The shift from control to elimination: implications for diagnostics

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de worm³

LCNTDR

NATURAL HISTORY MUSEUM
Introduction

- Soil-transmitted helminths (STHs) are part of the NTDs and account for a high burden of disease
- Morbidity control with MDA is the current STH strategy
- Future strategies should aim at moving from control to elimination of STHs

World Health Organization (WHO) 2014
The challenge

The switch from control to elimination from the diagnostic point of view

Effects of MDA, economic development, improved sanitary conditions and health education

Reduced prevalence, more low-intensity infections

Current diagnostic methods have a low sensitivity for these low-intensity infections

More sensitive diagnostic approaches are needed

Importance of detecting low-intensity infections
## Current and new diagnostic methods

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<tr>
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<th>Coprological stool methods</th>
<th>Molecular methods</th>
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<tr>
<td><strong>Advantages</strong></td>
<td>• Cheap</td>
<td>• Sensitivity drastically increased</td>
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<td></td>
<td>• Readily available</td>
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<td>• Easy to apply in field settings</td>
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<td><strong>Disadvantages</strong></td>
<td>• Lower sensitivity</td>
<td>• Higher costs</td>
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<td>• Risk of missing low intensity infections</td>
<td>• Difficult to implement in field settings</td>
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<td>• Risk of contamination</td>
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The lack of gold standard diagnostic methods makes validation of new diagnostic approaches challenging.

Adapted from Johansen; Acta Tropica 141 (2015) 161-169
Advances in PCR methodology

- Ribosomal and mitochondrial targets in PCR may be sub-optimal for low-intensity infections and lack of species-specificity
- New PCR approaches have been developed that target species-specific repetitive non-coding repeat DNA
- The high repetition sequences have a rapid evolutionary divergence: ideal for distinguishing even closely related species (i.e. *A. duodenale* and *A. ceylanicum*)
- Molecular approaches are becoming cheaper, easier to conduct and field based methods are in development
- PCR enables to detect smallest volumes of parasite DNA, ideal for detecting low-intensity infections.

Quantitative PCR (qPCR)

- qPCR allows to **quantify** the detected genetic material (DNA, RNA)
- qPCR is faster in detecting amplified DNA, no separate readout is needed
- Sensitivity is increased
- Lower amounts of material can be used
- Throughput is considerably higher than conventional PCR

- Possible challenges: qPCR is more expensive and more difficult to implement in field settings

- Today’s possibility of multi-parallel assays helps to drastically reduce cost of the PCR
- Additionally, the assay can be optimized for the geographic location (i.e. what pathogens should be included) as the assays can run independently
- Pooling of samples can further reduce costs

qPCR in DeWorm3

- Define molecular cut-offs to define transmission interruption
- Optimize stool collection, processing and storage
- Identify optimal extraction and pooling methodologies
- Build capacity at multiple sites for a systematic and harmonized approach to molecular diagnosis of STHs
- Create a biobank of stored parasite genetic network for the NTD community
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