State of the art diagnostics for Neglected Tropical Diseases

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Human African trypanosomiasis
Buruli ulcer
Chagas Disease
Dengue
Echinococcosis
Leishmaniasis
Leprosy
Lymphatic filariasis
Rabies
Schistosomiasis
Trachoma

Transmission control
Integrated vector management
Veterinary public health
Water and environmental sanitation
Behavioural change education

Preventive chemotherapy
Soil-transmitted helminthiases
Schistosomiasis
Lymphatic filariasis
Onchocerciasis
Trachoma
Foodborne trematode infections
Cysticercosis

Eradication
Dracunculiasis
Yaws

Intensified case management, surgery and chronic care

Behavioural change education
## Elimination and Eradication
### Targets and Milestones

<table>
<thead>
<tr>
<th>Category</th>
<th>2015</th>
<th>2020</th>
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<tbody>
<tr>
<td><strong>Eradication</strong></td>
<td>• Dracunculiasis (guinea-worm disease)</td>
<td>• Yaws</td>
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<tr>
<td><strong>Global elimination</strong></td>
<td></td>
<td>• Lymphatic filariasis</td>
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<td></td>
<td></td>
<td>• Leprosy</td>
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<tr>
<td></td>
<td></td>
<td>• Human African trypanosomiasan</td>
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<td></td>
<td></td>
<td>• Blinding trachoma</td>
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<tr>
<td><strong>Regional elimination</strong></td>
<td>• Onchocerciasis in Latin America</td>
<td>• Human rabies transmitted by dogs in the South-East Asia and Western Pacific regions</td>
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<tr>
<td></td>
<td>• Human rabies transmitted by dogs in Latin America</td>
<td>• Schistosomiasis in the American and the Western Pacific regions</td>
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<tr>
<td></td>
<td>• Schistosomiasis in the Eastern Mediterranean, Caribbean, Indonesia and Mekong River basin</td>
<td>• Visceral leishmaniasis in the Indian subcontinent</td>
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<tr>
<td></td>
<td>• Chagas disease transmission through blood transfusion interrupted</td>
<td>• Chagas disease intra-domiciliary transmission in the Region of the Americas</td>
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<tr>
<td><strong>Country elimination</strong></td>
<td>• Human African Trypanosomiasan in 80% of foci</td>
<td>• Onchocerciasis in selected countries in Africa</td>
</tr>
<tr>
<td></td>
<td>• Onchocerciasis in Yemen</td>
<td>• Schistosomiasis in selected countries in Africa</td>
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</tbody>
</table>
Only STH infections of moderate/heavy intensity cause morbidity. For this reason only **quantitative** methods (that count the number of eggs in the faeces are considered optimal). The diagnostic method should ideally also be **low cost** (to reduce the financial burden for the control programme) and using very **simple and possibly re-usable lab material** (to reduce the difficulties in procurement).

At the moment only a few parasitological **methods** respond to these criteria:

- Kato Katz, Mc master and MINI-Flotac. WHO is preparing a series of training video on these three methods.
Schistosomiasis - tools for assessing progress of control

- **Morbidity control**
  - Kato-Katz technique
  - CCA tests
  - Urine filtration/haematuria
  - Antigen detection tests

- **Elimination as a public health problem**
  - Kato-Katz technique – indicator is < 1% of heavy infections
  - CCA tests
  - Hatching test
  - Antibody tests: to identify hot-spots of transmission
  - Antigen and parasite DNA detection tests

- **Interruption of transmission**
  - Antibody detection tests for humans and reservoir hosts/serology
  - Tests to detect parasite DNA in human and snail intermediate hosts

These tools are either available or require further development into field applicable formats.
Schistosomiasis - need for diagnostic tools

- For routine testing of individuals in health facilities
- For epidemiological assessment (mapping)
- For monitoring progress of control programmes — when do we need to change control strategies
- For assessment of praziquantel efficacy and treatment outcomes
- For surveillance
- For verification of interruption of transmission
## Diagnostic used in lymphatic filariasis

