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A novel bacteriophage-based assay stratifies tuberculosis risk in recent household contacts of pulmonary tuberculosis: A prospective observational cohort study

02. Bacterial infection & disease

2a. Tuberculosis and other mycobacterial infections (incl antimycobacterial drugs, treatment & susceptibility/resistance, diagnostics & epidemiology)

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Background In the vast majority, tuberculosis (TB) arises from pre-existing latent Mycobacterium tuberculosis (Mtb) infection (LTBI). TB prevention strategies focus on screening programmes to treat LTBI. Interferon gamma release assays (IGRAs) are currently used for LTBI but are poorly predictive of the 5-10% that will progress to TB. Studies suggest greatest risk in those with recently acquired infection when immune control has not been achieved. Actiphage is a novel bacteriophage-based assay that we have previously shown can detect circulating Mtb in TB and some with LTBI. We investigate the hypothesis that Actiphage can identify a subset with LTBI that have features of active Mtb infection which may associate with increased risk of TB progression. We utilise 18FDG PET-CT (PET-CT) scanning to visualise the burden of active inflammation associated with LTBI and correlate this with Actiphage results at baseline, repeating the scan after 3 months to characterise infection trajectory.

Methods 21 healthy adult household contacts of pulmonary TB were tested with IGRA, Actiphage and PET-CT at baseline. PET-CT findings were classified as positive, indeterminate or negative based on pre-specified criteria. (Table1) Participants with positive PET-CT findings were investigated for active TB and if negative had a repeat scan after 3 months to characterise infection trajectory. All participants were followed for 12 months and received no TB prevention therapy.

Results In our cohort, Actiphage had sensitivity and specificity of 68.8% and 80.0% respectively, for predicting FDG uptake on PET-CT, compared with 81.3% and 20.0% using IGRA. 10 participants had persistent or progressive infection on follow-up PET-CT, with six receiving TB treatment. When including prospective outcome, baseline Actiphage result had sensitivity and specificity of 80.0% and 64.0% to discriminate between contacts with resolving and progressive infection.

Conclusions In this pilot study, detection of Mtb in blood using Actiphage early in LTBI was associated with an active and progressive state of infection with a likely higher risk of developing to clinical disease. Screening with Actiphage had high sensitivity and specificity for stratifying TB risk in recently exposed household contacts, supporting evaluation in larger cohorts.

Table 1

Definition of PET-CT descriptors	
Positive	▪ FDG avid mediastinal and hilar lymph nodes ▪ FDG avid area in lung parenchyma
Indeterminate	▪ Low absolute SUVmax uptake (<3) ▪ Uptake in anatomical regions with alternative diagnosis ▪ Uptake in anatomical regions that may be associated with Mtb infection
Negative	▪ No FDG accumulation above of physiological uptake

Keyword 1
bacteriophage
Keyword 2
bacteraemia
Keyword 3
human tuberculosis

Conflicts of interest

Do you have any conflicts of interest to declare?
I have no potential conflict of interest to report