A 69-year-old man was hospitalized due to increasing difficulty in breathing and cough. During previous hospitalizations, he had been treated for arteriosclerotic vascular disease with myocardial infarction and chronic obstructive pulmonary disease (COPD). His COPD now was found to be acutely exacerbated, so he was treated with 60 mg of methylprednisolone. The patient complained of intermittent episodes of diarrhea and shortness of breath, which did not always occur concurrently. The patient was a veteran who had served in the South Pacific in the 1940s and Vietnam in the 1960s.

A complete blood count with differential revealed an increased white blood cell count (18.5 × 10⁶/L [18,500 cells/µL]) and an elevated eosinophil count (0.06 [6%]) on admission. However, subsequent eosinophil counts fell to within normal range (0–0.02 [0%–2%]). A week after the patient’s admission, a Gram's stain and culture of a routine sputum specimen were found to be unremarkable, except for an unusual displacement of bacterial colonies on the primary culture media. On his 11th day in the hospital, the patient experienced a significant drop in his hemoglobin (76 g/L [7.6 g/dL]) and hematocrit (0.22 [22%]); a stool specimen was negative for occult blood. A second sputum sample submitted for a routine Gram's stain and culture exhibited roundworm larvae on the smear (Fig 1) and significant bacterial displacement on the primary culture media (Fig 2). The examination demonstrated three stages of the roundworm *Strongyloides stercoralis* (Fig 3). Tests for gastric and fecal occult blood were positive 2 to 3 weeks after admission; blood cultures (4 sets) were negative.

A purpuric rash developed on the patient’s lower extremities and spread upward to his abdomen. Although he was treated with thiabendazole, his condition continued to deteriorate, and he died of strongyloidiasis 32 days after admission.

The autopsy revealed numerous small foreign-body granulomas and necrotic material throughout the lungs and small bowel mucosa. The necrotic material may have been larvae of the genus *Strongyloides* but could not be identified definitively as such because the necrosis was pervasive.

**Clinical Background**

*Strongyloides stercoralis* is a free-living roundworm that adapts to a parasitic existence. Most common in tropical and subtropical climates, *S stercoralis* is found worldwide. In North America, this roundworm is endemic in southeastern regions, including Kentucky, Tennessee, Florida, and southern Appalachia.¹⁻³

Infective filariform (threadlike) larvae invade the host by penetrating unbroken skin and entering the bloodstream. Passing through the right heart, the larvae reach the capillaries of the lungs, where they break into the alveoli and develop into adolescent worms. These worms migrate to the epiglottis, are swallowed with sputum, and reach the small intestine, where they mature. The parasitic females are parthenogenic. They live buried in the mucous crypts of the duodenum and upper jejunum where they produce eggs that develop rapidly into rhabditiform (rod-shaped) larvae. These larvae traverse the intestinal lumen and, in most cases, are evacuated in the feces to continue maturation in the soil.⁴⁻⁵

Rhabditiform larvae can develop into filariform larvae in the intestine or perianal area, reinfecting the host and completing their life cycle.
This form of internal development, "autoinfection," is responsible for the longevity of some infections with *S. stercoralis* that can persist for decades. In the immunocompetent individual, host-parasite equilibrium is maintained through cell-mediated immunity. Accordingly, latent infections often are difficult to recognize because worms are sustained at low levels. Symptoms of chronic strongyloidiasis range from larva currens (itching at the site of entry) and mild gastrointestinal disease, to Löffler's syndrome, asthma, pneumonitis, and severe diarrhea. A high incidence of chronic strongyloidiasis has been observed among former Allied prisoners of war who worked on the Burma-Thailand railroad (the construction of which was depicted in the film *The Bridge on the River Kwai*).

In the immunocompromised host, hyperinfection results as reproduction of the parasite accelerates, and, through autoinfection, large numbers of filariform larvae invade various tissues and body fluids. Hyperinfection usually affects the lungs and gastrointestinal tract but can result in a disseminated infection involving many organs. Lymphatic malignancies, malnutrition, and immune disorders, including acquired immune deficiency syndrome, predispose patients to this often fatal opportunistic infection. Immunosuppressive drugs, specifically corticosteroids, have been implicated in impairing resistance to *S. stercoralis*. These drugs may act on the intraintestinal larvae as molting hormones and directly assist in the development of a systemic infection. Consequently, before administration of immunosuppressive therapy, patients who have been in areas in which *S. stercoralis* is endemic should be screened carefully for the presence of this parasite.

Symptoms of hyperinfection with *S. stercoralis* include severe pneumonitis, gastrointestinal hemorrhage, and an intense allergic response to the parasite invading various organ systems. Sepsis, which theoretically occurs when filariform larvae transfer bacteria through the bowel wall, can cause life-threatening secondary infections in patients with hyperinfection syndrome. Progressive petechial and purpuric lesions are often manifest, attributable to local vascular injury as filariform larvae migrate to the skin in a disseminated pattern.

