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Volunteer exposure study of paratyphoid fever in a controlled setting

Submission date 17/02/2026	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 25/02/2026	**Overall study status** Ongoing	
Last Edited 29/04/2026	**Condition category** Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

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Study information

Scientific Title
Salmonella Paratyphi A controlled human infection model in an endemic setting: determining safety, dose escalation, and correlates of protection

Acronym
PARACHIM

Study objectives
To determine the dose (in colony forming units) of Salmonella Paratyphi A, challenge strain NVGH308, needed to produce a 60% to 75% attack rate when ingested with sodium bicarbonate solution, in healthy adult volunteers in Pakistan.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 31/07/2025, Aga Khan University Ethical Review Committee (AKU-ERC) (National Stadium Road, Karachi, 74800, Pakistan; +92 21 3493 0051; erc.pakistan@aku.edu), ref: 2025-11238-35664

2. Approved 17/12/2025, National Bioethics Committee (NBC) (Shahrah-e-Jamhuriat, G-5/2, Islamabad, 44000, Pakistan; +92 51 9224325; nbcpakistan@nih.org.pk), ref: 4-87/NBCR-1336/25-26/1041

3. Approved 08/08/2025, Oxford Tropical Research Ethics Committee (OxTREC) (Research Governance, Ethics & Assurance, Research Services, University of Oxford, Boundary Brook House, Churchill Drive, Headington, Oxford, OX3 7GB, United Kingdom; +44 1865 282585; oxtrec@admin.ox.ac.uk), ref: 1782933

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Active

Assignment

Sequential

Purpose
Basic science

Study type(s)

Health condition(s) or problem(s) studied
Salmonella Paratyphoid A

Interventions
This is an inpatient dose-finding controlled human infection model (CHIM) study of Salmonella Paratyphi A infection in healthy adult participants in Pakistan. In total, up to 60 participants will be recruited. Participants will be challenged with S. Paratyphi A (strain NVGH 308) beginning at a dose of 1-5 x 103 CFU/30 ml, the dose previously established to give a desired 'attack' rate of approximately 66% (as per prior Oxford Vaccine Group S. Paratyphi A studies: OVG 2013/07, REC Ref: 14/SC/0004; OVG 2014/01, REC Ref: 14/SC/1204, OVG 2018/07, REC Ref: 21/SC/0330). Because of pre-existing immunity in an endemic country, we anticipate that a higher dose of challenge may be required to successfully reach the target attack rate; the programme will therefore run as a dose-escalation study, increasing a log of the dose at a time for each cohort of 3-5 participants enrolled. Given this study is the first SPA CHIM in Pakistan, we will start with a cohort of 3 participants. The first cohort will be further split into two groups (1+2 participants with an interval of at least 7 days to monitor the safety closely. The first dose review by the Data Safety Monitoring Board (DSMB) will be conducted after the first 3 participants have been challenged and followed up for 14 days. The second cohort will be another 3 participants. After we challenged the first 6 participants (cohorts 1 and 2), the DSMB will review the safety data and if there are no safety concerns, we will increase the cohort size to 5 participants. A dose review will be done after each of the cohorts reaching the 14 days of follow-up.
To ensure safety of the participants and also because of the lower reliability of closed-sanitation systems in Karachi, the study will be run on an inpatient basis at Aga Khan University (AKU) to ensure that volunteers are managed in a containment environment that avoids risk of onward transmission of paratyphoid A in the community (and conversely infection of the volunteers from contaminated water at home), and, as such, they will stay in an in-patient facility for the 10-20 days following oral challenge until at least 5 days of antibiotics have been received by the participants but not earlier then day 10 post-challenge.
Gut microbiome analysis
This part of the study will assess the impact of antibiotic (Ciprofloxacin) on the gut microbiome and its reservoir of antimicrobial resistance (AMR) genes in a setting with high antibiotic use. Stool samples will be collected at defined time points: before the challenge, after challenge before stating antibiotics, during antibiotic treatment, and at follow-up intervals. The project leverages metagenomic long-read sequencing to generate detailed microbial assemblies, enabling linkage of AMR genes to specific bacterial hosts and mobile genetic elements, providing insights into the effects of antibiotics on gut microbiota in a low-resource, endemic setting.

Intervention Type
Other

Primary outcome(s)

1. Dose of Salmonella Paratyphi A needed to produce a 60–75% attack rate measured using the proportion of participants developing Salmonella Paratyphi A infection at within 14 days following oral challenge

Key secondary outcome(s)
1. Human physiological response to Salmonella Paratyphi A challenge measured using participant symptom profiles, temperature measurements, and recorded clinical and laboratory observations at solicited event time points in the 21 days after challenge and within 14 days after challenge

2. Sensitivity of the predefined criteria for Paratyphoid A infection measured using determination of challenge dose per kg ingested and analysis of attack rate using alternative diagnostic criteria at paratyphoid diagnosis or 14 days post challenge

3. Characteristics of bacterial dynamics after challenge measured using microbiological assays of blood, stool, and urine, including quantitative assessment of bacteraemia at at 6 months post challenge

4. Human immune response to challenge measured using immunological laboratory assays assessing innate, humoral, cellmediated and mucosal responses, including antigenspecific antibodies, cell-mediated responses, functional assays, mucosal IgA, and cytokine and acute phase reactant profiles at 6 months post challenge

5. Immunological correlates of protection for S. Paratyphi A infection measured using immunological markers, including S. Paratyphi Aspecific antibody titres and serum bactericidal assay titres at baseline and at 6 months post challenge

