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Lessons on Parasitic Disease Control and Elimination

PARASITIC DISEASE CONTROL AND ERADICATION

Change and challenge is in the wind as 2008 comes to an end. The same is true when examining this month's ReachMD XM 160 special series Focus on Global Medicine. We take a look at both the changes and the challenges impacting global medicine.

Parasitic infections have a major impact on the developing world. The modes of transmission, treatment, and preventions vary widely. Whereas one parasitic infection is nearing eradication without the use of any drug therapy or vaccine, innovative approaches involving immunology, molecular biology, and genetics may be required for the elimination of another. What have we learned from the guinea worm and the hookworm and how can these principles be applied to help reduce other infectious diseases. You are listening to ReachMD, The Channel for Medical Professionals. Welcome to a special segment, Focus on Global Medicine.

I am your host, Dr. Jennifer Shu, practicing general pediatrician and author. Our guest is Dr. Michael Cappello, professor of Pediatrics, Microbial Pathogenesis, and Epidemiology and Public Health at the Yale School of Medicine and Director of the Yale World Fellows Program.

DR. JENNIFER SHU:

Welcome, Dr. Cappello.

DR. MICHAEL CAPPELLO:

Thank you, Jennifer.

DR. JENNIFER SHU:

Let's us start by talking a little bit about the hookworm and you have been doing some innovative research which I would love to get into, but can you give us a little bit of background about how common hookworm infections are both in the United States and globally?

DR. MICHAEL CAPPELLO:

Well, hookworm infection presently infects about 700 million people worldwide, although there are approximately 2 billion people who are at risk for infection within endemic communities and these are mostly countries or exclusively countries in resource limited settings up to 70%, 80% even 90% of people within a specific community could be infected. In United States, hookworm was endemic in the southern part of the country actually up until the early to mid part of the 20th century. This disease was eradicated in the United States to a large part to the efforts of the Rockefeller Sanitary Commission which was the precursor of the Rockefeller Foundation. They worked to educate people and to provide diagnosis and treatment facilities throughout the Southeastern part of the United States. Along with economic development, we were able ultimately to eradicate the disease here, but we still see it as a major cause of illness in resource limited countries.

DR. JENNIFER SHU:

Can you tell us how the hookworm infection is transmitted and is it contagious from person to person or animals, that kind of thing?

DR. MICHAEL CAPPELLO:

Right, so most of the hookworm infections in humans are caused by two species of hookworm, the first is *Ancylostoma duodenale* and the second is *Necator americanus* and these infections are acquired when eggs are excreted in the feces of an infected individual; those eggs when they reach the soil, if you have the right degree of humidity and temperature, those eggs will hatch and release larvae. The larvae then undergoes 2 successful moults to the L3 or third stage infectious larvae, and at point if those larvae are fortunate enough to come in contact with a permissive host, in this case humans, either penetrating the skin through the feet; they can penetrate the skin in any part of the body. In the case of *Ancylostoma* larvae, they are also infectious if they are ingested on contaminated food to start the infection. Those larvae then will migrate through the blood stream ultimately end up in the heart and lungs. They cut across the alveolar space into the airway. They climb up the airway, they are swallowed and they end up in the small intestine. At that point, they undergo the final molt to the adult hookworm stage and there you have both males and female hookworms that will mate in the intestine, the females will then release eggs and those eggs are excreted in the feces of the infected individual. So that's essentially the life cycle of this infection. There is very little risk of person to person transmission except that within closed communities where you have a high prevalence of infection and poor sanitation, there is a lot of maintenance or transmission of the life cycle itself and so I think that one of the challenges in dealing with hookworm control is trying to get into communities and educate them about the risk of acquiring infection and also about fairly low techniques that they can take to prevent transmission.

DR. JENNIFER SHU:

Great. Now you mentioned that the hookworm can go to multiple sites in the body, what kind of clinical manifestations might be expected in patients?

DR. MICHAEL CAPPELLO:

Well, most of the disease, if you will, caused by hookworm is really attributed to the adult worms which live in the small intestine. They actually have very sharp teeth or cutting plates and used those to attach to the intestinal mucosa and they literally chew on that plug of tissue within their buccal capsule. In the course of that process, they lacerate small blood vessels and blood is literally sucked into and leaks around the site of attachment, and each of these worms, although they are relatively small less than a cm in length, each of these

adult worms can cause us up to about 0.2 cc of blood loss per day. So if you have, let's say you are living in a developing country of relatively low dietary iron intake and you have a couple of hundred adult hookworms living in your gut, it really doesn't take long for you to develop fairly significant iron deficiency and anemia. So in addition to blood loss, infected people also will lose serum proteins through the course of blood feeding. There is also a fair amount of intestinal inflammation that can occur. There is a malabsorption syndrome that's been associated with hookworm in people living in endemic areas and the cumulative effect of all of this really is fairly significant malnutrition, anemia. In children, you see substantial growth delay and even cognitive deficits. Children with hookworm infection do not go as well in school. Adults with hookworm infection tend not to be as productive at work, in particular if their work required substantial physical labor. So the cumulative effect over time within communities can in fact be quite substantial in terms of economic impact

DR. JENNIFER SHU:

Now it seems like there is a pretty clear clinical picture, but is it also important to diagnose hookworm, especially in developing countries where you may not have the resources for that healthcare testing?

