

# Emerging Parasitic Infections in Transplantation

Roberta Lattes · Laura Linares · Marcelo Radisic

Published online: 29 September 2012  
© Springer Science+Business Media, LLC 2012

**Abstract** This article concentrates on parasitic infections that are novel in solid organ transplantation for which there are meaningful data. It also addresses some issues that are either exceptional or a cause for new concern and where the evidence for a well-established recommendation is lacking.

**Keywords** Parasitic infections · Leishmaniasis · Chagas disease · Malaria · *Strongyloides* · Microsporidia · Free-living amebas · Echinococcal diseases

## Introduction

Parasitic diseases affect billions of people throughout the world. In recent years, the number of papers addressing this subset of infections in the solid organ transplant recipient has grown steadily. This increase in documented cases reflects greater awareness, more accessible diagnostic tools, the existence of active transplant programs in geographical areas where parasitic infections are highly prevalent, and the increase in leisure tourism to endemic areas, in addition to expanding migration of individuals from endemic countries to all corners of the world. Reduced use of cyclosporine—which has intrinsic antiparasitic activity—in favor of alternative immunosuppressive agents may have contributed to the increasing prevalence of parasitic infections in transplant recipients [1]. Lastly, increased long-term survival of transplant recipients may also have contributed to the increased occurrence of these parasitic infections.

Many parasites cause chronic infections in the human host with very few or no clinical manifestations in the immunocompetent host. Thus, parasitic diseases may affect transplant recipients as a result of the recrudescence of latent infections or from de novo acquisition by means of natural infection, transmission by the transplanted organ and transmission from blood products transfused either before or after transplantation. As a result, transplant teams should be aware of the scenarios where the risk of post-transplant parasitic infection is enhanced.

Briefly, the highest risk is noted in organ donors or recipients who live or have lived or have traveled extensively or are originally from endemic areas. This includes “medical tourism,” migration from underprivileged areas to the western world and altruistic donors from those areas [2]. Also, deceased donors with an unclear diagnosis may pose a significant risk of unforeseen and rare parasitic infections [3].

## Leishmaniasis

Leishmaniasis is caused by a heterogeneous group of protozoan parasites, belonging to the genus *Leishmania* and causes a variety of different clinical syndromes. Leishmaniasis can be classified geographically into New World and Old World disease; clinical syndromes can be divided into visceral, cutaneous, or mucocutaneous leishmaniasis. Each species of *Leishmania* tends to be associated with a single sandfly vector, a major animal reservoir, and a major clinical syndrome.

It is estimated that 350 million people are at risk of acquiring the infection and that 12 million may be infected [4]. The first case of leishmaniasis in a transplant recipient was reported in 1979 [5]. Since then, approximately 100 cases have been described with the majority in kidney transplant recipients, although it has sporadically been

---

R. Lattes (✉) · L. Linares · M. Radisic  
Transplant Infectious Disease Section,  
Department of Transplantation,  
Instituto de Nefrología/Nephrology,  
Cabello 3889,  
Buenos Aires 1425, Argentina  
e-mail: roberta.lattes@gmail.com

diagnosed in all solid organ recipients. Post-transplant leishmaniasis is mainly attributed to reactivation of an infection acquired earlier in the patient's life. However, de novo infections may occur in recipients who have been exposed to the phlebotome sandfly vector or to contaminated blood products. Although transmission through the graft is regarded as possible, it has not been conclusively proven. Visceral leishmaniasis is by far the most frequent clinical presentation, whereas cutaneous and mucocutaneous presentations are rare in the transplant setting. Visceral leishmaniasis should be suspected in a patient with epidemiological risks and a prolonged febrile illness with splenomegaly, liver enlargement and pancytopenia. Transplant recipients seem to have an increased risk of disease recurrence either as a relapse—in spite of effective treatment—or as a reinfection [6]. It can occur from 1 month to 5 years after initial diagnosis and can be identified in up to 46–60 % of previously diagnosed patients [6], provided active follow-up is maintained long enough.

Serology may be used as a preliminary diagnostic tool as up to 90 % of transplant recipients with active infection test positive for antileishmanial antibodies [5]. The sensitivity of standard microbiological diagnostic methods largely depends on the parasite burden, and may reach 90 % in transplant

patients. Microscopy with identification of amastigotes in tissue specimens and positive cultures are used as gold standard methods. More recently DNA testing has become possible. The value of using this newer methodology is twofold. First, the timing for a positive DNA test seems to precede that of standard methodologies, and it is therefore an early diagnostic tool which allows earlier treatment. Second, the test could be used for treatment monitoring as well as for relapse diagnosis [6].

Liposomal amphotericin B (L-AmB) is regarded as the first-line treatment for visceral leishmaniasis (4 mg/kg/day on days 1–5 and 10, followed by once a week infusion until day 38) [2•]. An alternative suggested treatment could be a sequential combination of L-AmB+miltefosine (2.5 mg/kg/day orally for 28 days) [2•].

