COR-NTD 2020
Virtual Meeting, November 12 – 14
Integrating for Impact

A Multi-pronged Approach to NTD Surveillance

Session Date: 11/13/20

Session Time: 9:00 AM - 12:00 PM EST

Session Description: Surveillance is the backbone of effective public health programs. As NTD programs reduce infection prevalence and scale down or stop interventions, conducting surveillance is essential to ensuring that program gains are sustained. Maintaining disease-specific surveillance efforts can be costly and difficult to justify when health systems face many competing priorities, challenges that will only intensify following the COVID-19 pandemic. WHO has identified the development of multiplex-based diagnostic platforms and coordination across sectors for surveillance as priorities in the 2030 NTD road map. Development of new approaches to integrated surveillance requires innovation, both in the realm of the technology and the degree of coordination across disease platforms as well as in data analysis and utilization. In this session, three different strategies for carrying out integrated surveillance will be highlighted: 1) detection of pathogens in vectors; 2) environmental sampling; and 3) monitoring antibody responses in human populations. Speakers will discuss recent advances in the development of these surveillance platforms and the challenges that must be addressed to ensure their wider use. The discussion will focus on defining future research needs and next steps.

Session Chairs: Diana Martin, Amy Pickering and Nils Pilotte

Session Rapporteur: Justine Marshall

KEY DISCUSSION POINTS

What key findings and data did the group identify via presentations? What issues were raised in discussions?

Integrated serological surveillance: lessons learned from multiple country experiences and next steps for success – Diana Martin, CDC

- Antibodies can provide information about infection prevalence in a population. Multiplex technology allows detection of hundreds of antigens simultaneously in a single sample.
- Serology can be a useful metric for most NTDs but there are specificity concerns for some antigens/pathogens (cross-reactivity).
- Non-standard surveys may not provide sampling that is granular enough to find pockets of transmission.

- Integrated serosurveillance can piggyback on an existing single disease survey. It is important to coordinate during study planning to either expand the study design (collecting additional/different samples, e.g. adding blood spot collection) or introduce multiplex at sample processing (providing the samples were collected with consent for future testing).
- Limitations include inappropriate sampling frame (NTDs highly focal) or timing (seasonality/timeframe).
- Challenges of integrated serosurveys include longer timeframes, more planning and engagement, protocol development and piloting, trade-offs in terms of data strength for different diseases.

Lessons from Serosurveillance for NTDs – Kim Won, CDC

- The aim of surveillance is to detect a signal to intervene at the earliest moment. Serology can show us the presence of disease (antigens/antibodies) long before a manifestation of clinical disease. Three pieces of the puzzle must come together for simultaneous consideration:
    - The use case for serosurveillance (why & when) is important – clearly define the program decision to be made, e.g. Is MDA required?
    - Identify the program platform (where & who), e.g. TAS for LF? What are the requirements for decision-making?
    - Finally, we need to determine the test performance and testing platform choice (what) – taking into consideration sensitivity/specificity of diagnostics. E.g., Which diagnostic can provide the data we need?

Monitoring STH transmission through serology: a feasible solution? – Johnny Vlaminck, University of Ghent

- Serology for STH has been limited to date due to the ease of copromicroscopic diagnosis of STH infection in humans. But serological monitoring of STH transmission is attainable and advantageous.
- Advantages of serology for STH include: confidence on sample origin due to directly observed collection; improved compliance due to more acceptable sample production and transportation; easier integration with other surveillance/diagnostics platforms due to single matrix; necessity of high throughput as prevalence decreases and more samples are required to locate cases; and ability of serology to measure more than just patent infections.
- Antibody diagnosis is an indicator of community exposure to parasites, important for the control of STH.
- Cross-sectional study of 600 SAC in Jimma, Ethiopia in 2015 and 2018 where stool and finger-prick blood samples were collected from each participant. The stool samples underwent copromicroscopy diagnosis, and the blood spots were run on two ELISA tests (*Ascaris* haemoglobin antigen and *Ascaris* Lung L3 antigen). All three diagnostics showed

strong decreases in prevalence following MDA. This shows that we can use serology to monitor changes in infection intensity.

