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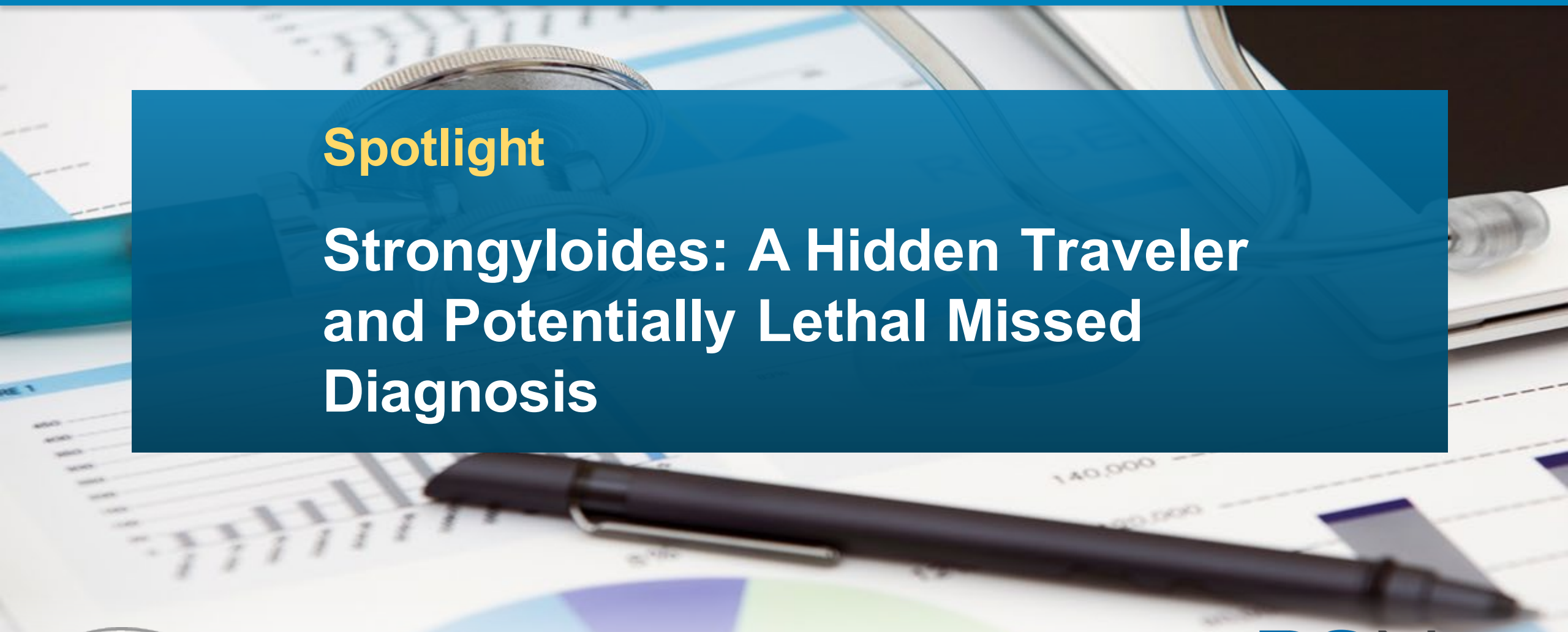

Spotlight

Strongyloides: A Hidden Traveler and Potentially Lethal Missed Diagnosis

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

PSNet
PATIENT SAFETY NETWORK

Source and Credits

- This presentation is based on the November 2022 AHRQ WebM&M Spotlight Case
  - See the full article at https://psnet.ahrq.gov/webmm
  - CME credit is available
- Commentary by: Narath Carlile MD MPH, Clyde Lanford Smith MD MPH DTM&H, James H. Maguire MD and Gordon D. Schiff MD
  - AHRQ WebM&M Editors in Chief: Patrick Romano, MD, MPH and Debra Bakerjian, PhD, APRN, RN
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Objectives

At the conclusion of this educational activity, participants should be able to:

- Recognize common and serious pitfalls in diagnosis of *Strongyloides* and potential consequences of failure to diagnose this infection
- Summarize approaches to diagnosis and treatment of *Strongyloides* infection
- Identify patients who should be tested for *Strongyloides* infection

STRONGYLOIDES: A HIDDEN TRAVELER AND POTENTIALLY LETHAL MISSED DIAGNOSIS

This case highlights serious pitfalls in the diagnosis of *Strongyloides stercoralis* infection and strategies to improve identification of patients at risk of this infection