Controversial issues addressing which donors or recipient candidates should be tested prior to transplantation are summarized in Table 1. It is difficult to state at this time which would be the best course of action if a positive test should become available at the time of transplantation. Similarly, undefined issues on follow-up methods after leishmaniasis has been diagnosed in a transplant recipient for the first time and the use of secondary prophylaxis are shown in Table 2.

**Table 1** Pretransplant screening in donors and recipients

Disease	Should be evaluated	Tests	Significance	Action/Comments
Visceral leishmaniasis	From endemic areas: Bangladesh, Brazil, India, Nepal, Sudan, southern Europe	Serology; PCR peripheral blood	History of past exposure; risk of reactivation or transmission	Consider screening donors and transplant candidates from endemic regions
Chagas disease	All natives from endemic areas; born to mothers from endemic areas (most Latin-American countries)	Serotests EIA, IHA; confirm with IFA or RIPA; PCR of blood samples of infected transplant candidates and of infected living donors during pretransplant work-up	Two different positive antibody tests for chronic infection diagnosis; positive PCR evidence of low-level parasitemia, with negative direct methods (Strout test)	Donor: If positive do not use heart. Monitor closely all other organ recipients of Chagas-positive donors. For infected recipients and for negative recipients of organs from infected donors, sequential post-transplant monitoring with Strout test and PCR is highly recommended. Either recipient or living donor with positive PCR before transplantation: would defer transplant to allow treatment for 30 days
Malaria	Endemic areas	Blood smears, latex agglutination, enzyme-linked and indirect fluorescence antibody assays: $\geq 1:64$	Assume active infection	Pre-transplant treatment if possible; Blood smears monitoring in recipient
Strongyloidiasis	Endemic areas; unexplained eosinophilia (even intermittent)	Stool examination, modified Baermann's technique, stool culture on a blood agar plate, ELISA, serum indirect fluorescent antibody test, PCR and gastrointestinal aspiration or biopsy	Diagnosis of intestinal strongyloidiasis	Treat the candidate with positive diagnosis; empirical treatment before transplantation if strong suspicion of risk

**Table 2** Parasitic diseases in organ transplantation—controversies

Disease	Situation	Controversial Issues
Visceral leishmaniasis	After post-transplant diagnosis and completion of treatment	Secondary prophylaxis; follow-up with PCR
Chagas disease	Infected donor immediately after transplantation	Prophylactic treatment of recipient vs. sequential monitoring
	Infected recipient immediately after transplantation	Prophylactic treatment of recipient vs. sequential monitoring
		No data on evolution to chronic disease (myocardiopathy) after transplantation
Malaria	Infected deceased donor	Discard organs vs. use organs and monitor for transmission
Strongyloidiasis	Donor preconditioning with corticosteroids	Risk of transmission of reactivated undiagnosed disease
	Duration of treatment in severe disease	2 weeks vs. parasite clearance
	Impaired intestinal absorption	Parenteral ivermectin

### Chagas Disease

Chagas disease used to be a public health problem only in Latin-American countries. However, due to migration and globalization, it has now spread worldwide accounting for an estimated 8

million to 10 million infected people with approximately 300,000 infected individuals living in the US [7].

The infecting agent *Trypanosoma cruzi* in endemic areas is transmitted mostly (up to 80 %) by a triatomine insect vector that serves as the parasite intermediate host. Transmission by unscreened blood transfusion, from infected mother to fetus, by laboratory accidents and by organ transplantation has been documented in those areas and these are the predominant epidemiological risks in the Western world. Human disease has two distinct phases: the acute and the chronic infection. The acute infection may resolve spontaneously, but without specific treatment the infection continues and leads to chronic infection or disease. Chronic *T. cruzi* infection can be asymptomatic for life or may evolve in approximately 30 % of patients into irreversible disease of the heart (27 %), the esophagus and the colon (6 %) and/or the peripheral nervous system (3 %) [8•]. Diagnosis in the acute phase is achieved by direct parasitological tests, including the examination of whole blood preparations and concentration methods (Strout test) and rarely by serological tests. In the chronic stage diagnosis is performed by serological tests

(Table 1). All these tests have good sensitivity but less than optimal specificity, and show considerable variation in reproducibility and reliability in the results [9•]. The most commonly used are: enzyme immunoassay, indirect hemagglutination and indirect immunofluorescence (IFA) [10]. A new enzyme-linked immunosorbent assay test system (Ortho-Clinical Diagnostics) has been licensed by the FDA for blood screening purposes [11]. IFA and radioimmunoprecipitation assay are used mainly as “confirmatory” tests [8•]. Assays based on polymerase chain reaction (PCR), which have recently been standardized, have been used in clinical research and should provide useful tools for rapid diagnosis [12•]. However, at present WHO still recommends that at least two different serological methods of testing be used for *T. cruzi* infection diagnosis [9•].

