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Malaria Update from the Annual Meeting of the American Society of Tropical Medicine and Hygiene

SPECIAL REPORT BY LIN H. CHEN, MD

Synopsis: *At the 52nd Annual Meeting of the American Society of Tropical Medicine and Hygiene, Dr. Monica Parise from the Centers for Disease Control and Prevention presented her annual update on prevention and treatment of malaria. The CDC Malaria Branch held an expert meeting on malaria chemoprophylaxis in January 2003 with input from the Division of Global Migration and Quarantine, during which the experts reviewed more than 1700 references.*

SIX DRUGS WERE EXAMINED IN DETAIL: CHLOROQUINE, HYDROXYCHLOROquine, mefloquine, doxycycline, atovaquone/proguanil, and primaquine. Experts discussed several questions about each drug, including the indications, dosing (how much before trip, loading dose, split dose), efficacy, adverse drug reactions, contraindications, precautions regarding cardiovascular disease, fine motor skills, drivers, drug interactions, and safety in pregnancy, breast-feeding, and children.

Overall recommendations are in agreement with existing policy. For areas with chloroquine-resistant *Plasmodium falciparum* (CRPF), options for chemoprophylaxis will be simply alphabetized. Primaquine is added as a second-line chemoprophylaxis agent. Chloroquine-proguanil is eliminated as an option in areas of CRPF prevalence. For chloroquine-sensitive *P falciparum* (CSPF) areas, recommendations will explicitly state that mefloquine, doxycycline, and atovaquone/proguanil might be used. In order to assess tolerance, the medication could be started as early as 3-4 weeks before exposure. A statement will be made about avoiding the purchasing of medications overseas due to potentially suboptimal drug quality. In addition, information on adverse drug reactions will be disseminated and the importance of antimalarials communicated. Rates of mild/moderate and severe adverse drug reactions are needed.

Regarding chloroquine (CQ) and hydroxychloroquine (HCQ), CQ remains the first choice for CSPF because there are more data. No eye exam is required due to very low risk of retinitis, even with long-term use. Twice-weekly dosing remains an option. No glucose-6-phosphatase deficiency (G6PD) screening is necessary prior to using either CQ or HCQ. Further discussion should explore tolerance of CQ vs HCQ and long-term use of HCQ in children.

The literature reviews reveal that doxycycline does *not* interfere with oral contraceptive efficacy. Doxycycline is preferred over minocycline for malaria prophylaxis on the basis of efficacy, experience, and potential side effects. However, long-term use of doxycycline needs to be further discussed. The dose of primaquine for terminal prophylaxis should increase to 30 mg base/d × 14 days for all areas. Primaquine should be avoided for primary or terminal prophylaxis in G6PD deficiency. No new insights emerged regarding candidates for terminal prophylaxis. Concerns regarding myelosuppression and the use in young children need to be addressed.

Atovaquone/proguanil efficacy is adequate as first-line malaria chemoprophylaxis. Efficacy is adequate against *P vivax* to recommend it in areas with *P vivax* predominance, but terminal prophylaxis is still recommended. Safety in children weighing 5-11 kg remains to be assessed.

Members of the expert panel recognize that mefloquine has become difficult to prescribe because of its potential side effects. There is no good explanation for long-term neuropsychiatric adverse drug reactions. However, gender differences exist, since women are more likely to experience adverse events than males. Adverse drug reactions may last weeks because of mefloquine's long half-life. The panel concluded that it is acceptable to use mefloquine for persons with a prior history of febrile seizures. No statement was felt necessary regarding the concurrent use of alcohol and mefloquine. It is also acceptable in persons needing fine motor skills, but the course may start 3-4 weeks early. Permissive language regarding loading doses will be added. Questions remain regarding split-dose prophylaxis, monitoring of liver function tests, and the use during pregnancy.

Primaquine is approved as a second-line drug for primary prophylaxis. Efficacy in recent trials was 88-94% against *P falciparum* and 85-92% against *P vivax*. The drug is well tolerated. Gastrointestinal upset is the most common adverse drug reaction. The most serious side effect is hemolysis in patients with G6PD deficiency; therefore, G6PD needs to be tested before this medication is used. Methemoglobinemia is also fairly common. Primaquine is well tolerated up to 1 year.

