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Early use of genomics to guide acquisition investigation of *Salmonella* Typhi

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Case report

Abstract

Background

As most *Salmonella* Typhi (*S*. Typhi) cases notified to public health units in Australia are acquired overseas, a case without recent travel raises concerns of local transmission. We describe a case of *S*. Typhi in a hospital inpatient without recent travel, where early use of genomic sequencing suggested remote acquisition from Chile in the 1980s, with chronic asymptomatic carriage. This facilitated the stand-down of a complex acquisition investigation.

Case

A notification of *S*. Typhi on stool culture was received for a female aged over 90 years living in Melbourne, Australia in October 2023. She had been hospitalised for three weeks (unrelated illness) and transferred into a residential aged care facility (RACF) six days prior to the result being known. She was asymptomatic and the sample was collected due to a recent ward gastroenteritis outbreak.

Investigation

Epidemiological investigation identified the case had emigrated to Australia in 1981 from Chile. Recent typhoid-like illness, overseas travel or contact with travellers from endemic areas were excluded. Subsequent genomic sequencing identified the isolate was multilocus sequence type 2 and did not cluster with any strains isolated in Victorian or international databases, most closely clustering with historical South American strains, with potential in-host changes over time.

Management

The case was presumed infectious throughout their hospital stay, with chronic carriage. There were 18 contacts, of whom 14 provided screening samples and were negative. Antibiotic case clearance was not recommended by the treating clinician due to patient comorbidity, treatment toxicity risks and unlikely treatment success without gallbladder removal. Enhanced infection control measures were instituted in the RACF (e.g. private bathroom, contact precautions for personal care, no food preparation). No additional cases were reported after two incubation periods (60 days).

Conclusion

Early genomic sequencing enhanced the efficiency of the public health investigation by rapidly confirming overseas acquisition and chronic carriage, obviating the need for extensive local upstream investigation.

Keywords: typhoid; genomics; public health; infection prevention and control; aged care

Background

Salmonella Typhi is not endemic in Australia and most cases are acquired overseas.[1,2] The purpose of the public health response in Australia is to determine the source of infection and prevent onward transmission. The incubation period is typically 8–14 days (range: 3–60 days). Cases are considered infectious if bacteria are present in stool, and some cases become chronic carriers.

On 16 October 2023, the North Eastern Public Health Unit (NEPHU) received a laboratory notification from the Microbiological Diagnostic Unit Public Health Laboratory (MDU-PHL) of a confirmed case of *Salmonella* Typhi detected in a faecal sample from a female aged over 90 years. The case lived with her family prior to being admitted to hospital on 18 September for stroke management. She was transferred to a rehabilitation facility on 24 September. On 9 October, the case passed a green-coloured formed stool. The case did not report systemic illness, fever, malaise or headache. Prompted by staff vigilance due to a recent norovirus outbreak, a faecal sample was collected on 10 October. Before the results were received, the case was transferred to a residential aged care facility for permanent nursing care.

In lieu of a clear onset of acute symptoms, the date of the green-coloured stool was used as symptom onset for initial investigation. The case had been in a hospital setting for the 14-day incubation period. Looking back further to 60 days, the case had spent nearly one third of this time in health services, with the remainder confined to her home.

The case reported no overseas travel in the past five years, and no contact with known cases of *Salmonella* Typhi, returned travellers from endemic countries, or unwell people.

Given these findings, an urgent investigation was initiated to explore the possibility of undetected local transmission, particularly in the sensitive setting of a healthcare facility. As the case did not exhibit symptoms consistent with typhoid at the time of sample collection, chronic carriage was also considered.

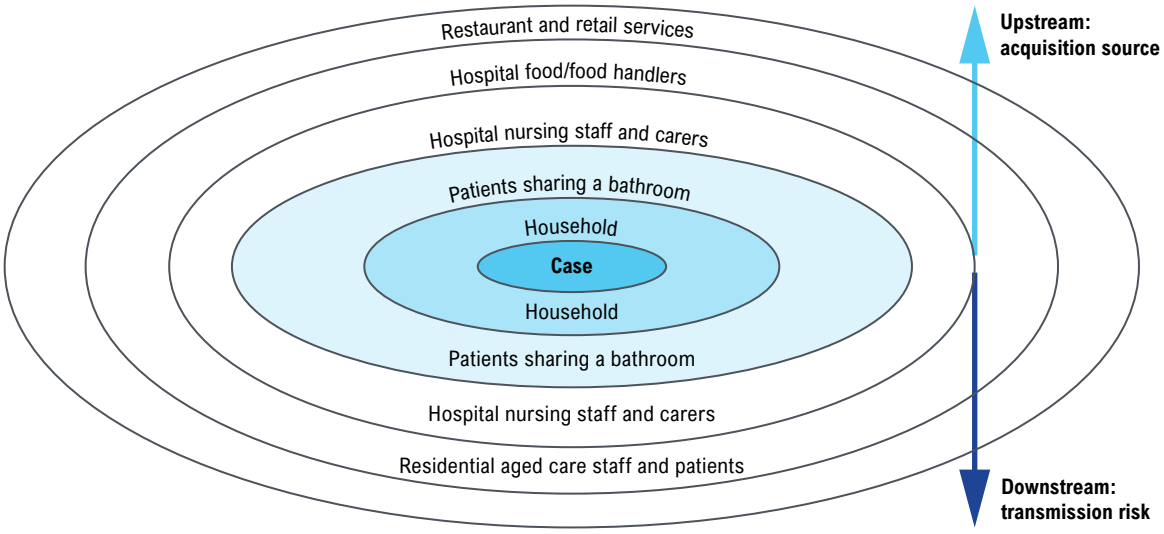
Ethics approval was not required as per Austin Health's Research Office. Informed consent for publication was obtained from the case's next of kin.

