Effective diagnostic tests and anthelmintic treatment for *Strongyloides stercoralis* make community control feasible

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**SUMMARY**

*Strongyloides stercoralis* is endemic in tropical and subtropical countries, and is prevalent particularly in economically impoverished people. Although an estimated 30 to 100 million people worldwide suffer from *S. stercoralis* infection and it is a life-long disease, it remains a neglected tropical disease. Faecal testing for *S. stercoralis* is very insensitive. The prevalence of *S. stercoralis* in Indigenous Australians (up to 60%) is much higher than previously thought, and its prevalence in Papua New Guinea is likely to be much higher than currently believed. When *S. stercoralis* and the HTLV-1 virus coexist in the one person, both diseases progress more quickly than when either infection is on its own. When people become infected with *S. stercoralis*, they develop acute strongyloidiasis which may be life-threatening. At any time during the course of the disease, if the immune system is suppressed, most often by corticosteroid drugs, infected people may develop hyperinfective strongyloidiasis and they will die unless the underlying *S. stercoralis* infection is effectively treated. The use of serology for diagnosis, together with ivermectin treatment, has revealed that it is possible to eradicate *S. stercoralis* from the patient, and serology can also define the effectiveness of treatment. The reservoir of infection is humans; the free-living stages are short-lived. Mass treatment may be effective at eliminating *S. stercoralis* from a community. Safe water and effective sanitation alone do not lead to elimination of *S. stercoralis*. Up-to-date knowledge of *S. stercoralis* has been revealed through the workshops of the National Strongyloides Working Group in Australia and is summarized here. Much of this information is now available on the world wide web, and the addresses of relevant web sites are given.

**Introduction**

*Strongyloides stercoralis* (Bavay 1876) Stiles and Hassal 1902 was first described in France by Bavay in 1876 as *Anguillula stercoralis*. The genus *Anguillula* was preoccupied by an eel genus, so in 1879 Grassi erected a new genus *Strongyloides* for roundworms previously known as *Anguillula*. In 1902, Stiles and Hassall showed that the correct name is *Strongyloides stercoralis* (1). This species is widespread particularly throughout tropical and subtropical areas of the world. Estimates of the number of people affected vary from 30 to 100 million (2). *S. stercoralis* occurs in Papua New Guinea (PNG) (3) but its extent is unknown. Surveys by Alan Kelly in the early 1970s did not reveal *S. stercoralis* (4). Its presence in Morobe Province was revealed in the early 1980s by using a filter paper culture technique (JMS, unpublished data).

*S. stercoralis* is a nematode tissue parasite that causes a life-long disease unless eradicated by treatment (5). It can cause an overwhelming infection called hyperinfection, or disseminated strongyloidiasis, when an infected person’s immune system is suppressed (6). Corticosteroids play an
important role in triggering hyperinfection (7). Other drugs and conditions that suppress the immune system also lead to hyperinfection, and in about 10% of the cases the cause is not clear (8). Human T-cell leukaemia virus type 1 (HTLV-1) occurs in some parts of PNG and West Papua (9). Coinfection with S. stercoralis and HTLV-1 causes accelerated progression of both diseases (10) and resistance to anthelmintic treatment for S. stercoralis (11,12).

Although disease caused by S. stercoralis is now diagnosable and treatable (5), it has been neglected. It is now classified by the World Health Organization as a neglected tropical disease.

There are a number of reasons why S. stercoralis has been neglected. These are elaborated later. Briefly they are:

- The disease has been difficult to diagnose. The symptoms are non-specific and secondary infection often masks the underlying cause of the disease. Faecal testing is insensitive. Although the sensitivity of the specific IgG test is high, patients in the acute or hyperinfective phase of the disease may not have the antibodies. Consequently there has been gross under-diagnosis of the disease, as well as gross underestimation of its prevalence and its contribution to morbidity and mortality. In a retrospective study in Queensland from 1998 to 2002, of 120 hospital admission records of patients who tested positive for Strongyloides, only 6 gave strongyloidiasis as the primary diagnosis. The primary diagnosis of the remaining 114 was one of the following: gastrointestinal disorder, respiratory disorder, failure to thrive, genitourinary disorder, skin disorder or sepsis (13). All these conditions are features of S. stercoralis infection, and it is likely that the true primary cause of disease in these cases was in fact S. stercoralis infection.