Finally, sulfadoxine-pyrimethamine is no longer recommended for self-treatment. Atovaquone/proguanil is now the drug of choice. Statements will specifically recommend avoidance of halofantrine. A summary report will be provided in the near future.

Abstract Summaries

Additional interesting reports on malaria from the *Supplement to the American Journal of Tropical Medicine and Hygiene* (2003;69[3]) are as follows:

Many of the studies presented had examined malaria epidemiology. MacLean et al reported an analysis of malaria surveillance data obtained at the McGill University Centre for Tropical Diseases. Data showed an increase in malaria cases from 1981 to 2002, with a dramatic increase in incidence between 1996 and 1998 attributed to *P vivax* acquired in India, where a malaria epidemic was identified concurrently. The study is an illustration of the potential of travelers to act as sentinels for infectious disease outbreaks and changing epidemiology (*Abstract #58*). Alger et al studied the prevalence, incidence, and recurrence of malaria in northern Honduras. Study subjects were examined with malaria smears in December 1998, August 1999, December 1999, and September 2000. The baseline prevalence of malaria was 7.1% (range, 9.8-21.5%), with a 4.3% prevalence of *P falciparum* (range, 3.4-10.0%). The incidence of *P vivax* infection was higher in children up to 14 years old, whereas the incidence of *P falciparum* was greater in older persons (*Abstract #256*). Maguire et al evaluated residents for malaria at select locations of the Sanma and Shefa provinces of the Republic of Vanuatu. Malaria smears indicated a mean malaria prevalence of 22% (range, 4-33%), predominantly *P falciparum* (73%), followed by *P vivax* (25%). The gametocyte rate among persons with *P falciparum* was 54%. Primaquine was apparently removed from the national malaria treatment guidelines in 1991, which may explain the finding of a high gametocyte rate (*Abstract #277*). MacArthur et al investigated 3 autochthonous cases of *P vivax* malaria in Loudoun Country, Va; 2 presented in August 2002 and 1 in March 2003. Entomologic vector investigation showed *Anopheles quadrimaculatus* and *A punctipennis*. Parasite DNA analysis suggested a single source in spite of the long lag time for the third case. Although uncommon, autochthonous cases of malaria continue to occur within the continental United States (*Abstract #279*).

Several aspects of malaria immune response were reported. Njama et al assessed the prevalence of asymptomatic parasitemia and its association with symptomatic malaria in Ugandan children between the ages of 6 months and 5 years living in Kampala. A total of 283 subjects had routine blood smears done at enrollment and approximately every 30 days. The risk of developing symptomatic malaria within 30 days was 50% in the subjects with a positive routine smear compared to 9% in those with a negative smear. Six percent of the subjects had asymptomatic parasitemia that was preceded and followed by a negative routine smear. Njama et al conclude that asymptomatic parasitemia should be treated and that a reduction of transmission intensity may

reduce symptomatic malaria (*Abstract #6*). Similarly, Diemert et al used monthly malaria smears to evaluate the association of symptomatic malaria episodes following asymptomatic parasitemia in 2 Malian villages. Diemert et al also found that routine monthly assessment of parasitemia correlated with subsequent clinical malaria (*Abstract #15*). Legorreta-Herrera et al used a mouse model to study the effect of early treatment of malaria in modification of cross protection for further infections. They evaluated 5 groups of mice infected with *P chabaudi*, in which each group was treated once with pyrimethamine on day 0, 5, 7, or 9, or no treatment (control group). Each group was divided further 8 weeks later and infected with *P chabaudi*, *P yoelii 17XL* (lethal), or a mixture of the 2 parasites. Mice with early treatment (day 0 or 5) died, whereas mice with later treatment (day 7 or 9) or no treatment survived. This study in mice showed that infection with *P chabaudi* induces immunity against the same parasite. The study also showed that infection with *P chabaudi* produces cross protection against *P yoelii* 17XL and that early treatment of the first infection reduced the cross protection effect (*Abstract #665*).