During the 1960s and 1970s, two drugs were introduced for treatment: nifurtimox (8–10 mg/kg/day) and benznidazole (5–7 mg/kg/day). When treatment is administered for 30 to 60 days, parasitic cure is achieved in 60 % to 100 % of acute cases and 20 % to 60 % of infections acquired up to 10 years before [13, 14]. According to recent evidence trypanocidal treatment might modify the outcome of chronic infections as well [15–18]. Protocols with newer treatment strategies using ravuconazole (ravuconazole prodrug E1224) or posaconazole alone or in combination with either antiparasitic drugs (phase II trial of posaconazole: Clinical Trial for the Treatment of Chronic Chagas Disease with Posaconazole and Benznidazole; NCT01162967) or amiodarone have been performed or are under development [19, 20•, 21]. In recent years, organ transplantation has become more prevalent in endemic areas. As a result, organ transplantation in individuals infected with *T. cruzi* has become more common, with a steadily growing number of infected individuals on the waiting list [8•]. A substantial number of papers addressing the issue can be found in the literature. Most are either case reports or single-center experiences with a small number of cases. However, some guidelines can be proposed (Table 1) [1, 8•, 22•]. Also, some still unanswered questions are summarized in Table 2.

Most of the experience in chronically infected individuals is related to kidney transplant [8•, 23] or to heart transplant [24•] procedures, with only very few cases in liver transplant recipients. In kidney recipients reactivation has been shown to occur mainly within the first post-transplant year or after a significant increase in immunosuppression (i.e. treatment of rejection). Reactivation after transplantation occurs in 10 % to 35 % of recipients, but it varies greatly among transplant centers and has decreased over time [8•]. There is no proven explanation for this variation. However, it is possible to speculate that the use of more accurate reactivation diagnosis tests, and lower maintenance immunosuppression dosages is a plausible cause. Reactivation in nonheart recipients can be completely asymptomatic with initially isolated parasitemia. When clinical manifestations

occur, the more common clinical symptoms include subcutaneous involvement (similar to erythema nodosum) and panniculitis. Tenderness and limb involvement are characteristic. If diagnosis and consequently treatment are delayed lesions can evolve into painful ulcers. Myocarditis and encephalitis have also been described but are quite uncommon. Good responses to 30 days of treatment, with adequate graft and patient survival in long term follow-up, have been reported [8•, 23]. Although published experience in non-kidney recipients is scant, most, with the exception of heart transplant recipients, generally follow a similar course [8•].

The myocardium and the heart conduction system are the main targets of chronic parasitic infection. Therefore, the infection may evolve into severe heart disease. Heart transplantation is now accepted as the treatment of choice for chronic chagasic cardiomyopathy in spite of infection reactivation risk [24•, 25]. Over the past 20 years, Chagasic cardiomyopathy has become the second leading reason for heart transplantation in one center in Brazil [26]. Reactivation has been reported to occur in 26.5 % [27] to 42.9 % [24•]. A wide spectrum of reactivation diseases, including asymptomatic parasitemia, fever, subcutaneous involvement and myocarditis have been described. Chagasic myocarditis may pathologically resemble rejection and assessment of the tissue to detect parasites is critical. In general, reactivation occurs early after transplantation and relapses after treatment are frequent (one to eight episodes per patient) [28], suggesting that sterilization is not always achieved. Early diagnosis, careful monitoring and good response to treatment allow an adequate survival. Prophylactic treatment early after transplantation has been studied in a small cohort of patients but did not prevent reactivation [25, 27].

Evidence shows that asymptomatic parasitemia may occur either as the only manifestation of recurrence or as the preliminary step before tissue invasion [23]. It has therefore been recommended that blood from all infected recipients be prospectively and sequentially monitored to identify the circulating parasite using direct parasitological tests, preferably the Strout method [8•]. PCR-based tests may prove to be beneficial and allow earlier identification of parasitemia [24•], but have not yet been approved for standard of care. Efforts have been made to standardize PCR methods and specific primers have been identified that have the best sensitivity and reproducibility for clinical use [12•]. However, as intermittent low-burden parasitemia—of no clinical relevance—may occur in chronically infected individuals, PCR methods that allow parasitic load measurement may possibly better reflect the correlation of a positive test with clinically relevant parasitemia. Also, all available tissue specimens, including protocol endomyocardial biopsies, should be evaluated for the presence of amastigote nests [8•]. Serology has no utility in the diagnosis of reactivation.

The use of organs from infected donors poses a different set of questions. In the early 1990s transmission to negative recipients from known infected donors was first reported in kidney transplant recipients [29, 30]. Later, transmission from positive donors was detected by systematic search for parasitemia in 18 % of seronegative kidney recipients, and all were cured with trypanocidal treatment [23]. But it was not until 10 years later and after the first reports of accidental transmission in the US from unselected donors that the transplant community felt that more answers were needed [31, 32]. Transmission is not the rule, and has been documented to occur in up to 18 % of kidney transplants [8•, 23]. Also, recent data on nine liver transplant recipients from infected donors show a 22 % transmission rate that was identified through parasitemia monitoring with no clinical manifestations of disease [33]. Nonetheless, acceptance of such donors is debatable. In countries where the disease is endemic, not all transplant teams accept organs from infected donors, but the acceptance is growing with informed consent from the patient and provided follow-up methods are available. Sequential monitoring should be employed for post-transplant follow-up, combined with a high level of suspicion and early initiation of trypanocidal treatment should be used if such a patient develops clinical manifestations of disease transmission or parasitemia.