- The sensitivity of faecal testing is low. Until recently, practitioners have relied on faecal testing for diagnosis. This means that there has been an underestimation of prevalence and an overestimation of the efficacy of anthelmintic drugs (14,15).

- The disease has been difficult to cure. There was a lack of effective drugs (until ivermectin became available). In addition, the ability of the worms to multiply in the host means that all the worms must be eliminated in order to effect a cure. So it is important to be able to determine whether a treated person has been effectively treated. The IgG diagnostic test has made this possible (16).

- A mistaken belief that free-living stages of S. stercoralis persist in the environment. In fact, the free-living stages are short-lived (17,18).

As a result, health authorities have not seen the need to carry out mass treatment to control S. stercoralis. Australia, in spite of having an excellent health system, has not come to grips with S. stercoralis in its midst. Although S. stercoralis is rare in mainstream Australia, it is hyperendemic throughout tropical and subtropical Indigenous Australia. Estimates of prevalence in various Indigenous settlements are between 4.5% and 60% seropositive (19-25) and between 2% and 41% positive by stool testing (19,26,27). In central Australia, it coexists with HTLV-1 (28).

In 2001, a group of concerned professionals came together at a workshop in Nhulunbuy in the Northern Territory and formed the National Strongyloides Working Group (NSWG) of the Australasian College of Tropical Medicine to investigate S. stercoralis. Since then, the NSWG has held biennial National Workshops on Strongyloidiasis in order to share information about S. stercoralis and to make recommendations on how to tackle the disease. This has resulted in bringing together information about S. stercoralis, some of which would not otherwise have entered the public arena.

What we now know gives us the tools to enable the disease to be controlled. This paper will summarize this information and refer to more detailed material, much of which is available on the world wide web on the Aboriginal Resource and Development Services web site at http://www.ards.com.au/health_strong.htm or the James Cook University web site at http://www.jcu.edu.au/school/phtm/PHTM/ss/.
**Strongyloides stercoralis life cycle**

The life cycle is represented schematically in Figure 1. It is described in detail by Speare (5) and is available at http://www.jcu.edu.au/school/phtm/PHTM/ss/acrrm-cd/CD-Index.pdf. A patient education flip chart about *S. stercoralis*, the life cycle, the disease, and how to prevent and treat it, is available in plain English at http://www.ards.com.au/StrongFront.pdf. Infective filariform larvae are illustrated in Figure 2. There are a number of features in the life cycle that have implications for the treatment of patients and control of the disease.

The parasitic females actively burrow through the intestinal absorptive epithelium counteracting the movement of epithelial cells as they migrate towards the tips of the villi (30), and filariform larvae can migrate anywhere in the body (31). Thus *S. stercoralis* is a tissue parasite in intimate association with the host.

![The Life Cycle of Strongyloides stercoralis](image)

Figure 1. Schematic representation of the life cycle of *Strongyloides stercoralis*. Updated and modified from Zaman (29).
S. stercoralis has the ability to multiply in the body by the autoinfective cycle. Some rhabditiform larvae develop into infective filariform larvae in the lower part of the gut, and enter the body proper through the side of the lower gut or the skin around the anus (5). As a consequence, S. stercoralis causes a life-long disease, and hyperinfection occurs particularly when type 2 immune responses are suppressed (32). In addition, a person is cured only when treatment has eliminated every worm in the body. A single worm may reestablish a patent infection by the autoinfective cycle.

The infective larvae can migrate anywhere in the body (31). So larvae can cause symptoms anywhere in the body, and bacteria carried by the larvae from the gut may seed secondary infection anywhere in the body.

