

INFECTIONS CONNECTED WITH ORGAN AND TISSUE TRANSPLANTATION

Agnieszka E. Laudy^{1*}, Stefan Tyski²

¹Department of Pharmaceutical Microbiology and Bioanalysis, Medical University of Warsaw, Poland

²Department of Pharmaceutical Microbiology and Laboratory Diagnostic, National Medicines Institute, Warsaw, Poland

Submitted in May 2024, accepted in June 2024

Abstract: Transplantology is a branch of medicine that is developing rapidly. Transplanted whole organs or segments of organs may be recovered from either living or deceased donors. New methods of preserving transplanted solid organs, including the kidney, liver, heart, lung, and pancreas, as well as tissues, such as the cornea and skin, are being developed. Preservation fluid, which is used to perfuse and store the donated organ or tissue, should reduce biological deterioration of organs and tissue, attenuate ischemia/reperfusion-induced cell/tissue injury, and protect against damage. Lowering the storage temperature of organs significantly reduces the risk of damage. Efforts are also made to shorten the time between collecting the organ or tissue from the donor and transplanting it in the recipient. However, during transplantation, the recipient may become infected, primarily with bacteria and fungi. Infections of organ recipients occur most often due to unhygienic organ collection, improper handling and transport, and inappropriate preservation conditions, especially contamination of preservation fluid. The literature on contamination of organ preservation fluid and infections in graft recipients is very diverse, both in terms of the isolated bacterial and fungal species and the number of incidents. A large percentage of contaminating microorganisms belong to the generally non-pathogenic skin microbiota, but there are also cases of multidrug-resistant bacteria. Besides, the transplanted organs themselves may pose a danger. They may contain latent microorganisms, mainly viruses and parasites, that could be activated in a patient who has been subjected to immunosuppression to reduce the risk of organ rejection.

1. Introduction. 2. General aspects of transplantology and organ preservation. 3. Bacterial infections in organ transplant recipients and contamination of preservation fluid. 3.1. Infections associated with kidney transplantation. 3.2. Infections associated with liver transplantation. 3.3. Infections associated with pancreas and lung transplantation. 3.4. Infections associated with corneal and skin transplantation. 4. Fungal infections in organ transplant recipients. 5. Viral infections in organ transplant recipients. 6. Parasitic infections in organ transplant recipients. 7. Conclusions.

Keywords: contamination of organ preservation fluid, infections in organ recipients, microbial contamination of transplants (grafts), post-transplant infections, transplantology

1. Introduction

Organ transplantation (or grafting) amongst humans has developed over the past 70 years (Giwa *et al.* 2017). The first successful transplantation of the human kidney between identical twins was performed by dr. Joseph E. Murray in 1954 (Merrill *et al.* 1956). In 1990, Murray and E. Donnall Thomas were awarded with Nobel Prize in Physiology or Medicine for “their discoveries that have enabled the development of organ and cell transplantation into a method for the treatment of human disease” (The Nobel Prize, 1990). Currently, transplantation is the only effective therapy for patients with end-stage disease. So, transplants can

save lives, but they can also restore function in patients with vital organ failure, thus improving their quality of life. Several factors are responsible for therapeutic success: selection of the right donor with a high-quality and efficacious organ; preservation of the organ to ensure it is in a good condition for transplantation; ensuring there is enough time to organize staff, facilities, and equipment, and to perform the tests and the actual procedure; appropriate immunosuppressive medication; and post-transplant care of the organ recipient (Jing *et al.* 2018).

European Committee (Partial Agreement) on Organ Transplantation of the Council of Europe developed special guide for specialists, intended to ensure the

* Corresponding Author: A.E. Laudy, Department of Pharmaceutical Microbiology and Bioanalysis, Medical University of Warsaw, S. Banacha Str. 1b, 02-097 Warsaw, Poland, e-mail: alaudy@wp.pl

© 2024 Agnieszka E. Laudy and Stefan Tyski

This is an open access article licensed under the Creative Commons Attribution-NonCommercial-NoDerivs License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Cite as:

Infections connected with organ and tissue transplantation. Laudy A.E. and Tyski S., ADV MICROBIOL-NY, 2024, 63, 2, 65–80
<https://doi.org/10.2478/am-2024-0006>

quality and safety of the donation and transplantation of organs, tissues and cells as well as technical guidance to ensure the safety and quality of human organs intended for transplantation (European Committee (Partial Agreement) on Organ Transplantation of the CE, Guide 2022). The chapter 8 of this guide draws attention to risk of transmission of microbial diseases, especially viral infections. The issues related to infections of people – potential organ donors, are also discussed. Moreover attention is paid to geographic distribution, endemic zones and risks of infectious diseases, that can be transmitted by solid organ transplantation.

Considering the data collected during the collaboration between the World Health Organization (WHO) and the Spanish Transplant Organization (Organización Nacional de Transplantes [ONT]), the most frequently transplanted solid organs (grafts) regardless of geographical region, are, in order: kidney, liver, heart, lung and pancreas (ONT-WHO Global Observatory on Donation and Transplantation, 2022). Over 150,000 these organs were transplanted in 2022 (Table I). According to Finger *et al.* (2023), the percentage of patients from the United States who survived with an implanted organ for 1 and 5 years is 90.9% and 78.6%, respectively, for heart transplants; 86.7% and 47.3%, respectively, for a single lung transplant; 87.7% and 58.6%, respectively, for a double-lung transplant; 80.9% and 50.2%, respectively, for a heart-lung transplant; 92.3% and 83.3%, respectively, for a liver transplant from a living donor; 91.2% and 75%, respectively, for a liver transplant from a deceased donor; 98.8% and 92.1%, respectively, for a kidney transplant from a living donor; 96.3% and 83.3%, respectively, for a kidney transplant from a deceased donor; and 90.9% and 79.6%, respectively, for a pancreas transplant. In addition to the above mentioned solid organs, small bowel, eyes and cornea, bones, and soft tissues/skin called vascularized composite allotransplant, are also grafted.

The aim of this review is to draw attention to the infections of organ recipients and to recognize the severity of the microbiological problem connected with the use of preservation fluid (PF) for organs before transplantation. PF contains substances that protect cells against degradation, but does not contain antimicrobial agents. Thus, it is interesting to investigate how often infections occur in organ recipients due to contaminated PF. Attention should also be paid to latent infections, mainly viruses, that develop in immunosuppressed organ recipients, as well as to parasites that may be transmitted along with the transplanted organ and that may cause infection in the organ recipient. This review provides information for microbiologists working in transplantation units, as well as medical staff directly involved in the transplantation process.

2. General aspects of transplantology and organ preservation

There are four types of transplants based on the genetic relationship between the donor and the recipient: xenotransplant, where the donor is an animal and the recipient is a human; allotransplant, where the donor and recipient are from the same species; isotransplant, where the donor and recipient are identical twins; and autotransplant, where the donor and recipient are the same person. The chance of organ rejection decreases in the order given above (Oli *et al.* 2022). Transplanted organs, either the whole organ or segments/fragments, may be recovered from either living or deceased donors (for the latter, donors who have been declared brain dead or after cardiac death). Living donor donation often takes place between related people; however, there are also anonymous and altruistic donors.

In the initial period of transplantation, organs were preserved at room temperature with the use of blood-

Table I
Organ transplants in different geographical regions in 2022 (ONT-WHO Global Observatory on Donation and Transplantation).

Organ transplantation in 2022	Geographical region							
	Poland	European	Americas	Eastern Mediterranean	Western Pacific	South-East Asia	African	Global
Kidney	874	25,361	39,196	6,364	18,219	12,696	286	102,122
Liver	362	9,840	13,387	1,817	8,325	4,067	(-)	37,436
Heart	173	2,444	4,996	184	1,090	274	(-)	8,988
Lung	93	2,073	3,313	55	1,199	144	(-)	6,784
Pancreas	18	611	1,171	56	158	30	(-)	2,026
Small bowel	(-)	40	90	14	23	3	(-)	170
Total organ transplants	1,520	40,369	62,153	8,490	29,014	17,214	286	157,526

(-) – data not available

based perfusates. Chemically defined cell culture media were developed in the 1950s (Jing *et al.* 2018). The use of blood-based perfusates versus chemically defined preservative solutions is still a concern. There are unfavorable phenomena related to blood, including hemolysis, thrombus formation, immune-mediated responses, and blood-borne infectious transmission, mainly of a viral origin (Jing *et al.* 2018). During the development of transplantology, researchers found that lowering the temperature of PF reduces biological deterioration of organs, attenuates ischemia/reperfusion-induced cell/tissue injury, and protects organs from damage. Cooling reduces cellular metabolism and the oxygen requirements. The aspects of cellular injury and microvascular dysfunction in the pathogenesis of ischemia/reperfusion during organ preservation have been discussed elsewhere (Petrenko *et al.* 2019; Datta *et al.* 2021). Renal preservation by ice cooling was first used during kidney transplantation (Calne *et al.* 1963).

