

to gain weight, even though it seemed that my eating and activity habits had not changed. When I turned 55, I cut out powdered doughnuts and began to walk more. Now, at age 57, I am 10 pounds lighter, my wife is happier that there is less powdered sugar on the seat of the car, and I have a little more energy. As I

reflect on my BMI of 27.3, however, I am now looking for more small steps. My office is located on the fourth floor of a building with both stairs and an elevator. Hmmmm.

Dr. Byers is a professor of preventive medicine at the University of Colorado School of Medicine, Denver.

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FOCUS ON RESEARCH

Chagas' Disease — Can We Stop the Deaths?

James H. Maguire, M.D., M.P.H.

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Nearly 100 years since its discovery by the Brazilian physician Carlos Chagas, the protozoan parasite *Trypanosoma cruzi* remains perhaps the most common cause of myocarditis worldwide. The lethality of Chagas' heart disease is undisputed, as the survival curves presented by Rassi et al. in this issue of the *Journal* illustrate with chilling clarity (pages 799–808). More than 10 million Latin Americans carry the parasite, and at least 1 million of them will die unless scientific and political breakthroughs lead to new strategies and tools for diagnosis, treatment, and increased access to medical care.¹

Chagas' disease (American trypanosomiasis) afflicts impoverished people in the Americas from Mexico to southern South America. Blood-sucking triatomine bugs that transmit *T. cruzi* live in thatched roofs and cracks in the walls of poorly constructed homes. Massive rural-to-urban migrations of populations that have occurred since the 1970s have brought Chagas' disease to Latin American cities and periurban *favelas*, where transmission through blood trans-

fusion and transplacental transmission have resulted in many new cases. The exodus of millions of Latin Americans to more developed countries accounts for the estimated 100,000 or more chronically infected persons now living in the United States and more than a dozen transfusion- and transplantation-associated cases in the United States, Canada, and countries in Europe, which do not



Triatomine Insect

screen donors serologically for Chagas' disease.

The evolution of disease due to *T. cruzi* is insidious. Except for a small percentage of persons in whom fulminant myocarditis or meningoencephalitis develops, all patients survive the acute stage of infection. A vigorous immune response then reduces the number of parasites to nearly undetectable levels that remain so for life, un-

less infection is reactivated by AIDS or immunosuppressive therapy. For poorly understood reasons, only 10 to 30 percent of infected persons have clinical manifestations of chronic Chagas' disease. The heart and gastrointestinal tract are the principal targets, and symptoms usually do not appear for 15 to 30 years.

The gastrointestinal features of the disease occur rarely among populations living north of the equator. Inflammation and destruction of autonomic ganglia lead to the dysphagia of Chagas' megaesophagus and prolonged constipation of Chagas' megacolon. Heart disease is the more common and more severe manifestation. There is controversy over the pathogenesis of the lesions of Chagas' cardiomyopathy, which consist of chronic inflammatory infiltrates, diffuse and focal fibrosis, and loss of myocardial cells. Current evidence suggests that parasites that persist in the myocardium and the inflammatory and immunologic reaction to them are primarily responsible for the pathology.¹

Right bundle-branch block or

left anterior hemiblock precedes other manifestations of chronic heart disease in the majority of cases. Progression of disease leads to cardiac dilatation and biventricular failure. Prominent features of advanced Chagas' heart disease include left ventricular apical aneurysm and combinations of complex ventricular arrhythmias, sinus bradyarrhythmias, and intraventricular and atrioventricular conduction block. The most common modes of death are sudden death, progressive heart failure, and to a lesser extent, embolism of mural thrombi to the brain or other organs.

Rassi and colleagues report their evaluation of 424 patients with known Chagas' heart disease as the basis for a risk score to predict the likelihood of death. Among persons in their high-risk category, the 10-year mortality was 84 percent. Mortality was considerably lower among those classified as low risk (10 percent) or intermediate risk (44 percent), but the long-term outlook for many of these persons is not promising, given the progressive nature of the disease. Indeed, the prognosis for patients with Chagas' cardiomyopathy may be worse than that associated with other dilated cardiomyopathies.

Population-level data are as alarming as those from clinic-based populations such as that of Rassi et al. In one study of a rural community in Brazil, 60 percent of persons 20 years of age or older had serologic evidence of *T. cruzi* infection, and 14 percent of infected persons had right bundle-branch block on electrocardiography.² Mortality over a six-year period was approximately 20 percent among young and middle-aged persons with right bundle-branch block. Among those

who also had at least one ventricular extrasystole, mortality was 60 percent, or 14 times that among uninfected persons.

Given these grim statistics, what can be done? Medications to improve cardiac function or suppress arrhythmias, as well as implantation of pacemakers or defibrillators, prolong life but do not halt the progression of the disease. Cardiac transplantation is an option for those with end-stage disease, since survival rates are as high as those among patients who receive transplants because of other cardiomyopathies. In this regard, the risk score developed by Rassi et al. will help guide decisions about appropriate therapy and the allocation of limited resources.

In the past, benznidazole and nifurtimox, the only available drugs with activity against *T. cruzi*, were believed to be ineffective and too toxic for treating chronic infections. However, according to a recent report, a 60-day course of benznidazole therapy eliminated infection in more than 60 percent of chronically infected children.³ Evidence is mounting that antiparasitic treatment may prevent or retard the progression of cardiac disease, even in adults.⁴ Nonetheless, more clinical trials and better drugs are needed.

Clearly, the best solution is to prevent *T. cruzi* infection in the first place. In 1991, the six Southern Cone countries (Argentina, Bolivia, Brazil, Chile, Paraguay, and Uruguay) initiated a program to curtail transmission of the parasite through vector control and the screening of blood donors (Peru later joined the effort as well).¹ Remarkably, transmission has been virtually eliminated in much of the region, and several million cases of infection and tens

of thousands of deaths have been averted. This success has led to similar programs in the other areas of Latin America where Chagas' disease is endemic.

Difficult challenges lie ahead for the elimination of transmission, and millions of people remain chronically infected, including some living in the United States and other countries where the disease is not endemic. Yet there are reasons for optimism: the commitments of governments and the international community, the generosity of donors, new candidate drugs and partnerships for their development, new national programs to identify and treat infected children, and the sequencing of the *T. cruzi* genome, which opens prospects for new drugs and diagnostic tools and an increased understanding of the mechanisms of disease.⁵ Political will, good science, and unfailing financial support can remove this killing disease from the list of the most neglected "poor people's diseases."

Dr. Maguire is a professor of epidemiology and preventive medicine at the University of Maryland School of Medicine, Baltimore.

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