S. stercoralis does not persist in the environment. There is a maximum of one generation of free-living S. stercoralis (33) and the infective larvae survive for only two weeks even in ideal conditions (34). They are all dead within 3 weeks of faecal contamination. The reservoir of infection is infected people.

Infective filariform larvae have narrow tolerance limits for survival. Their optimum temperature range is 20 to 28 degrees Celsius and they die in the refrigerator and in the heat (5). They die within a few hours on dry soil in the sun and within 3 days on dry soil in the shade (17). So it is essential to store faecal samples correctly and for as short a time as possible, particularly when using diagnostic tests that depend on the presence of viable larvae in the faeces.

Strongyloidiasis: progression of the disease

The three phases of strongyloidiasis

The progression of the disease is summarized in Table 1. There are three phases of strongyloidiasis: acute, chronic and hyperinfective (disseminated).

Acute strongyloidiasis

In the 1950s, Tanaka infected himself with infective filariform larvae through the skin and, 27 days later, rhabditiform larvae first appeared in the faeces (5). The worms multiply in the body, and as the numbers increase, the symptoms become more intense. This is acute strongyloidiasis. In children, the infection sometimes causes wasting and hypokalaemia (36). In adults, it sometimes causes dysentery (35). Some mortality may occur at this stage. Eventually
**TABLE 1**

**Progression of Disease Due to Strongyloides Stercoralis: Changes in Behaviour of the Worms, Larval Output, Effectiveness of the Diagnostic IgG Test, Immune Status, and Symptoms as the Disease Progresses**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Worms</th>
<th>Larvae/ml stool</th>
<th>Specific IgG test</th>
<th>Immunity</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Number of females in gut increases via the autoinfective cycle, then larval output slows as immunity increases.</td>
<td>0 to &gt;1000. Stool test negative or positive (35)</td>
<td>Negative, equivocal or positive</td>
<td>'Window period' before specific IgG levels become raised. Immune response increases, antibodies IgE, IgA, IgM and IgG increase, number of eosinophils increases.</td>
<td>Marked skin, lung and digestive system symptoms, severe diarrhoea, wasting and hypokalaemia in children; can be fatal (36).</td>
</tr>
<tr>
<td>Chronic</td>
<td>Low larval output by stunted females reduces migration of larvae in tissues. Immunity keeps the number of worms low, but worms persist.</td>
<td>0 to 400. Stool test usually negative</td>
<td>Positive or equivocal</td>
<td>Immune response is strong, antibodies IgE, IgA, IgM and IgG are raised, eosinophilia is present in about 70%.</td>
<td>Skin, lung and digestive symptoms mild to moderate and may be intermittent; at least 70% have symptoms (37).</td>
</tr>
<tr>
<td>Hyperinfective (Disseminated)</td>
<td>Females recover (38); numbers of females, migrating larvae and larvae in stools increase. The person will die unless they get effective treatment.</td>
<td>400 to &gt;1000. Stool test usually positive</td>
<td>Positive, equivocal or negative</td>
<td>Immune suppression causes the antibodies IgE, IgA, IgM and IgG and the number of eosinophils to decrease (39).</td>
<td>Severe skin, lung and digestive system symptoms; other organs may be affected. Secondary infection with gut bacteria in 50%, which may present as pneumonia, meningitis or septicaemia. Case fatality rate 70% (8).</td>
</tr>
</tbody>
</table>

*Information from R. Speare unless otherwise indicated*
the immune system responds with type 2 immunity (40) that attacks the females in the gut and the larvae migrating through the tissues. The effect on the females is marked reduction in the rate of reproduction (38,41). The immune response slows the migration of larvae through the tissues, and probably kills some of the migrating larvae (42). The overall effect is a reduction of the worm load, but the immune system is not able to eliminate the worms.