Data on malaria medication efficacy included a report by De Boever et al on the efficacy of Malarone™ (atovaquone and proguanil hydrochloride) in a post-marketing surveillance. An estimated 1.28 million people had been prescribed atovaquone/proguanil as of April 2003, with most prescriptions written for malaria prophylaxis. Up to that point, 48 post-marketing prophylaxis failures and 15 falciparum malaria treatment failures were reported. Five cases of clinical failure have been documented to have a genetic mutation in codon 268 of cytochrome-b gene, which results in a reduced parasite binding affinity of atovaquone. The countries from which failure has been confirmed include Nigeria, Mali, Cameroon, Ivory Coast, Kenya, and Gabon (*Abstract #245*). Filler et al investigated reported malaria chemoprophylactic failure among travelers in a US university exchange program. A post-travel questionnaire was used to evaluate cases of malaria reported among a group of American University staff and students who traveled to Ghana. Twenty-five of the 33 travelers completed the questionnaire. Twenty-four of the 25 took a chemoprophylactic drug recommended by the CDC (atovaquone/proguanil 15, mefloquine 6, doxycycline 3), but only 14 (56%) reported complete compliance. Twenty reported symptoms consistent with possible malaria during the trip, and 13 were evaluated medically. Six were diagnosed with malaria and were treated with antimalarial drugs, in spite of appropriate chemoprophylaxis in 3 of these travelers. Some of the travelers in the group decided to discontinue chemoprophylaxis because of the impression that the drugs were ineffective. Upon return, 5 travelers with a reported microscopic diagnosis of malaria were tested for anti-*Plasmodium* antibodies and all were negative. Filler et al documented the frequency of misdiagnosis occurring in malaria-endemic countries, misconceptions regarding efficacy, and poor compliance with chemoprophylaxis, drug resistance, safety issues resulting from misdiagnosis, and unnecessary treatment for malaria (*Abstract #57*).

Smith et al examined responses to treatment of *P falciparum* in HIV-infected and HIV-uninfected individuals in Siaya, Kenya. Febrile adults found to be parasitemic with *P falciparum* were recruited and were tested for HIV, molecular analysis of *P falciparum* resistance, and sulfa drug levels. Subjects represented 3 groups: HIV-positive CD4 < 200 (n = 43), HIV-positive CD4 > 200 (n = 79), and HIV-negative (51). All subjects were treated with SP (national guidelines) and followed for 28 days. Parasite density on day 0 was 4 times higher in HIV-positive CD4 < 200 subjects than the other 2 groups, and there were significant differences between the baseline parasitemias of the 3 groups. Twenty-one of the 28 failures (6 early treatment failures and 22 late parasitologic failures) were among the HIV positives, which suggested a negative effect of HIV on treatment of *P falciparum* malaria (*Abstract #273*).

A number of combination therapies for malaria treatment were presented. Sihuincha et al studied the efficacy of artesunate-mefloquine in treating uncomplicated *P falciparum* malaria in patients detected by the national malaria program in Loreto, Peru. *P falciparum* parasites have been increasingly resistant to CQ and sulfadoxine-pyrimethamine (SP) in Amazonian Peru. Peru included mefloquine plus artesunate as standard treatment in the National Malaria Control Program beginning in November 2001. Efficacy of the regimen using artesunate (4 mg/kg/d for 3 days) and mefloquine (12.5 mg/kg/d for 2 days starting on day 2 of treatment) was studied among 143 patients. Ninety-two percent of patients cleared parasitemia within 24 hours; another 8% cleared parasitemia by 48 hours. A total of 89% of patients defervesced within 24 hours and another 11% within 48 hours (*Abstract #262*). Pitmang et al compared the efficacy of combination SP + CQ to that of SP alone in treating uncomplicated *P falciparum* malaria in Nigerian patients. A total of 120 patients were treated with the combination, while 116 were treated with SP alone. The combination group cleared their parasitemia more quickly (75% vs 42% by day 3) and had greater clinical improvement by day 14 (95% vs 72%). RI, RII, and RIII resistance was lower in the combination group

compared to the SP group (7.9%, 3.5%, 1.8% vs 23%, 17%, 5%, respectively). Although parasite resistance to SP and CQ is well established, the combination of SP + CQ for malaria appears to be more effective than monotherapy and may lead to a longer use of these drugs (*Abstract #442*). In contrast, a randomized trial by Obonyo et al compared treatment of *P falciparum* with either SP alone or in combination with artesunate for 1 (As1) or 3 days (As3) in Kenya. Treatment failure by day 14 was highest in the SP group (26%), compared to 16% in SP + As1, and 9.4% in SP + As3. Failure rates by day 28 were 46%, 38%, and 26%, respectively. The study demonstrated high resistance to SP and inadequate efficacy of the combination of SP + As in Kenya (*Abstract #791*).

