

# Corneal Transplantation from Donors Serologically Positive for *Trypanosoma cruzi*

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## ABSTRACT:

**Introduction:** Chagas disease, caused by infection with *Trypanosoma cruzi* (*T. cruzi*), can be transmitted by solid organ transplantation but risk of transmission by corneal tissue is undefined.

**Objectives:** The primary objective in this study is to describe patient cases following corneal transplantation at risk for *T. cruzi* transmission and summarize the outcomes.

**Methods:** This retrospective case series describes four patients who received corneal transplants from donors found to be serologically positive for *T. cruzi* only after corneal transplantation of donated tissue had been performed. In 2011, two Descemet's Stripping Automated Endothelial Keratoplasties (DSAEK) were performed using corneas from a single donor. In 2018, corneas from a second positive donor were used for a DSAEK and a penetrating keratoplasty (PK) in two other patients. The patient with a PK elected for a repeat transplant, while those with DSAEKs did not undergo further transplant.

**Results:** None of the recipients developed signs or symptoms of ocular or systemic Chagas disease. All laboratory testing for evidence of infection yielded negative results.

**Conclusion:** These cases suggest that the risk of Chagas disease transmission is low in corneal transplants, including both DSAEK and PK.

**Key words:** Chagas disease, corneal transplant, DSAEK, endothelial keratoplasty, penetrating keratoplasty, *Trypanosoma cruzi*

Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK) is a partial-thickness corneal transplant involving the inner layers of the cornea, while penetrating keratoplasty (PK) is a full-thickness corneal transplant. All types of corneal transplantation, including DSAEK and PK, have been associated with bacterial, fungal, and viral transmission and secondary infections.<sup>1-6</sup> Transmission of infectious disease after corneal grafting is more likely in the setting of positive cultures of donor rim cornea.<sup>3,6,7</sup> *Trypanosoma cruzi* is a bloodborne protozoan parasite that causes Chagas disease, a systemic illness which can involve widespread dissemination of the organism. It is most commonly spread by triatomine insects, commonly known as "kissing bugs." *T. cruzi* has been transmitted via solid-organ transplantation, including heart, liver, kidney and pancreas transplantation.<sup>8</sup> Animal studies have shown *T. cruzi* parasites and their DNA in corneal tissue as well as ocular muscle and nearby connective tissue in infected animals,<sup>9</sup> and specifically, in corneal epithelium and stroma.<sup>10</sup> To date, there have been no published reports of transmission or lack of transmission of parasitic disease through corneal grafting procedures.

## METHODS

We present a retrospective case series of four patients who received corneal tissue from two donors who had

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serologically tested positive for *T. cruzi*. The Centers for Disease Control and Prevention (CDC) tested the donors and identified four cases in which corneal transplants had been performed before the donor test results were available. Both donors had undergone all required testing for organ donation as per the U.S. Food and Drug Administration regulations and standards of care, but this did not initially include serology for *T. cruzi*. The patients were included in this study when the authors were informed by the eye banks about these events.

## RESULTS

In June 2011, eyes from a single donor were used for DSAEKs in two patients (Cases 1 and 2). Both of these patients elected to retain their grafts. As of six months later, they had not developed evidence of *T. cruzi* infection. In June 2018, eyes from a second positive donor were used for a DSAEK (Case 3) and a PK (Case 4). The patient with a DSAEK did not undergo further surgery, but the patient with a PK strongly desired to replace the graft and had a repeat PK on postoperative day 13. As of eight months postoperatively in Case 3 and six months in Case 4, they had not developed evidence of *T. cruzi* infection.

### Cases 1 and 2

Case 1 is a 73-year-old female with a history of keratoconus and a PK in the left eye sixteen years prior, who underwent a DSAEK in 2011 in the left eye for graft failure. Case 2 is an 82-year-old female with history of Fuch's dystrophy, who underwent a DSAEK in 2011 in the right eye for chronic corneal edema. Her postoperative course was complicated by late failure of the graft to attach and she underwent repeat bubble placement at the first postoperative month with successful attachment of the graft thereafter.

A single donor was used for the corneas in both Case 1 and Case 2. The donor was tested for *T. cruzi* infection because the heart valves were to be used for transplantation. Both enzyme-linked immunosorbent assay (ELISA) testing and indirect fluorescent antibody testing of the donor were unequivocally positive for antibody to *T. cruzi*. Results of this testing became available only after the corneas had been used for transplant, and the corneal surgeon was notified by the CDC, where the confirmatory testing had been performed. Heart tissue from the donor later underwent histopathological analysis for *T. cruzi* amastigotes, which showed several suspicious areas but no definitive trypanosomes.

Both patients in Cases 1 and 2 were informed of the donor's status on the fourth postoperative day, and the risks

involved were discussed at length. Both patients were offered surgery to replace the graft, and after an in-depth conversation of the risks, benefits, and alternatives, they declined further surgery.

