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# The National Strongyloides Working Group in Australia 10 workshops on: commendations and recommendations

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**S**trongyloidiasis, caused by the intestinal helminth *Strongyloides stercoralis*, is commonly found in developing nations in tropical and subtropical regions.<sup>1</sup> Strongyloidiasis was omitted by the World Health Organization (WHO) as one of the Soil Transmitted Helminths in their Neglected Tropical Diseases Roadmap and can therefore be considered one of the most neglected tropical diseases.<sup>2,3</sup> Despite its reputation as a disease of developing countries, strongyloidiasis remains an important disease in Australia, particularly for Aboriginal and Torres Strait Islanders, and those living in remote communities.<sup>4,5</sup>

The majority of people infected with *S. stercoralis* present with a chronic form of strongyloidiasis.<sup>6</sup> Infected people may be asymptomatic, or they may suffer primarily with gastrointestinal, respiratory<sup>7</sup> and/or dermatological symptoms, ranging in severity from mild and intermittent to severe and unrelenting.<sup>6</sup> Due to the autoinfective life-cycle, almost unique among human intestinal helminth infections, infection may be life-long. Secondary infection may cause pneumonia, meningitis or septicaemia,<sup>8-10</sup> and is more likely to occur in immunosuppressed individuals, particularly those treated with corticosteroids. Returned service personnel and those who have migrated from, lived in, or travelled through endemic areas, may develop severe disease many decades after initial infection.<sup>11-14</sup>

Control and prevention measures must incorporate education, environmental health, effective diagnostics, and appropriate treatment of infected persons. Commonly used anthelmintics such as albendazole, mebendazole, and pyrantel are not effective

against *S. stercoralis*, leaving patients with residual worms that subsequently multiply and re-establish infection. Ivermectin is currently recommended as the most effective treatment option.<sup>15,16</sup>

The pioneering work on strongyloidiasis in Australia was performed by Professor David Grove and his colleagues for World War II ex-prisoners of war who were still infected 40 years after returning home.<sup>17</sup> Grove developed an enzyme-linked immunosorbent assay (ELISA) based on the detection of antibodies to *Strongyloides* in serum, which became a routine pathology test for diagnosing strongyloidiasis from 1987.<sup>18</sup>

## National Strongyloides workshops

The first National Workshop on Strongyloidiasis was held in Nhulunbuy in 2001. A community elder asked "We've had Strongyloides for so long, why hasn't something been done?" In response to this, the National Strongyloides Working Group (NSWG) was formed as a special interest group of the Australasian College of Tropical Medicine. The chairperson, Emeritus Professor Rick Speare from James Cook University, is an internationally recognised expert on strongyloidiasis. The group has expanded to consist of several multidisciplinary experts including parasitologists, veterinary and molecular scientists, pathologists, environmental health officers, medical practitioners, health promotion and prevention professionals, and other interested parties. The stated aims of the group are to:

- raise awareness of strongyloidiasis
- inform health professionals and community members about the disease

and its prevention, diagnosis, treatment, and control

- advocate on behalf of affected people for appropriate changes to government policy in relation to prevention, diagnosis, and treatment, based upon current research.

The ultimate goal is eliminating the disease from Australia.

Much has been achieved in Australia since the first meeting of this interest group of concerned experts. These achievements deserve recognition. Here we describe the achievements and make a series of recommendations for consideration for research and clinical practice in the future.

## Achievements to date

*1. The establishment of a sustained working group that has facilitated information exchange as well as communication of scientific information to the government, clinicians, and the general public*

In late 2015, the 10<sup>th</sup> National Workshop on strongyloidiasis was held in Adelaide. The working group has grown to include a representation of health professionals including researchers, clinicians, parasitologists, health promotion experts, Indigenous health workers, and Indigenous community members.

*2. Working with Indigenous communities with a concomitant reduction in disease burden in some communities*

There have been successful outcomes in a number of Indigenous communities that have been engaged in developing community-based mechanisms to reduce *S. stercoralis* infections. Working group members have been involved in developing, in partnership with these communities, a number of approaches, including engagement strategies,<sup>19</sup> a clinical audit approach,<sup>20,21</sup> mass drug administration approaches,<sup>22,23</sup> infrastructure upgrades, and community-based education programs.<sup>24</sup> The effectiveness of ivermectin in eliminating *S. stercoralis* from the body, and establishing a criterion for cure using *Strongyloides* serology, was demonstrated at Miwatj Health, an Indigenous health organisation in the Northern Territory.<sup>20</sup> The effectiveness of mass drug administration of ivermectin in eliminating *S. stercoralis* in more than 80% of those treated, along with low reinfection rates, has been demonstrated in two remote Aboriginal communities.<sup>22,23</sup>

3. CDC correction to *Strongyloides* life cycle

Following requests by the NSWG, the US Centers for Disease Control and Prevention altered their graphic describing the *S. stercoralis* life cycle (<http://www.cdc.gov/parasites/strongyloides/biology.html>) to illustrate that the free-living stage of the nematode's life cycle is limited to a maximum of one generation (Figure 1). This has important implications for both treating infected people and environmental control in preventing transmission.