Interest in herbal therapies was also evident at the meetings. Aderounmu et al reported on the antimalarial activity of 4 commonly used medicinal plants in Nigeria. Four plants, *Enantia chlorantha*, *Azadirachta indica*, *Morinda lucida*, and *Cymbopogon giganteus*, were evaluated for their activity against *P falciparum* in vitro. The crude extracts of these plants inhibited parasite growth. *E chlorantha* inhibited parasite growth by 68.9% and appears to be a promising anti-malarial (*Abstract #639*). Waters et al evaluated in vitro anti-malarial activity of traditional herbal remedies from Kenyan plants. The genera *Erythrina* and *Millettia* contained anti-malarial compounds that appeared to kill both drug-sensitive and drug-resistant parasites (*Abstract #643*). Given the development of *Plasmodium* parasite resistance, potentially useful plants or compounds should continue to be identified and further explored. ■

Truths and Consequences: The Parasites of Dogs and Cats

CONFERENCE COVERAGE

Problems in human health when pets contaminate the environment.

By Maria D. Mileno, MD, and Frank J. Bia, MD, MPH

An intriguing symposium was presented at the 52nd Annual Meeting of the American Society of Tropical Medicine and Hygiene, which addressed various enigmatic parasitic infections of animals, and the serious problems that animal parasites may cause in humans.[1] The chair for this excellent symposium was Dr. Leonard Marcus, VMD, MD, who has previously highlighted numerous infections for the medical community that are transmitted by animals and their parasites. They can reach humans in a variety of ways, including nosocomial transmission.[2] The Companion Animal Parasite Council (CAPC) is currently writing guidelines for diagnosis, treatment, prevention, and control of internal and external parasites in dogs and cats. One of Dr. Marcus' major objectives in organizing this symposium was to introduce CAPC to a medical audience, explain its significance for practicing physicians, and enhance cooperation between MDs and veterinarians. The web site will be www.capcvet.org and on it will appear the long and short guidelines that can be downloaded, biographies of participants, and links to other organizations such the American Association of Veterinary Pathologists and the American Heartworm Society.

This symposium began with an excellent summary of the importance of flea control in cats and dogs by Dr. Michael Dryden of Kansas State University. The common cat flea, *Ctenocephalides felis*, not only affects cats but also accounts for most flea infestations of dogs. It is associated with infestation of about 50 other animal species. The consequences of animal flea infestations have implications for both animals and humans. These include anemia in animals and their general annoyance to humans, along with flea allergy dermatitis, delusional parasitosis, and the potential for transmission of human diseases such as murine typhus. Occasionally, ova of the dog tapeworm, *Dipylidium caninum*, are ingested by larval fleas in which they develop into cysticercoid larvae. Infection of children may occur following accidental ingestion of an infected flea. Dr. Dryden noted that cat and dog fleas are somewhat unique, since they become permanent ectoparasites of animals unless effectively treated. The home environment of the animal then becomes heavily flea contaminated. These premises are difficult to eradicate fleas from, and resistance to available agents has even become a problem in this context. Flea infestation of a home will generally require extensive treatment of the premises.

Although the cat flea is a major problem for both dogs and cats, the rat flea offers other possibilities. A recent CDC report in *MMWR* indicates that 47 cases of murine typhus, the zoonotic disease caused by *Rickettsia typhi*, were identified in 5 islands of Hawaii during 2002: Maui had 35 cases, Molokai had 6, Oahu reported 3, Kauai had 2, and Hawaii had just 1.

Symptoms and their frequency (%) included fever (98), malaise (89), headache (87), myalgia (81), loss of appetite (81), chills (81), arthralgias (72), nausea (60), vomiting (54), backache (53), abdominal pain (51), stiff neck (42), and skin rash (40). Severe disease complications occurred in 10 of these cases including acute renal failure, gastrointestinal bleeding, meningitis, encephalitis, pneumonitis, and CHF with pleural effusion. Peridomestic rodents and the oriental rat flea (*X cheopis*) have maintained the endemicity of murine typhus on the Hawaiian Islands. Before World War II, this disease was widespread in the continental United States, but improved rodent and ectoparasite control practices decreased transmission, with fewer than 50 cases reported annually from Hawaii, California, and Texas combined. While rodent depopulation programs are important, insecticides, which prevent arthropods from transmitting disease to humans, must also be considered and used.