Chronic strongyloidiasis

The infection persists. This has been shown by studies of World War 2 ex-prisoners of war who acquired S. stercoralis in prison camps during the war and had the infection for up to 57 years (37,43,44). This phase is called chronic strongyloidiasis. The person has fewer worms, and intermittent symptoms. Infected people remain infected for the rest of their life (5).

Hyperinfective strongyloidiasis

In some people, the number of worms continues to increase slowly, and hyperinfective strongyloidiasis develops with no obvious cause. Most cases of hyperinfective strongyloidiasis are associated with suppression of the immune system, particularly type 2 immunity. This topic has been reviewed by Keiser and Nutman (32). A study of fatal strongyloidiasis in the literature showed that the most common precipitating factor was the administration of corticosteroid drugs (60%) (7,8). Some deaths were due to other conditions and other drugs that suppress type 2 immunity (30%). There was no obvious cause of hyperinfection in a few cases (10%) (8). Unfortunately, corticosteroids are sometimes given to patients for respiratory symptoms that are actually due to S. stercoralis larvae migrating through the lungs (45,46). An endoscopic and histopathological study of the duodenum in hyperinfection was published recently (47).

Symptoms

A summary of the symptoms is given in Table 1. The symptoms of S. stercoralis infection have been described in detail by Grove (37) and summarized by Speare (5). Briefly, the majority of symptoms are non-specific. This is a major impediment to diagnosis of the disease. The severity of the symptoms varies according to the number of worms in the body, and which organs are affected depends on where the larvae have migrated to. The most frequent symptoms are associated with the skin, digestive system and lungs, but any other organ may be affected, including the joints and central nervous system. Fatigue is common. Secondary infection may make its presence felt as pneumonia, septicaemia or meningitis, or abscesses in any organ or in the muscles. The only symptom that is pathognomonic for S. stercoralis infection is larva currens. It consists of itchy linear urticarial rashes (Figure 3) that move at 2 to 10 cm per hour (37).

Immune regulation of S. stercoralis infection

In chronic strongyloidiasis, the level of infection with S. stercoralis is regulated by the type 2 component of the immune system. IgA, IgM, IgG and eosinophils are lower in severe strongyloidiasis than in mild or moderate strongyloidiasis (39).

The effects of antibodies on filariform larvae in the body have been investigated by experimental work in mice. Both IgG and IgM are important in killing filariform larvae in the body, but the role of eosinophils is not clear. Brigandi et al. (42) showed that eosinophils are associated with IgG-mediated killing of filariform larvae in mice. IgM together with complement and neutrophils was protective against filariform larvae (48). Similarly, IgG together with complement and neutrophils was protective against filariform larvae (40).

With respect to the stages in the gut, IgA and IgE play a role in modulating larval output (43), probably by reducing parasitic female fecundity by impairing their ability to feed and excrete. When stunted females that were not producing larvae were taken from immune dogs and transplanted into naive dogs, they recovered and reproduced (38).

The level of IgG4 rises in people who have been infected with S. stercoralis for a long time (49). Experimental evidence is consistent with the hypothesis that IgG4 blocks IgE-mediated immune responses (43).

Diagnostic tests

There are two main possibilities for diagnosing S. stercoralis available in Australia: examination of faeces for rhabditiform larvae or filariform larvae, and
examination of the blood for specific antibodies to *S. stercoralis*. Sputum and duodenal fluid are sometimes examined for *S. stercoralis* larvae.

Tests are currently being developed in the USA based on recognizing antigenic material from *S. stercoralis* in the blood or faeces (50). This may overcome the problem of changing immune status during the progression of the disease.

**Faecal testing**

Faecal testing has high specificity but poor sensitivity. The most sensitive faecal test is the agar plate culture.