Currently, there are two ways to preserve organs: static cold storage (0–8°C) and dynamic storage based on machine perfusion (Jing *et al.* 2018; Guibert *et al.* 2011). Using perfusion equipment, which provide enhanced nutrient and oxygen delivery, various procedures have been developed depending on the temperature (Jing *et al.* 2018; Petrenko *et al.* 2019): hypothermic machine perfusion (0–12°C), midthermic machine perfusion (13–24°C), subnormothermic machine perfusion (25–34°C), and normothermic machine perfusion (35–38°C). Besides, controlled oxygenated rewarming (8–20°C) has been used to preserve kidneys and livers. In this method, the perfusate temperature rises gradually to weaken ischemia/reperfusion injury (Jing *et al.* 2018). PF continuously pumped by machine perfusion systems through the organ (e.g., kidney) provides nutrients and oxygen, carries away toxic waste products, and delivers buffers that absorb metabolites produced by the organ (e.g., lactic acid and adenosine monophosphate). The use of an ultra-low temperature to protect tissues and organs has also been considered.

It should be underlined, that PF in unopen containers must be sterile (European Pharmacopoeia 11, 2023, 2.6.1. Sterility). These preparations are prepared by specialized manufacturers that meet the requirements of Good Manufacturing Practice (GMP). The microbiological quality of these fluids should be similar to fluids used for cell culture.

Many chemically defined solutions that can replace blood have been evaluated and used to preserve tissues and organs before transplantation (Guibert *et al.* 2011; Latchana *et al.* 2015; Jing *et al.* 2018; Petrenko *et al.* 2019; Datta *et al.* 2021; Finger *et al.* 2023). However there is no consensus among transplantation centers as to which of PFs is the best (Salehi *et al.* 2018). The compositions of several PFs are listed in Table II. These

solutions are intended to provide appropriate physiological and biochemical conditions, oxygenation, and temperature to ensure cell survival and to reduce damage associated with ischemia/reperfusion injury. The most known and frequently used PFs in solid organ transplantation are EC or Euro-EC (Collins *et al.* 1969) and UW (Belzer *et al.* 1968; Southard and Belzer 1995). Generally, PFs contain electrolytes, buffers, antioxidants, and pharmacological agents. Importantly, PFs do not contain antimicrobial agent, except for the modified UW liquid listed in Table II (Guibert *et al.* 2011), which contains penicillin G (200,000 IU/L). PFs can be differentiated based on the Na⁺/K⁺ ratio. High Na⁺ and low K⁺ concentrations correspond to extracellular solutions, whereas high K⁺ and low Na⁺ concentrations correspond to intracellular solutions, which are intended to prevent cellular edema by maintaining intracellular ion concentrations upon cold-induced dysfunction of Na⁺/K⁺ pumps (Jing *et al.* 2018; Datta *et al.* 2021).

Taking into account the risk of infection of the organ recipient through contaminated PF, it is recommended to perform a microbiological examination of a PF sample taken from the container in which the organ was stored just after removing the organ to transplantation process. The test should be performed in accordance with the procedures applicable in a given microbiological laboratory for clinical samples taken from the patient. Public Health England (PHE) in partnership with the NHS described in UK standards for microbiology investigations (UKSMIs) Document “Abdominal organ transport fluid testing” (UK Standards for Microbiology Investigations, B62, 2020). According to these recommendations, the sample of specimen from fluid surrounding the organ should be taken immediately after the organ has been lifted from the transport bag for implantation. Volume of transport fluid to submit for analysis differs depending on the size of organ being transplanted. A minimum of approximately 5% of the total volume in the organ transport bag should be used for analysis (ideally a minimum of 20 mL). PF fluid should be centrifuged at 1200×g for 5 min. and spread on appropriate media such as blood agar, Sabouraud agar and CLED agar (for *Enterobacteriales*). All cultured microorganisms should be identified to species level. A separate issue is transplantation of corneas, the most commonly transplanted human tissue (Fabre *et al.* 2021). Corneal disease is the second major cause of blindness worldwide (Li *et al.* 2019). Corneal transplantation, also known as keratoplasty, involves replacing part of the recipient’s corneal tissue with tissue taken from a deceased donor. The first recorded therapeutic corneal transplantation on a human, unfortunately unsuccessful, was reported in 1838; the first successful human corneal transplant was performed by Zirm in 1905 (Crawford *et al.* 2013).

Table II
Composition of preservation solutions (Jing *et al.* 2018; Guibert *et al.* 2011; Finger *et al.* 2023; Petrenko *et al.* 2019; Latchana *et al.* 2015; Datta *et al.* 2021).

Solution	Electrolytes (nmol/L)	Buffer	Antioxidant	Colloid/ Impermeant	Amino acids	Other	pH	Osmolality (mOsm/L)	Intracellular/ Extracellular
EC (Euro-Collins)	K ⁺ (115), Na ⁺ (10), Mg ²⁺ (5), Cl ⁻ (15)	Phosphate (50; 57.5; 60), Bicarbonate (10)	-	-	-	Glucose (19.5; 180; 195)	7.3; 7.4	340; 355; 375	I
UW (University of Wisconsin, Viaspan)	K ⁺ (125), Na ⁺ (25), Mg ²⁺ (5), Cl ⁻ (20)	Phosphate (25)	Glutathione (3), Allopurinol (1)	Pentafraction - HES (50 g/L), Lactobionate (100), Raffinose (30)	-	Sulphate (5), Adenosine (5) Insulin (40 U/L), Dexamethasone 16 mg/L, Penicillin G 200,000 UI/L)	7.40 (25°C)	320; 324	I
Celsior	K ⁺ (15), Na ⁺ (100), Mg ²⁺ (13), Ca ²⁺ (0.25), Cl ⁻ (28; 41.5; 71)	Histidine HCl (30)	Glutathione (3), Mannitol (60)	Lactobionate (80), Mannitol	Histidine, Glutamate (20)	Sucrose	7.30 (20°C)	242; 360; 368	E
HTK (Custodiol)	K ⁺ (9; 10), Na ⁺ (15), Mg ²⁺ (4), Ca ²⁺ (0.015), Cl ⁻ (32; 50)	Histidine (180) Histidine HCl (18)	Tryptophan (2), Mannitol (30), α -Ketoglutarate (1)	Mannitol	Histidine, Tryptophan, Glutamate		7.02 -7.20 (25°C)	310	E
HTK-New (Custodiol-N)	K ⁺ (10), Na ⁺ (16), Mg ²⁺ (8), Ca ²⁺ (0.02), Cl ⁻ (30)	Histidine (124), N-acetyl-L-histidine (57)	Tryptophan, α -Ketoglutarate (2)	-	Histidine, Glycine (10) Tryptophan (2), Alanine (5), Arginine (3), Aspartate (5)	Sucrose (33), Deferoxamine (25 $\times$ 10 ⁻³), LK-614 (7.5 $\times$ 10 ⁻³)	7.0-7.1	302	E
IGL-1 (Institut Georges Lopez-I)	K ⁺ (25; 30), Na ⁺ (120; 125), Mg ²⁺ (5), Ca ²⁺ (0.03-0.5), Cl ⁻ (0; 20)	Phosphate (25)	Glutathione (3), Allopurinol (1)	Lactobionate (100), Raffinose (30), PEG-35 (0.03; 1)	-	Nitroglycerin, Adenosine (5) Sulphate (5)	7.40 (25°C)	290; 320	E
LPDG (Perfadex)	K ⁺ (6), Na ⁺ (138), Mg ²⁺ (0.8), Ca ²⁺ (0.3), Cl ⁻ (142)	Phosphate (0.8), Tris or Bicarbonate (1)	-	Dextran 40 (50)	-	Glucose (5) Sulphate (0.8)	7.4	295	E
Ep4 (EP-TU)	K ⁺ (26), Na ⁺ (141), Mg ²⁺ (4), Cl ⁻ (103)	Phosphate	-	Dextran 40	-	Glucose (10)	-	-	E
ET-Kyoto (ETK)	K ⁺ (44), Na ⁺ (100)	Phosphate (25)	-	Pentafraction - HES (30), Trehalose (41; 120)	-	Sulphate, Gluconate (100), Dibutyl cAMP	7.4	370	E
HOC - hyper- tonic citrate	K ⁺ (79), Na ⁺ (84), Cl ⁻ (30)	Citrate	Mannitol (185)	-	-	-	-	-	I
PBS - phosphate buffered sucrose	Na ⁺ (120)	Phosphate (60)	-	-	-	Sucrose (140)	7.40	310	I
Scot	K ⁺ (5), Na ⁺ (118), Mg ²⁺ (1.2), Ca ²⁺ (1.75), Cl ⁻ (128.9)	-	-	PEG-20 (30)	-	Glucose (11)	7.50	302	E
HTK-TiProtec	K ⁺ (93), Na ⁺ (16), Mg ²⁺ (6; 8), Ca ²⁺ (0.05), Cl ⁻ (103)	Phosphate (1) or Histidine (198) N-acetyl-L-histidine (30)	α -Ketoglutarate (2)	-	Glycine (5; 10) Tryptophan (2), Alanine (5), Aspartate (5; 8)	Glucose (10), Sucrose (20; 37), Deferoxamine (82 $\times$ 10 ⁻³), LK-614 (17 $\times$ 10 ⁻³)	7.0	305	I
KH (Krebs- Henseleit)	K ⁺ (5.9), Na ⁺ (143), Mg ²⁺ (1.2), Ca ²⁺ (1.25), Cl ⁻ (125.2)	Phosphate (1.2) Bicarbonate (25)	-	-	-	Sulphate (1.2), Glucose (11)	7.8	380	E