Although there is significant controversy about which potential donors should be screened in nonendemic areas and which screening methods are preferred, recent donor screening and recipient monitoring guidelines have been published to guide local decisions (see Table 1) [8•, 22•]. The use of prophylactic benznidazole remains controversial. Some advocate its use, but randomized evidence is lacking. Others prefer to monitor for active infection and to treat after parasitemia is detected because of the potential toxicity of trypanocidal drugs, the low rate of reactivation and transmission and the generally good outcome with treatment (see Table 2) [8•, 22•, 34].

## Malaria

Malaria is the cause of more than 300 million acute cases and over 1 million deaths per year which occur mostly in underdeveloped regions. It is transmitted to humans through the bite of the female *Anopheles* mosquito but blood transfusions have been found to be responsible for some cases in endemic areas and occasionally in countries with large immigrant populations [35]. After successive exposures to the disease a partial and incomplete immunity is produced that explains the lack of detectable parasitemia and the higher incidence of asymptomatic disease in adults from endemic regions. This results in a potentially critical situation at the time of organ donor assessment, as donors from endemic

regions might have undetectable levels of circulating parasites and present a risk even if they have been away from those areas for a long time.

Very few cases have been described in transplant recipients [2•]. Still, malaria is potentially fatal in the transplant recipient. Transmission via the graft seems to be the main mode of acquisition of the disease, although some cases have been traced to blood or blood products transfused to the recipient, even well before transplantation, and to mosquito bites after transplantation. Clinical manifestations usually start in the early post-transplant period (10 to 21 days after transplantation) [2•] and have been described in kidney, liver and heart recipients. Clinical manifestations are often nonspecific. Fever has been reported as the most frequent presenting symptom, but it often lacks the typical paroxysmal or cyclic pattern. The four different main plasmodia species that infect humans, *Plasmodium ovale*, *P. vivax*, *P. malariae* and *P. falciparum*, have all been diagnosed in solid organ transplant recipients. In most post-transplant recipients, the diagnosis is made by the identification of the parasite in blood smears in febrile patients with unexplained hemolysis and thrombocytopenia [1]. Early diagnosis and conventional specific treatment usually result in prompt and uneventful recovery.

Geographical distribution of resistance to antiplasmodium drugs has changed over time. As a result, identification of the specific plasmodium species and local resistance patterns informs optimal treatment of infected patients. As a general rule *P. vivax*, *P. malariae* and *P. ovale* can be treated with a 3-day course of chloroquine, whereas *P. falciparum* infection may be treated with chloroquine, when sensitive, or with artemisinin derivative combinations, atovaquone-proguanil, mefloquine, halofantrine or quinine in combination with another drug, such as doxycycline, clindamycin, or artesunate, depending on local resistance. Since quinine may reduce the drug levels of calcineurin inhibitors (cyclosporine and tacrolimus), close monitoring of blood levels is needed.

### Strongyloidiasis

*Strongyloides stercoralis* is an intestinal helminth that infects about 80 to 100 million persons from temperate, subtropical and tropical regions worldwide, including Africa, Southeast Asia, Latin-America, southeastern US and southern Europe [36]. *Strongyloides stercoralis* is able to complete its life cycle both in the environment and in the human host. As a consequence, the parasite has an “autoinfective” cycle that results in decades long persistent infections [37•]. The spectrum of disease includes acute infection, chronic intestinal infection, asymptomatic autoinfection, symptomatic autoinfection, hyperinfection syndrome and disseminated disease.

Immunosuppressed patients—especially those under corticosteroid treatment—as well as those coinfecting with HTLV I are more prone to develop hyperinfection syndrome and disseminated disease [37•].

In the transplant recipient, in spite of immunosuppressive treatment, the disease may be limited to prolonged and intermittent gastrointestinal symptoms that need to be differentiated from drug-related adverse effects. A high index of suspicion together with a thorough parasite investigation in the appropriate samples (i.e., in stool and duodenal aspirate) are needed to make a diagnosis. Eosinophilia is frequently absent in patients receiving corticosteroid therapy, and hence lack of eosinophilia should not be misleading in this particular set of patients (see Table 1).

