“Typhoid Control and Elimination Efforts in Samoa in the Shadow of COVID-19”

Samoa Typhoid Fever Control Program
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Samoa Expanded Program on Immunization (EPI)
Teuila Pati

BMGF: Duncan Steele, Kirsten Vannice, Jessica Long, Supriya Kumar, Shauna Metschke, Anita Zaidi
The Polynesian Triangle within Oceania

- Distance from New Caledonia to Easter Island: 7149 km
- Distance from Easter Island to Tonga: 7347 km
- Distance from Tonga to New Caledonia: 8119 km
Epidemiological Model of Typhoid Fever and its Use in the Planning of Antityphoid Immunization and Sanitation Programmes

B. CVJETANOVIC, B. GRAB & K. UEMURA

*Bull. Wld. Hlth Org. 1971; 45:53-75*

Used demographic and disease burden data from Samoa (1960s) for the model to predict the impact from use of vaccine and sanitation interventions.

**Population:** ~150,000;

**Annual crude typhoid incidence:** 72/100,000

*Predicted that high coverage with an effective vaccine would have a strong impact*
In 2012, the Samoan gov’t became deeply concerned about endemic typhoid
2013 – Gov’t of Samoa & WHO invited MM Levine to Samoa as a WHO Consultant to design a Samoa Typhoid Fever Control Program
A plan for a Samoa Typhoid Fever Control Program was crafted.
Initial external funding came from the BMGF
3 Phases of the Samoa Typhoid Fever Control Program

• Preparatory Phase (~24 months)
  • Strengthen clinical microbiology
  • Create epidemiologic investigation capability

• Original Attack Phase Plan (~3 years)
  – Mass vaccination with Typbar-TCV of all Samoans 1-45 yrs of age
  – Routine toddler vaccination (Typbar-TCV, age 12 mos)
    – Ty21a live oral vaccine for persons > 45 years of age

• Consolidation Phase (3-5 yrs)
  – Enhanced surveillance for residual cases
  – Environmental microbiology to detect S. Typhi in wastewater & sewage
  – Intensive search to find all chronic carriers
  – Rx of chronic carriers (Samoan strains are ciprofloxacin-sensitive)
Expeditiously visit household (or school or workplace) of every confirmed typhoid case
• Epidemiologic investigation, questionnaire
• **Determine water source & sanitation facility**
• **3 stool cultures** from all contacts
• **Detect subclinical acute & chronic infections**
• Serum from all adult contacts for **Vi serology**
• **RUQ ultrasound of adult contacts** to find gallstones using hand-held POCUS device
• Place **Moore swabs in septic tank** (or latrines) and in intakes of untreated piped river water
• MDU performs whole genome sequencing of *S. Typhi* isolates within 3 weeks
Typhoid in Samoa by Island and Region

Savaii
Pop'n 44,797 (22.3%)
19 districts

Upolu
Pop'n 156,077 (77.7%)
24 districts

Incidence of confirmed typhoid fever (cases per 10^6 population in 2019)

- None (0)
- Very Low (1-9)
- Low (10-49)
- Medium (50-99)
- High (100-199)
- Very high (200-500)

Health facilities
- Hospital
- Health Center
- Rural District Hospital

Small triangles indicate three Upolu districts (▲) and one Savaii district (▼) that are geographically divided.

Typhoid remains endemic in Samoa, with a 2019 crude incidence of 69.7 cases/10^5.

Aggregated data from 2008-2019

Typhoid incidence is low among young children < 5 years, increases steadily from ages 5-24 yrs, peaks in ages 25-29 yrs, and then declines.

Savaii typhoid case clusters, June 19 – August 19, 2019

**FAMILY I (SATUPAITEA/SALELOLOGA)**
1. 21 yo M, BC+ on June 19, 2019
2. 13 yo M, BC+ on July 5, 2019
3. 17 yo f, BC+ on July 30, 2019
4. 18 yo M, BC+ on Aug 7, 2019

**FAMILY O (SALELOLOGA/SALELAVALU)**
1. 14 yo M, BC+ on June 22, 2019; he was ill while visiting family on Upolu in mid-June 2019
2. 1 yo M, BC+ on July 17, 2019
3. 9 yo f, BC+ on July 18, 2019
4. 17 yo f, BC+ on July 22, 2019

**FAMILY P (SALELOLOGA)**
1. 15 yo M, BC+ on July 23, 2019
2. 14 yo M, BC+ on Aug 1, 2019

**FAMILY S (SALELAVALU)**
1. 36 yo M, BC+ on June 27, 2019
2. 15 yo f, BC+ on Aug 15, 2019

**NON-FAMILY CASES (SALELAVALU)**
1. 7 yo f, BC+ on July 29, 2019
2. 29 yo M, BC+ on Aug 1, 2019

**FAMILY F/O (VAILELE, UPOLU) (relatives of family O)**
1. 1 yo M, BC+ on July 11, 2019; his 14 yo M uncle from Savaii, while ill with fever and malaise, visited these relatives on Upolu in June 2019
2. 23 yo M, BC+ on Aug 19, 2019. Father of the 1 yo M Upolu case; he visited Savaii during the 2nd week of Aug 2019
Even if a remediable mode of amplified transmission cannot be detected in Samoa, the susceptibility of Samoans to typhoid fever can be greatly diminished by the use of vaccines:

- **Vi-TT for all Samoans age 1 to 45 yrs**
- **Vi-TT for all toddlers age 12 mos**
- Ty21a live oral vaccine for persons age > 45 years (doesn’t stimulate Vi antibodies)
Total blood culture-confirmed typhoid fever cases (all ages) by 2-month intervals, on Upolu, January 2018 through April 2023.
Definitions of CONTROL and ELIMINATION of TF in Samoa

