Update on enteric fever, South Africa

Background
South Africa is endemic for enteric fever caused by *Salmonella* Typhi, although the prevalence of disease is much lower than most other countries in sub-Saharan Africa. It is a Notifiable Medical Condition, meaning that all laboratory-confirmed cases must be officially reported to the Department of Health. However, reported cases significantly underrepresent the true number of cases. The likelihood that enteric fever cases are identified and diagnosed depends on many factors, including how ill the patient is, how aware of the disease healthcare workers are, whether blood culture tests are done, and how accessible laboratory testing for blood cultures is. Blood culture tests are not performed at all levels of health care and are not a routine investigation in many South African healthcare settings; blood culture tests are usually performed only for selected patients who are admitted to hospital. This means that many cases of enteric fever are likely missed across the country, especially those cases with milder disease as well as cases in areas of the country where the necessary laboratory testing is not readily accessible.

The number of reported enteric fever cases in South Africa has declined over the last few decades, and larger outbreaks have become less common. The most recent large outbreak occurred in Delmas in 2005, with over 2900 cases.

After the outbreak in Delmas in 2005, the number of enteric fever cases in South Africa has remained stable with less than 150 cases per year (an average of 97 cases per year) – Figure 7.

![Figure 7. Laboratory-confirmed enteric fever cases, South Africa, 1 January 2003 – 21 April 2022](image-url)
Over the past decade (since 2012), Gauteng Province usually reported the most cases per year followed by Western Cape, Mpumalanga and KwaZulu-Natal provinces (Figure 8).

During 2020 and 2021, the total number of enteric fever cases across the country (89 cases in 2020 and 134 cases in 2021) was similar to previous years. However, at a provincial level there was an increase in the number of cases reported from Western Cape and North West provinces in 2021 (Figure 9, arrows showing case numbers for WC (green line) and NW (red line)) with a concurrent decrease in the number of cases reported from Gauteng (blue line).

For Western Cape Province, the increase in cases for 2021 was clearly attributable to increased numbers of cases in only 3 districts (City of Cape Town Metro, Cape Winelands and Garden Route), and in North West Province the increase was solely due to cases in a single district (Dr Kenneth Kaunda District). Cases continue to be reported from both provinces in 2022.

Public and private laboratories throughout the country submit *Salmonella* Typhi isolates to the Centre for Enteric Diseases (CED), NICD, for further investigation. All isolates are investigated using whole-genome sequencing (WGS) and core-genome multilocus sequence typing (cgMLST) analysis. cgMLST analyses 3002 genes to assess genetic relatedness. A cluster is defined as a group of *Salmonella* Typhi isolates that on cgMLST analysis differ from each other by ≤5 alleles – this means that they are highly genetically related. Unfortunately, not all isolates are received, so cases with missing isolates cannot definitively be linked to or excluded from clusters.

**Genomic surveillance**

Fifty-eight cases of enteric fever have been reported nationally in 2022 to date (21 April 2022). Gauteng Province reported most cases (48%; 28/58), followed by Western Cape Province (22%; 13/58). North West and KwaZulu-Natal provinces each reported 10% (6/58) of the total cases, Free State Province reported three cases, and Eastern Cape and Limpopo provinces each reported a single case (Figure 9).

**Figure 8.** Proportion of laboratory-confirmed enteric fever cases by province, South Africa, 1 January 2003 – 21 April 2022.
i. Western Cape Province
The current status of the three clusters in Western Cape Province is summarised in Table 2 and Figure 10. The City of Cape Town cluster now comprises 18 cases, with five cases identified in 2022. The Garden Route cluster has 15 cases, with two cases identified in the current year. The last case in the Winelands cluster was identified in May 2021. Although six laboratory-confirmed cases of enteric fever were reported from the Winelands District between July 2021 and January 2022, none could be linked to the Winelands cluster on cgMLST.

Table 2. Western Cape Salmonella Typhi clusters, January 2020 – 21 April 2022*

<table>
<thead>
<tr>
<th>District</th>
<th>Number of cases</th>
<th>Date of first case</th>
<th>Date of most recent case</th>
</tr>
</thead>
<tbody>
<tr>
<td>City of Cape Town</td>
<td>18</td>
<td>November 2020</td>
<td>February 2022</td>
</tr>
<tr>
<td>Cape Winelands</td>
<td>11</td>
<td>July 2020</td>
<td>May 2021</td>
</tr>
<tr>
<td>Garden Route</td>
<td>15</td>
<td>August 2020</td>
<td>February 2022</td>
</tr>
<tr>
<td>Grand Total</td>
<td>44</td>
<td>July 2020</td>
<td>February 2022</td>
</tr>
</tbody>
</table>

*The results of WGS and cgMLST analysis are still pending for isolates from recent cases detected in City of Cape Town Metro, so case numbers may change as these results become available.