4. Disseminated strongyloidiasis was added to the Northern Territory CDC's notifiable disease register in 2011

Disseminated strongyloidiasis, defined as the detection of *S. stercoralis* by microscopy in a specimen not derived from the gastrointestinal tract, has been added as a new disease (May 2011, version 6) in the Centre for Disease Control NT Notifiable Diseases.<sup>25</sup> The NSWG continues to advocate for inclusion of strongyloidiasis (by laboratory notification) in notifiable disease registers of all states and territories as we lack adequate data about the prevalence of the disease or its progression to severe disease. Laboratory notification of strongyloidiasis would provide incidence data and enable a systematic evidence-based approach to addressing this public health issue.

5. Ivermectin use for strongyloidiasis is now accessed through the Pharmaceutical Benefits Scheme (PBS) using a streamlined authority

code, a process that improves workflow and removes systematic discouragement to prescribing for practitioners

At the time the NSWG was formed, ivermectin required telephone authorisation from Medicare on the Pharmaceutical Benefits Scheme (PBS) and, as a result, clinicians were reluctant to prescribe it. Downscaling the requirements to a streamlined PBS authority code removed this psychological barrier, resulting in clinicians being more likely to prescribe ivermectin for strongyloidiasis. The NSWG, in collaboration with health professionals, the organisation One Disease at a Time, and Merck Sharpe & Dohme, achieved this.

6. Pathology tests for strongyloidiasis have been further developed

These developments include molecular methods for *S. stercoralis* in faecal specimens [real-time PCR<sup>26</sup> and loop-mediated isothermal amplification (LAMP)],<sup>27</sup> which are promising but not yet commercially available. Serology has been successfully performed using blood spots on filter paper, improving issues associated with collection of blood from young children and specimen transportation and storage from remote areas.<sup>28</sup>

Recommendations

1. Further engagement and collaborations with affected Indigenous communities, with the goal of elimination of the disease

Further work is needed to engage, communicate and progress towards

prevention and elimination of strongyloidiasis with Indigenous communities. Only with communities' involvement will strongyloidiasis be eliminated in Australia. Inclusion of Indigenous Elders and Traditional Owners in decision-making is crucial.

2. Greater understanding of the environmental factors influencing survival and transmission of *S. stercoralis*

Currently, clinical approaches to treating strongyloidiasis are the focus of interventions. However, understanding the environmental factors that allow the nematode to survive in the environment (soil, wet areas inside and outside the house, and waste water reservoirs) and to be transmitted to people, will increase the number of tools at our disposal for preventing and controlling the disease.<sup>29</sup> This is particularly important if ivermectin resistance emerges in *S. stercoralis*, as it has in sheep infected with *S. papillosus*.<sup>30</sup>

3. Greater understanding of the role that dogs have in transmission of *S. stercoralis*

The role that dogs might play in transmission of *S. stercoralis* to humans is not clear. *Strongyloides* larvae have been found in dogs in central Australia, but the species is unknown (Speare per obs). Studies using animal models have demonstrated that dogs can develop patent infections with *S. stercoralis*.<sup>31</sup> As dogs and people live closely together, controlling *S. stercoralis* in dogs might be key to transmission reduction and requires further investigation.