The scheduled use of a 30-day residual adulticide, such as fipronil, on pet animals is suggested before the home becomes infested and presents owners with a more difficult problem in eradication. Topical application of these agents on the animal's coat will kill newly emerged adult fleas before they can lay eggs, *and* also eliminate all stages of various tick species, including deer ticks that transmit Lyme disease, babesiosis, and ehrlichiosis. Fipronil acts by collecting within the oils of animal skin and hair follicles. Because it continues to be released from hair follicles onto the skin and coat over time, it has prolonged action for both tick and flea control. Travelers who know they will be staying in homes where dogs and cats are commonly present may want to invest in a supply of one of these very effective agents for animals and bring it with them on their travels to prevent discomfort and disease transmission to both themselves and their children.

The female sand flea presents other possibilities for human infections. A brief article appeared recently in *Infections in Medicine* and described a 25-year-old researcher who was studying bats in the Comoros Islands. Frequently not wearing shoes and crawling on his hands and knees, he developed itchy erythematous papules that eventually looked like typical lesions of tungiasis, containing a gravid female, which appeared as a central punctum that eventually blackened. They were asymmetrically located on palms and soles, and the fleas were removed with a sterile needle. The sand fleas, or *Tunga penetrans* jiggers, are about 1 mm and reside in earthen floors of homes, sandy soil, and beaches. Common hosts are humans, dogs, cats, horses, pigs, and birds. Complications can include secondary bacterial infection, autoamputation, tetanus, and even gangrene.

Although the focus of this symposium was on dogs and cats in North America, the scope of these problems will generally encompass most travelers as well. A review of the 4 major infections discussed included toxocariasis, hookworm infections, and *Baylisascaris procyonis* epidemiology and infection, in addition to a potentially emerging pathogen, *Echinococcus multilocularis*.

Peter Schantz reviewed the life cycle and clinical implications of *Toxocara* infections. Unless dams are treated for *Toxocara* infections, ova will be passed into the soil where they larvate, and these larvated ova of the parasite are quite hardy. They survive best when protected from sun in dry climates and, at times, have been documented to overwinter. Following ingestion, migrating larvae can penetrate the gut wall and travel to the liver and blood and disseminate throughout the body. The tissue phase of animal infections may last for years, and these organisms can be transmitted transplacentally. Interestingly, the parasites shed a glycoprotein that protects them from immunologic attack. There is a strong tropism of *Toxocara* organisms for the neurological system, particularly the eyes, in paratenic hosts. Paratenesis refers to the passage of an infective agent by one or a series of hosts, in which an infectious agent is transported between hosts but does not undergo further development. Four distinct categories of clinical infections include 1) visceral larva migrans (VLM); 2) ocular larva migrans (OLM); 3) neurological larva migrans; and 4) covert toxocariasis. Patients with low-level exposures to ova may present only with eosinophilia, while children and others who display pica may ingest thousands of eggs simultaneously. Hence, children with pet dogs are the most likely to present with VLM.

Of note, 58% of all US households have a dog or cat residing with them. Travelers to the United States, or other locations in which working or pet dogs are present around children, must be aware of their potential to infect young children with *Toxocara* ova. Children may present with retinal granulomas, including a white pupil, which is a serious finding and indicates infection will likely result in visual loss. Diagnosis can be made serologically by appropriate ELISA testing. Note that these ocular manifestations of toxocariasis have occasionally been mistaken for ocular malignancies.

In endemic countries, humans who are infected with hookworm have increasing rates of infection with age, as opposed to other infections such as ascaris and whipworm infection. The latter tend to

peak in childhood, which implies some degree of immune regulation upon repeated exposures. *Ancyclostoma* spp. other than *duodenale*, such as *A caninum* or *A braziliense*, represent hookworm parasites of dogs and cats, which can potentially be shed by these animals and spread to humans. They are the cause of cutaneous larva migrans, which so commonly affects travelers to tropical countries. Unlike toxocariasis, canine hookworm infection can also be transferred by direct skin contact with contaminated soil, after which larvae may migrate for days and weeks, occasionally reaching ectopic sites in the human intestine, causing eosinophilic enteritis. Negative stool examinations and the presence of only a single adult male or nongravid female may characterize these human GI infections. Prevention during travel can minimize risk. Picking up after dog excrement, treating house pets with an antihelminthic agent on a regular basis, as well as excluding dogs and cats from playgrounds, will make a significant effect on prevention of childhood infection, particularly during travel.