<table>
<thead>
<tr>
<th>Field assay</th>
<th>Detection target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood film</td>
<td>Microfilariae</td>
</tr>
<tr>
<td>Alere Filariasis Test Strip (FTS)</td>
<td>Filarial antigen</td>
</tr>
<tr>
<td>Binax Now Filariasis ICT</td>
<td></td>
</tr>
<tr>
<td>Brugia Rapid™ test</td>
<td>Antifilarial antibody</td>
</tr>
</tbody>
</table>

- **Blood film**: Used for detection of microfilariae (Mf) in blood films.
- **Alere Filariasis Test Strip (FTS)**: Detects filarial antigen.
- **Binax Now Filariasis ICT**: Used for rapid detection of filarial antigen.
- **Brugia Rapid™ test**: Detects antifilarial antibodies.
Diagnostic used in lymphatic filariasis

- **Mapping**
  - Blood film or FTS/ICT
  - Mf or Ag≥1%

- **MDA**
  - Baseline
  - Mid-term (optional)
  - Follow-up [TAS Eligibility]

- **Surveillance**
  - FTS/ICT Brugia Rapid
  - Potential for use: Antibody, xenomonitoring

- TAS1
  - 2
  - 3
  - Pass
# Main diagnostic tests for onchocerciasis

<table>
<thead>
<tr>
<th>Type of test</th>
<th>Basis</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>REMO</td>
<td>Palpable nodules</td>
<td>Mapping</td>
</tr>
<tr>
<td>Skin snip</td>
<td>Microscopy mf</td>
<td>Mapping and M&amp;E</td>
</tr>
<tr>
<td>O-150 PCR</td>
<td>DNA detection</td>
<td>M&amp;E and surveillance</td>
</tr>
<tr>
<td>Ov-16 in kids</td>
<td>Antibody detection</td>
<td>Mapping, M&amp;E and surveillance</td>
</tr>
<tr>
<td>Skin snip PCR</td>
<td>DNA detection</td>
<td>Surveillance in low prevalence</td>
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</table>
Diagnostics needed for dengue

Patient management

- To distinguish dengue from other diseases with similar clinical presentation (e.g., malaria, chikungunya, zika, etc)
- To assess severity of infection
- To provide rapid results

Surveillance and outbreak management

- Inexpensive
- Easy to use
- Stable at temperatures >30°C
- Can be used in remote areas (e.g., Pacific islands)

Adapted from Dengue diagnostics: proceedings of an international workshop 4-6 October 2004 WHO/TDR Geneva, Switzerland TDR/IRM/DIAG/DEN/05.1
Dengue diagnostics

- Requires better quality rapid tests with high sensitivity and specificity
- Should not have cross reaction to chikungunya and zika viruses
- Quality assurance of rapid tests should be ensured
Chagas disease

- The biggest challenge is to increase diagnosis (at present <10%), challenges are biomedical, psychosocial, access, etc.
- Acute phase diagnosis - made through parasitological tests (direct or through concentration/centrifugation techniques)
- Chronic phase diagnosis - done through two serological tests; a third test may be needed for doubtful or inconclusive cases
Chagas disease

- High sensitivity and sensitivity serological tests available: the challenge - a rapid diagnosis for use in rural areas, slums, etc.
- Commercialized serological rapid diagnostic tests and last-generation serological tests currently being evaluated by WHO
- Markers of cure or markers to assess therapeutic response also needed, since results of serological tests remain positive for years after successful parasitological treatment
Buruli ulcer and yaws - current tools

Buruli ulcer
- PCR targeting IS2404 - the most widely used method in endemic countries

Yaws
- Standard lab-based serology
  - treponemal (TPHA, TPPA)
  - non-treponemal (RPR)
- Rapid syphilis test: combined dual treponemal and non-treponemal tests. Very useful for field use
- PCR
Buruli ulcer and yaws - gaps and future needs

Buruli ulcer

- Point-of-care diagnostic test
- Thin layer chromatography (TLC) that can detect toxin mycolactone in tissue. The toxin is unique to BU and detection confirms the disease. Field studies to start by year end.
- Antigen to capture test converted into lateral flow. Still in development stage by researchers

