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## Media Release

### **New study casts doubt on the way in which tuberculosis (TB) is transmitted**

#### **Results from the first fingerstick blood test to meet WHO standards for TB released**

#### **First study shows face mask sampling can 'diagnose' or detect infectious individuals.**

**Tuesday, 19th October, 2021** – The virtual [52<sup>nd</sup> Union World Conference on Lung Health](#) (WCOLH) opened today by announcing three major scientific developments that will potentially impact the global response to tuberculosis (TB), the world's second biggest infectious disease killer behind COVID-19.

The event takes place against the backdrop of ongoing COVID-19 vaccine inequity, with the pandemic continuing to impact the delivery of TB services in many low- and middle-income countries.

COVID-19 and TB are today the world's two leading infectious disease killers. The novel coronavirus pandemic has refocused attention on how infectious diseases transmit from person to person and has catalysed innovations in sampling and diagnostics. The disruption to TB services during the pandemic has only highlighted just how important it will be going forward that testing for and treating TB are made simpler and easier to access.

### **Researchers question assumptions of how TB is transmitted**

In the opening press conference today, researchers from the University of Cape Town in South Africa announced results from their study of TB positive people carried out in the specially constructed Respiratory Aerosol Sampling Chamber (RASC) which suggest that coughing, thought previously to be the main means of spreading TB, might not be the primary driver of TB transmission. Instead, tidal, or regular, breathing may be a far more significant contributor to the aerosolization of *Mycobacterium tuberculosis*, the bacterial cause of TB.

“This study is an important step forward in our understanding of aerosol transmission of disease and its findings are as relevant for COVID-19 as they are for TB,” said **Guy Marks**, President of The Union, convenor of the World Conference. “It will hopefully generate more focus on the topic of airborne spread of respiratory diseases.”

Lead author of the study, **Ryan Dinkele** of the University of Cape Town, said if tidal breathing is a primary driver, or even as important as cough in TB transmission, then symptomatic screening for TB-transmitters may not be useful in slowing the spread of the disease.

“The current approach, which relies on the testing and treatment of passively identified individuals may not be a reliable response to preventing transmission, as it depends on

people feeling sick enough to seek treatment,” said Dinkele. “It may also shed light onto why constructing transmission chains is so challenging in high TB burden settings.”

### **Fingerstick blood test can detect TB in less than an hour.**

The development of a fast and accurate, non-sputum-based point-of-care triage test for tuberculosis (TB) would have a major impact on combating the TB burden worldwide. A new fingerstick blood test has been developed by Cepheid (Xpert-MTB-Host Response (HR)-Prototype).

**Jayne Sutherland** of the MRC Unit The Gambia at LSHTM, reported interim results of the Xpert-MTB-HR prototype trialled in a prospective, multi-site study across Gambia, Uganda, South Africa and Vietnam. The device is the first to meet the WHO target product profile for a Triage test for TB regardless of HIV status or geographical location. It takes under 1 hour and uses fingerstick blood, rather than sputum, which reduces biohazard risk and increases likelihood of diagnosis in individuals who cannot readily produce sputum such as children and people living with HIV.

### **Face-mask sampling can predict acquired *Mycobacterium tuberculosis* infection in household contacts**

**Caroline Williams**, Clinical Lecturer in Infectious Diseases at the University of Leicester in the UK, reported on the use of masks to see if bacteria could be detected on the mask and therefore could potentially be used to detect infectiousness earlier than with sputum. Mask sampling could detect viable bacteria and those patients with higher levels on their mask correlated with increased infectiousness determined by new infections in their close contacts.

### **TB and COVID-19 survivor Uvi Naidoo and The Union Ambassador, Film & TV Actor Claire Forlani, address the media**

Earlier in the press conference pediatric TB doctor **Uvi Naidoo** described his experience of surviving TB a few years ago and two bouts of COVID-19 in 2020.

It took a little over three years of treatment until he was cured of MDR-TB. He sustained numerous life-threatening complications – many due to dated TB tools and drugs still in use today. 10 years later today, Naidoo acquired severe COVID-19 twice from patients he treated within the past year. Like many other nurses, doctors and the general public he has seen death on a personal and heartfelt level.

“While admitted for COVID-19, I saw patients’ demise from COVID19, medical colleagues break down from sheer emotional and physical fatigue and watched my whole family admitted to ICU for COVID19, losing my dear father,” said Naidoo.