The most common test used is the direct smear. This is a particularly insensitive test for the early stage of acute strongyloidiasis, for chronic strongyloidiasis and for the early stages of hyperinfective strongyloidiasis due to the very low larval output in the faeces. Conway et al. (51) summarized the relative sensitivity of various faecal tests. In these studies, the estimated number of people infected was the number positive by any one of a number of faecal tests. The estimated sensitivity of the direct smear (3 studies) varied between 0% and 52%, formalin-ether concentration (3 studies) between 13% and 55%, nutrient agar plate culture (5 studies) between 78% and 100%, Harada-Mori filter paper culture (3 studies) between 7% and 58%, and Baermann concentration (1 study) 60%. The latter three tests require viable larvae, and therefore correct handling of specimens.

However, the true sensitivity is probably about half these estimates, judging by sensitivity estimates in two studies on patients who had a previous positive faecal test. In a study using the Baermann technique, 35% were positive by the first examination (14). In a study using the agar plate test, 58% were positive after one test (15).

People coinfected with HTLV-1 are more likely to return a positive direct faecal smear. In a study in Japan, 61% of people with both *S. stercoralis* and HTLV-1 had a positive direct faecal smear whereas only 18% of those with *S. stercoralis* and no HTLV-1 had a positive direct faecal smear (52).

It is important to note that an estimate of
sensitivity depends on the mix of patients being tested. If they are mostly in the acute or hyperinfective phase, then the sensitivity of faecal testing will be higher than if they are mostly in the chronic phase, because the larval output is higher in severe strongyloidiasis (39). Also, if there are several larvae per field in a direct smear, it indicates that the patient has, or is heading for, severe disease (5).

Implications of the insensitivity of faecal testing

- The diagnosis of *S. stercoralis* infection has frequently been missed.
- People who were considered ‘cured’ still had the infection.
- The efficacy of drugs for *S. stercoralis* infection has been overestimated. The efficacy of thiabendazole has been thought to be high, but in fact the main effect of the drug is to inhibit reproduction in parasitic females (53), resulting in negative faecal testing after treatment.
- Grove’s morbidity study (37) underestimated the extent of symptoms due to *S. stercoralis* infection because some of the ‘control’ group were later found to have *S. stercoralis* (D. Grove, personal communication).
- Estimations of the specificity of serology have been underestimated because false positives were defined as positive serology and negative faecal testing.

Serum-specific IgG ELISA

The first application of the use of the enzyme-linked immunosorbent assay (ELISA) to detect antibodies to *S. stercoralis* was carried out in France in 1978 (54). This test was further developed in Australia to detect IgG antibodies to *S. stercoralis* in 1981 (55).

In Australia today, blood testing consists of the determination of IgG antibodies to *Strongyloides ratti* antigen in the serum by ELISA. It is now routinely available in four major laboratories using a single source of antigen for routine testing. The sensitivity of the test is estimated to be 93% and the specificity 95%. The specificity approaches 100% in the mid to high positive range (20).

A commercial kit tests for specific IgG using a preparation of *S. stercoralis* filariform larvae as the antigen. It gives comparable results (56). Some private laboratories offer this test.

The sensitivity of the IgG test is probably much higher for people with chronic strongyloidiasis (see Table 1). In a study that compared returned travellers with immigrants from areas where *S. stercoralis* is endemic, the sensitivity of the IgG test was lower in travellers (73%) than in immigrants (98%) (57). The authors did not offer an explanation for their results. It is likely that the travellers had contracted *S. stercoralis* recently and some were still in the ‘window period’ before developing immunity and producing the specific IgG antibodies, whereas most of the immigrants probably had chronic strongyloidiasis. This would account for the difference in the two groups.

People with hyperinfection may be negative with the IgG test, depending on how severely their type 2 immune responses are depressed. In addition some elderly World War 2 ex-prisoners of war with *S. stercoralis* infection are negative by the IgG test (WP, unpublished observations).

There have been efforts to improve the specificity of the test by using monoclonal antibodies. It appears that there is no single antigen from *S. stercoralis* larvae that is universally recognized by immune sera (58). So perhaps the strength of the current test is the number of antigenic components in the preparation used for testing.

Studies in Japan suggest that *Strongyloides* serology may be less sensitive in patients infected with HTLV-1. This implies that patients with borderline serology should be treated, as is done in central Australia (L. Einsiedel, personal communication).