PEG polyethylene glycol, HES - hydroxyethyl starch, LK-614 - iron chelator. All units are shown as (mmol/L) unless otherwise indicated; Dextran 40, Pentafraction, PEG are in g/L

Currently, donor tissue is routinely retrieved by eye banks either through *in situ* excision of the cornea or enucleation of a complete eyeball. Of note, these tissues still carry ocular surface microbiota upon arrival at the eye bank, and these microorganisms may be a source of infection. Eye tissues are stored either in hypothermic storage at 4°C for 5–10 days (an approach mainly used in the United States) or in organ culture at 31–37°C for up to 35 days (an approach mainly used in Europe) (Li *et al.* 2019; Gibbons *et al.* 2020; Fabre *et al.* 2021). The mission, history, and tasks of the European Eye Bank Association and Eye Bank Association of America (EBAA) have been presented elsewhere (Jones *et al.* 2012; EBAA 2021).

In a systematic review, Gimenes *et al.* (2022) compared several specially developed corneal storage media with *Optisol*-GS, the most widely used medium to preserve corneas for transplantation. All of them contain antibiotics, most often gentamicin and streptomycin. However, considering the incidence of devastating fungal infection, most often caused by *Candida* sp., amphotericin and voriconazole have sometimes been added to *Optisol*-GS (Layer *et al.* 2014; Mistò *et al.* 2020; Gimenes *et al.* 2022). There are also objections to supplementation of hypothermic corneal storage media with amphotericin, mainly due to the high cost and low effectiveness of this antifungal chemotherapeutic at low concentrations (Tu 2021). On the other hand, Gibbons *et al.* (2020) concluded that the use of the fungicidal amphotericin B for endothelial keratoplasty was more cost-effective than the use of the fungistatic voriconazole or caspofungin. While the opinions are divided, cost-effectiveness also plays a role in developing treatments.

To minimize the risk of infections in organ recipients caused by microorganisms that contaminate tissues, a special monograph was introduced into the European Pharmacopoeia in 2023: “Microbiological Examination of Human Tissues” (Ph. Eur. 2023). An example of the content included in this source is a microbiological control strategy for cornea. This example was elaborated because the preservation of ocular tissue and corneal transplantation deserves special attention due to the large number of grafts performed (Chu 2000; Jones *et al.* 2012). In addition, to ensure long-term storage of corneas, Chaurasia *et al.* (2020) suggested their sterilization by gamma irradiation (17–23 kGy from a cobalt-60 source). This strategy effectively stabilizes tissue grafts and eradicates contaminating microorganisms, including viruses.

In addition to the above-mentioned preservation methods, cryopreservation has also been developed (Whaley *et al.* 2021). It requires freezing the tissue/organ to a temperature below 0°C to slow deterioration by reducing the rate of metabolism. Such pre-

served material, like bone marrow, blood components, and gametes, can be stored for many weeks (Datta *et al.* 2021; Ozgur *et al.* 2023). However, problems arise when large organs and other three-dimensional structures are cooled below 0°C, because ice crystals can form immediately inside cells and cause severe mechanic destruction. Cryoprotective agents (CPAs) are crucial for cryobiology (Elliott *et al.* 2017; Jang *et al.* 2017; Whaley *et al.* 2021). Solutions containing alcohols (e.g., methanol, ethanol, glycerol, ethylene glycol, and propylene glycol), sugars (e.g., trehalose, sucrose, mannitol, and raffinose), polymers (e.g., polyethylene glycol, dextrans, and hydroxyethyl starch), dimethyl sulfoxide, dimethyl acetamide, and glutamine, among other components, are commonly used for cryopreservation of microorganisms and cells. CPAs can mitigate cryoinjury caused by ice nucleation, crystal growth, and cellular dehydration during freezing, all of which influence post-thaw survival (Elliott *et al.* 2017; Ozgur *et al.* 2023). Considering the penetration of CPA into solid organs, it is necessary to use hypothermic perfusion with CPAs at a temperature of 10°C prior to cooling the material to –80°C (Elliott *et al.* 2017). Microorganisms that contaminate tissues or organs do not multiply at such a low temperature. Supercooling (to about –10°C) in the presence of CPAs largely protects cells against the negative impact of ice crystal formation (Ozgur *et al.* 2023). Experimental results concerning vitrification – rapid cooling to below –100°C to form a noncrystalline glassy phase in animal, rabbit, and rat organs (e.g., heart, liver, kidney), are promising (Ozgur *et al.* 2023; Berendsen *et al.* 2014), based on the successful cryopreservation of hepatocytes, pancreatic islets, gametes, and stem cells (Whaley *et al.* 2021). However, rewarming vitrified material and preserving functionality and viability are notable challenges. A thorough understanding of the chemical and biological processes behind freezing and thawing will be necessary for the future development of a safe and effective cryopreservation method (Weissenbacher *et al.* 2019).

There are a myriad of sources of infections in organ recipients (Oriol *et al.* 2019; European Committee (Partial Agreement) on Organ Transplantation of the CE 2022; Li *et al.* 2022; Manuel *et al.* 2023). Endogenous pathogens, mainly viruses and less often parasites, may be present in the transplanted organ and transmitted to the recipient. The donor might be unaware of their infection or be asymptomatic, especially when latent viruses become virulent in a recipient subjected to immunosuppression due to the risk of transplant rejection. Exogenous microorganisms in PF may occur during the procurement process – for example, they may come from the surface of the donor’s body or from the environment. Most often, infections in organ recipients occur due to unhygienic organ collection, improper

handling and transport, and inappropriate preservation conditions, especially contamination of the PF used for perfusion and storage. Antibiotic therapy in recipients before transplantation reduces the risk of developing infection in case a contaminated organ is transplanted.

Besides, some potential organ recipients often travel abroad, mainly to Asian countries, to reduce costs and to shorten the waiting time for transplantation. In some geographic regions, there is limited medical and microbiological screening of donors. Furthermore, in countries where payment for organ donation is legal, donors typically come from lower socioeconomic areas where endemic infections such as tuberculosis and malaria may occur (Len *et al.* 2014).

Len *et al.* (2014) developed and proposed recommendations for screening donors and recipients prior to organ transplantation to minimize transmission of donor-derived infections. The authors considered latent and acute bacterial, fungal, viral, and protozoal infections. In addition, the Infectious Diseases Community of Practice of the American Society of Transplantation has published guidelines concerning screening of donors and candidate prior to solid organ transplantation (Malinis *et al.* 2019). Moreover, the online medical portal *emedicine.medscape.com* provides current information on transplantation of the kidney (Collins 2021), liver (Manzarbeitia and Arvelakis 2022), pancreas (Rao and Finger 2022), intestines (Andacoglu and Greenstein 2021), lung (Whitson 2022), and heart (Botta and Mancini 2023), as well as post-transplantation complications and infections accompanying the transplantation of these organs.

Although immunosuppressive therapies are involved at the time of transplantation, the early post-transplant period (up to 1 month) is notable for hospital-acquired infections, especially related to surgical procedures including implant placement and the use of medical devices like intravenous and urinary tract catheters. The intermediate post-transplant period (months 1–6) is the time where there is the greatest risk for opportunistic infections. In stable recipients, infections are less frequent 6 months after transplantation (Fishman 2017; Sawinski and Blumberg 2019). Transmission of infection during transplantation of solid organs grafts is uncommon but potentially life threatening. Fishman (2017) provided a comprehensive overview of the epidemiology of infections during organ transplantation, diagnosis, and therapy. Regardless of whether infections are directly related to the process of organ transplantation, one should remember that these severely ill and immunosuppressed patients are also exposed to nosocomial pathogenic microorganisms in their environment. For this reason, some microorganisms isolated from infected patients may differ from microorganisms found in contaminated PF.

3. Bacterial infections in organ transplant recipients and contamination of preservation fluid

Microbiological contamination of PF is a potential source of post-transplantation infections and requires patients to be treated with antibiotics or antimicrobial chemotherapeutics. The most frequently isolated microorganisms from these fluids are staphylococci, Gram-negative rods, and *Candida* spp. strains (Sotiropoulos *et al.* 2018). An important issue that requires microbiological and clinical analysis is whether all isolated microorganisms should be treated as actual pathogens and antimicrobial therapy should be implemented in recipients (Manuel *et al.* 2023). Moreover, the protocols for screening organ or tissue donors for infectious risks are inconsistent and vary according to the type of graft, national standards, and the availability of the screening tests.

