically

Nanoro demographic health surveillance (DHS)
- Nanoro DHS catchment area spans 594.3 km² with a population density of 125/km²
- Holoendemic for *Plasmodium falciparum*, seasonal peak
- HIV prevalence 0.9% in 2013
- Population lives in close proximity to livestock

Zoonotic versus human-to-human reservoir and transmission?
Kariuki (2006): genetic relatedness iNTS isolates to isolates from livestock, soil, water and human stool (PGFE)
Dione (2007): genetic relatedness *Salmonella* gastroenteritis isolates to isolates from livestock

Clinical Research Unit of Nanoro (CRUN): Research institute with Health and Demographic Surveillance System (HDSS) in Rural African area.

**Study design**

- **Blood culture surveillance**
- **Blood culture confirmed iNTS**
- **Household visit**
- **Drinking water**
- **Household member stool**
- **Livestock stool (pooled)**

**Index isolate**
*Salmonella* from blood culture

**Household isolate**
*Salmonella* isolate obtained from household sampling

**Paired isolates**
Same serotype *Salmonella* isolate obtained from blood culture and household sampling

**Multilocus variable tandem repeat (MLVA) and Whole Genome Sequencing**
Household visits

- 29 household visits representing 32/42 (76.2%) eligible index patients
  - 2 households had two index patients, one household had a patient with recurrent infection

<table>
<thead>
<tr>
<th></th>
<th>Total obtained</th>
<th>Nrs. of Salmonella</th>
<th>Different serotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household members stool samples</td>
<td>290</td>
<td>18 (6.2%)</td>
<td>9 serotypes</td>
</tr>
<tr>
<td>Livestock pooled samples</td>
<td>186</td>
<td>16 (8.6%)</td>
<td>13 serotypes</td>
</tr>
<tr>
<td>Water samples</td>
<td>30</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Pairs and clusters

- 3 households (4 index patients; 3 household members): all *Salmonella* Typhimurium

- Clusters among household members
  - Drac 1 household 2 human stool samples
  - Derby 2 households 7 human stool samples

- Three serotypes (Brancaster, Tennessee, Muenster) were found in both human stool samples and livestock, but not in the same household.
### Study results

<table>
<thead>
<tr>
<th>May 2013 to August 2014</th>
<th>Serotypes of index patients</th>
<th>Serotypes in stool samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blood sample</td>
<td>Household members</td>
</tr>
<tr>
<td><em>Salmonella Typhimurium</em></td>
<td>26</td>
<td>3</td>
</tr>
<tr>
<td><em>Salmonella Enteritidis</em></td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>All other serotypes</td>
<td>1</td>
<td>15</td>
</tr>
</tbody>
</table>

- *Salmonella Binningen* -
- *Salmonella Brancaster* -
- *Salmonella Give* -
- *Salmonella Llandorff* -
- *Salmonella Poona* -
- *Salmonella Schwarzengrund* -
- *Salmonella Vilvorde* -
- *Salmonella non-typeable* -
- *Salmonella I 3,19:z:-* -
- *Salmonella I 4:b:-* -
**Paired *Salmonella* Typhimurium isolates obtained from index patients and corresponding household members**

<table>
<thead>
<tr>
<th>Household visit</th>
<th>* Days between sampling</th>
<th>Village</th>
<th>Index patient</th>
<th>Household member</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age (months)</td>
<td>Age (years)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sex</td>
<td>Sex</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Malaria diagnosis</td>
<td>MLVA type</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>17</strong></td>
<td>10</td>
<td>Boulpon</td>
<td>46</td>
<td>negative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>2-8-7-9-0210</td>
</tr>
<tr>
<td><strong>24</strong></td>
<td>8</td>
<td>Nazoanga</td>
<td>13</td>
<td>positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>2-7-10-8-0210</td>
</tr>
<tr>
<td><strong>28</strong></td>
<td>11</td>
<td>Nazoanga</td>
<td>42</td>
<td>negative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F</td>
<td>2-7-12-NA-0210</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td>11</td>
<td>negative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>2-7-10-8-0210</td>
</tr>
</tbody>
</table>

MLVA: multilocus variable number tandem-repeat analysis

* Number of days between inclusion of the index patient and the household visit.

** Two index patients from the same family, presenting with a 4-day delay.
Geographic distribution of isolates
Each index/household pair genetically strongly related

Isolates from the same village often closely related

Close clonal relation to isolates from DRC;

All Sequence Type (ST) 313 – Lineage II
Strengths and Limitations

Limitations
- Time between presentation index patient / household sampling
- Limited number of paired cases
- No food sampling
- No follow-up stool samples
- Water culture techniques; notoriously difficult to culture *Salmonella* from water

Strengths
- Despite logistic restraints 32 households sampled
- Good coverage
- Area of high co-habitation;
- Whole Genome Sequencing
• Limited overlap between serotypes obtained from human and livestock sources (in contrast to western countries)

• Strong genetic association between *Salmonella* Typhimurium isolates obtained from blood culture and stool samples from household members of the patient.

• Strong genetic association between *Salmonella* Typhimurium isolates obtained from human sources living within the same village around the same time.

• Incremental arguments for role of humans in transmission of pediatric iNTS.  
  Dione et al (2007): Overlapping serotypes but wide genetic variation between isolates from human gastroenteritis cases and livestock  
  Kariuki et al (2006): No evident genetic relatedness (PFGE) between isolates from iNTS cases and livestock living in the same compound in Kenya

• Vessel for transmission still uncertain: further research into day-to-day water and prepared food could provide insight.

In conclusion
Please feel free to ask your questions