*Strongyloides kellyi*, a *S. fuelleborni*-like species of *Strongyloides*, is endemic only in parts of Papua New Guinea. *S. kellyi* does not have an autoinfective cycle. It is likely that *S. kellyi* antibodies would cross-react in this test (I. Sampson, personal communication), but *S. kellyi* infections are readily identified by faecal testing. Past work
on the IgG test indicated that *Wuchereria bancrofti*, *Ascaris lumbricoides*, *Necator americanus* and *Toxocara canis* are unlikely to cross-react (55).

A major advantage of the IgG test is the opportunity to identify people with chronic strongyloidiasis so that they can be treated and relieved of their non-specific symptoms, and not become victims of hyperinfective strongyloidiasis at a later date.

**Eosinophilia**

Eosinophilia defined as >400/µl varies in different series between 60% and 90% (59). 57% of patients with *S. stercoralis* at Royal Darwin Hospital from mid-1991 to mid-1992 had eosinophilia (60). Eosinophilia is also present in people infected with other helminths, so it is not a reliable test for *S. stercoralis*.

**Value of the IgG test in monitoring the effectiveness of treatment**

The value of the IgG test has been the subject of debate among medical practitioners in Australia. It was mistakenly believed that a positive IgG test does not distinguish between past and current infection. Though this is true for viral infections, it is not true for parasitic infections. People treated with anthelmintic drugs often returned a negative faecal test, and the practitioner then erroneously assumed that the person was cured, and a positive IgG test was assumed to be past infection rather than failure of treatment.

The advent of the drug ivermectin enabled the clarification of the value of the IgG test (16). An Australian Indigenous medical clinic instituted a monitoring program based on the identification of strongyloidiasis using the IgG test followed by treatment with albendazole for three days, and then retesting several months later. They found that although the test results showed lower IgG levels after treatment, most did not become negative (22). This result was disappointingly similar to earlier studies using thiabendazole (61-63) or albendazole (63,64) as the anthelmintic. Then they used ivermectin (200 µg per kg body weight) as the anthelmintic treatment. On retesting after six months, most of the patients treated with ivermectin were negative by the IgG test. Thus the value of the IgG test for diagnosis and the efficacy of treatment with ivermectin were clarified at the same time. In addition, the value of the IgG test in monitoring the effectiveness of treatment was established (16). Since that time, these conclusions have been confirmed during a community control program in another Indigenous community (23). However, there are some patients who test negative by the IgG test who may still have a few worms and later the symptoms recur (WP, unpublished observations).

**Anthelmintic treatment**

**Effects of anthelmintics on *S. stercoralis***

David Grove and others conducted a number of studies examining the effect of anthelmintic drugs on migrating larvae and parasitic adults of *S. ratti* (53). The effects of the drugs on *S. stercoralis* in people are likely to be similar. The results are summarized as follows:

- **Ivermectin**: there is dose-dependent eradication of adults in the gut and larvae in the tissues, and surviving larvae do not mature.
- **Albendazole**: there is also dose-dependent eradication of adults in the gut and larvae in the tissues.
- **Thiabendazole** does not kill adult worms but reduces larval output; it has no effect on larvae in the tissues.
- **Cambendazole** eliminates adults and larvae.
- **Mebendazole** kills adults but not larvae, and is between 100 and 1000 times less effective than cambendazole.

Of these drugs, thiabendazole is no longer commonly used because of the side-effects of nausea and neuropsychiatric symptoms. There were a number of trials of cambendazole during the early 1980s, but it was withdrawn from the market by the manufacturer because of rare severe reactions in cattle (61). Mebendazole is completely unreliable (61). Albendazole 400 mg for 3 days is commonly prescribed. The estimated efficacy of this regimen was 38% compared with 83% for ivermectin (65). This
is probably an overestimate for both drugs because it relied on faecal testing for defining cure. The estimate of Archibald et al. of the efficacy of albendazole at 400 mg twice daily for 3 days was 75% (66). Their definition of cure was all of three criteria: negative faecal test, negative IgG test and no symptoms. In another study, the efficacy of one dose of ivermectin at 200 μg per kg body weight was 68% and of ivermectin followed by a second course of either ivermectin or albendazole was 83%, using a negative IgG test alone as the criterion for cure (16).