A number of publications have focused on PF contamination or infections in solid organ recipients. Mattner *et al.* (2008) investigated the extent to which bacterial and fungal donor organ contamination caused post-transplant nosocomial infections in solid organ transplant recipients. Out of 282 organ recipients (140 lung, 71 liver, 51 heart, and 16 heart-lung recipients), 150 (53.2%) received contaminated organs. The lung and heart-lung transplants were the most contaminated based on PF or organ swab microbiological examination. In the lung transplant group, 126 Gram-positive bacteria, 102 Gram-negative rods, and 57 fungi were isolated, whereas in the heart-lung transplant group, 18 Gram-positive bacteria, 5 Gram-negative rods, and 6 fungi were cultured. Of note, polymicrobial contamination was frequent.

Colvara Mattana *et al.* (2011), analyzed 136 PF samples used to store kidneys and pancreas. The contamination rate of these samples was 27.9%, mainly by coagulase-negative staphylococci, *Bacillus* spp., and *Enterococcus* spp. (representing 55% of contaminated PF samples). The authors concluded that infections of the organ recipients were not associated with contaminated PF. Sotiropoulos *et al.* (2019) reviewed 19 studies published from 2000 to 2016 regarding bacterial and fungal contamination of PF samples used to store solid organs before transplantation. Of 5647 patients, 1428 (25.3%) had positive microbial cultures. The bacteremia data showed a wide range (0%–69%), which precluded the authors for drawing conclusions or making recommendations.

Peghin *et al.* (2024) recently described skin and soft tissue infections in solid organ transplants. The authors drew attention to the possibility of infections caused by staphylococci and streptococci, as well as microorganisms that are rare in such a situation, including *Nocardia* sp., *Bartonella* sp., and *Mycobacteria*. Some of these

infections may be related to the patient's hospital stay and the environmental contamination there.

Isabel Oriol together with a group of Spanish researchers (Oriol *et al.* 2016; Oriol *et al.* 2018; Oriol *et al.* 2019) have conducted multicenter investigations, systematic reviews, and meta-analysis on the impact of culture-positive PF on solid organ transplantation for several years. In one study, they found that 46 out of 50 liver grafts had been stored in contaminated PF, but only in 14 cases were there pathogenic microorganisms. They mainly isolated coagulase-negative staphylococci. There was no infection among the recipients (Oriol *et al.* 2016). The authors also emphasized that the examination of PF immediately before implantation has the greatest diagnostic value. In another large multicenter cohort study, out of 622 transplanted organs (362 kidneys, 166 livers, 51 lungs, 32 hearts, and 11 multiple organs) and PF samples, as many as 389 (62.5%) were microbiologically contaminated, but only one fourth of positive samples contained "high risk" pathogens; *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, and *Enterobacter cloacae* dominated (Oriol *et al.* 2019). PF contamination could be directly linked to the development of infection in only five patients. The authors concluded that clinical monitoring of solid organ recipients infected with microorganisms present in contaminated PF, regardless of their species, is important to make the proper diagnosis and to determine whether the situation requires the treatment of infections associated with PF (Oriol *et al.* 2018). Yahav and Manuel (2019), in a commentary on the publication of Oriol (Oriol *et al.* 2019), and Yu *et al.* (2019) also called for an increase in evidence, especially in terms of precise characterization of contaminating microorganisms, to limit the use of antibiotics in the prevention and treatment of infections.

What is important, Cervera *et al.* (2014) described recommendations for the management of multi-drug-resistant (MDR) bacteria in solid organ transplant patients, considering infections with methicillin-resistant *S. aureus* (MRSA); vancomycin resistant enterococci; and extended-spectrum beta-lactamase (ESBL)-, AmpC-, and carbapenemase-producing Gram-negative rods. Recently, Pilmis *et al.* (2023) analyzed MDR *Enterobacterales* infections in the context of abdominal solid organ transplantation, paying attention to donor screening for gastrointestinal tract colonization by these MDR Gram-negative bacteria. The authors also considered the prevalence of bacterial infections, including those caused by MDR Gram-negative bacteria, in kidney and liver recipients. The prevalence of infections was up to 65%, and the prevalence of MDR pathogens was up to 20%. While Bodro *et al.* (2013) analyzed the outcomes of bacteremia caused by drug resistant

Enterococcus faecium, *S. aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *E. cloacae* (ESKAPE pathogens) in solid organ transplant recipients. In the 6-year study, there were 276 bacteremia cases among 190 recipients, of which 54 (19.6%) cases were caused by drug-resistant ESKAPE strains. These strains were found in 24 kidney recipients, 21 liver recipients, and 9 heart recipients. Carbapenem- and quinolone-resistant *P. aeruginosa* strains predominated in the above recipient groups – 13, 9, and 5, respectively – followed by ESBL-producing *K. pneumoniae* – 7, 3, and 1 cases respectively.

Complications related to organ and tissue transplantation and PF contamination are primarily caused by bacteria that grow aerobically. Anaerobic bacteria generally do not pose a significant threat to transplant recipients, with the exception of *Clostridioides difficile*, a common nosocomial pathogen in hospital wards that causes infections especially in immunocompromised patients, such as organ recipients. The American Society of Transplantation Infectious Diseases Community of Practice (Mullane *et al.* 2019) developed guidelines to address the prevention and management of *C. difficile* infections in solid organ transplant recipients. The incidence of *C. difficile* infections varies by the type and number of organs transplanted. The prevalence of these infections in the solid organ transplant population ranges from a low of 3.2% in the pancreatic transplant population to 12.7% in those receiving multiple organ transplants (Mullane *et al.* 2019). It should be mentioned that Audet *et al.* (2011) examined PF contamination in the context of liver transplantation. Apart from a number of aerobic bacteria (mainly coagulase-negative staphylococci), they isolated anaerobes, four strains of *Propionibacterium* sp., and a strain of *Veillonella* sp. These bacteria did not cause infection in organ recipients.

Bacterial infections are generally connected with organ storage and surgical procedures and are not latent in nature, with the exception of *Mycobacterium* spp. infections. Transplant recipients are immunocompromised and vulnerable to developing tuberculosis. There have been a number of cases of tuberculosis reactivation in recipients of organs contaminated with *Mycobacterium tuberculosis* (Sidhu *et al.* 2014; Abad *et al.* 2019; Nguyen Van *et al.* 2024; Hyun *et al.* 2024). Screening of latent tuberculosis infection in donors is the cornerstone of the tuberculosis preventive strategy in recipients (Malinis and Koff 2021).

The use of antibiotics to decontaminate grafts has been evaluated (Paolin *et al.* 2018). The authors examined bacterial contamination profiles of 11,129 tissue samples as allografts retrieved from multi-tissue donors. The tissues were incubated twice at 4°C for 24–28 hours in a decontamination solution containing

ceftazidime (24 mg/L), lincomycin (120 mg/L), polymyxin B (100 mg/L), and vancomycin (50 mg/L). The samples were analyzed microbiologically. Immediately after tissue retrieval, 6130 (55%) of the samples were contaminated. Using subsequent decontamination, the number of bacteria decreased – to 1955 samples after the first decontamination step and to 113 samples after the second decontamination step. Coagulase-negative staphylococci were the dominant bacterial group.

Louart *et al.* (2019) drew some interesting conclusions when considering the risk of contamination of organ procurement in different locations. Their multivariate statistical analysis of 2535 grafts indicated that 285 (11%) were microbiologically contaminated, of which 20% were skin grafts, 12% were arterial grafts, 9% were heart valves, and 7% were corneal grafts. Regarding the location of organ retrieval, 47% were collected in standard operating rooms, 39% in dedicated non-operating rooms (hospital mortuaries), and 14% in intensive care units. The authors concluded that although standard operating rooms provide the best place to procure grafts, dedicated non-operating rooms led to a lower risk of tissue microbial contamination. This may be related to the fact that corneal samples, which constituted approximately 60% of the analyzed grafts, were mainly recovered from deceased patients stored in a cooled room. The authors reported that the percentage of contaminating microorganisms varied depending on the place of tissue collection. For tissues collected in standard operating rooms, 65.5% of the microbes were Gram-positive bacteria, 17.2% were Gram-negative rods, and 14.8% were fungi isolated. In dedicated non-operating rooms, 26.4% of the isolated microbes were Gram-positive bacteria, 39% were Gram-negative rods, and 20.7% were fungi. Finally, for the tissues collected in intensive care units, 64.3% of the microbes were Gram-positive bacteria, 24.3% were Gram-negative rods, and 5.7% were fungi (Louart *et al.* 2019).