Case Details

- 70-year-old man with hypertension and osteoporosis with a medical history notable for:
  - A history of multiple myeloma (diagnosed 10 years prior, treated with chemotherapy and steroids, in remission)
  - A history of a pulmonary embolus (treated with a course of anticoagulation, not on anticoagulation now)
  - Seen numerous times in primary care clinic for diarrhea (attributed to viral or unknown causes) and with intermittently elevated eosinophilia.
- Originally from Haiti, moved to the US in the 1980s, travels frequently to Haiti, the Dominican Republic, Central America

Case Details

- Patient had been living independently and frequently traveling with his wife until recently.
- Two months ago, he had worsening abdominal pain and was found to have gangrenous cholecystitis and a blood stream infection. He was admitted to the hospital and treated with medications and surgery.
- Recently he was seen again with severe vomiting and was found to be hypotensive.
- He was admitted to the intensive care unit.

Case Details

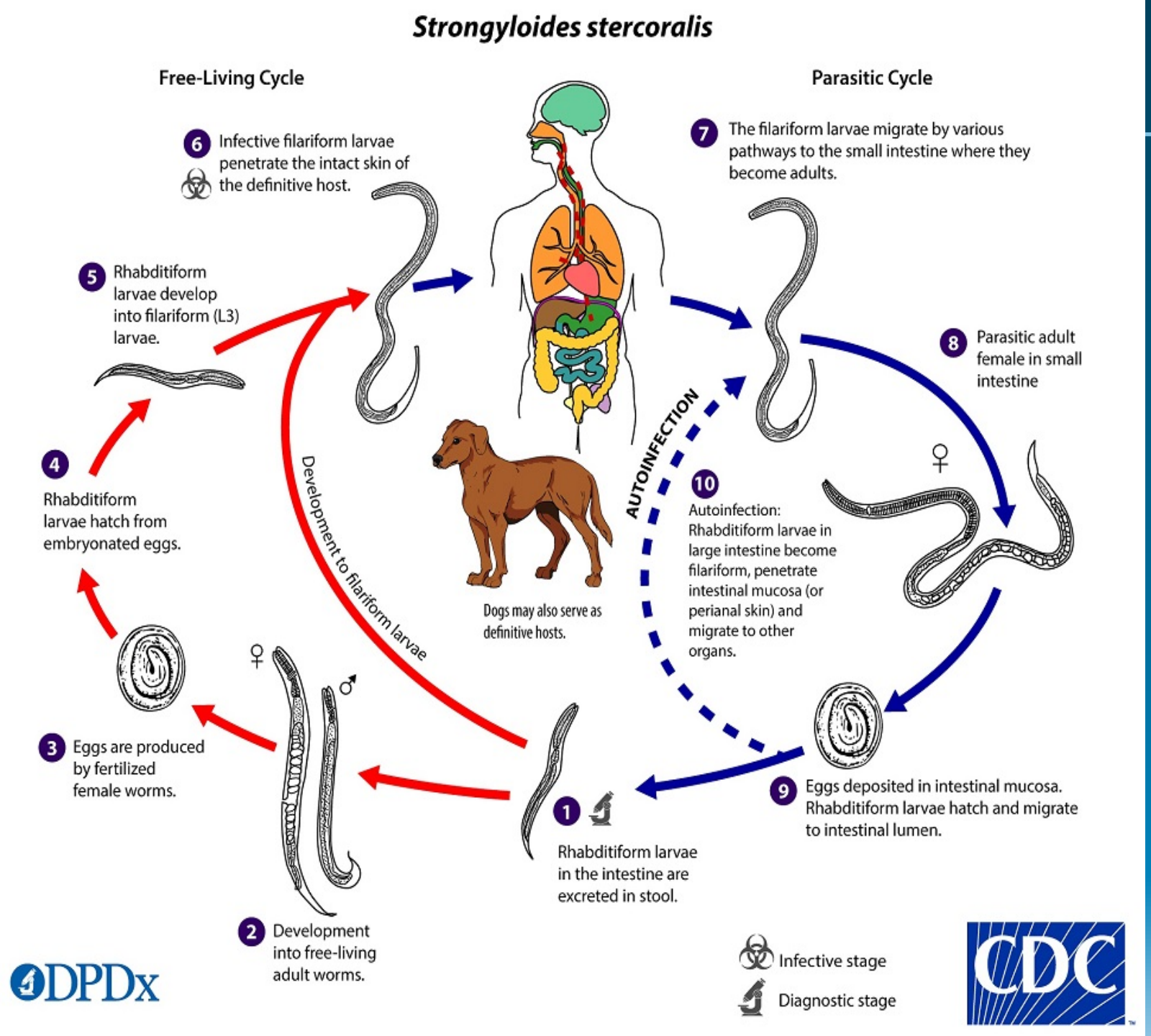
- He was treated with fluids, pressors, and broad-spectrum antibiotics.
- An upper endoscopy was performed for concern of gastrointestinal bleeding, during which biopsies were taken
- Microscopic examination of the biopsy specimens unexpectedly showed that his duodenum was heavily infiltrated with the parasitic helminth – *Strongyloides stercoralis*.