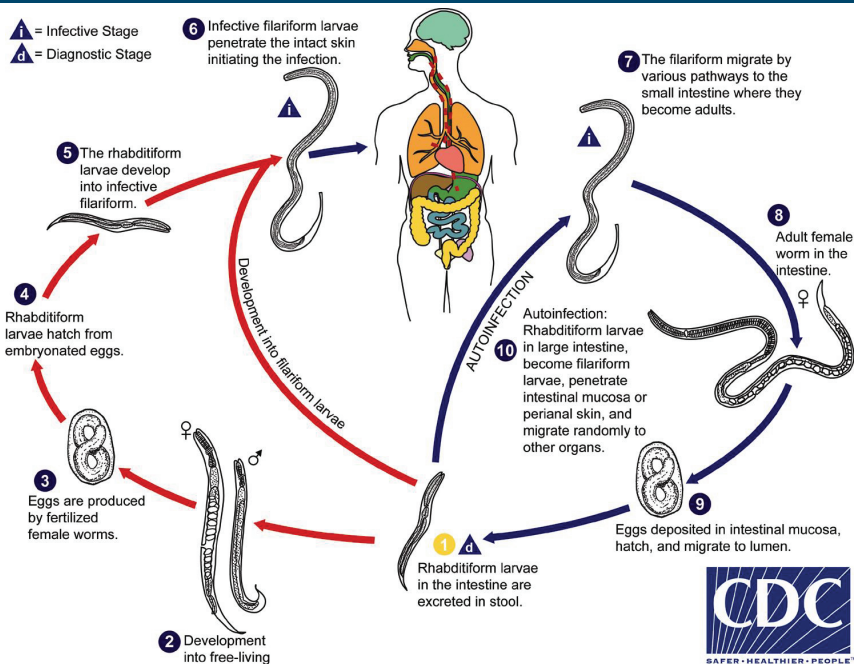
4. Greater understanding of barriers to control in communities

Barriers to prevention and control in communities include: insufficient knowledge of the disease by health bureaucrats and clinicians; insufficient and poorly maintained housing and health infrastructure; and a lack of understanding of the parasite by health professionals and communities that includes the life cycle, symptoms, criteria for cure, and strategies for preventing transmission.<sup>5</sup>

5. Improved availability and utilisation of current diagnostic techniques

Diagnostic techniques for the detection of *S. stercoralis* are not yet ideal and require careful interpretation. Microscopy is most useful in acute and severe strongyloidiasis, when there is a heavy larval output.<sup>32</sup> Sensitivity of faecal microscopy is poor in chronic strongyloidiasis because larvae are not evenly distributed through the faecal sample and may be shed intermittently. Culture methods, such as agar plate culture, are more sensitive, but require live larvae.

Figure 1: Altered US CDC graphic illustrating that the free-living stages of the nematode's life cycle is limited to a maximum of one generation.



Larvae may not survive transportation to the laboratory as they are killed by extended refrigeration, exposure to high temperatures, and the use of preservatives such as sodium-acetate, acetic acid and formalin (SAF). Furthermore, formalin-ethyl acetate concentration, commonly used in Australian diagnostic pathology labs, may remove rather than concentrate larva in stool.<sup>33</sup> Although current molecular detection methods don't require live larvae, they are not sensitive in stool samples where there is a low larval load<sup>26</sup> and cannot be used on SAF-preserved samples. Serology remains the best available diagnostic test. A positive test indicates a current infection, except during the window period following infection before the host has mounted an immune response to the parasite, and 3–6 months following effective treatment. False negatives may occur in those who are significantly immunosuppressed.<sup>33</sup> Educating clinicians about the need to consider strongyloidiasis in differential diagnoses, and to ensure the use of optimal specimen collection and processing techniques for the detection of strongyloidiasis is intrinsic to an effective control program.<sup>6</sup> There is a critical need to develop rapid, sensitive, and field portable diagnostic techniques for the detection of strongyloidiasis that can be effectively performed by personnel with limited training and in resource limited settings. A simple test to definitively identify cases of systemic disease would also be highly beneficial.

### 6. Continued advocacy for inclusion of strongyloidiasis on the notifiable diseases register nationally<sup>34</sup>

Lack of data is one of the major barriers to controlling and eliminating the disease.<sup>32</sup> Notification would provide the data for an accurate estimate of incidence to inform the necessary public health action at individual, community, regional and national levels.<sup>31</sup>

### 7. Continued advocacy for a strategy for the elimination of strongyloidiasis in Australia that respects the needs of all groups of people suffering from strongyloidiasis

Each Aboriginal community or region needs a program to eliminate the disease devised and led by the community.<sup>19,29</sup> In other groups, a standardised process for identifying infected individuals, treating them, and monitoring for cure, is required. Advocacy includes identifying opportunities to extend collaboration and joint approaches with other communities, groups and agencies fighting similar diseases, such as hookworm, where joint efforts could be more effective.

## Conclusion

There have been a number of achievements in the control and treatment of strongyloidiasis, and the work of the NSWG significantly contributes to these achievements. However, the NSWG will not rest while this preventable and treatable disease remains endemic in our Indigenous communities in Australia.

## Dedication

This work is dedicated to the memory of Rick Speare and Frank O'Donohoo, both of whom were taken from us before their time and, through their work, will continue to have a significant and lasting impact on public health in Aboriginal communities and on the control of strongyloidiasis in Australia.

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