More commonly reported after transplantation are the devastating outcomes of strongyloidiasis hyperinfection syndrome—with a mortality rate close to 50 %—and of disseminated infection—with a reported mortality close to 80 %. The severe clinical disease may present with pulmonary involvement, bacterial sepsis or bacterial meningitis with gram-negative rods from intestinal flora, in addition to acute and severe abdominal disease including bloody diarrhea, adynamic ileus, intestinal obstruction and gastrointestinal hemorrhage, and these may be accompanied by a petechial rash that is inhabited by larvae. Strongyloidiasis has been reported in all solid organ transplant recipients and has been attributed mainly to the reactivation of a dormant infection in the recipient. Donor-related transmission has been assumed in some transplants where the bowel of the donor was involved and the recipient had no history of prior infection [38]. However, recent evidence shows transmission from the donors in kidney transplant recipients [39•]. The proposed mechanism for this to occur could be related to the use of corticosteroids in the preconditioning regimen of donors which could trigger the reactivation and spread of an asymptomatic infection [39•]. The occurrence of severe strongyloidiasis in transplant recipients belongs almost entirely either to the immunosuppression era before cyclosporine use, or more recently to the cyclosporine-sparing or T-cell-depleting immunosuppressive regimens [1].

There is no diagnostic gold standard methodology; all employed techniques fail in sensitivity, specificity or availability in some areas [36]. Diagnostic methods that could be employed during pretransplant evaluation are summarized in Table 1. Definitive diagnosis is achieved by identification of larvae in clinical specimens, although this might prove difficult to achieve. Treatment should be given before transplant with a confirmed diagnosis and also if the epidemiological burden is high, regardless of the severity of symptoms. Ivermectin is nowadays the treatment of choice, especially in severe forms of the disease. Two weeks of daily treatment (200 µg/kg orally) has been suggested for intestinal strongyloidiasis in the transplant recipient [37•]. Patients with



severe disease (hyperinfection, dissemination) might benefit from more prolonged courses of treatment, or even until parasitological eradication is achieved. For those who are unable to use the oral route, ivermectin enema [40], or subcutaneous ivermectin 1 % solution (approved only for veterinary use) have been employed [41]. Alternative treatments include the use of tiabendazole at a dose of 25 mg/kg orally twice a day for 3 days or albendazole at a dose of 10 mg/kg/day, but their efficacy in immunocompromised hosts is less than satisfactory.

### Microsporidiosis

Microsporidia are currently considered emerging pathogens responsible for life-threatening infections in organ transplant recipients. Infections caused by these parasites should be considered in the differential diagnosis of chronic diarrhea when no other pathogen is identified.

Microsporidia are obligate, spore-forming, intracellular, highly diverged parasites that are related to fungi [42]. They are ubiquitous and highly resistant to degradation; they can infect a wide range of animals and have the ability to survive in the environment for many months. Fecal–oral and urinary–oral routes seem to account for most infections, although person-to-person transmission as well as water-born and food-born transmission have been described [40]. A cluster of cases in transplant recipients was linked to an outbreak in the general population in Lyon, France, in 1995 [43]. Cell-mediated immunity is paramount in controlling microsporidial infection. *Enterocytozoon* infections are generally limited to the intestine and have been reported in solid organ transplant recipients to cause non-bloody, watery, and chronic diarrhea, marked fatigue, abdominal discomfort, weight loss and prolonged fever. *Encephalitozoon* species infect macrophages, disseminating widely and may cause a systemic infection with involvement of the intestinal and hepatobiliary tracts, the respiratory tract, sinuses, kidney, eye, and the brain.

Microsporidial coinfection with other more common intestinal pathogens has been well described [44], and therefore needs to be thought of when specific treatment for an identified pathogen does not result in resolution of symptoms. Routine examination of stool does not always result in identification of microsporidia. Special staining techniques and PCR methods are needed to reach a diagnosis.

Treatment with albendazole or with purified oral fumagillin (60 mg/kg/day for 14 days) has been used in transplant recipients, but parasite clearance is not always achieved in spite of apparent resolution of diarrhea. Reduction of immunosuppression and replacing mycophenolate mofetil with azathioprine should be considered when dealing with this infection [44]. Prevention can be achieved through avoiding

contact with known reservoir hosts, especially pets, thoroughly cooking meat, boiling drinking water and refraining from swimming in lakes, rivers and swimming pools.

### Free-Living Amebas

Infection due to free-living amebas has been increasingly reported in immunocompromised patients, but it is still very rare in solid organ transplant recipients [45, 46]. The spectrum of the disease in the general population includes: chronic skin involvement (granulomatous lesions, ulcers and subcutaneous abscess); sinus disease; disseminated disease with skin, bone, lung and intraabdominal organ involvement; and granulomatous encephalitis that has an insidious, protracted, progressive course and an almost always fatal outcome, with a post-mortem diagnosis in most [47, 48]. Donor-transmitted *Balamuthia mandrillaris* granulomatous amebic encephalitis has been reported recently with devastating effects in the recipients unless preemptive treatment is administered early after transplantation [3, 49]. The need for thorough pretransplant evaluation looking for unusual infecting organisms in donors with undiagnosed lesions or infrequent diagnosis cannot be over-emphasized.

