ABSTRACT  The prevalence of antibodies against *Strongyloides* in the serum of newly-arrived Indochinese immigrants was determined. Sera that had been stored in the State Health Laboratories, Queen Elizabeth II Medical Centre, Nedlands, WA 6009, Ian A. Sampson, BAppSc, Senior Technologist, Serology Section, State Health Laboratories. David L. Grove, MD, FRACP, DTM&H, Associate Professor, Department of Medicine, The University of Western Australia. Reprints: Associate Professor D. L. Grove.

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Perth, were stratified according to age and sex, then samples were selected at random. Two hundred and ninety sera that had been obtained from persons between the ages of one and 69 years were examined by an indirect fluorescent antibody test. Five per cent of children who were aged between one and two years gave positive reactions. The positive reaction rate in this population increased by approximately 7% per year until the age of seven to eight years at which point it levelled off. Approximately half of all older children, teenagers and adults had positive antibody responses, indicating past or present infection with *Strongyloides stercoralis*. This parasite is an extremely unusual worm in that it is able to replicate within the human host. Consequently, infection may persist for years.

Strongyloidiasis is endemic in another Australian population group: Indochinese immigrants
Furthermore, immunosuppression may result in fatal, disseminated infection. 

Strongyloidiasis is now recognized in three major Australian population groups: Aborigines who are living in the north of the country; World War II veterans who were prisoners in southeast Asia; and Indochinese immigrants. The salient features of the clinical manifestations, diagnosis and treatment of strongyloidiasis are reviewed.

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Strongyloides stercoralis is one of the major intestinal worm infections of humans. Infection with this roundworm is acquired when infective larvae penetrate the intact skin. These migrate by way of the bloodstream and the lungs to the gut, where they burrow into the small intestinal mucosa and develop into adult worms. Gravid female worms release larvae which are passed in the faeces and deposited on the soil; there, they develop by one of two means into infective larvae and may infect a new host.

However, this parasite has a peculiar biological behaviour for a worm as it has the capacity to replicate within the human host. Some of the first-stage larvae that are released into the small intestine are presumed to moult twice to become infective larvae, then to invade either the mucosa of the large bowel (internal autoinfection) or penetrate the perianal skin (external autoinfection); in either event, larvae migrate through the tissues back to the bowel, thus repeating the life-cycle. It is this ability to replicate which accounts for the long duration of infection that may be seen. Furthermore, in immunosuppressed patients, worms may multiply unhindered and disseminate throughout the body with disastrous consequences.1

Strongyloidiasis has been well recognized hitherto in two population groups in Australia. The infection is endemic in the northern parts of the country, particularly among Aborigines. For example, faecal examinations have revealed the parasite in 6% of persons who were tested in Fitzroy Crossing in Western Australia.4 In addition, strongyloidiasis is common in Australian veterans of World War II who were prisoners of war in southeast Asia; nearly 30% of such persons who were living in Perth who were investigated were shown to be infected.5

Since 1972, nearly 100,000 Indochinese immigrants, mainly from Vietnam, have been admitted into this country.4 Since sera from Vietnamese subjects now constitute some 30% of the specimens that are submitted to this laboratory for testing for Strongyloides antibodies, and as many of these give positive results, we undertook a more detailed seroprevalence study. In addition, this is the first report of the rate of acquisition of Strongyloides antibodies in children who have lived in an endemic area.

Patients and methods

Sera had been collected as a routine from Vietnamese immigrants who had arrived in Perth in 1982-1983; these sera had been stored in liquid nitrogen. Sera were divided into age groups - each year between the ages of one and nine years was considered separately and each decade thereafter. Ten specimens from patients of each sex in each age bracket were selected at random. Insufficient sera were available for the three to four and four to five years’ age groups, so data from these two age groups were combined. Additionally, there were 30 serum specimens in the 50-years-and-over age group. The parasitological status of these individuals is uncertain. However, it is known that of 2012 Vietnamese persons who arrived in Western Australia in 1982-1983, the following numbers of cases with various parasites were found by examination of the stools: Trichuris trichiura, 73 cases; hookworm, 42 cases; Giardia lamblia, 36 cases; Ascaris lumbricoides, 27 cases; S. stercoralis, 24 cases; Hymenolepis nana, nine cases; Opisthorchis sinensis, four cases; Entamoeba histolytica, one case; and Enterobius vermicularis, one case (J.B. Iveson, personal communication). Most of these persons had received standard treatment with pyrantel pamoate before their faeces were tested.