STRONGYLOIDES: A HIDDEN TRAVELER AND POTENTIALLY LETHAL MISSED DIAGNOSIS

The Commentary

By Narath Carlile MD MPH, Clyde Lanford Smith MD MPH DTM&H, James H. Maguire MD and Gordon D. Schiff MD

PATHOPHYSIOLOGY



Strongyloides (threadworm)

A parasite endemic to tropical and subtropical regions of the world.

- **Classic Life Cycle:** travels from skin (usually entering through bare feet) to the lungs and then to the GI tract of host
- **Hyperinfection Syndrome:** Exaggerated form of classic life cycle (parasite burden and turnaround increase and accelerate)
- **Disseminated Disease:** Parasite present in areas of body outside of locations of classic life cycle (i.e., organs other than skin, GI tract, or lungs). Tends to occur in the immunocompromised[2]

Pathophysiology

- Reinfection can continue throughout the lifetime of the host patient, a process known as autoinfection.
- Usually, the host's immune system prevents the number of worms from increasing but cannot clear the infection completely.
- This process results in an ongoing low level of infection, affecting up to 30% of the population in endemic areas, in which worms continue to release larvae that reinfect the host or become a source of infection to others.
- In patients with a weakened immune system (e.g., by steroids or other immune suppressing medications, viruses such as human T-cell lymphotropic virus type 1 (HTLV-1), or severe malnutrition), *Strongyloides* replication can increase, leading to a build-up of large numbers of worms, the so-called hyperinfection syndrome.
- Hyperinfection with *Strongyloides* is often fatal.

Pathophysiology

- While this patient's intermittent episodes of diarrhea may have been due to strongyloidiasis, he was fortunate not to develop disseminated strongyloidiasis despite receiving several courses of treatment with steroids.
- It is rare for *Strongyloides* itself to cause gangrenous cholecystitis and there was reportedly no suggestion of this infection on pathologic examination of the gallbladder specimen.
- Translocation of *Strongyloides* larva through the bowel wall (usually lower in the intestine), especially in the setting of delayed intestinal transit, could contribute to bacteremia but is less likely to have been a factor in the present case.

DIAGNOSIS AND TREATMENT

Diagnosis and Treatment

- A key issue for this patient was to recognize his risk for *Strongyloides* infection based on his history of residence and travel.
- In tropical and subtropical areas, people who live in rural areas with poor sanitation have a greater risk of acquiring strongyloidiasis from fecally contaminated soil than people who live in developed urban areas and are less likely to walk barefoot.
- Suspecting and testing for *Strongyloides* is warranted for all patients with these risk factors who are about to start steroids or other immunosuppressive treatment.

Diagnosis and Treatment

- Testing in the United States can be done by examination of stool specimens for larvae, OR serum antibody testing.
  - However, the sensitivity of a single stool test for detecting larvae is only 30%, and even with multiple specimens reaches only 70-80%.
  - Therefore, screening using an antibody test from a sample of blood is preferred because of its greater sensitivity and specificity, and a positive serological test indicates a high probability of infection.[3,4]

Diagnosis and Treatment

- All persons with positive stool or serological tests should receive treatment with ivermectin, which is highly effective. Other widely used antiparasitic agents, such as albendazole, are less effective.
  - A single dose or two of ivermectin is usually effective for persons with chronic strongyloidiasis, but successful treatment of disseminated infection requires prolonged courses of daily treatment.[1,2]
  - One important caveat applies to patients from parts of Central and West Africa, where infection with the parasite *Loa loa* is also found.
  - Treatment with ivermectin can be fatal for persons with a heavy burden of *Loa loa* infection; the combination of *Strongyloides* and *Loa loa* infection thus requires specialized treatment at dedicated centers.

Diagnosis and Treatment

- This patient was from a country in which *Strongyloides* is endemic and he should have been screened for *Strongyloides* infection before any immunosuppressant medications were started.
  - Since strongyloidiasis can last for life, ideally all persons at risk should be screened, but it is imperative to screen patients who are about to receive or who have recently started steroids or other immunosuppressive medications.
  - Persons at risk for *Strongyloides* infection should be treated empirically if immunosuppression needs to be initiated before the results of testing become available (e.g., for acute COVID-19).
  - Thus, all providers, including primary care physicians, oncologists, rheumatologists and pulmonologists who frequently administer immune suppressive medications, should keep *Strongyloides* in mind and be proactive with appropriate testing.