### Echinococcal Diseases

Two different entities caused by the cestode genus *Echinococcus* are recognized in human disease. Although quite different from each other, both pose intriguing puzzles at the time of solid organ transplantation. *Echinococcus granulosus* is a parasite of domestic dogs that causes hydatid cysts (cystic echinococcosis) and is endemic in many countries in the world. *Echinococcus multilocularis* is a parasite of wild canines that causes alveolar echinococcosis and is predominant in Central Europe and in rural China [50]. Hydatid cysts are most frequently asymptomatic and the course of the disease is generally benign. Cysts may develop in any organ, but they are predominantly found in the liver or the lung. When symptoms do occur, they originate from the mass effect of the enlarging cyst or from the leakage, rupture, or bacterial infection of the cyst. In alveolar echinococcosis, larvae proliferate more rapidly making alveolar cysts grow indefinitely behaving as slow-growing cancers that in all cases require wide surgical resections to avoid further growth and recurrence.

In transplant candidates, cystic echinococcosis may be diagnosed at the time of pretransplant evaluation when intriguing cystic images are found on routine chest radiography or in the abdominal imaging. Also, they may be unsuspected and diagnosed in the living donor or accidentally found in the deceased donor at the time of organ

procurement. Although limited data are available, it is plausible to speculate that benign, cystic echinococcosis may have an accelerated growth with immunosuppressive treatment [50], and hence a prudent approach would be to treat the recipient either before or after transplantation with albendazole (400 mg twice daily) for 3 months to 2 years. The need for surgical removal of the cysts before transplantation is very limited but antiparasitic treatment should still be administered.

Although there has been no documented transmission from donors it should be remembered that liver cysts are inhabited by viable larvae which makes it necessary to avoid rupture of the cysts at the time of organ procurement.

In alveolar echinococcosis, *E. multilocularis* larvae nest in the liver and proliferate indefinitely making alveolar cysts grow, invade locally and spread to distant organs. The disease is lethal in approximately 10 years from diagnosis unless it is promptly identified and radically excised by surgery [51]. Recent reports provide evidence that long-term treatment with benzimidazole may slow the progression of the disease. Liver transplantation has been attempted in severe cases with better results achieved if transplantation is performed before blood vessel involvement. Immunosuppression can enhance the parasitic growth and the risk of recurrence; therefore, immunosuppression should be reduced to a minimum as early as possible. Recently, the first report of a rapidly progressive hepatic alveolar echinococcosis in a renal transplant recipient was published [52]. Available data seem to indicate that the disease might have been acquired immediately after transplantation and that the rapid progression correlated with the unusually intense immunosuppression regimen employed in this particular case.

## Conclusions

Parasitic diseases are increasingly recognized as an emerging threat by transplant teams throughout the world. These infections might originate from undiagnosed infected donors, from reactivation in infected recipients and from post-transplant exposure, and may cause substantial morbidity and mortality, especially if they are not recognized early and properly treated. Transplant physicians should consider parasitic infections during the assessment of transplant candidates and prospective donors from endemic regions. Transplant clinicians should also be mindful of the potentially rapid course of parasitic disease after transplantation and the complex drug interactions of available antiparasitic agents. Many questions remain unanswered, but there is a lack of large multicenter, randomized studies, so the best strategy remains a matter of opinion and relies mostly on expert opinion.

**Disclosure** No potential conflicts of interest relevant to this article were reported.

## References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

- Kotton CN, Lattes R. Parasitic infections in solid organ transplantation. *Am J Transpl*. 2009;9(s4):s234–51.
- Muñoz P, Valerio M, Eworo A, Bouza E. Parasitic infections in solid-organ recipients. *Curr Opin Organ Transplant*. 2011;16(6):565–75. *Updated perspective of the most common parasitic diseases occurring in solid organ transplant. Includes a thorough review of published papers.*
- Centers for Disease Control and Prevention (CDC). Notes from the field: transplant-transmitted *Balamuthia mandrillaris* – Arizona, 2010. *MMWR Morb Mortal Wkly Rep*. 2010;59(36):1182.
- Barsoum RS. Parasitic infections in organ transplantation. *Exp Clin Transplant*. 2004;2(2):258–67.
- Antinori S, Cascio A, Parravicini C, Bianchi R, Corbellino M. Leishmaniasis among organ transplant recipients. *Lancet Infect Dis*. 2008;8(3):191–9.
- Simon I, Wissing KM, Del Marmol V, Antinori S, Rimmelink M, Nilufer Broeders E, Nortier JL, Corbellino M, Abramowicz D, Cascio A. Recurrent leishmaniasis in kidney transplant recipients: report of 2 cases and systematic review of the literature. *Transpl Infect Dis*. 2011;13:397–406.
- Bern C, Montgomery SP. An estimate of the burden of Chagas disease in the United States. *Clin Infect Dis*. 2009;49:e52–4.
- The Chagas' Disease Argentine Collaborative Transplant Consortium, Casadei D. Chagas' disease and solid organ transplantation. *Transpl Proc*. 2010;42:3354–9. *Data on follow-up of infected recipients and of naive recipients transplanted with organs from infected donors in large transplant centers from an endemic area. Guidelines on follow-up after transplantation.*
- Otani M, Vinelli E, Kirchoff L, et al. WHO comparative evaluation of serologic assays for Chagas disease. *Transfusion*. 2009;49:1076–82. *Comprehensive comparison of different serological diagnostic methods with evaluation of sensitivity and specificity of available tests.*
- Pirard M, Iihoshi N, Boelaert M, et al. The validity of serologic tests for *Trypanosoma cruzi* and the effectiveness of transfusional screening strategies in a hyperendemic region. *Transfusion*. 2005;45(4):554–61.
- Gorlin J, Rossmann S, Robertson G, et al. Evaluation of a new *Trypanosoma cruzi* antibody assay for blood donor screening. *Transfusion*. 2008;48(3):531–40.
- Schijman AG, Bisio M, Orellana L, et al. International study to evaluate PCR methods for detection of *Trypanosoma cruzi* DNA in blood samples from Chagas disease patients. *PLoS Negl Trop Dis*. 2011;5(1):e931. *Intralaboratory and interlaboratory comparison of different PCR primers to evaluate those with the highest correlation to known positive samples.*
- Rodrigues Coura J, de Castro SL. A critical review on Chagas disease chemotherapy. *Mem Inst Oswaldo Cruz*. 2002;97(1):3–24.
- Sosa Estani S, Segura EL. Treatment of *Trypanosoma cruzi* infection in the undetermined phase. Experience and current guidelines of treatment in Argentina. *Mem Inst Oswaldo Cruz*. 1999;94 Suppl 1:363–5.
- Amato Neto V. Etiological treatment for infection by *Trypanosoma cruzi*. *Mem Inst Oswaldo Cruz*. 1999;94 Suppl 1:337–9.