“We’ve all been humbled. There have been far too many gaps for too long and too many continue to suffer. From the political realm to basic sciences and clinical bedside, it’s high time we all show we care. It’s time to roll up our sleeves in service to those that really need us.”

Union Ambassador, actress **Claire Forlani**, said the coronavirus pandemic has highlighted the absence of interest and care from those communities most affected by the virus.

“Is it any wonder that vaccine inequity is front and center,” said Forlani. “The failure to deliver COVID-19 vaccines to low- and middle-income countries and to end tuberculosis are two sides of the same coin - a devaluation of human life in poor countries.”

### **Indonesia and South African Health Ministers and WHO DG Tedros to speak**

Later today Indonesian Health Minister **Budi Gunadi Sadikin** will address the Opening Session. Indonesia, India and the Philippines, are the three countries whose TB responses have been most impacted by COVID-19, according to the [WHO Global TB report](#) released last week. WHO Director-General **Dr Tedros Adhanom Ghebreyesus** and South African Minister for Health **Joseph Phaahla** will also address the conference this week.

The Official Opening Press Conference can be viewed [here](#):

ENDS

Today’s [Official Opening Press Conference](#) featured the following studies:

#### **Cough-independent aerosolization of *Mycobacterium tuberculosis* suggests a significant role for tidal breathing in tuberculosis transmission (TBS-08-04)**

Disrupting *Mycobacterium tuberculosis* (*Mtb*) transmission remains an attractive anti-tuberculosis (TB) strategy, however our limited understanding of how particulate matter (including *Mtb*) is aerosolized in the peripheral lung during respiration undermines this approach. This study aimed to compare the aerosolization of *Mtb* and particulate matter from TB-positive patients during three respiratory manoeuvres: Tidal Breathing (TiBr), Forced Vital Capacity (FVC), and Coughing.

GeneXpert-positive patients ( $n = 39$ ) were recruited from TB clinics in Cape Town, South Africa. Bioaerosols were sampled within a Respiratory Aerosol Sampling Chamber (RASC), with real-time assessment of CO<sub>2</sub> concentration and particle numbers stratified into 5 size categories. *Mtb* bacilli were detected using fluorescence microscopy.

On average, single TiBr manoeuvres produced 6-20 times fewer particles than either FVC or cough. No differences were observed across all manoeuvres in the proportions of particles detected in the size categories ranging from 0.5 to 5µm; however, cough produced proportionately fewer particles >5µm in diameter compared to FVC ( $p = 0.026$ ). *Mtb* were detected consistently for all manoeuvres after the five-minute sampling, with 66%, 70%, and 61% of the samples positive for *Mtb* in TiBr, FVC, and cough respectively. Although a single TiBr manoeuvre produced approximately 1.6- and 2.2- times fewer *Mtb* than FVC and cough, respectively, TiBr and cough produced 64.5 and 3.8 *Mtb* bacilli per hour. These findings suggest that coughing significantly increases particle aerosolization compared to TiBr, however, this increase in particle production does not appear to be associated with increased aerosolization of *Mtb*, with TiBr producing more *Mtb* per particle compared to coughing. If the number of organisms detected reflects infectivity, this would suggest that TiBr might contribute to asymptomatic transmission in high-burden endemic settings.

- Oral Abstract presentation (OA)
- Track: Theme: Bioaerosols Threats and opportunities.
- Session Channel: 7
- Session Date and Time: Thursday 21 October, 16:40 – 17:25 (CEST)
- Presenter: R. Dinkele, University of Cape Town, Cape Town, South Africa

## **Diagnostic accuracy of the Cepheid 3 gene host-response fingerstick blood test in a prospective, multi-site study (LB-1786-22)**

**Background:** The development of a fast and accurate, non-sputum-based point-of-care triage test for tuberculosis (TB) would have a major impact on combating the TB burden worldwide. A new fingerstick blood test has been developed by Cepheid (Xpert-MTB-Host Response (HR)-Prototype). Here we describe the first prospective findings of the MTB-HR prototype.

**Methods:** Fingerstick blood from adults presenting with symptoms compatible with TB in South Africa, The Gambia, Uganda and Vietnam was analysed using the Cepheid GeneXpert MTB-HR prototype. Accuracy of the Xpert MTB-HR cartridge was determined in relation to GeneXpert Ultra results and a composite microbiological score (GeneXpert Ultra and liquid culture) with patients classified as having TB or other respiratory diseases (ORD).