In many cases, it is quite difficult to locate a proper organ donor. Sometimes, there is not enough time to find one and a patient qualified to receive a transplant dies. Kieslichova *et al.* (2019) presented a case report in which both kidneys, the liver, pancreatic islets, and the heart were transplanted to five organ recipients from a deceased patient with antibiotic-sensitive *K. pneumoniae* and *E. coli* in her sputum. Appropriate antibiotic prophylaxis and antibiotic therapy were administered to four of the five patients who developed ESBL-producing *K. pneumoniae* and ESBL-producing *E. coli* infections. It turned out that these strains were present in the transport medium in which the organs were stored during organ procurement. The two kidney recipients died, but the remaining three patients survived the operations with good graft function.

3.1. Infections associated with kidney transplantation

There have been many studies related to renal infection after kidney transplantation and contamination of PF used to store kidneys. Bertrand *et al.* (2013) pointed out that contamination of PF used to store kidney grafts has been examined using various methods. Sometimes, the methods used did not allow the detection of microorganisms because of incorrect growth conditions (e.g., media, temperature, and incubation time). Furthermore, the authors analyzed 200 kidney transplantations (with kidneys from a deceased donor) performed over a 3-year period. During the hospitalization period, 62 patients who received a kidney stored in contaminated PF, regardless of whether they received prophylactic antibiotic therapy, did not exhibit any invasive blood, urinary, peritoneal, or wounds infections related to the microorganisms isolated from the PF. Coagulase-negative staphylococci were mainly isolated. In a large study on infection in renal transplant recipients, Sawinski and Blumberg (2019) noted that bacterial infections are a major cause of morbidity and mortality after organ transplantation. The most common infections (23–75%) in kidney transplantation are those related to the urinary tract. Moreover, reactivation of tuberculosis may occur in transplant recipients. Opportunistic bacteria, including with *Nocardia* sp. and *E. coli*, remain the most common organism causing urinary tract infections (Parasuraman *et al.* 2013). Reticker *et al.* (2021) showed that out of 152 kidney transplant recipients, as many as 67% received organs stored in contaminated PF. However, 80% of these microorganisms can be considered to be part of the normal skin microbiota. Sixty-seven percent of patients who underwent transplantation with kidneys stored in contaminated PF were treated with antibiotics for 5 days. There was no difference in the incidence of infection between patients who received an organ stored in contaminated PF and patients who received an organ stored in culture-negative PF. Similarly to the aforementioned study, Yansouni *et al.* (2012) analyzed 331 PF samples, almost half of which had stored kidneys. They found that 62.2% of the PF samples were contaminated. However, high-risk organisms, mainly *Enterobacteriaceae* and *S. aureus* strains, accounted for only 17.8% of the isolated microbes.

Li *et al.* (2022) conducted a retrospective study to elaborate the association between organ PF pathogens and early infections after kidney transplantation. They analyzed clinical data from 514 kidney transplant donors and 808 recipients between 2015 and 2020. They found that 329 recipients showed early infections after transplantations connected with contaminated PF. The dominant pathogen isolated from the PF samples was *Staphylococcus epidermidis* (10.2%). In addition, 34.6%

of the PF samples contained pathogenic bacteria from the ESKAPE group, 21% of the PF samples were contaminated with *Candida* sp. Thirty-five percent of the infections were caused by microorganisms belonging to both groups. The recipients infected with ESKAPE pathogens and *Candida* sp., in comparison to recipients with other pathogens, had higher rate of bloodstream and transplant-site infections, 14.1% versus 6.9% and 16.7% versus 3.5%, respectively. Yu *et al.* (2019) made similar observations in a retrospective analysis of 1002 PF samples associated with kidney transplantation for microbiological contamination. They isolated 1036 microorganisms. As many as 275 (26.5%) of the recipients' PF samples were contaminated with ESKAPE pathogenic strains. It is worth noting that in the group of microorganisms obtained, 14.4% were *Candida* spp., including 6.3% of *Candida albicans*. The authors stated that patients whose PF is contaminated with ESKAPE pathogens have a significantly increased risk of infections during the early post-transplant period. Corbel *et al.* (2020) analyzed 4487 kidney grafts procedures and carefully examined the possibility of infection in the recipients. The percentage of contaminated PF samples that stored kidney grafts from living and deceased donors was similar, 20.5% and 24.1%, respectively. Nearly 60% of PF contaminants were polymicrobial. The most frequently isolated microorganisms were coagulase-negative staphylococci (65.8%) and *Enterobacteriaceae* strains (28%).

Saad *et al.* (2020) analyzed infections in the first year after renal transplant and concluded that the most often complications are the bacterial urinary tract infections (44.2%). Veroux *et al.* (2010) analyzed 62 PF samples used to store kidneys and found that 38.7% of samples were contaminated with at least one microorganism. There were five species of coagulase-negative staphylococci (13 strains) among the PF samples contaminated with bacteria. Bacterial contamination evolved without symptoms in most patients treated with prophylactic intravenous piperacillin-tazobactam therapy. Six patients received kidneys from PF contaminated with *C. albicans*.

PF contamination with MDR microorganisms possesses a great danger to organ recipients. Zhang *et al.* (2022) analyzed carbapenem-resistant *K. pneumoniae* infections in kidney transplant recipients. Among 206 PF samples tested, 20 were contaminated with carbapenem-resistant *K. pneumoniae* strains. An infection developed in 15 patients, and 6 of them died. All isolated strains were susceptible to ceftazidime-avibactam, and all but one strain were susceptible to tigecycline.

Ranghino *et al.* (2016) evaluated the clinical impact of microbial contamination of PF used to store kidneys. During a 3-year single-center retrospective study, the authors examined 290 PF samples and clinical

data from patients who received a kidney transplant from deceased multi-organ donors. All of the patients received prophylactic broad-spectrum antibiotics intravenously during surgery and at least for 9 days after transplantation. If yeasts were present in the PF, fluconazole or caspofungin therapy was introduced. Of the 290 PF samples, 101 (34%) were contaminated with one or more microorganisms, mainly with coagulase-negative staphylococci (47 strains belonging to 9 species) and *E. coli* (17 strains). In addition, 10 *C. albicans* strains were isolated. The authors found that although PF contamination is frequent, the incidence of PF-related infections is very low. Preemptive therapy did not help to reduce the rate of PF-related infections, so a reasonable reduction in the use of antibiotic therapy could be made. The authors recommended close clinical and microbiological monitoring of the recipient when PF is contaminated to establish a diagnosis and to start the appropriate antibiotic therapy as soon as possible (Ranghino *et al.* 2016).

Transplant centers follow different approaches concerning the use of antibiotic prophylaxis before surgery and during the first post-transplant week. A nationwide survey regarding perioperative antibiotic prophylaxis in France indicated that antibiotic prophylaxis practices during the perioperative kidney transplant period are very heterogeneous, and this situation requires the development of a special guidelines (Le Berre *et al.* 2020). Of note, 107 of 139 respondents (77%) reported the existence of local practice guidelines for surgical antibiotic prophylaxis in kidney transplant recipients. Only 18 of 139 respondents (13%) reported that they used the following drugs for prophylaxis during the early post-transplant period: cephalosporins (13/18), fosfomycin (3/18), fluoroquinolones (1/18), glycopeptides (1/18), and fluconazole (1/18). The median drug prescription duration was 5 days.

3.2. Infections associated with liver transplantation

In solid organ transplant recipients, the second most commonly described complication (after infections related to kidney transplantation) is infection that result from contaminated PF used to store liver grafts. During a 4-year retrospective study (2007–2010), Sauget *et al.* (2011) showed that among 137 transplanted organs (90 kidneys and 47 livers), 54.5% of PF samples were contaminated with bacteria. Coagulase-negative staphylococci were dominant (66.4%), followed by *Enterobacteriaceae* (8.3%) and anaerobic bacteria, namely *Propionibacterium* spp. (7.5%). The following strains were also isolated from the transplanted kidneys and their PF samples: *Lactobacillus* spp. (4.9%); streptococci and enterococci (2.9%); anaerobic *Peptostreptococcus* spp. (2%); *S. aureus* (2%); and single strains of *Pseudomonas* sp.,

Bacillus sp., and *Micrococcus* sp. However, the dominant bacteria causing infections in transplant recipients were *Enterobacteriaceae* (54.3%), coagulase-negative staphylococci (17.2%), and streptococcal and enterococcal strains (15.5%). Pulsed field gel electrophoresis of the DNA of bacteria isolated from contaminated PF revealed no clonal identity, with the exception of a pair of *E. coli* strains. These findings indicate a small risk of developing infections in patients whose transplanted organs were stored in contaminated PF.