Soil epidemiology: a new tool for STH surveillance? – Amy Pickering, Tufts University

- Soil epidemiology presents a sensitive and low-cost new tool to complement existing stool-based tools (Kato-Katz and multiplex PCR).
- Environmental surveillance can detect asymptomatic infections, and STH lifecycle involves stages in soil, so good opportunity to detect parasites. STH eggs have been found to be common in soil in communities where STH infections are endemic.
- Environmental surveillance can be applied for various use cases.
- Advantages of soil surveillance include: cost-effective as one location represents multiple households and can give information about transmission locations; lower sample refusal rates; and increased performance of highly sensitive and specific eDNA molecular tools.

Detecting Soil Transmitted Helminths in the Environment in Endemic Communities: experiences from the field – Sitara Ajjampur, Christian Medical College, Vellore, India

- A pilot study to detect STH in the environment in endemic communities was carried out in India and Benin, leveraging the DeWorm3 study sites.
- Approx. 100 households were recruited at each site, and HH soil samples were collected from HH entrance and near the HH water source. Water samples were also collected from stored HH drinking water containers. eDNA was extracted from 20g soil and tested by qPCR for STH. Samples also underwent microscopy diagnosis. Environmental prevalence data is linked to human infection prevalence data from the same HH collected through the DW3 study.
- HH entrance soil was more contaminated than water source soil. HH water samples yielded low levels of eDNA and will not be tested further.
- Findings show that soil qPCR results seem to reflect human STH infections, even in low prevalence settings.
- The study investigated new eDNA methods including direct extraction of DNA from large quantities of raw soil and droplet digital PCR (ddPCR). Thorough assay validation is required to prevent confounding from zoonotic NTD species, especially in rural areas.
- Soil qPCR is a useful, cost-effective and logistically less challenging surveillance tool than stool collection.

Xenomonitoring for Integrated NTD Surveillance: Successes, Challenges and Paths Forward – Nils Pilotte, Smith College

- Xenomonitoring can play a role, but its operational role and translation into programmatic decision-making requires clarification.

- The opportunities of molecular xenomonitoring (MX) include greater reach than human surveillance, providing non-invasive indirect measurement of prevalence via transmission potential.
- Integrated trapping (flies and mosquitoes) and integrated detection show potential.
- MX in American Samoa showed that even non-vector species provided an indicator of *W. bancrofti* prevalence, with implications for the expanded utility of cross-species MX as a surveillance tool for LF. This study also showed no difference in the positivity rates by trap type, which is important for integration of MX into existing/multi-pathogen surveillance platforms.
- There are opportunities to utilise banked samples from previous studies to answer outstanding questions.

Panel discussion

Martha Saboya highlighted the lack of integration between serology projects and the opportunities to learn lessons from first phase to apply to second phase of surveillance. Pelagie Boko-Collins questioned the gains to be leveraged from the huge investment in vet entomology and emphasized the need to integrate entomology and epidemiology. Dziedzom de Souza noted that Ghana has medical entomologists but they are mostly focused on malaria and there is a need to improve NTD capacity. Sitara Ajjampur reminded the audience of the lab capacity in many countries like India: any lab that can do PCR for blood or stool can do for soil. The samples are stable and can be transported to central laboratories. We don't need to always think of this lab research as run in HICs.

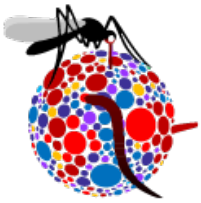
The panel discussed opportunities to leverage sewerage sampling, which only exist where there are sanitation systems, e.g. not possible in rural areas with single household toilets. These can be useful in urban areas. STH has successfully been detected in sewerage using PCR, but more work is needed to validate and interpret such assays.

For a full picture of NTDs we need to survey vectors, populations and environment: How can we put together serosurveillance, environmental surveillance and xenomonitoring into one integrated surveillance program?

Integrated surveillance should be led by country perspective and sustainable from national surveillance capacity. It is important to:

- Identify questions we are seeking to answer (Lessons from Serosurveillance for NTDs);
- Identify the platform and the technical (laboratory) analysis required; and
- Consider the data analysis and interpretation.