One of the problems of albendazole therapy is that it must be taken on three consecutive days. This makes it difficult to ensure that all the doses have been taken. An advantage of ivermectin is that a course is one dose, so the health professional can directly observe that the drug has been swallowed.

Absorption of anthelmintics

Both albendazole and ivermectin are lipophilic and are best taken with a fatty food such as full-cream milk (67). Ivermectin may be poorly absorbed in the fasted state in a critically ill patient (68).

Resistance to anthelmintic treatment

Two studies of patients who had been treated by two courses of ivermectin and then followed up indicated that 17% and 16% respectively were still IgG positive six months after treatment (16,23). If still positive after retreatment, they may be resistant to treatment and should be treated on a regular basis (41,69).

Resistance of S. stercoralis to treatment with albendazole is associated with elevation of the S. stercoralis-specific IgG4 antibody titre at the expense of IgG1 (70). IgG4 is thought to block IgE-mediated responses in human strongyloidiasis (43).

Patients who are immunosuppressed (71,72) as well as HTLV-1 patients (11,12,73,74) are frequently resistant to treatment.

Safety of ivermectin

Ivermectin affects gamma-aminobutyric acid (GABA)-mediated nerves. In many invertebrates including roundworms, muscle contraction is controlled by GABA-mediated nerves, and ivermectin causes paralysis. In mammals, such nerves occur only in the central nervous system, and the blood-brain barrier prevents ivermectin from entering the brain. People with conditions that may compromise the blood-brain barrier may be at risk of an adverse reaction when treated with ivermectin (5).

In general, ivermectin is a very safe drug (75). Its safety for very young children and pregnant women has not been established conclusively, so it should not be used routinely in these groups. If there is a clinical need to use ivermectin, it should be considered on a case-by-case basis. Data collected so far suggest that it is safe. During the oncocerciasis trials in Africa, some pregnant women were treated inadvertently. When the outcomes of these pregnancies were compared with the outcomes in those who were not treated, there was no significant difference between the two groups (76).

Ivermectin should be used with caution in people who may be coinfected with the eye worm Loa loa. This species is endemic in parts of Africa. Individuals with high densities of L. loa microfilariae have developed serious adverse effects when treated with ivermectin, and some have died (77).

Coinfection with HTLV-1

The rate of S. stercoralis infection is significantly higher in patients with HTLV-1 infection than in patients without HTLV-1 infection (74,78).

HTLV-1 is associated with an exacerbated type 1 immune response. Coinfection with S. stercoralis or Schistosoma mansoni decreases the activation of type 1 cells, which may influence the outcome of HTLV-1 infection (79). Helminths including S. stercoralis induce a type 2 response. HTLV-1 decreases the type 2 immune response that is effective against S. stercoralis (10), leading to hyperinfective strongyloidiasis.

HTLV-1 causes decreased levels of IgE and eosinophils, both of which are important in the immune response to S. stercoralis (74). The high production of IFN-γ observed in patients coinfected with HTLV-1 and S. stercoralis (73,80) decreases the production of IL-4, IL-5, IL-13 and IgE, molecules that participate in the host defence mechanism
against helminths (80). Although coinfection with HTLV-1 was associated with a decrease in levels of IgE and skin sensitivity, it did not affect the levels of IgG (10).

HTLV-1 patients are frequently refractory to anthelmintic treatment. Resistance to treatment with albendazole has been associated with high levels of serum IFN-γ and TGF-β-1 (73). Similarly, resistance to treatment with ivermectin by HTLV-1-positive patients has been demonstrated (11). This is probably due to impairment of immunity to S. stercoralis in people coinfected with HTLV-1.