There is considerable environmental contamination with eggs of the raccoon ascarid or roundworm, *Baylisascaris procyonis*, found fairly commonly in the United States, Europe, and Japan. This topic was nicely reviewed by Dr. K. Kazacos from the Purdue University School of Medicine. Unfortunately, the helminth can infect both dogs and humans in addition to raccoons, although there is no evidence for transplacental or mammary infection as a route for vertical transmission. Within the United States, this large roundworm is prevalent in the Midwest, the Northeast, and West Coast areas. Ova are commonly found in the environment. Although human cases have been diagnosed since the early 1980s, it is suspected that unrecognized cases have probably occurred since the 1950s. Raccoons and foraging dogs leave behind their feces, which may contaminate backyards, house surfaces, roofs, or even firewood bark. This infected fecal material may find its way into the home, and in one case a child was infected by licking contaminated wood bark.

This parasitic roundworm may first insidiously affect muscle, followed by central nervous system infection with ensuing encephalitis. It is estimated that *Balisascaris*-associated encephalitis has already affected approximately 100 different species of animals. There is a lag time or latent period between infection and severe CNS disease, which lasts from 1 to 3 weeks. Once neurological symptoms appear, some clinical cases have suggested rabies at first presentation, but on autopsy, infection was shown to be caused by *Balisascaris procyonis*. On MRI scanning, there may be characteristic deep white matter lesions and periventricular enhancement. This parasitic infection has also been associated with ocular larva migrans. One might suspect disease in persons with clinical neurological symptoms and a history of exposure, peripheral eosinophilia, and an eosinophilic pleocytosis in the CSF. Diagnosis can be made using IFA and ELISA techniques; antibodies may be found in the serum and/or CSF, and one can distinguish this infection from toxocariasis using ELISA techniques. Treatment should be instituted immediately if the disease is suspected. Treatment options include albendazole, although no regimen is particularly efficacious.[2] Corticosteroid therapy may be important as part of therapy for ocular or CNS disease in order to quell the severe inflammatory response associated with treatment.

On a final note for this symposium, the tapeworm of coyotes and red foxes, *Echinococus mulitlocularis*, now has established a focus of infection of dogs in central North America, including the Dakotas. Two human cases were described during the symposium. Farm dogs and cats will consume wild rodents, and prevention of both animal and human disease is accomplished by avoiding animals' consumption of such rodents, hand washing of fruits and vegetables, and the deworming of both dogs and cats with praziquantel. ■

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Participants and Topics

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- Dryden M. Tick and flea control in dogs and cats: Implications for human health.
- Schantz P. Zoonotic helminths of dogs and cats: Transmission, disease manifestations and prevention.
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Trypanosoma cruzi and the United States Blood Supply: Should We Be Testing All Donors?

CONFERENCE COVERAGE

By Mary-Louise Scully, MD

Synopsis: *Insuring that the blood supply is free of transmissible pathogens remains a challenge. Since 1987, 7 cases of transfusion-transmitted* Trypanosoma cruzi *infections have occurred in the United States/Canada. The chronic nature of Chagas disease and the increasing number of immigrants from endemic countries may warrant the need to institute universal testing for this parasite.*

Source: Leiby DA. Epidemiologic aspects of *Trypanosoma cruzi* in United States blood donors. ASTMH annual meeting. Philadelphia, Pa: December 5, 2003.

Trypanosoma cruzi, THE AGENT OF CHAGAS DISEASE, is a protozoan parasite that can cause lifelong, often untreatable, infection. Patients in the acute stage of illness, which is recognized in only 1-2% of infected patients, have demonstrable parasitemia, and IgM antibodies predominate. During latent/indeterminate and chronic stages of infection, patients have low levels of parasitemia and elevated IgG levels. It is estimated that there are 50,000-100,000 *T cruzi*-infected immigrants residing in the United States. Most infected patients are asymptomatic, and at this time there is no screening performed to identify *T cruzi*-infected blood donors.