Integration is one of the pillars of the new WHO NTD road map and SDG goals. The ultimate goal is to strengthen national capacity by putting together all the tools for countries to use.



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How can major regional NTD programs (e.g. Act to End NTDs) start to establish needs at regional levels? Do they have a role to strengthen lab and personnel capacity, standardize surveys, introduce quality controls and assurance measures?

KNOWLEDGE GAPS IDENTIFIED

What data and tools need to be generated to address the issues raised by the group?

Access to well-defined sample sets

Integrated serosurveillance requires antigen discovery to improve assays and a repository of well-characterized sera to validate those assays. This is also essential to develop STH serology further, e.g. biomarker discovery.
Serology needs to be validated as a programmatic tool, which requires WHO recommendations and policies.

STH serology: antibodies and assays

We know little about STH antibody response profiles – how quickly do antibodies arise, how long are they detectable, etc.
We need to delve further into assay development: antigen selection/production, species-specific vs pan-STH. These diagnostic tools can then be linked to program decision points.

Xenomonitoring

A clear definition of the epidemiology – entomology relationship is necessary and will occur only through modeling based on rigorous and high-quality data collections.
Need for more clearly defined data interpretation framework and for a minimum set of best practice study design and data collection recommendations for all xenomonitoring studies.

Costs of serosurveillance

Information about cost of regular serosurveillance as a public health surveillance tool is missing.

RECOMMENDED NEXT STEPS

What operational research and other actions need to be taken to address the knowledge gaps identified by the group?

Investment in biobanks

A biobank of clinically defined specimens to validate new tests (sera, vectors, stool, other?) would accelerate progress on serological diagnosis across NTDs.

Further studies on sampling strategies

For integrated serosurveillance, research is needed to evaluate alternative sampling approaches to determine if they would provide useful decision-making data.
Sampling strategies also need investigation for environmental surveillance of STH, e.g. appropriate site selection and effect of environmental parameters such as soil pH.

Longitudinal studies of antibody responses
Well-designed longitudinal studies are required to understand antibody response profiles for STH serology. Biomarker discovery research is also essential to advance STH serology and diagnostics.

Molecular xenomonitoring standardization
Research needs build along the following cycle:

- Quality data through standardized MX methods ("minimum information-collection standards") to help us understand the epidemiology – entomology relationship,
- More complete understanding of the epidemiology – entomology relationship to facilitate pipeline development (at a minimum it is essential to include basic epidemiology in all entomology studies), and
- Development of standardized collection and processing pipelines to facilitate integration.

Xenomonitoring implementation
Need to develop and agree upon xenomonitoring/integrated xenomonitoring implementation and interpretation guidelines with NTD stakeholders.
Need for personnel capacity building for xenomonitoring at program (country) level.

Strong protocols for integrated surveillance
Clear protocols for sample/data protection need to be in place before activities begin. This should be addressed early in the planning stage, and take into account the following:

- Emphasise upfront planning requirements and also coordination and cooperation between research projects so that the benefit of collections is maximised.
- Ensure consent is sought for future unknown testing, e.g. "samples will be stored for x time and may also undergo additional screening for diseases of public health concern as identified by MoH"
- Material Transfer Agreement must also specify future testing for collected samples, along with storage, disposal, etc. The regulatory framework around exporting samples depends heavily on the setting and/or country criteria.
- Don't immediately assume that samples will need to be exported; many countries have capacity for in-country samples processing.

Environmental surveillance
Need a thorough community study to validate results of the pilot study in Benin and India.

What are the remaining questions that we need to address to make this a scalable solution? STH has successfully been detected in sewerage using PCR, but more work is needed to validate and interpret these assays.

Health Information Systems
How can we leverage strengthened health information systems (HIS) to achieve NTDs surveillance to improve response? Could HIS play a role in the proposed multi-pronged approach for NTDs surveillance?

Integrated surveillance
Need a multiplex strategy that allows us to continue to monitor for NTD pathogens in a post-validation/verification setting when the national NTD Programs are no longer in place.
Need for longitudinal studies that combine surveillance at human, vector and environmental level. Or better yet, national integrated surveillance with rigorous M&E.
What about data platforms to bring surveillance together?