**Results:** When data from all sites (n=75 TB, 120 ORD) were analysed, TB score discriminated between TB and ORD with an AUC of 0.94 (CI, 0.91-0.97). When sensitivity was set at 90% for a triage test, specificity was 86% (CI, 75-97%) at a cut-off of 2.05. These results were not influenced by HIV status or geographical location. When evaluated against a composite microbiological score (n=80 TB, 111 ORD), the TB score was able to discriminate between TB and ORD with an AUC of 0.88 (CI, 0.83-0.94).

**Conclusions:** Our interim data indicate the Cepheid MTB-HR cartridge reaches the minimal target product profile for a point of care triage test for TB using fingerstick blood, regardless of geographic area or HIV infection status.

- Oral Abstract presentation (OA)
- Session Channel: 2
- Session Date and Time: Friday 22 October, 15:00 – 16:20 (CEST)
- Presenter: J. Sutherland, MRC Unit The Gambia at LSHTM, Fajara, Gambia

## **Face mask sampling of pulmonary tuberculosis patients predicts acquired *Mycobacterium tuberculosis* infection in household contacts (TBS-08-01)**

**Background:** *Mycobacterium tuberculosis* (Mtb) relies on airborne transmission. We have previously shown the utility of mask sampling to capture exhaled Mtb as a non-invasive diagnostic tool in pulmonary TB (pTB). Here we evaluate whether mask sampling can additionally stratify transmission risk in household contacts of pTB.

**Methods:** Mask sampling was performed on forty-six microbiologically confirmed pTB patients prior to commencing TB treatment. Patients were stratified according to quantitative mask Mtb capture, into high ( $\geq 20,000$  copies) and low/neg output ( $<20,000$  copies) IS6110 output groups. Transmitted Mtb infection was determined in 181 of their household contacts with serial QuantiFERON (QFT) testing at baseline and 6 months, and defined by QFT seroconversion, or increase in interferon- $\gamma$  of  $\geq 1$  IU/ml. Multilevel mixed-effects logistic regression was used to calculate adjusted odds ratios (AORs), correcting for household clustering and adjusted for significant co-founders ( $p=0.1$ ).

**Results:** Mtb was detected in 91% (42/46) mask samples with high output in 19 (45%) individuals. Household contacts of high output patients had a threefold increased risk of transmitted Mtb infection compared to contacts of patients with low/neg output: QFT conversion 26% vs. 14%; AOR 3.20 95%CI 1.26 - 8.12,  $p=0.01$ ; and interferon- $\gamma$  increase  $\geq 1$

IU/ml 34% vs. 15%; AOR 3.62, 95%CI 1.54 - 8.53, p=0.003. Neither conversion nor increase  $\geq 1$  IU/ml in QFT was associated with sputum bacillary burden, CXR score of disease extent/cavities or sleeping proximity.

**Discussion:** Mask sampling provides a novel non-invasive clinical tool for both diagnosis and stratification of infectivity risk in pTB patients, which can support and enhance TB control programmes for active case finding, stratified contact tracing and outbreak management. Like our previous work and published cough aerosol work, this study also highlights the superiority of aerosol sampling compared with traditional markers of infectivity, to better predict infection transmission risk in close contacts.

- Oral Abstract presentation (OA)
- Track: Theme: Bioaerosols Threats and opportunities.
- Session Channel: 7
- Session Date and Time: Thursday 21, 16:40 – 17:25
- Presenter: C. Williams, University of Leicester, Leicester, UK

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#### **About the [52nd Union World Conference on Lung Health](#)**

The Union World Conference on Lung Health, convened by [The Union](#), is the world's largest gathering of clinicians and public health workers, health programme managers, policymakers, researchers and advocates working to end the suffering caused by lung disease, with a focus specifically on the challenges faced by low-and lower-middle income populations. Of the 10 million people who die each year from lung diseases, some 80 percent live in these resource-limited settings.

Organising international conferences on TB and related subjects has been a core activity of The Union since its founding in 1920.

**Twitter:** @UnionConference

#### **About [The Union](#)**

The Union was founded in 1920 and is the world's first global health organisation. We are a global leader in ending TB, we fight the tobacco industry, and we solve key problems in treating major diseases. We use science to design the best treatments and policies for the most pressing public health challenges affecting people living in poverty around the world. The Union's members, staff and consultants operate in more than 140 countries and embody our core values of accountability, independence, quality and solidarity.

See how The Union is supporting the [COVID-19 response](#).

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