In a retrospective study, Chaim *et al.* (2011) analyzed contamination of PF samples in relation to recipient survival and acute cellular rejection in the context of liver transplantation. Fifteen of the 121 PF samples were contaminated with *K. pneumoniae* (n=6), *S. epidermidis* (n=5), and *A. baumannii* (n=3). Only one patient with a PF-associated infection (caused by *K. pneumoniae*) died. In a 4-year prospective study, Reimondez *et al.* (2021) investigated the risk of infections from contaminated PF in liver transplant recipients. Of the 88 PF samples tested, 33 showed the presence of bacteria and one third had polymicrobial contamination; *S. epidermidis* predominated. Five recipients became infected and received antibiotic therapy based on the antibiogram. Antibiotic prophylaxis with 3 g of intravenous ampicillin-sulbactam was routinely administered in all recipients 30 minutes before skin incision and four times a day up to 48 hours after surgery. There was no significant difference in infections between patients whose transplanted liver was stored in contaminated PF and patients whose transplanted liver was stored in uncontaminated PF. Garcia-Zamora *et al.* (2015) reported similar observations when analyzing 178 liver transplants. They found bacteria or fungi in 79 PF samples (44%). Staphylococci (64%) and *Enterobacteriaceae* (17%) strains were isolated most frequently. There were 25 postoperative infections, but only 4 out of 79 liver graft recipients (5%) who received a liver stored in contaminated PF developed a postoperative infection related to the microorganism isolated from the PF. These findings indicate the low dependence of such infections on PF contamination.

Hygienic practices and procedures during preservation of transplanted organs have reduced the extent of PF contamination. In a 1-year study (March 2007–March 2008) involving 60 PF samples in which transplanted livers were stored, all but one of the samples were contaminated (Ruiz *et al.* 2009). Strains of low pathogenicity such as coagulase-negative staphylococci, *Streptococcus viridans*, and *Corynebacterium* sp. accounted for 75% of the isolated microbes. Microorganisms isolated from post-transplant infections did not match the strains isolated from the PF samples.

Sometimes, organ transplants are performed from deceased donors who have various infections. In a ret-

rospective study, Tong *et al.* (2020) analyzed data from 211 liver donors, of which 82 (38.9%) were infected, to define whether, blood, bronchial aspirate, catheter, and urine samples had been subjected to microbiological examination. The most common isolates were *A. baumannii* (27 cases), *S. aureus* (22 episodes), and *P. aeruginosa* (13 cases). There were 17 cases of fungal infections, and *C. albicans* accounted for 53% of these cases. Among 82 liver donors, 51 were infected, of which there were 12 possible donor-derived infections and 39 non-possible donor-derived infections. The authors concluded that in the case of liver transplantation from an infected donor, the postoperative incidence of infection is high and the infection interval is short. When dealing with MDR bacteria, recipients may have serious complications and poor outcomes.

Berry *et al.* (2019) tested the effectiveness of intra-operative versus perioperative extended antibiotic prophylaxis in the context of liver transplant surgery. Liver transplant patients who received an extended 72-hour course of prophylactic antibiotics did not show a reduction in surgical site infections compared with patients who received a short course of antibiotics (the first dose 30 minutes prior to incision and the second dose 4 hours after initiation of the transplant procedure). There were 16 and 18 infections, respectively. Moreover, a similar number of vancomycin-resistant enterococci were isolated from each group.

3.3. Infections associated with pancreas and lung transplantation

Microbiological contamination of PF used to store pancreas transplants poses a great threat to recipients. The microbiological safety of islet preparations is particularly important. Meier *et al.* (2018) examined the microbiological purity of samples collected during islet isolation over a 10-year period. Microbial contamination of PF was found in 64.4% (291/452) of processed donor pancreas. Coagulase-negative staphylococci were isolated most frequently from pancreas PF (45%), followed by *S. aureus* (9.5%), streptococci (6.7%), and *Candida* spp. (5.3%). The procedure of preparing islets for administration to the recipient, although carried out under aseptic conditions, was also associated with the risk of contamination. The use of antibiotics and successive washing steps during pancreas digestion and islet isolation and purification helped to eliminate microorganisms inherited from procurement of the donor pancreas. After islet isolation and purification, 4.9% (22/452) of the preparations met the release criteria for transplantation. Finally, a total of 189 islet preparations were transplanted to 92 recipients (Meier *et al.* 2018).

Tran-Dinh *et al.* (2023) conducted a 6-year retrospective study on contamination of PF used to store

lung grafts before transplantation. The authors examined 271 patients and found that 83 patients (30.6%) received lung grafts stored in contaminated PF. The most common isolates were *S. aureus* (33 cases) and *E. coli* (13 cases). Additionally, five *Candida* spp. strains were recovered from contaminated PF samples. The authors concluded that there is a high prevalence of PF contamination, and this phenomenon may decrease the survival of lung graft recipients. They recommended routine microbiological testing of PF and treatment with targeted antibiotic therapy in case of infection after lung transplantation.

3.4. Infections associated with corneal and skin transplantation

Storing eye tissues in eye banks before keratoplasty for a certain period of time allows a number of tests to be performed, including an assessment of microbiological contamination (EEBA Technical Guidelines for ocular tissue, 2020). Deogaonkar and Roy (2023) analyzed 50 publications published from 2005 to 2021 regarding donor-related corneal infection. The post-keratoplasty infection rates were 0.2–0.77% for endophthalmitis and 6.5–10.5% for microbial keratitis. In analyzed articles, MDR Gram-negative rods and fungi (*Candida* spp. and *Aspergillus* spp.) were associated with contamination (Deogaonkar and Roy 2023). Thareja *et al.* (2020) reported slightly different observations. Apart from fungal infections, the most common causes of bacterial infection after keratoplasty were *Staphylococcus* and *Streptococcus* strains.

Mathes *et al.* (2019) performed a retrospective review (2006–2017) of the infection rates in a single eye bank, comparing corneas prepared and not prepared by the eye bank. The overall infection rate related to the donor tissue was low (2.3 in 10,000). The eye bank-prepared corneas were assumed to be more susceptible to infection due to exposure to elevated temperatures when removed from cold storage for processing. Additionally, handling corneas during eye bank preparation may increase the chance of tissue contamination. However, eye bank-prepared corneas were not linked to an increased risk of post-keratoplasty infections.

Ling *et al.* (2019) analyzed the current factors affecting corneal organ culture contamination and presented a flow diagram of donor tissue processing. The study included 4410 corneal samples, of which 110 (2.5%) were contaminated. Sixty-three fungal strains were isolated, including 38 *C. albicans* strains and 24 bacterial strains, of which coagulase-negative staphylococci dominated (14 strains).

Röck *et al.* (2017) retrospectively analyzed factors influencing the contamination rate of 1340 cultured corneas at the Tübingen Cornea Bank (Germany) from

2008 to 2014. The annual contamination rate ranged from 1.3% to 2.1%. Of note, half of the samples were contaminated with fungi, exclusively *Candida* sp., and half of the samples were contaminated with bacteria, predominantly *Staphylococcus* spp. The analysis showed an increased risk of contamination for septic donors compare with aseptic donors. The main source of fungal and bacterial contamination could be resistant skin microbiota. The mean monthly contamination rate was correlated with the mean monthly air temperature.

In a large retrospective analysis of organ-cultured human corneas in one French regional eye bank for the period of 2005–2018 (Fabre *et al.* 2021), among 127,979 donor corneas collected, 1240 samples (6.9%) were microbiologically contaminated. This group contained 930 (75%) bacterial strains, including 6 species of coagulase-negative staphylococci ($n=357$), non-enterobacteria Gram-negative rods ($n=339$), and enterobacteria ($n=140$) – and 272 (21.4%) fungal strains – including 225 *Candida* sp. strains (*C. albicans*, $n=130$) and 31 filamentous fungal strains. Besides, 38 (3.1%) microorganisms were not identified. There was some change in the annual average contamination rate and the microorganism groups from 2005 to 2018 (Fabre *et al.* 2021).

Li *et al.* (2019) investigated microbiological contamination in donor corneas preserved in the medium term, starting from the acquisition of eyeballs preserved and delivered in ice box to the eye bank. Eyeballs were soaked in 0.05% povidone iodine solution for 1–2 minutes, rinsed with sterile saline, and soaked in 2000 U/mL gentamicin sulphate solution for 10–15 minutes. Then corneal grafts were excised into medium-term preservation solution at 4–8°C for keratoplasty. After removal of the central corneas for transplantation, the corneo-scleral rims were put back into the medium for 1 month at 20–25°C. Eighty-two donor corneas were included in the study. The contamination rate was 9.8%; seven of the eight identified strains were fungi.

Skin transplants are performed primarily in people with severe burns. These injuries are a significant global health problem, with over 11 million people requiring medical intervention each year and approximately 180,000 deaths annually (WHO Fact Sheet 2023). The management of severe burn injuries involves preventing and treating burn shock and promoting skin repair through a two-step procedure of covering and closing the wound. Currently, split-/full-thickness skin autografts are the gold standard for permanent skin substitution (Šuca *et al.* 2024). Burns provide an ideal environment for bacterial growth. There is an increased risk of infection of the skin and/or soft tissues during the early stages, particularly from Gram-positive bacteria, followed by Gram-negative bacteria and fungi (Kelly *et al.* 2022).