Since 1987, a total of 7 US/Canadian transfusion cases of *T cruzi* have occurred. In 1999, a multiple myeloma patient was transfused with a platelet unit from a Chilean donor that was later confirmed as seropositive. Both the donor and recipient were parasitemic and serologically positive. Both were asymptomatic. Of note, the donor had emigrated from Chile 33 years earlier. The most recent transfusion case of *T cruzi*, from a Bolivian donor, occurred in Rhode Island in 2002.

Leiby and colleagues have looked at the effect of evolving donor demographics on the seroprevalence of *T cruzi* in Los Angeles and Miami.[1] From May 1994 to September 1998, blood donors in Los Angeles and Miami were queried regarding birth or time spent in a *T cruzi*-endemic country and then tested for *T cruzi* antibodies by radioimmunoprecipitation assay (RIPA). Seropositive rates were 1 in 7500 for donors in Los Angeles and 1 in 9000 in Miami. In addition, the seroprevalence rates in Los Angeles increased from 1996 to 1998, most likely secondary to minority donor recruitment efforts. The seroprevalence in directed donation was even higher, at 1 in 2400. Perhaps of greater concern are data suggesting congenital transmission of *T cruzi* across several generations.[2] Therefore, asymptomatic, yet transmissible, infection may be present not only in the immigrants from *T cruzi*-endemic countries, but also in their children and their children's children. Clearly, this enlarges the spectrum of the problem.

Chagas disease following solid organ transplantation has occurred in Latin America where *T cruzi* is endemic, but the first reported US case occurred in 2001. A 37-year-old woman who had received cadaveric kidney and pancreas transplants had a febrile illness, and *T cruzi* trypomastigotes were found on her peripheral blood smear.[3] Subsequently, the 2 other patients who had received organs from the same donor were culture positive for *T cruzi* as well. The donor had been an immigrant from Central America.

Another study looked at seroprevalence of *T cruzi* in more than 11,000 Baltimore/Houston postoperative cardiac surgery patients.[4] There were 6 (0.05%) confirmed seropositives, and 5 out of the 6 were Hispanic patients. Four of 6 patients had positive pre-operative serology tests. The other 2 patients were cardiac transplants, and both excised hearts were found to be positive for *T cruzi* by PCR. Therefore, all 6 patients were infected with *T cruzi* prior to surgery. Clinicians should consider the possibility of Chagas disease in patients from endemic areas, especially patients with cardiac conditions that could be consistent with chronic Chagas disease.

Strategies to alleviate this problem are being developed. Unlike many pathogens for which nucleic acid testing is best for donor screening, *T cruzi* serology is actually more useful because not everyone infected with *T cruzi* has detectable circulating parasites. The parasite can survive irradiation of blood products, and even leukoreduction fails to remove all *T cruzi* parasites. It is estimated that even if all blood donors were questioned for *T cruzi* risk factors, up to 4% of seropositive donors might still be missed.

Therefore, the path of the future may be the need for universal, serologic screening of blood donors for *T cruzi*. This would result in substantial cost, perhaps as high as an additional $50 million per year. However, since infection with this parasite is often chronic and generally untreatable, the long-term benefits may justify the expense. ■

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CME Questions

1. **Which of the following statements is *incorrect* regarding *T cruzi*?**
   a. *T cruzi* has been transmitted through blood products and organ transplants in the United States.
   b. Congenital transmission of *T cruzi* may occur.
   c. *T cruzi*-infected blood donors are often asymptomatic.
   d. Nucleic acid testing would be the best approach to identify *T cruzi*-infected blood donors.
   e. *T cruzi* can survive blood product irradiation.

2. **Which one of the following statements regarding malaria prophylaxis and treatment is true?**
   a. Chloroquine and hydroxychloroquine are no longer the prophylaxis of choice for chloroquine-sensitive *P falciparum* malaria in endemic regions, such as Haiti.
   b. Terminal prophylaxis is required when atovaquone/proguanil is used on a long-term basis to prevent vivax malaria.
   c. Minocycline is preferred over doxycycline for prophylaxis in patients using minocycline for treatment of acne, since it requires no change in medication and has equivalent efficacy.
   d. Primaquine cannot be used for primary malaria prophylaxis.
   e. Methemoglobinemia occurs in patients who are G6PD deficient and taking halofantrine.

Answers: 1.(d); 2.(b)

Readers are Invited. . .

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