DR. MICHAEL CAPPELLO:

Sure, I think that the value of effective and efficient diagnostics really has to do both with an individual situation, but also within communities and even within countries. In other words for us to get a handle on the global impact of infections like hookworm as well as the soil-transmitted nematodes, it's important to go into communities and actually find out which parasites are prevalent, what the level of intensity of infection might be within a particular community, what the rates of reinfection are following treatment. So there are a lot of reasons why effective diagnostic studies are important. At present, surprisingly the way we diagnose hookworm today is probably the way it was diagnosed 100 years ago and that's using fecal microscopy. So each of the intestinal nematode eggs have a distinct morphology and they can be identified using fairly standard microscopy of fecal egg preparations. Recently in our lab and also work done by other groups have focused on trying to develop more reproducible or reliable antigen detection assays as well as PCR based methods to both quantify the intensity of infection, but also to distinguish between the various hookworm species that might be present within a particular community.

DR. JENNIFER SHU:

It sounds like there is some excellent new diagnostic tests available on the horizon, what about new treatments or is the current treatment adequate?

DR. MICHAEL CAPPELLO:

So the current therapy for hookworm infection as well as the other major soil-transmitted nematodes, *Ascaris* and *Trichuris* really relies on a class of drugs called the benzimidazoles, and in particular, albendazole is the drug of choice for hookworm infection at least in terms of large scale community based treatment programs. Unfortunately, if you look at the data in some communities, treatment failure rates are probably upwards of 50% in some trials, and in fact in our experience recently in a study in central Ghana, we found that a 40% treatment failure rate within 3 communities in which hookworm was endemic, even more worrisome is the prospect of the emergence of resistance to the benzimidazoles, but we know from de-worming studies at in children is that probably multiple treatments per year are required in order to achieve the full health benefits of de-worming and if we were to embark on such an ambitious project on global scale, I think most of us who work in the field recognize that we are likely to see the emergence of resistance in human hookworm species in the same way that we have seen resistance in some of the veterinary nematode infections and so I think that as de-worming becomes more common and as people recognize that the need to de-worm multiple times in the course of a year, we are pretty certain that we will begin to see greater rates of resistance. There have been some reports to date to suggest that resistance is coming, but really that's been difficult to determine or at least define on a more molecular level. So I think that there is a pressing need at

this point in time for people to be thinking about developing new drugs and new treatments for hookworm infection as well as the other nematodes. As you know, it takes many years to develop effective antimicrobials and so the time to be working on drug discovery and drug development really is before you actually need these compounds. So we have done some work looking to identify new compounds that have activity against hookworm. We have been working to develop with our colleagues in Ghana methods that can be adapted to the field to actually detect the presence of resistance to albendazole and other agents and so I think that it's very important at this stage that people begin to anticipate that the current medicines that we use for hookworm and other intestinal nematode infections may not with us for more than the next decade.

DR. JENNIFER SHU:

Earlier you mentioned the importance of educating communities about preventing hookworm infections. What kinds of practices might prevent transmission of the hookworm and are they any vaccines or anything new on the horizon?

DR. MICHAEL CAPPELLO:

Well, I think we learned an important lesson from the Rockefeller Sanitary Commission, which as I mentioned earlier, was very effective at educating as well as diagnosing and treating people in the Southeastern United States who had fairly high rates of hookworm infection. So, education I think is very important, in particular the proper and safe disposal of human waste. The challenges that in very poor countries, these efforts may not be feasible, and in fact, on certain parts of the world that use human waste as fertilizer for their crops, I think it would be extremely difficult to get people to change behavior. So I think without a doubt, efforts at education and community based health interventions need to be really coupled with economic development and improvement in sort of people's general state of living and condition. With regard to vaccines, certainly there are groups that are focusing on the development of vaccines. There is at least one vaccine that has made it into human trials in the early stages. I think that ultimately because hookworm is so intimately woven into these poor rural communities, I think vaccines could ultimately have a very positive effect on controlling disease if not helping to eradicate it.

DR. JENNIFER SHU:

I would like to thank our guest, Dr. Michael Cappello. We have been discussing parasitic disease control and eradication.

I am Dr. Jennifer Shu, you've been listening to a special segment Focus on Global Medicine on ReachMD, The Channel for Medical Professionals. Please visit our web site at www.reachmd.com, which features on-demand pod casts of our entire library. Thank you for listening.

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