4. Fungal infections in organ transplant recipients

In addition to bacterial infections, organ recipients may experience fungal infections. Peghin *et al.* (2024) analyzed several skin and soft tissue fungal infections in solid organ transplant recipients. Infections in recipients were caused by strains from the following genera: *Candida* spp., *Cryptococcus* spp., *Aspergillus* spp., *Mucor* spp., *Fusarium* spp., *Histoplasma* spp., *Blastomyces* spp., and *Coccidioides* spp. It is extremely important to use appropriate diagnostic tests to detect the etiological factor of the infection. In addition, Sawinski and Blumberg (2019) reported that kidney transplant patients are at increased risk for opportunistic fungal infections, including *Candida*, *Aspergillus*, *Cryptococcus*, and *Pneumocystis*. Candidemia is most often an early post-transplant nosocomial infection of surgical drains or vascular access catheters. *Candida* infections may be observed in liver recipients with cholangitis, hematomas, or bile leaks (Fishman 2017). Invasive *Aspergillus* infections occur most often in debilitated or immunosuppressed organ recipients. Within 1-year after organ transplantation, opportunistic infections emerge, including by *Pneumocystis jirovecii*, which causes pneumonia, and by endemic fungi such as *Histoplasma capsulatum*, which causes Darling's disease (Fishman 2017).

Contamination of PF with yeasts during solid organ recovery can lead to life-threatening complications in the recipients. Fungal infections constitute a significant clinical problem in liver and kidney recipients. Botterel *et al.* (2010) analyzed 650 PF samples collected during a 5-year period in terms of fungal contamination using standardized procedures for systematic mycological culture. The yeast contamination rate was 4.1% and 3.1% for liver and kidney transplants, respectively. Strains belonging to the following species were identified: *C. albicans*, *Candida glabrata*, *Candida krusei*, *Candida tropicalis*, *Candida valida*, *Pichia etchellsii*, and *Rhodotorula* sp. Audet *et al.* (2011) analyzed 91 PF samples used in liver transplantation and detected 4 *C. albicans* strains, 1 *Aspergillus fumigatus* strain, and 1 *Saccharomyces* sp. strain. Stern *et al.* (2022) analyzed the PF of 1248 hepatic and 1273 renal transplants. They found that fungal contamination in the PF of hepatic and renal grafts was 1.2% and 0.86%, respectively. Although the incidence of fungal contamination was low, contaminated PF was associated with high mortality of organ recipients. *C. albicans* was the most common organism (70.4%), followed by *C. krusei* and *C. glabrata*. The above observations are consistent with those reported by Levesque *et al.* (2015) in a 5-year multicenter study of PF contamination after liver transplantation. Among 2107 PF samples, 28 (1.33%) were contaminated with *Candida* strains, 64% of which were *C. albicans*. Eight

recipients developed yeast-related complications and 1-year after transplantation, the mortality rate among this group of patients was 62.5%. Bachellier *et al.* (2014) mentioned *C. albicans* arteritis transmitted by PF after liver transplantation.

Ten years ago, the EBAA (Aldave *et al.* 2013) reported that from 2005 to 2010, the incidence of fungal infections after corneal transplantation showed an increasing trend. Thirty-one cases of culture-proven fungal keratitis (n=14) and endophthalmitis (n=17) were reported out of 221,664 corneal transplants performed using corneal tissue distributed by domestic eye banks.

Thareja *et al.* (2020) noticed that in post-keratoplasty infections, the main fungal pathogen is *C. albicans*, followed by *C. glabrata*. Besides, *Alternaria* sp. and *Cladosporium* sp. may also cause infections. Based on the findings, the authors proposed antifungal supplementation of PF to eliminate contaminated fungi. The arguments for and against supplementation of PF with voriconazole, caspofungin, amphotericin B, and betadine have been discussed. Malinis and Boucher (2019) provided recommendations regarding screening of solid organ donors for histoplasmosis, coccidioides, and cryptococcosis.

5. Viral infections in organ transplant recipients

The laboratory serological tests to detect viral infections, especially latent ones, should be performed in both organ donors and recipients (Grossi 2018; Malinis and Boucher 2019; Sawinski and Blumberg 2019). The risk of infection for recipients may be associated with the following viruses: herpes viruses (e.g. human herpes virus [HHV]6, HHV7, and HHV8); Kaposi sarcoma herpesvirus; cytomegalovirus (CMV); herpes simplex virus (HSV); varicella zoster virus (VZV); Epstein-Barr virus (EBV); retroviruses, including human immunodeficiency virus (HIV) and human T cell lymphotropic virus-1 and 2; and hepatitis viruses, including hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis E virus (HEV). Other rare viruses may also pose a threat: West Nile virus, Chikungunya virus, Zika virus, dengue virus, lymphocytic choriomeningitis virus, and rabies virus (Fishman 2017; Peghin *et al.* 2024). Saad *et al.* (2020) analyzed infections in the first year after renal transplant and found that the most frequent viral infections were caused by CMV (21.8%) 31–180 days after transplantation.

The U.S. Public Health Service has published recommendations on how to reduce the risk for transmission of several viruses through solid organ transplantation (Jones *et al.* 2020). In 2021, the Centers for Disease Control and Prevention realized that this recommendation might be unnecessary for pediatric organ

transplant candidates. Thus, a year later the guidelines were updated to specify that solid organ transplant candidates aged < 12 years at the time of transplantation who have received postnatal infectious disease testing are exempt from the recommendation for HIV, HBV, and HCV testing during hospital admission for transplantation (Free *et al.* 2022).

6. Parasitic infections in organ transplant recipients

In addition to bacteria, fungi, and viruses, parasites including *Toxoplasma gondii*, *Trypanosoma cruzi*, *Strongyloides stercoralis* and *Leishmania* spp., and amoebas including *Balamuthia* spp. and *Naegleria* spp. can cause infections related to transplants (Fishman 2017; Grossi 2018; Malinis and Boucher 2019; Peghin *et al.* 2024). Toxoplasmosis constitutes a significant danger in heart transplant recipients, when a *Toxoplasma* seropositive heart is transplanted into a *Toxoplasma* seronegative recipient. Toxoplasmosis has also been transmitted to liver and kidney recipients (Malinis and Boucher 2019). Transmission of *Strongyloides* spp., an intestinal nematode endemic to the tropics and subtropics, via transplantation has been described with significant mortality and morbidity (Malinis and Boucher 2019; CDC 2012; Peghin *et al.* 2024).

7. Conclusions

Implantology is a field of medicine that has recently shown quite dynamic development. The number of people receiving solid organ and tissue transplants has increased markedly. After successful organ transplantation, many people with end-stage organ failure can live for a long period of time. The surgical process of transplantation involves the risk of infections, primarily with bacteria and fungi. This is facilitated by the contamination of PF in which an organ is stored, as well as non-compliance with hygiene procedures. The published data regarding the extent of contaminated PF and the bacterial and fungal strains are very diverse and largely depend on the level of the transplantation centers and the procedures they follow. The second area of microbiological danger for transplant recipients is related to the possibility of transmitting mainly viruses and parasites with the transplanted organ. Latent microorganisms like *Mycobacteria* and viruses may be reactivated in the body of a patient subjected to immunosuppression after transplantation. Opinions on the scope and method of antibiotic prophylaxis for organ donors and recipients are divided. Contamination of PF with essentially non-pathogenic microorganisms and their transfer to the organ recipient rarely results in severe infection. How-

ever, post-transplantation infections caused by MDR bacteria should undoubtedly be detected quickly and treated with the appropriate antibiotics.