Epidemiological and genomic investigations

A multidisciplinary incident management team was convened on 17 October 2023, comprising public health clinicians from local and state departments, geriatric and infectious diseases clinicians, infection prevention and control teams and MDU-PHL staff.

The investigation included assessment of both upstream sources of infection and downstream individuals at risk of infection (Figure 1). Household contacts and patients who had shared a bathroom with the case were considered the highest-risk groups and faecal screening samples were requested.

Figure 1: Epidemiological investigation plan, *Salmonella* Typhi acquisition investigation,[a] Melbourne, Australia, 2023



a Shaded area represents contacts deemed at high risk, with faecal sample screening requested.

Hospital staff were not considered contacts as appropriate standard precautions had been used.

Review of statewide epidemiology identified 12 typhoid cases in the 60 days prior to this case's notification. All were associated with overseas travel, with no epidemiological links to the current case, indicating that acquisition from hospital or a retail food source was unlikely.

During the case interview, it was noted that the case had emigrated from Chile to Australia in 1981. Investigation revealed a significant typhoid epidemic had occurred in Chile around this time, with over 70,000 cases over a ten-year period.[3] The case did not recall a past typhoidal illness and reported that they and their family were all vaccinated for typhoid prior to migration.

An in-home carer—originally from India, a typhoid-endemic country—had provided care from July 2023 until hospital admission. The carer was overseas for the duration of the investigation. Although a faecal sample could not be obtained, their employer was able to confirm there had been no recent illness, sick leave, other travel, and no other employer.

Given the working theory of chronic carriage, genomic sequencing was prioritised to inform the investigation. MDU-PHL completed genomic analysis within 7–10 days of receiving the sample (Figure 2). The isolate was confirmed as multilocus sequence type (MLST)-2 (senterica_achmann_2) and did not cluster with any sequences from Victorian or publicly available international databases on the National Center for Biotechnology Information's sequence read archive (pathogen detection portal ID PDT001981732.1).[4] Phylogenetic analysis shows the isolate most closely clustered with historical strains from Chile which were associated with chronic carriage,[5] supporting the hypothesis of chronic carriage with potential acquisition during the Chilean typhoid epidemic and with potential in-host changes over time (Figure 2). This early genomic sequencing facilitated the stand-down of a potentially complex local acquisition investigation.

Infection prevention and case management

The case had previously been living independently but was now, post-stroke, requiring nursing assistance for personal care and continence, increasing the risk of faecal oral transmission. A plan for ongoing management of a chronic carrier within a sensitive setting was required, balancing the public health versus the individual risks. It was decided not to attempt antibiotic clearance due to treatment toxicities, frailty and low likelihood of success without gall bladder removal for the case.