Early diagnosis and treatment can influence the outcome of disseminated strongyloidiasis. Thiabendazole is the drug of choice. Ivermectin, an alternative antiparasitic drug, is under study as an alternative therapy for patients who cannot tolerate or who do not respond to thiabendazole.

**Role of the Laboratory**

Proper specimen collection and handling are critical to an accurate diagnosis with respect to the severity of *S. stercoralis* infections. Recovery of exclusively rhabditiform larvae is diagnostic of strongyloidiasis, whereas observation of filariform larvae is indicative of hyperinfection. Duodenal aspirates should be centrifuged and the sediment examined as a wet mount within an hour of being taken. Fecal material is an excellent nutrient medium for the growth of roundworm larvae. Stool samples, therefore, must be submitted promptly for direct microscopic examination and fixed or refrigerated. Otherwise, rhabditiform larvae will develop into the filariform stage in vitro within 24 hours, falsely indicating a condition of hyperinfection. This caveat is emphasized in a study in which two of four cases were falsely positive for filariform larvae because specimens were stored improperly.
The formalin–ethyl acetate sedimentation method is acceptable for the direct examination of stool specimens. Studies show, however, that 50% of infections will remain undetected when using stool microscopy. Increasing the number of stools examined improves sensitivity but is impractical for most laboratories because it requires more time. Baermann's test, which concentrates larvae for study, further increases the sensitivity of stool examination, although this method is not performed commonly in clinical laboratories. Alternatives to direct stool microscopy include culture of stool specimens (coproculture) and microscopic examination of duodenal aspirates. These methods are recommended when worm numbers are low, as is often the case in chronic infections.

Strongyloides stercoralis larvae must be differentiated from hookworm because the two roundworms are quite similar in appearance. The rhabditiform larvae are 380 μm long and possess a short buccal cavity, a large hourglass-shaped esophageal bulb, and a pronounced genital primordium. Hookworm larvae have a long buccal cavity and an inconspicuous genital primordium. Growing to 630 μm, filariform larvae of S. stercoralis have a notched tail and a slender esophagus that occupies up to one half of the body length.

Serologic methodologies offer increased sensitivity (84%–92%) when compared with direct microscopic examination. Enzyme-linked immunosorbent assays (ELISA) use somatic S. stercoralis larva as the antigen for the detection of Immunoglobulin G antibodies specific to S. stercoralis. Cross-reactivity occurs in patients infected with Ascaris lumbricoides, Loa loa, or hookworm. High indexes of both positive (.97) and negative (.95) predictive values recommend this test as a useful and cost-effective method for screening individuals exposed to endemic areas and candidates for immunosuppressive therapy. Preabsorption of serum specimens to remove cross-reactivity with other parasitic worms enhances both the sensitivity and specificity of ELISA tests. Positive ELISA results can be followed with more specific tests, such as stool examinations, for definitive diagnosis.

A Gram's stain of the patient's initial sputum specimen suggested mixed normal flora, and the culture grew microbes consistent with normal respiratory flora. The primary plates exhibited bacterial colonies displaced from the streak marks made during specimen inoculation, a finding that was suspected initially of being caused by insect contamination.

Other laboratory findings of interest in this patient's case were gastric aspirates (submitted in lieu of stool or duodenal aspirates), an ELISA test for S. stercoralis, and eosinophil counts. The aspirates exhibited adult, rhabditoid, and numerous stages of ova that had not been seen in the sputum specimens. The reason for the multiple parasitic stages in the gastric aspirates is unclear but may have been due to a complication of the patient's obstructive bowel condition. An ELISA test for S. stercoralis was performed during
the course of the infection. Although the patient was hyperinfected, the result (4.1 = SD) was considered a “low positive” according to the test’s reference ranges. An elevated eosinophil count can also indicate a parasitic infection. However, eosinophilia may occur only at the onset of infection, and, as the parasite disseminates, the eosinophils may fall within normal limits. Infections with *S. stercoralis* should be suspected in any individual who has previous exposure to endemic areas, regardless of the eosinophil count.

**Conclusion**

Investigating unusual observations in the laboratory can be critical in the diagnosis. Larvae were first detected in the Gram's stain of this patient's second sputum sample. The first evidence of strongyloidiasis occurred; however, when displacement of the bacterial colony was observed on primary culture plates from the initial sputum sample. Gastric secretions exhibited multiple stages of this parasite, including the diagnostic rhabditiform larvae, when stool or duodenal aspirates were unavailable.

**References**