



Current Topics

Heart Drug Helps To Beat Chagas, Leishmania Parasites

Amiodarone, a drug long used for treating irregular heart rhythms, can also be effective against Chagas disease and leishmaniasis skin lesions, according to Alberto Paniz-Mondolfi at Columbia University in New York, N.Y., and his collaborators in Venezuela. Both these parasitic diseases are endemic in Central and South America, affecting millions. Moreover, cases in which patients are coinfecting with these parasites are on the rise, the clinical researchers report.

Trypanosoma cruzi, a protozoan parasite that is transmitted by reduviid bugs, causes Chagas disease, which was discovered 100 years ago. During the chronic phase of an infection, these parasites can affect organs such as the heart, damaging muscle tissue and causing arrhythmias. Drugs that target this parasite show limited effectiveness, and toxic side effects restrict their use. Meanwhile, sand flies transmit *Leishmania* spp., another type of protozoan parasite. They cause leishmaniasis, which develops in several forms. For example, cutaneous leishmaniasis causes skin ulcers, whereas visceral leishmaniasis affects organs such as the liver and spleen. Here again, available therapy is unsatisfactory. For example, widely used pentavalent antimonials can damage the heart, kidneys, and liver. Thus, better drugs are needed for treating individuals infected with either or both these parasites. Vaccines are also needed.

A month after a Chagas patient received amiodarone for his heart ar-

rhythmia, his levels of circulating antibodies against *T. cruzi* dropped dramatically, according to Paniz-Mondolfi. Subsequent treatment with the antifungal drug itraconazole lowered those levels below detectable limits. Details appear in the May 2009 issue of *Chemotherapy* (55:228–233).

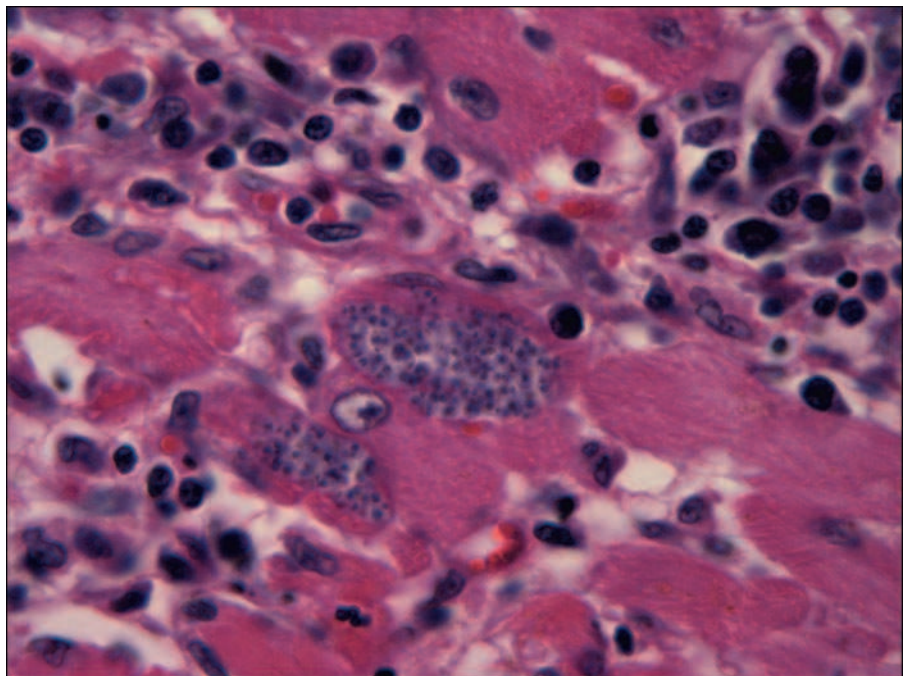
Separately, amiodarone was given to a patient with cutaneous leishmaniasis to stabilize an irregular heart rhythm. Surprisingly, after a month, the leishmaniasis lesions healed without other treatments. Details of that case study appear in the June 2008 *Therapeutics and Clinical Risk Management* (4:659–663).

Since those cases, Paniz-Mondolfi and his colleagues successfully treated 12 more Chagas and leishmaniasis pa-

tients with amiodarone or amiodarone-itraconazole combination therapy, and are planning to conduct clinical trials on larger numbers of such patients.

When used against fungi, azole drugs block ergosterol biosynthesis and interfere with membrane biosynthesis. In treating heart arrhythmias, amiodarone disrupts mitochondrial calcium homeostasis. When combined to treat *T. cruzi* or *Leishmania mexicana*, the two drugs prove remarkably potent in killing the parasites. Details appear in the April 2009 *Antimicrobial Agents and Chemotherapy* (53:1403–1410) and the February 2006 *Journal of Medicinal Chemistry* (49:892–899).

“Chagas patients treated with ami-



T. cruzi infecting heart tissue. *T. cruzi* nests in cardiac muscle with surrounding inflammatory cell reaction. Researchers find that drugs used to treat cardiac arrhythmia also have activity against these trypanosomes. (Micrograph courtesy of Alberto Paniz-Mondolfi.)

odarone for arrhythmias improved overall more than patients treated with other anti-arrhythmia drugs, and we wondered why," Paniz-Mondolfi says. "These basic science results explain what we see clinically in patients."

"It's an excellent example of the piggy-back approach to the chemotherapy of tropical diseases," says Roberto Docampo, a professor of cellular biology at the University of Georgia, Athens. The drug combination is attractive because both types of drugs are already approved for use in humans and much is known about their pharmacokinetics and side effects. Although long-term use of amiodarone for arrhythmia can be toxic, "its use in combination with imidazole to kill parasites could be shortened because of their synergistic effects," he says.

Treating Chagas patients early with amiodarone and antifungal drugs of the azole type might eliminate the chronic phase that leads to heart problems, Paniz-Mondolfi says. More generally in terms of both Chagas and leishmaniasis, he adds, "In developing countries we need to provide patients with an immediate solution, and amiodarone and itraconazole are generic, cheap, and abundant."

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