16. Viotti R, Vigliano C, Lococo B, et al. Long-term cardiac outcomes of treating chronic Chagas disease with benznidazole versus no treatment. *Ann Intern Med*. 2006;144:724–34.
17. Viotti R, Vigliano C. Etiological treatment of chronic Chagas disease: neglected ‘evidence’ by evidence-based medicine. *Expert Rev Anti Infect Ther*. 2007;5(4):717–26.
18. Marin-Neto JA, Rassi Jr A, Avezum Jr A, et al. The BENEFIT trial: testing the hypothesis that trypanocidal therapy is beneficial for patients with chronic Chagas heart disease. *Mem Inst Oswaldo Cruz*. 2009;104 Suppl 1:319–24.
19. Le Loup G, Pialoux G, Lescure FX. Update in the treatment of Chagas disease. *Curr Opin Infect Dis*. 2011;24(5):428–34.
20. • Bern C. Antitrypanosomal therapy for chronic Chagas' disease. *N Engl J Med*. 2011;364:2527–34. *A thorough review of the most important issues of the disease with an exhaustive review of available treatments and ongoing treatment protocols.*
21. Veiga-Santos P, Barrias ES, Santos JF, et al. Effects of amiodarone and posaconazole on the growth and ultrastructure of *Trypanosoma cruzi*. *Int J Antimicrob Agents*. 2012;40(1):61–71.
22. • Chin-Hong P, Schwartz BS, Bern C, et al. Screening and treatment of Chagas disease in organ transplant recipients in the United States: recommendations from the Chagas working group. *Am J Transplant*. 2011;11(4):672–80. *Thorough review of available methods for screening and for diagnosis.*
23. Riarte A, Luna C, Sabatiello R, et al. Chagas' disease in patients with kidney transplants: 7 years of experience 1989–1996. *Clin Infect Dis*. 1999;29(3):561–7.
24. • Diez M, Favaloro L, Bertolotti A, et al. Usefulness of PCR strategies for early diagnosis of Chagas' disease reactivation and treatment follow-up in heart transplantation. *Am J Transplant*. 2007;7(6):1633–40. *The first comparison of parasitemia diagnosis in the transplant setting using standard methods vs PCR.*
25. Bocchi EA, Fiorelli A. The paradox of survival results after heart transplantation for cardiomyopathy caused by *Trypanosoma cruzi*. First Guidelines Group for Heart Transplantation of the Brazilian Society of Cardiology. *Ann Thorac Surg*. 2001;71(6):1833–8.
26. Godoy HL, Guerra C, Viegas RF, et al. Infections in heart transplant recipients in Brazil: the challenge of Chagas' disease. *J Heart Lung Transplant*. 2010;29(3):286–90.
27. Campos SV, Strabelli TM, Amato Neto V, et al. Risk factors for Chagas' disease reactivation after heart transplantation. *J Heart Lung Transplant*. 2008;27(6):597–602.
28. Fiorelli AI, Santos RHB, Oliveira Jr JL, et al. Heart transplantation in 107 cases of Chagas' disease. *Transplant Proc*. 2011;43(1):220–4.
29. de Faria JB, Alves G. Transmission of Chagas' disease through cadaveric renal transplantation. *Transplantation*. 1993;56(3):746–7.
30. Vazquez MC, Riarte A, Pattin M, Lauricella M. Chagas' disease can be transmitted through kidney transplantation. *Transplant Proc*. 1993;25(6):3259–60.
31. Zayas CF, Perlino C, Caleindo A, et al. Chagas disease after organ transplantation—United States, 2001. *MMWR Morb Mortal Wkly Rep*. 2002;51:210–2.
32. Centers for Disease Control and Prevention (CDC). Chagas disease after organ transplantation—Los Angeles, California, 2006. *MMWR Morb Mortal Wkly Rep*. 2006;55(29):798–800.
33. McCormack L, Quiñonez E, Goldaracena N, et al. Liver transplantation using Chagas-infected donors in uninfected recipients: a single-center experience without prophylactic therapy. *Am J Transplant*. 2012. doi:10.1111/j.1600-6143.2012.04160.x.