Serum anti-Strongyloides antibodies were measured by the immunofluorescent assay with the infective larvae of Strongyloides ratti as described by Grove and Blair. These antibodies are known to have no significant cross-reactivity with the antigens of Ascaris and Dirofilaria. The specificity of this assay has since been confirmed further by showing that preabsorption of Strongyloides antibody-positive sera with hookworm antigens did not affect the titre of anti-Strongyloides antibodies, whereas preincubation with Strongyloides antigens produced a 16-fold fall in titre. Sera were screened at a dilution of one in 10 in phosphate-buffered saline. Previous studies have shown that when a dilution of one in eight is used, the test has a sensitivity of approximately 96%.6 Briefly, infective larvae were incubated with the test serum at 37 °C for one hour, washed several times by centrifugation, incubated with fluoresceinated antihuman globulin (Tago, Burlingame, California, USA), washed three times, then examined for cuticular fluorescence with an ultraviolet microscope. Only sera which produced strong, generalized cuticular fluorescence were considered to have given a positive result.

Results

The percentage of seropositive persons in each group is indicated in the Figure. Five per cent of children in the second year of life gave positive responses. The percentage of seropositive children rose progressively at a rate of 7% per year until the age of about seven to eight years old at which time approximately half the children were seropositive. A similar seropositive rate was seen in all subsequent age groups.

It should be noted that border-line reactions were not considered to be positive results. If they had been, approximately 80% of the adults would have been seropositive.

Discussion

The major purpose of this paper is to draw attention to the fact that there is now another population group in this country, namely, Indochinese immigrants, in which strongyloidiasis is prevalent. Therefore, this diagnosis may need to be considered in some of these individuals. A definitive diagnosis of strongyloidiasis is made by finding larvae, usually in the stools, sometimes in duodenal fluid, and occasionally in tissues or other body fluids. However, these techniques are frequently insensitive and the diagnosis may be missed. For example, in a study of ex-servicemen who had suffered from chronic strongyloidiasis for more than 35 years, multiple examinations of faeces and/or duodenal fluid were often necessary to reach the diagnosis. Indeed, in one patient with pathognomonic larva currens, the diagnosis was never proved in spite of prolonged investigation.7

On the other hand, serological examination is both much less unpleasant for the patient and technician and much more sensitive; it has the capacity to allow the diagnosis to be reached when the worm burden is low and the parasites are likely to be missed on microscopic examination.3 However, two caveats must be added. First, assays for the presence of antibody are unable to differentiate between past and present infection. Little information is available concerning how long antibodies persist after the successful treatment or spontaneous elimination of the infection.
should that occur. Antibody titres fell, but not markedly, six months after treatment with thiabendazole.\(^4\) What can be said is that veterans who had undoubtedly been exposed to the parasite while living under grossly unhygienic conditions during World War II had no serological evidence of previous infection 35 years later.\(^3\) Secondly, antibody assays give no indication of the intensity of infection, that is, the worm burden. Both of these problems may be solved if an assay to detect the presence of Strongyloides antigens can be developed. Meanwhile, a reasonable initial course of action is to examine the faces for evidence of infection when strongyloidiasis is suspected, then to proceed to serological investigation if the results of this are negative. This assay can be ordered through the State Health Laboratories in Perth.