• **CONTROL** - <5 autochthonous cases/10^5/yr
  – Initially in priority target age groups (0-19 yrs; 20-45 yrs)
  – Ultimately in all ages (including >45 years)

• **ELIMINATION** - 0 autochthonous cases/10^5/yr
  – Systematic search for chronic typhoid carriers in Samoans >45 years
    • RUQ POCUS, stool cultures, Vi serology
    • Rx with 4 wks of oral ciprofloxacin or 2 weeks of i.v. ampicillin
    • Monitor all chronic carriers annually; health education
## Annual Total Typhoid Cases among Upolu Residents, by Age Group and Year

<table>
<thead>
<tr>
<th>Year</th>
<th>All ages</th>
<th>0-4 yrs</th>
<th>5-19 yrs</th>
<th>20-45 yrs</th>
<th>&gt;45 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Inc/10^5</td>
<td>Cases</td>
<td>Inc/10^5</td>
<td>Cases</td>
</tr>
<tr>
<td>2018</td>
<td>114</td>
<td>73.1</td>
<td>6</td>
<td>28.8</td>
<td>44</td>
</tr>
<tr>
<td>2019</td>
<td>103</td>
<td>65.5</td>
<td>9</td>
<td>42.8</td>
<td>39</td>
</tr>
<tr>
<td>2020</td>
<td>50</td>
<td>31.5</td>
<td>7</td>
<td>33.0</td>
<td>18</td>
</tr>
<tr>
<td>2021</td>
<td>34</td>
<td>21.2</td>
<td>3</td>
<td>14.0</td>
<td>13</td>
</tr>
<tr>
<td>2022</td>
<td>22</td>
<td>13.6</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>2023*</td>
<td>4</td>
<td>2.4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* January through April
What S. Typhi genotypes are in Samoa?

306 Samoan S. Typhi from 1983-2020, by year and genotype

Genotypes 3.5.4/3.5.3 comprise 95.4% (292/306)

Sikorski et al., mBio. 2022 (5):e0192022. PMID: 36094088
Dyson & Holt, J Infect Dis. 2021;224(12 Suppl 2):S775-S780. PMID: 34453548
How do Samoan S. Typhi genotypes compare globally?

306 Samoan S. Typhi from 1983-2020 versus 4,934 global S. Typhi

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Samoa</th>
<th>Non-Samoan</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5.4</td>
<td>285</td>
<td>1*</td>
</tr>
<tr>
<td>3.5.3</td>
<td>7</td>
<td>1*</td>
</tr>
<tr>
<td>4.1</td>
<td>11</td>
<td>137</td>
</tr>
<tr>
<td>2.2.1</td>
<td>1</td>
<td>19</td>
</tr>
<tr>
<td>2.3.2</td>
<td>1</td>
<td>49</td>
</tr>
<tr>
<td>3.5</td>
<td>1</td>
<td>92</td>
</tr>
<tr>
<td>Others</td>
<td>0</td>
<td>4,635</td>
</tr>
<tr>
<td>Subtotals</td>
<td>306</td>
<td>4,934</td>
</tr>
<tr>
<td>Total N</td>
<td>5240</td>
<td></td>
</tr>
</tbody>
</table>

*Australian isolations of unknown travel origin

Maximum-likelihood phylogeny

Genotype 3.5.3 is nested within genotype 3.5.4

Genotypes 3.5.4/3.5.3 are essentially exclusive to Samoa

Sikorski et al., mBio. 2022 (5):e0192022. PMID: 36094088
Dyson & Holt, J Infect Dis. 2021;224(12 Suppl 2):S775-S780. PMID: 34453548

Special Acknowledgement: Corin Yeats, PhD and Jason Sahl, PhD
Sub-lineages for epidemiologic analysis

- Molecular subtyping by genotype and sub-lineage

- **Hypothesis**: similar isolates represent a network or chain of infection via a common vehicle and/or source


186 Samoan *S. Typhi* from 2018-2020
WGS and epidemiologic linkages of infections

Epidemiologic linkages, e.g.
- Familial contact; same or different household
- Known recent gathering
- Repeat positive culture after 1 month

Dataset: 12 examples of epidemiologic linkages (EL) and 3 repeat positive (RP) cultures from same individual ~1 month apart

Epidemiologic linkages are supported by SNP cutoffs

Phylogeny supports 10/12 epidemiologic linkages with 0-3 SNP differences

EL5: different sub-lineages, 28 SNPs
EL11: same sub-lineage, 9 SNPs

SNP cutoff is not defined for S. Typhi
- ≤10 for S. enterica (Burnsed, 2019)
- ≤4 for S. Typhi (Schürch, 2018)

1-3 SNPs separate repeat positives cultures from same individual ~1 month apart

Genomic epidemiology during Consolidation Phase

- Unique genotypes (3.5.4/3.5.3) permit monitoring for importation
- Validated WGS framework and SNP typing to compare relatedness:

<table>
<thead>
<tr>
<th>Isolate Source*</th>
<th>Epidemiologic Tool</th>
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<tr>
<td>Sparse cases</td>
<td>-Blood culture surveillance (central and peripheral)</td>
</tr>
</tbody>
</table>
| Asymptomatic shedders (“carriers”) | -Household “SWAT team” investigations  
                                      -Village-level POCUS surveys for carriers |
| Environment     | -Moore swabs in septic tanks, sewers, and waterways |

*Culture-based methods required
A sunset on typhoid in Samoa? Stay tuned...