Figure 9. Enteric fever cases by province, South Africa, 1 January 2003 – 21 April 2022
ii. North West Province

As at 21 April 2022 there are 36 cases in the Klerksdorp cluster. While most cases hail from North West Province (64%, 23/36), cases belonging to this cluster have also been identified in four other provinces (Table 3 and Figure 11).

Table 3. Klerksdorp *Salmonella* Typhi cluster cases by province, January 2020 – 21 April 2022

<table>
<thead>
<tr>
<th>Provinces</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>North West</td>
<td>23</td>
</tr>
<tr>
<td>Gauteng</td>
<td>6</td>
</tr>
<tr>
<td>Mpumalanga</td>
<td>4</td>
</tr>
<tr>
<td>KwaZulu-Natal</td>
<td>2</td>
</tr>
<tr>
<td>Free State</td>
<td>2</td>
</tr>
<tr>
<td>Grand Total</td>
<td>36</td>
</tr>
</tbody>
</table>
iii. Gauteng Province

Gauteng Province reported 28 cases in the current year to date. The number of cases reported in January, February and March 2022 is higher than those reported for the same months in previous years (Figure 12).

The distribution of the Gauteng cluster cases by district is shown in Figure 13. Unlike the clusters in Western Cape and North West provinces, the cases in this cluster are not localised to a single district. However, of the 6 cases for 2022 to date, 4 are from Ekurhuleni Metro. A case diagnosed in Rustenburg, North West Province, has also been linked to this cluster. The cases span a range of age groups as shown in Figure 14.
The relevant provincial and district departments of health are aware of all the above-mentioned clusters, and outbreak investigations are ongoing. Contamination of municipal water is extremely unlikely to be the source of infection in any of these clusters, due to the demographics of the cases (including their age profiles, places of residence, source(s) of drinking water and access to improved sanitation) and the slow growing nature of the clusters. It is likely that there are complex chains of transmission within the respective communities, mostly due to the presence of unrecognised cases and carriers who serve as reservoirs of infection and lead to ongoing transmission. This makes it challenging to investigate and identify source(s) within the communities.

No likely or definite source(s) of infection have been identified for the Western Cape clusters as yet. For the Klerksdorp cluster, contaminated water in an illicit underground gold mine in the City of Matlosana has been identified as a common source of infection for a subset of the cases. However, multiple concurrent patterns of transmission are likely occurring in this cluster, including ongoing exposure of miners working underground, where miners with acute illness or asymptomatic *Salmonella Typhi* carriage cause persistent contamination of underground source(s) of drinking water and/or food. Infected miners (who are acutely ill, asymptomatic carriers, or are shedding during convalescence following acute illness), may then unknowingly transmit infection to household contacts through contamination of food or water in the home. Cases for which the source of infection or exposure is unknown have also been reported, suggesting community transmission. Infected persons who travel may become sources for new chains of transmission in other provinces.

In addition to the 36 confirmed cases in the Klerksdorp cluster, an additional 11 people were identified who had clinically compatible illness and were epidemiologically linked to a confirmed Klerksdorp cluster case; these were classified as probable cases. These probable cases were identified through interviews with confirmed case-patients (or their proxies), and were close contacts of case-patients who developed illness contemporaneously, in keeping with household-type transmission.
ENTERIC DISEASES

Prevention and control of enteric fever

Healthcare workers countrywide should be more aware of enteric fever, so that cases can be detected and treated appropriately. It is essential to follow up on all cases to ensure clearance of the organism and to screen household/close contacts for *Salmonella Typhi*. Chronic carriers need to be identified and managed appropriately.

Preventive measures for the public include:

- **Hand hygiene.** Wash hands with soap and safe water before eating or preparing food, and after using the toilet or changing a baby's nappy.
- **Food safety practice.** Follow the World Health Organization’s five keys to safer food: keep clean; separate raw and cooked; cook thoroughly; keep food at safe temperatures; and use safe water and raw materials.
- **Using safe water.** Contamination of municipal water is extremely unlikely to be the source of infection in any of these clusters. However, if people are concerned about the quality of water they use for drinking and cooking, then it is recommended to treat the water first by boiling it (place water in a clean container and bring to a boil for 1 minute) or treating it with household bleach (add 1 teaspoon of household bleach (containing 5% chlorine) to 20-25 litres of water, mix well and leave it to stand for at least 30 minutes before use).

Source: Centre for Enteric Diseases, NICD-NHLS; lindae@nicd.ac.za