34. Altclas JD, Barcan L, Nagel C, Lattes R, Riarte A. Organ transplantation and Chagas disease. *JAMA*. 2008;299(10):1134.
35. Mungai M, Tegtmeier G, Chamberland M, Parise M. Transfusion-transmitted malaria in the United States from 1963 through 1999. *N Engl J Med*. 2001;344(26):1973–8.
36. Montes M, Sawhney C, Barros N. *Strongyloides stercoralis*: there but not seen. *Curr Opin Infect Dis*. 2010;23(5):500–4.
37. • Roxby AC, Gottlieb GS, Limaye AP. Strongyloidiasis in transplant patients. *Clin Infect Dis*. 2009;49(9):1411–23. *Comprehensive review of Strongyloides infection in the transplant setting.*
38. Patel G, Arvelakis A, Sauter BV, Gondolesi GE, Caplivski D, Huprikar S. Strongyloides hyperinfection syndrome after intestinal transplantation. *Transpl Infect Dis*. 2008;10(2):137–41.
39. • Hamilton KW, Abt PL, Rosenbach MA, et al. Donor-derived *Strongyloides stercoralis* infections in renal transplant recipients. *Transplantation*. 2011;91(9):1019–24. *Demonstration of transmission from donor in kidney recipients. Hypothesis on what might the causes be.*
40. Tarr P, Miele PS, Peregoy KS, Smith MA, Neva FA, Lucey DR. Case report: rectal administration of ivermectin to a patient with *Strongyloides hyperinfection syndrome*. *AmJTrop Med Hyg*. 2003;68:453–5.
41. Lichtenberger P, Rosa-Cunha I, Morris M, et al. Hyperinfection strongyloidiasis in a liver transplant recipient treated with parenteral ivermectin. *Transpl Infect Dis*. 2009;11:137–42.
42. Didier ES, Weiss LM. Microsporidiosis: current status. *Curr Opin Infect Dis*. 2006;19(5):485–92.
43. Rabodonirina M, Cotte L, Radenne S, Besada E, Trepo C. Microsporidiosis and transplantation. A retrospective study of 23 cases. *J Eukaryot Microbiol*. 2003;50(Suppl):583.
44. Galvan AL, Sanchez AM, Valentín MA, et al. First cases of microsporidiosis in transplant recipients in Spain and review of the literature. *J Clin Microbiol*. 2011;49(4):1031–6.
45. Fung KT, Dhillon AP, McLaughlin JE. Cure of *Acanthamoeba cerebral abscess* in a liver transplant patient. *Liver Transpl*. 2008;14(3):308–12.
46. Vernon SE, Acar BC, Pham SM, Fertel D. *Acanthamoeba* infection in lung transplantation: report of a case and review of the literature. *Transpl Infect Dis*. 2005;7(3/4):154–7.
47. Duarte AG, Sattar F, Granwerth B, Aronson JF, Wang Z, Lick S. Disseminated acanthamoebiasis after lung transplantation. *J Heart Lung Transplant*. 2006;25(2):237–40.
48. Barete S, Combes A, de Jonckheere JF, et al. Fatal disseminated *Acanthamoeba lenticularis* infection in a heart transplant patient. *Emerg Infect Dis*. 2007;13(5):736–8.
49. Centers for Disease Control and Prevention (CDC). *Balamuthia mandrillaris* transmitted through organ transplantation—Mississippi, 2009. *MMWR Morb Mortal Wkly Rep*. 2010;59(36):1165–70.
50. Kern P, Grüner B, Wahlers K. Diagnosis and course of echinococcal diseases in the transplant setting. *Transpl Infect Dis*. 2011;13:217–21.
51. Bresson-Hadni S, Vuitton DA, Bartholomot B, et al. A twenty-year history of alveolar echinococcosis: analysis of a series of 117 patients from eastern France. *Eur J Gastroenterol Hepatol*. 2000;12:327–36.
52. Geyer M, Wilpert J, Wiech T, et al. Rapidly progressive hepatic alveolar echinococcosis in an ABO-incompatible renal transplant recipient. *Transpl Infect Dis*. 2011;13(3):278–84.