DIAGNOSTIC CONSIDERATIONS

Diagnostic Considerations

- Although *Strongyloides* infects millions of people worldwide, screening is not common during normal immigration procedures, nor after individuals return from visits to countries where it may be endemic, and it is not routinely considered by U.S. physicians.[5]

Diagnostic Considerations

- Elevated eosinophil counts can be an important clue to a possible parasitic infection, but eosinophilia also occurs in many other conditions, such as infectious diarrhea, inflammatory bowel diseases and atopic conditions.[6]
  - Inflammatory bowel diseases can present with similar symptoms but are much more likely to have an associated finding of blood in the stool. Further testing to rule out inflammatory bowel disease requires colonoscopic examination and biopsy.
  - There are also other eosinophilic gastrointestinal diseases (EGIDs) such as eosinophilic esophagitis and eosinophilic gastroenteritis, but these conditions usually present with upper gastrointestinal symptoms such as nausea, vomiting, and early satiety.
  - Atopic conditions such as asthma can elevate eosinophil counts but are not commonly associated with diarrhea.[4]
  - Often, a white cell "differential" count is not automatically performed when a CBC (complete blood count) is ordered. However, in a patient with the appropriate social or travel history, screening for *Strongyloides* infection should include a CBC with "differential" and an antibody test, especially before initiation of any steroid or immunosuppressive medications.

Diagnostic Considerations

- Using the DEER taxonomy to better characterize what happened in the diagnostic process in this case, we can see that errors occurred in several aspects of the patient's care – including in history taking, testing, and assessment.
- There was a "failure/delay in eliciting a critical piece of history data"; specifically, overlooking his elevated eosinophil count, which should have raised suspicion of a potential parasitic infection.
  - Recognizing and following up on this abnormal test result in a timely manner could have prevented such a long delay in his diagnosis. In addition, in his numerous physician visits for diarrhea, there was failure to consider the diagnosis of a parasitic infection, failure to order indicated tests, and too much weight placed on competing explanations for his eosinophilia and diarrhea.[6]

SYSTEM CONSIDERATIONS

System Considerations

- Limited knowledge of parasitic helminths by US clinicians puts a large population of patients in iatrogenic danger.[7]
- All clinicians, especially those in primary care, critical care, rheumatology, pulmonology, and oncology, should be aware of the importance of identifying patients who should be screened for *Strongyloides* infection based on their social and travel history.
- Clinicians who prescribe immunosuppressive medications should also know how to treat these patients before they receive corticosteroids or other medications that could put them at risk of hyper-infection.
- Building awareness among at-risk patients and families about strongyloidiasis and screening options, along with the availability of curative treatment, could be helpful.

System Considerations

- Health departments can play a greater role in alerting clinicians and laboratories to the most recent epidemiological findings, to heighten clinical suspicion for strongyloidiasis and the capacity to treat.[7]
- Clinician education can be supported by protocols or computerized reminders (e.g., triggered by an initial prednisone order for patients who have lived or extensively traveled in tropical and subtropical regions).
  - But such computerized reminders need to be designed and implemented with sensitivity, to avoid adverse prejudicial or legal harms, given potential stigma and discrimination that can be associated with recent migration and/or chronic parasitic disease. [8-10]

TAKE HOME POINTS

Take-Home Points

- *Strongyloides* infection is common in tropical and subtropical regions and is not infrequently seen in immigrant and low-income communities in the US.
- The social and travel history of patients is critical to identify who is at risk for this infection, especially when combined with unexplained GI symptoms or eosinophilia.
- Any patient who is being considered for treatment with steroidal or immunosuppressive medications and who is at risk of *Strongyloides* infection should be screened and treated, if necessary, before beginning those medications.

Take-Home Points

- Screening in the United States should be done with an antibody test on a blood sample.
- Eosinophilia can be a clue to underlying *Strongyloides* infection but do not be deterred by its absence. Likewise, a stool test for *Strongyloides* larvae is diagnostic if positive, but given its poor sensitivity, a negative finding does not rule out infection. An antibody test is preferred for ruling out infection.
- Ivermectin is a curative treatment for *Strongyloides*, but re-infection can occur if there is ongoing exposure.
- *Strongyloides* hyperinfection has a high mortality even with treatment. It should be completely preventable with appropriate screening. Diagnostic delays can significantly increase the risk of death.

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