**Transmission**

Aspects of the life cycle and transmission of S. stercoralis and also effective control measures are well understood, and have been summarized by Feachem et al. (81), except that it is now known that there is a maximum of one free-living generation (33), and the stages in the soil are short-lived, about 2 weeks (34). Galliard showed in the 1950s that the worms die within a few hours in the open, or 2 to 3 days in the shade if the soil is dry (17).

Transmission may be indirect, by contact with infective filariform larvae on damp soil or damp vegetation, or direct, by faecal contamination of the skin. With rare exceptions, larvae in direct faecal smears are rhabditiform. Infective filariform larvae are observed rarely (82,83), and these can be passed on to others by faecal contamination.

There is evidence that transmission of infection occurs indoors. There have been reports of high rates of infection with S. stercoralis in mental institutions in USA, Canada, USSR and Chile (18) and of clustering of people infected with S. stercoralis in households in Jamaica (84) and Bangladesh (85). Transmission in these circumstances could be either direct or indirect.

**Community control**

The reservoir of infection with S. stercoralis is infected people. Its free-living stages are short-lived and sensitive to heat, cold and drying. This means that treatment of people has the potential to eliminate this species from the community. Prociv (26) found that, in children of an Australian Indigenous community, prevalence of S. stercoralis was reduced from 26% to below 6% six months after thiabendazole treatment. This level was sustained for at least the ensuing three years. He concluded that sustained chemotherapy would have eliminated S. stercoralis from the community without any change in living conditions.

In situations where there is safe water, effective sanitation and good personal hygiene, an infected person does not pass on the infection. This has been shown to be true in a study of ex-prisoners of war infected with S. stercoralis during World War 2, none of whom gave the infection to their wives (86).

Specific IgG testing is valuable in identifying people with chronic strongyloidiasis in the communities where it is endemic, because in this situation most infected people have the chronic form of the disease.

Community control should take place in the overall context of other diseases that are present in the community. In Papua New Guinea, other parasitic diseases include Plasmodium spp, Wuchereria bancrofti, Strongyloides kellyi, Nectator americanus, Ascaris lumbricoides, Trichuris trichiura, Sarcoptes scabiei and enteric protozoa. For example, ivermectin treatment should be effective against Strongyloides spp, W. bancrofti and Sarcoptes scabiei, and albendazole for three days is effective against A. lumbricoides, N. americanus and T. trichiura. Because A. lumbricoides and T. trichiura are persistent in the environment, ongoing treatment would be required to eliminate these from the community.

**Conclusion**

It is now possible to diagnose and treat Strongyloides stercoralis infection. This means that it is possible to identify people with chronic strongyloidiasis and treat them so that they can be relieved of their non-specific symptoms and not become victims of hyperinfective strongyloidiasis at a later date.

Recent studies have shown the value of IgG ELISA serology for identifying people with Strongyloides infection and monitoring the effectiveness of anthelmintic treatment. They have also shown that past treatments have been ineffective and that ivermectin is the most effective and expedient treatment
available, particularly when two courses are given. Failed treatment can usually be identified by retesting with the serum IgG test six months after treatment. Those who return a test that is not low or negative should be retreated. This process can be used to identify people who are resistant to treatment.

Longer-term retesting perhaps at two years, or self-referral when the symptoms return, may be able to identify the few who are negative six months after treatment but are still infected. For this reason, anyone who has ever tested positive for *S. stercoralis* could still have the disease. They should receive prophylactic anthelmintic treatment before being given corticosteroids or any other medication that depresses the immune system.

HTLV-1 patients, those on immunosuppressant drugs and others who are resistant to treatment should receive anthelmintic treatment on a regular basis.

Because the free-living stages are short-lived, it is possible to achieve community control by mass treatment with ivermectin. Safe water and good sanitation alone are not sufficient to eradicate *S. stercoralis*.

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This paper is dedicated to the memory of Dr Helena Vrbova.

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