Completion date
10/12/2027

Eligibility

Key inclusion criteria
1. Willing and able to give informed consent.
2. Aged 18 -55yrs.
3. In good health as determined by medical history, physical examination and clinical judgment of the study team.
4. Available for all required appointments (agree to being residential in Karachi until confirmed clearance).
5. Able to comply with all study requirements, including infection control precautions.
6. Agree to medical record review.
7. Agree to avoid antipyretic/anti-inflammatory treatment from challenge until advised by a study doctor or until 14 days after challenge.
8. Agree to refrain from donating blood for the duration of the study.
9. Agree to avoid vaccination during the study period.
10. For participants of childbearing potential, they should be willing to ensure that they or their partner use effective contraception until confirmed clearance.
11. Agree to remaining admitted in the hospital and take leave from work for a period of 10-20 days

Healthy volunteers allowed

Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. History of significant organ/system disease that could interfere with study conduct or completion, in the opinion of the study team. Including, for example, but not restricted to:
1.1 Cardiovascular disease
1.2 Respiratory disease
1.3 Haematological disease
1.4 Endocrine disorders
1.5 Renal or bladder disease, including history of renal calculi
1.6 Biliary tract disease, including biliary colic, asymptomatic gallstones or polyps or previous cholecystectomy
1.7 Gastro-intestinal disease including chronic diarrhoea, inflammatory bowel disease, irritable bowel syndrome or diseases requiring use of regular antacids, H2-receptor antagonists, proton pump inhibitors, laxatives or prokinetic agents
1.8 Neurological disease
1.9 Metabolic disease
1.10 Psychiatric illness requiring hospitalisation, or other mental health condition
1.11 Known or suspected drug abuse
1.12 Known or suspected alcohol misuse
1.13 Infectious disease
1.14 Coagulation disorder
2. Known or suspected impairment of immune function, alteration of immune function, or prior immune exposure that may alter immune function to paratyphoid, resulting from, for example:
2.1 Congenital or acquired immunodeficiency, including IgA deficiency
2.2 History of auto-immune disease
2.3 Human Immunodeficiency Virus or symptoms/signs suggestive of an HIV-associated condition
2.4 Receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months or long-term systemic corticosteroid therapy
2.5 Receipt of immunoglobulin or any blood product transfusion within 3 months of study start
2.6 History of cancer (except squamous cell or basal cell carcinoma of the skin and cervical carcinoma in situ)
3. HLA-B27 positive.
4. Moderate or severe depression or anxiety as classified by the Hospital Anxiety and Depression Score at screening or challenge that is deemed clinically significant by the study doctors.
5. Weight less than 50 kg.

6. Presence of implants or prosthetic material.
7. Anyone taking long-term medication (e.g. analgesia, anti-inflammatories or antibiotics) that may affect symptom reporting or interpretation of the study results or that may interact with antibiotics used for treatment of paratyphoid A (in particular drugs that could prolong corrected QT interval).
8. Contraindication to fluoroquinolones, macrolide antibiotics, co-trimoxazole, cefixime or ceftriaxone.
9. Family history of aneurysmal disease.
10. Participants who are pregnant, lactating or unwilling to ensure that they or their partner use effective contraception from 30 days until three negative stool samples confirm clearance.
11. Scheduled elective surgery or other procedures requiring general anaesthesia during the study period.
12. Participants who have participated in another research study involving an investigational product that might affect risk of paratyphoid infection or compromise the integrity of the study within the 30 days prior to enrolment, or who plan to enrol in another research study during the follow-up study period.
13. Significant blood donation or planned blood donation prior to enrolment.
14. Detection of any abnormal results from screening investigations (at the clinical discretion of the study team).
15. Prolonged corrected QT interval (>450 milliseconds) or significant clinical abnormality on ECG screening.
16. Evidence of HIV or Hepatitis B or Hepatitis C infection.
17. Presence of gallbladder abnormalities such as stones/calculi or polyps, as seen on ultrasound.
18. Presence of any degree of haematuria.
19. Inability to comply with any of the study requirements (at the discretion of the study staff and the participant's General Practitioner).
20. Any other social, psychological or health issues which, in the opinion of the study staff, may:
20.1 Put the participant or their contacts at risk because of participation in the study
20.2 Adversely affect the interpretation of the primary endpoint data
20.3 Impair the participant's ability to participate in the study

Temporary Exclusion at Challenge:
21. Acute or acute-on-chronic infection within the previous 5 days, that is considered clinically significant by the Investigator.
22. History of any systemic antibiotic therapy during the previous 5 days for short-acting antibiotics and 15 days for long-acting antibiotics.
23. Any systemic corticosteroid (or equivalent) treatment in the previous 14 days, or for more than seven consecutive days within the past 3 months.
24. Therapy with antacids, proton pump inhibitors or H2-receptor antagonists or prokinetic agents within 24 hours prior to challenge.
25. Receipt of any vaccine in the preceding 7 days.
26. Plan to receive any vaccine within 21 days following challenge.

Date of first enrolment
05/06/2026

Date of final enrolment
05/04/2027

Locations

Countries of recruitment
Pakistan

Study participating centre
Aga Khan University
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Sponsor information

Organisation
Aga Khan University

ROR
https://ror.org/03gd0dm95

Funder(s)

Funder type

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	Informed consent form	04/06/2025	17/02/2026	No	No
Participant information sheet		10/07/2025	17/02/2026	No	Yes
Protocol file		10/07/2025	17/02/2026	No	No