Both patients underwent diagnostic testing for *T. cruzi* 6 months after their DSAEKs. They both had negative indirect fluorescent antibody testing (titer < 1:32), negative polymerase chain reaction (PCR) testing, and negative enzyme immunoassays (EIA) using a cutoff of 0.30. Both wet mount slides of blood samples and hemoculture were negative for the organism.

### Cases 3 and 4

Case 3 is an 85-year-old male who underwent DSAEK in 2018 with revision of a tube shunt in the left eye for secondary corneal edema. He had a complex ocular history, including advanced primary open angle glaucoma, corneal neovascularization, and recurrent trichiasis of the left lower eyelid. He had previously undergone multiple surgeries including Ahmed glaucoma drainage device, Scheie procedure, trabeculectomy with needle bleb revisions, cataract extraction, posterior capsulotomy, and argon laser trabeculoplasty.

Case 4 is a 59-year-old man had a history of traumatic open globe, Baerveldt and Ahmed glaucoma drainage device placement, vitrectomy, dislocated scleral sutured intraocular lens (IOL) subsequently replaced with an anterior chamber IOL, and PK in the left eye. He underwent a repeat PK in 2018 for primary graft failure.

Corneas from a single donor were used in Cases 3 and 4. The donor tested positive for antibody enzyme-linked immunosorbent assay (EIA) and immunoblotting with trypanomastigote excreted-secreted antigens (TESA blot) of *T. cruzi* performed at the CDC. The results of donor testing were reported to the eye bank twelve days after release of the eye tissue. The corneal tissue had already been implanted, and the transplanting surgeons were rapidly notified.

The patient from Case 3, who had received a DSAEK, was informed of the donor's status on the tenth postoperative day and offered surgery to replace the graft. After an in-depth discussion of the risks, benefits, and alternatives, the patient declined further surgery. His testing eight months after surgery was negative for both *T. cruzi* antibody via ELISA and immunoblot assay (TESA).

The patient from Case 4, who had undergone a PK, was notified on the ninth postoperative day. He strongly desired to have the graft removed and underwent a repeat full-thickness corneal transplant on postoperative day 13. Blood

tested by enzyme immunoassay for *T. cruzi* antibodies taken at the time of repeat PK surgery was non-reactive and pathological examination of the explanted graft was grossly normal. Pathological analysis of the explanted graft tissue was also negative for *T. cruzi* parasites. Repeat blood testing 6 months later was also nonreactive for *T. cruzi* antibodies.

## DISCUSSION

The first widespread screening for *T. cruzi* infection in the United States began in 2007 with the American Red Cross and Blood Systems testing all blood donors. Screening is now routinely performed in all major U.S. blood donation centers.<sup>11</sup> Survey data as of 2010 showed that individual organ procurement organizations, on the other hand, either did not screen for *T. cruzi* infection (81%) or had protocols for targeted testing based on regional and individual donors' risk of the disease (19%).<sup>12</sup> The American Society of Transplantation published updated guidelines in 2019 for screening organ donors for Chagas disease.<sup>13</sup> The Chagas in Transplant Working Group, which is associated with the Disease Transmission Advisory Committee of the Organ Procurement and Transplantation Network, recommends serologic testing of potential donors who were born in South America, Central America or Mexico.<sup>8</sup> However, these recommendations are not mandatory, may not be followed as a standard for all organizations, and are not enforced by federal guidance. It is therefore possible that corneas from infected donors may be implanted without the donor being tested for the disease.

Little is known about the role of Chagas disease in corneal transplantation. Most infected donors are in the chronic phase with no detectable parasitemia and are diagnosed on the basis of serologic testing. In the chronic phase, *T. cruzi* may be found in many tissues of the body but has a predilection for cardiac myocytes. The presence of trypanosomes in the circulating blood may increase the risk of transmission with corneal transplants. Parasitemia occurs in both acute phase infection and reactivated chronic infection, which can occur in immunocompromised patients. In turn, infection may be more likely in immunosuppressed cornea recipients. The risk of transmission may also be higher with penetrating keratoplasty than with lamellar transplants or DSAEK, due to the presumably reduced burden of parasite in smaller amounts of tissue and the fact that animal models failed to identify *T. cruzi* in the endothelium, instead finding *T. cruzi* in greater concentration toward anterior corneal structures.

It is unknown whether current corneal tissue storage solutions have activity against *T. cruzi*. Gentamicin and

streptomycin are used at <1% concentration in Optisol GS- (Bausch + Lomb, Rochester NY) and LIFE4°C (Numedis Inc., Isanti MN) corneal storage solutions. Gentamicin has been found to have in vitro activity against *Trypanosoma brucei*,<sup>14</sup> but to our knowledge, neither gentamicin or streptomycin have been tested against *T. cruzi*. It is uncertain whether corneal tissue storage solutions play a role in mitigating the risk of *T. cruzi* transmission.

More investigation is needed to characterize the risks of DSAEK and other corneal transplants in the setting of donors positive for Chagas disease. This report provides evidence that the risk of *T. cruzi* transmission is likely low in DSAEK and PK patients.

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