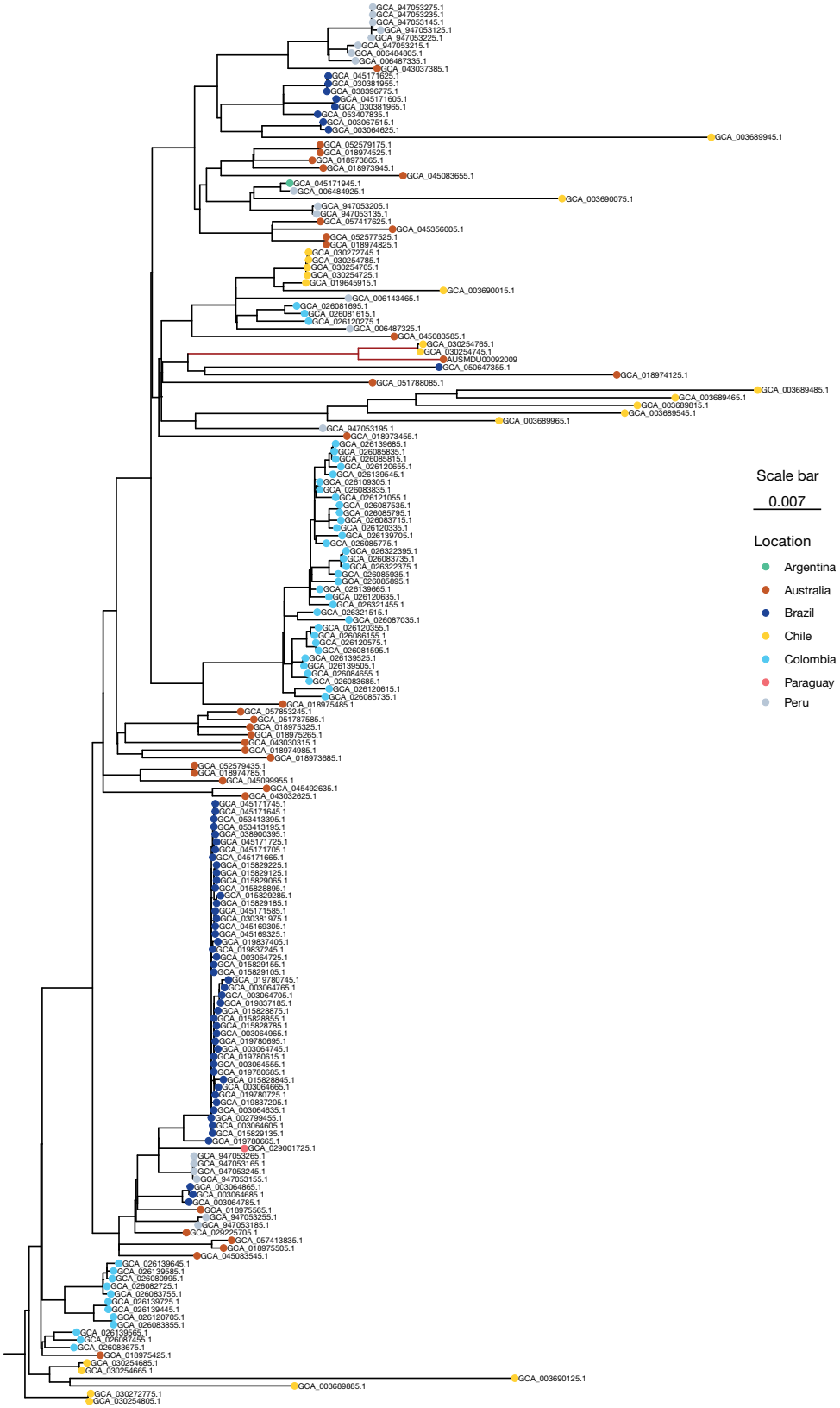
The case was distressed at having been kept in isolation during the investigation and so it was deemed appropriate for them to be able to move freely around their residential home. Faecal screening was conducted for 14 of the 18 identified close contacts, including 11 co-residents and three household contacts. All returned negative results for *Salmonella* Typhi.

Residential aged care staff were advised to implement enhanced personal protective equipment for activities involving toileting and personal care, but routine use was not deemed necessary. Vaccination of staff against typhoid was not recommended. The facility was advised to house the case in a single room with a private bathroom and, as far as practicable, to avoid shared bathroom use or involvement in food preparation activities. No specific environmental cleaning requirements beyond standard protocols were recommended.

Conclusion

Chronic carriage should be considered in typhoid case investigations, as carriers are asymptomatic and a potential reservoir for infection. This is increasingly relevant in the context of rising migration from typhoid-endemic countries. Early access to genomic sequencing can guide public health investigations, distinguishing chronic carriage from local transmission, with the latter requiring significantly more investigation. Antibiotic clearance is complex in chronic carriage and requires specialist input and risk assessment. This case highlighted the importance of a tailored and proportionate public health response, and the need for multidisciplinary collaboration to ensure that the delivery of this response was timely, effective, and coordinated.

Figure 2: Maximum-likelihood phylogenetic tree of *Salmonella enterica* serovar Typhi,[a] Melbourne, Australia, 2023



a Tree shows Victorian case (highlighted in red) pictured in relation to genome sequences from South America and key representative Victorian genomes (one representative per cluster). Tree was inferred using IQTree v2.1.4-beta with GTR+F+G4 model with 1000 bootstraps from a core genome alignment using the Victoria case as a reference genome. The genetic distances between the Victorian case and the Chilean genome sequences (red branch) suggest they belonged to the same ancestral group but were not very closely related (i.e. not direct or local transmission). All other Victorian isolates were not genomically related to the Victorian case (not pictured).

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