Yaws

- Sufficient tools to achieve eradication
- Need to strengthen capacity for PCR in yaws endemic countries
Visceral leishmaniasis

- **Current field-level diagnostics**
  - Serological tests: rapid tests (rK39) and DAT
  - Parasitological tests (gold standard): lymph node, spleen and bone marrow aspirates

- **Gaps**
  - More sensitive rapid tests needed
  - Parasitological tests: low sensitivity (60-85%); unavailable in certain endemic areas

- **Future needs**
  - Rapid, highly sensitive/specific, non-invasive test to differentiate active VL from parasitic exposure and from cured VL patients (e.g. urine-based)
  - Should be able to follow-up therapy efficacy
  - Should be useful for the diagnosis of VL in *Leishmania/HIV*-co-infected patients
  - Should be user-friendly under field conditions
Cutaneous leishmaniasis

- **Current field-level diagnostics**
  - Parasitological tests (gold standard): dermal scraping or aspiration for direct examination
  - Clinical diagnosis: common in many endemic areas

- **Gaps**
  - Parasitological tests: low sensitivity (64-90%) and invasive

- **Future needs**
  - Rapid, highly sensitive/specific, non-invasive test
  - Should be user-friendly under field conditions
HAT - current tools and strategies

- Card Agglutination Test for Trypanosomiasis (CATT) is a serological test for active mass-screening of at-risk population
- Rapid Diagnostic Test (RDT) being under evaluation, mostly for passive screening
- Trypanolysis (TL) being re-tooled and recently introduced in the diagnostic algorithm
- Confirmatory parasitological tests: Gland puncture, Capillary Tube Centrifugation (CTC) and mini Anion-Exchange-Centrifugation Technique (mAECT)
- Molecular tests developed (i.e. PCR and LAMP) – unfortunately not accurate to add value to diagnosis process of HAT
- For disease staging, lumbar puncture, cerebrospinal fluid WBC count and parasite detection is still the only method available
HAT - diagnostics gaps and future needs

- Maintain active case-finding surveys in well-defined areas according to the epidemiological situation, and adapt strategies to the new available tools
- Reinforce passive case-finding to improve access to diagnosis
- Strengthen innovative case-finding strategies and expand to peripheral health system in defined regions to ensure sustainability of control and surveillance
- Introduce simpler and affordable diagnostic tools for use by non-skilled staff in rural areas
- However
  - Should serological tests be applied to all individuals seeking health care from at-risk areas or only to selected cases (according to the clinical signs for example)?
  - How to increase specificity of serological testing
Taeniasis - neurocysticercosis diagnostic situation

Taeniasis

- Stool-microscopy
- Self-identification of infection through visual observation of worm segments in stool (easy, low cost, low sensitivity and specificity)
- Coproantigen detection with ELISA (sensitivity up to 96, relatively easy to perform)

Cysticercosis/NCC

- **Serology**: varying results also possible with urine, saliva and for NCC cerebrospinal fluid (CSF)
  - Antibody detection
  - Antigen detection is more suitable for detection of active infections, being the Ag-ELISA - the most commonly used test. This test can also vary regarding sensitivity (55-92%) and specificity (83-84%)
  - Other serological tests available are radioimmunoassay, hemagglutination, the complement fixation test, dipstick assay, latex agglutination and immunoblot techniques
Taeniasis - neurocysticercosis diagnostic situation

- **NCC**: Diagnosis can be complicated since serology alone not enough to prove or dismiss a case
  - Serology tests can be accurate if CFS is used. This is invasive and painful.
  - In certain NCC patients the parasite dies and a calcified cyst remains. These patients may or may not show NCC symptoms and antibody detection tests may show positive or negative results independently
  - For an accurate NCC confirmation, neuroimaging techniques are needed. However, these are expensive and often not available in endemic areas

- *Taenia solium/cysticercosis* is a re-emerging zoonosis. Research priorities include development of more sensitive, low cost and specific diagnostic tests
Thank you