Diagnostic TPP for *Strongyloides stercoralis* control programs

Strongyloides stercoralis is a soil-transmitted helminth affecting an estimated 300-600 million people globally. Similar to the other STHs, its transmission is characterized by a sequence of events entailing open defecation by infected individuals and maturation of worm stages in the environment, with consequent presence of infectious larval stages of the worm in the soil. Finally, mainly infection occurs through skin penetration of infective larvae (autoinfection is also possible).

Epidemiology

S. stercoralis is most prevalent in areas with inadequate access to water and sanitation, and poor hygiene. These areas include parts of South-East Asia, Africa, Western Pacific regions, and South and Central America. Clinically, the infection can range from subclinical to severe disease manifestations, mostly involving skin, intestine and respiratory tract. A deadly complication, hyperinfection or dissemination, can also occur in immunosuppressed people.

Public Health Response

The World Health Organization (WHO) recommends implementation of preventive chemotherapy (PC), during which a single dose of 200 μg/kg of ivermectin is periodically administered to both school-age children and adults living in endemic areas. Ivermectin is safe for healthy persons or persons with other infections, except for people with high *Loa loa* parasitaemia, who are at risk of developing severe encephalopathy. In such circumstances, it is considered more cost effective to treat all populations at risk than to apply an individual 'test-and-treat' approach.

The initiation of these annual large-scale deworming programs is recommended when the detected prevalence of *S. stercoralis* larvae in stool, diagnosed through Baermann method or agar plate culture, exceeds 5% in a school-based survey or 10% in a community-based survey. When deploying serology-based assays, the detected prevalence thresholds for initiating deworming are higher (school-based survey: 15%; community-based survey: 25%). Re-assessment of prevalence to evaluate continuation of drug distribution is recommended after a 5 year-period.

However, this approach is not sufficient to interrupt transmission without additional measures such as increased access to clean water and sanitation, and education and behavioural change. Additional operational research is also needed to determine the frequency of prevalence reassessment and the characteristics of communities that respond well to deworming compared to those where prevalence remains persistently high despite good, reported treatment coverage.

Available Diagnostic Tools

Since the 1990s, Kato-Katz has been the WHO recommended diagnostic standard for quantifying STH eggs in stool. However, Kato-Katz is not adequate for the detection of *S. stercoralis*. Among parasitological methods, Baermann method and agar plate culture (APC) demonstrated the highest sensitivity and should hence be preferred. Chief limitations of Baermann and APC are that they require fresh stool samples, not more than 24 hours between pre-analytic phase and reading, and the need for skilled microscopists trained specifically on the recognition of *S. stercoralis* larvae. A variety of new diagnostic tests are available, including antibody-based assays (e.g. ELISA and lateral flow assays) and DNA-based methods (qPCR). Each of these tests have important advantages and disadvantages. Important advantages are the ability to simultaneously detect parasites other than STHs (qPCR with appropriate targets and in-lab serology) and the possibility of using preserved samples that allow testing them over longer periods of time compared to Baermann/APC (qPCR, serology). Chief limitations of these tests are the need for well-equipped laboratories with well-trained and skilled technicians (mainly in the case of qPCR), higher cost for reagents/kits (qPCR and serology), and lack of standardized protocols and commercially available kits (qPCR).

Diagnostic Technical Advisory Group

The WHO Department of Control of Neglected Tropical Diseases (NTD) manages a diverse portfolio of twenty diseases, each with its own unique epidemiological and diagnostic challenges. The Strategic and Technical Advisory Group (STAG), the principal advisory group to the WHO for the control of NTDs, decided that a single WHO working group would help ensure that a unified approach could be used to identify and prioritize diagnostic needs, and to inform WHO strategies and guidance on the subject.

Thus, the Diagnostic Technical Advisory Group (DTAG) was formed as an advisory group to the Department of Control of Neglected Tropical Diseases. The first meeting of the DTAG was held in Geneva, Switzerland, on 30 and 31 October 2019.

DTAG members discussed priorities for the year ahead as well as how to manage the complexity of supporting the diagnostics agenda across the entirety of the WHO NTD portfolio. Recommendations were made, based on the understanding that they would be reviewed at the next meeting, as it had been made clear that all NTDs had diagnostic needs which would have to be addressed in due course.

One of the recommendations was that TPPs for diagnostics were needed for *S. stercoralis* that would facilitate implementation of *S. stercoralis* control programs based on mass drug administration.

Purpose of the TPP

Baermann method and APC can be used for the detection of *S. stercoralis* infection at population level, but the challenges of obtaining fresh stool samples, the technical

characteristics of the techniques, and the need for trained personnel and equipment, limit a rapid scaling up of the implementation of the control programs for *S. stercoralis*. The purpose of this TPP proposed by the WHO Department of Control of Neglected Tropical Diseases is to guide the development of new diagnostic tools to support reliable decisions on whether *S. stercoralis* control programs should be implemented.

Brief summary of TPP

In vitro/ex vivo laboratory-based (minimum) or point-of-sampling test (ideal) that allows for detection of analytes specific to *Strongyloides* spp. in all age groups. For laboratory-based tests, tests can be performed in regional or national diagnostic testing laboratories by trained laboratory technicians (<1-week training) and specific requirements for portability and transport should not exceed those of standard laboratory equipment. For point-of-sampling tests, health personnel and community health workers should be able to perform and interpret the test with only a single day of training and any equipment used for reading the test should be highly portable and battery powered if it needs electricity at all. The test should be specific (Sp) (≥98 %) and have a sensitivity (Se) of at least 50%, though different Se/Sp combinations are possible. The test should allow for a throughput of at least 30 samples per hour for a laboratory-based test and four per hour for a point-of-sampling test, and its cost should not exceed 6 US$ per test.