By means of this assay, which is both highly sensitive and specific, approximately 50% of older children and adults had evidence of past or present infection. Similar observations of a high frequency of infection have been found in two other surveys of persons who were living in endemic areas. Approximately 75% of normal Filipino adults had immunofluorescent antibodies in a titre of one in eight or more,\(^2\) while Douce et al., with an enzyme-linked immunosorbent assay, found anti-Strongyloides antibodies in 45% of the adult population of a Thai village.\(^7\)

Clearly, strongyloidiasis is widespread in southeast Asia. What is uncertain is how many of these individuals have active, clinical or subclinical infections. It is likely that a proportion of those individuals are genetically endowed with the capacity to eradicate infection while infection persists in the remainder. Thus, only between one-quarter and one-third of the veterans who were mentioned earlier had chronic infections in spite of the fact that most individuals had probably been exposed to infection.\(^4\)

As far as we are aware, this is the first occasion in which the rate of acquisition of seropositivity in a population has been studied. Both the rate of the acquisition of infection, and the ultimate proportion of the population which is infected, roughly parallel that of hookworm, the other major soil-transmitted intestinal nematode infection. For example, Udsone found the following prevalences of infection: 37% (one to four years old); 65% (five to nine years old), 68% (10-14 years old), 71% (15-19 years old) and 62% (20 years old).\(^6\)

Many patients with chronic strongyloidiasis are asymptomatic, although cutaneous and gastrointestinal manifestations are common. The classic triad consists of abdominal pain, diarrhoea and urticaria. Cutaneous manifestations are the most characteristic feature and are present in two-thirds of patients. Many subjects have urticarial eruptions in which crops of stationary wheals that resemble mosquito bites appear, particularly on the buttocks and around the waist. These wheals last for one to two days and recur at irregular intervals. Less commonly, larva currens is found; this urticarial rash may migrate in a serpiginous fashion at the rate of several centimetres an hour and last for up to one to two days. A variety of non-specific gastrointestinal symptoms is seen in these patients more frequently than in the general population. These include indigestion, cramping lower abdominal pains, intermittent or persistent diarrhoea, pruritus ani, and weight loss.\(^3\)

Clinical manifestations of more profound significance supervene if disseminated infection develops. Overwhelming strongyloidiasis is being recognized increasingly in patients who are immunosuppressed either as a result of disease, because of the administration of immunosuppressive agents, or both.\(^6,10\) In this condition, patients may present with severe, generalized abdominal pain and abdominal distension which is indicative of intestinal obstruction; shock and jaundice may then appear. Massive larval infiltration of the lungs may result in coughing, wheezing and shortness of breath. A spectrum of neurological features that ranges from confusion to coma indicates cerebral involvement. A high fever develops frequently, and sepsis with Gram-negative organisms, which may lead to pneumonia or meningitis, is often found.

The standard recommended therapy for strongyloidiasis is thiabendazole in the dose of 25 mg/kg by mouth twice a day for three days. Unfortunately, this drug is toxic and is not always effective. Most patients complain of side-effects, particularly nausea, vomiting, malaise, dizziness, feelings of disembodiment, and smelly urine. Confirmation of effective therapy may be difficult since worm burdens are often low before treatment, and a partial reduction in worm numbers may make it almost impossible to detect any remaining parasites. One recent study suggested that up to one-third of patients may not be cured with a single course of thiabendazole.\(^6\) Ideally, patients should be reassessed six and 12 months after therapy.

Mebendazole has been used for the treatment of strongyloidiasis but its efficacy in humans is uncertain.\(^11\) Certainly, both thiabendazole and mebendazole have been shown to be ineffective in normal and immunosuppressed dogs with experimental infections.\(^12\) Another benimidazole, cambendazole, was more effective in mice\(^13\) and in dogs\(^12\) although it could not always be relied upon in the latter host. This drug has been used with apparent success in a number of human clinical studies,\(^14\) but is not recommended for human use by the manufacturers and recently has been withdrawn from the veterinary market. The current anthelmintic therapy of strongyloidiasis is frequently unsatisfactory; experimental studies have suggested that ivermectin\(^15\) or cyclosporin\(^16\) may prove valuable. For the moment, thiabendazole must be relied upon and repeated courses of treatment given if necessary.

In summary, the possibility of strongyloidiasis in Indo-Chinese immigrants should be considered if the clinical circumstances are appropriate. The diagnosis may be reached by serological examination, and the efficacy of treatment with thiabendazole needs to be monitored. Finally, it must be remembered that approximately 42 000 Australians served in Vietnam. Although these individuals may have been less exposed to infection than are the indigenous inhabitants, some of these persons have been infected, and at least one fatal case of disseminated strongyloidiasis in a Vietnam veteran has been reported.\(^17\)

References


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