ORCID

Agnieszka E. Laudy <https://orcid.org/0000-0002-5989-4462>

Stefan Tyski <https://orcid.org/0000-0003-3352-038X>

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

References

1. Abad C.L.R., Deziel P.J., Razonable R.R.: Treatment of latent TB infection and the risk of tuberculosis after solid organ transplantation: Comprehensive review. *Transpl. Infect. Dis.* **21**, e13178 (2019)
2. Aldave A.J., DeMatteo J., Glasser D.B., Tu E.Y., Iliakis B., Nordlund M.L., Misko J., Verdier D.D., Yu F.: Report of the Eye Bank Association of America medical advisory board subcommittee on fungal infection after corneal transplantation. *Cornea*, **32**, 149–1454 (2013)
3. Andacoglu O.M., Greenstein S.M.: Intestinal transplantation. *Mescape*, **March** (2021) <https://emedicine.medscape.com/article/1013245>
4. Audet M., Piardi T., Panaro F., Ghislotti E., Gheza F., Cag M., Jarzembowski T.M., Flicoteaux H., Wolf P., Cinqualbre J.: Incidence and clinical significance of bacterial and fungal contamination of the preservation solution in liver transplantation. *Transpl. Infect. Dis.* **13**, 84–88 (2011)
5. Bachellier P., Addeo P., Saouli A.-C., Woehl-Jaegle M.L., Ellero B., Oussoultzoglou E., Marcellin L.: *Candida albicans* arteritis transmitted by preservation fluid after liver transplantation. *Ann. Transplant.* **19**, 64–67 (2014)
6. Belzer F.O., Ashby B.S., Gulyassy P.F., Powell M.: Successful seventeen-hour preservation and transplantation of human-cadaver kidney. *N. Engl. J. Med.* **278**, 608–610 (1968)
7. Berendsen T., Bruinsma B., Puts C.F., Saeidi N., Usta O.B., Uygun B.E., Izamis M.-L., Toner M., Yarmush M.L., Uygun K.: Supercooling enables long-term transplantation survival following 4 days of liver preservation. *Nat. Med.* **20**, 790–793 (2014)
8. Berry P.S., Rosenberger L.H., Guidry C.A., Agarwal A., Pelletier S., Sawyer R.G.: Intraoperative versus extended antibiotic prophylaxis in liver transplant surgery: a randomized controlled pilot trial. *Liver Transplantation*, **25**, 1043–1053 (2019)
9. Bertrand D., Pallet N., Sartorius A., Zahar J.R., Soussan R.S., Lortholary O., Legendre C., Mamzer M.-F.: Clinical and microbial impact of screening kidney allograft preservative solution for bacterial contamination with high-sensitivity methods. *Transpl. Int.* **26**, 795–799 (2013)
10. Bodro M., Sabé N., Tubau F., Llado L., Baliellas C., Roca J., Cruzado J.M., Carratala J.: Risk factors and outcomes of bacteraemia caused by drug-resistant ESKAPE pathogens in solid-organ transplant recipients. *Transplantation*, **96**, 843–849 (2013)
11. Botta, D.M., Mancini, M.C. Heart transplantation. *Medscape* **June** (2023) <https://emedicine.medscape.com/article/429816>
12. Botterel F., Foulet F., Legrand P., Soria A.-M., Farrugia C., Grimbert P., Matignon M., Lauzet J.-Y., Guerrini P., Bretagne S.: Yeast contamination of kidney, liver and cardiac preservation

- solutions before graft: need for standardization of microbial evaluation. *J. Hosp. Infect.* **76**, 52–55 (2010)
13. Calne R.Y., Pegg D.E., Pryse-Davies J., Brown F.L.: Renal preservation by ice-cooling: an experimental study relating to kidney transplantation from cadavers. *Br. Med. J.* **2**, 651–655 (1963)
 14. Centers for Disease Control and Prevention (CDC): Transmission of *Strongyloides stercoralis* through transplantation of solid organs-Pennsylvania, 2012. *MMWR* **62**, 264–266 (2013)
 15. Cervera C., Van Delden C., Gavalda J., Welte T., Akova M., Carratala J.: Multidrug-resistant bacteria in solid organ transplant recipients. *Clin. Microbiol. Infect.* 2014, **20**(Suppl. 7), 49–73 (2014)
 16. Chaim F.H.M., Boin I.F.S.F., Ataide E.C., Stucchi R.S.B.: Perfusion fluid contamination in relation to recipient survival and acute cellular rejection in orthotopic liver transplantation: retrospective analysis. *Transplant. Proc.* **43**, 1313–1315 (2011)
 17. Chaurasia S., Das S., Roy A.: A review of long-term corneal preservation techniques. *Indian J. Ophthalmol.* **68**, 1357–1363 (2020)
 18. Chu W.: The past twenty-five years in eye banking. *Cornea* **19**, 754–765 (2000)
 19. Collins G.M., Bravo-Shugartman M., Terasaki P.I.: Kidney preservation for transportation. Initial perfusion and 30 h ice storage. *Lancet*, **2**, 1219–1222 (1969)
 20. Collins B.H.: Kidney transplantation. *Medscape*, **December** (2021) <https://emedicine.medscape.com/article/430128>
 21. Colvara Mattana A.M., Rodrigues Marra A., de Oliveira Machado A.M., de Jesus Lopes Filho G., Salzedas Netto A.A., Miziara Gonzalez A.: Evaluation of the presence of microorganisms in solid-organ preservation solution. *Braz. J. Infect. Dis.* **15**, 528–532. (2011)
 22. Corbel A., Ladrière M., Le Berre N., Durin L., Rousseau H., Frimat L., Thilly N., Pulcini C.: Microbiological epidemiology of preservation fluids in transplanted kidney: a nationwide retrospective observational study. *Clin. Microbiol. Infect.* **26**, 475–484 (2020)
 23. Crawford A.Z., Patel D.V., McGhee C.N.: A brief history of corneal transplantation: from ancient to modern. *Oman J. Ophthalmol.* **6**(Suppl. 1), S12–S17 (2013)
 24. Datta S., Fitzpatrick A.M., Haykal S.: Preservation solutions for attenuation of ischemia-reperfusion injury in vascularized composite allotransplantation. *SAGE Open Medicine*, **9**, 1–13 (2021)
 25. Deogaonkar K. and Roy A.: Donor related corneal graft infection: a review of literature and preventive strategies. *Semin. Ophthalmol.* **38**, 219–225 (2023)
 26. Elliott G.D., Wang S., Fuller B.J.: Cryoprotectants: a review of the actions and applications of cryoprotective solutes that modulate cell recovery from ultra-low temperatures. *Cryobiology*, **76**, 74–91 (2017)
 27. European Committee (Partial Agreement) on Organ Transplantation of the Council of Europe (CD-P-TO: Guide to the quality and safety of organs for transplantation. 8th edition. European Directorate for the Quality of Medicines & HealthCare, Council of Europe, Strasbourg, France, 2022
 28. European Eye Bank Association: Past, Present, and Future. <https://eyebankingjournal.org/wp-content/uploads/2015/12/26-339-1-PB.pdf>
 29. European Eye Bank Association – EEBA Technical guidelines for ocular tissue. (2020) https://www.eeba.eu/files/pdf/EEBA_Technical_Guidelines_for_Ocular_Tissue_Revision11.pdf
 30. European Pharmacopoeia 11, 2.6.1. Sterility. (04/201:20601). European Directorate for the Quality of Medicines & HealthCare, Council of Europe, Strasbourg, France, 2023
 31. European Pharmacopoeia 11, 2.6.39. Microbiological Examination of Human Tissues. (01/2023:20639). European Directorate for the Quality of Medicines & HealthCare, Council of Europe, Strasbourg, France, 2023
 32. Eye Bank Association of America (EBAA) 2021. <https://restoresight.org/>
 33. Fabre L., Puyraveau M., Jeanvoine A., Thibaud G., Pizzuto J., Pouthier F., Delbosc B., Gauthier A.S.: Changes of contamination rate and microorganism evaluation in organ-cultured human corneas: a 14-year review from a French Regional Eye Bank. *Cornea* **40**, 696–703 (2021)
 34. Finger E.B., Namsrai B.-E., Rao J.S.: Organ preservation. *Medscape*. **October** (2023) <https://emedicine.medscape.com/article/431140-overview#showall>
 35. Fishman J.A.: Infection in organ transplantation. *Am. J. Transplant.* **17**, 856–879 (2017)
 36. Free R.J., Levi M.E., Bowman J.S., Bixler D., Brooks J.T., Buchacz K., Moorman A., Berger J., Basavaraju S.V.: Updated U.S. Public Health Service guideline for testing of transplant candidates aged <12 years for infection with HIV, Hepatitis B virus, and Hepatitis C virus – United States, *MMWR*, **71**, 844–846 (2022)
 37. Garcia-Zamora C. & Parrilla Paricio P. *et al.*: Clinical significance of contamination of the preservation solution in liver transplantation. *Transplant. Proc.* **47**, 2322–2323 (2015)
 38. Gibbons A., Leung E.H., Yoo S.H.: Cost-effectiveness of antifungal supplementation of corneal cold storage media. *Ophthalmology*, **127**, 582–88 (2020)
 39. Gimenes I., Pintor A.V.B., da Silva Sardinha M., Marañón-Vásquez G.A., Gonzalez M.S., Presgrave O.A.F., Maia L.C., Alves G.G.: Cold storage media versus Optisol-GS in the preservation of corneal quality for keratoplasty: a systematic review. *Appl. Sci.* **12**, 7079 (2022)
 40. Giwa S. & Toner M. *et al.*: The promise of organ and tissue preservation to transform medicine. *Nat. Biotechnol.* **35**, 530–542 (2017)
 41. Grossi P.A.: Donor-derived infections, lessons learnt from the past, and what is the future going to bring us. *Curr. Opin. Organ Transplant.* **23**, 417–422 (2018)
 42. Guibert E.F., Petrenko A.Y., Balaban C.L., Somov A.Y., Rodriguez J.V., Fuller B.J.: Organ preservation: current concepts and new strategies for the next decade. *Transfus. Med. Hemother.* **38**, 125–142 (2011)
 43. Hyun J.H. & Kang J.-M. *et al.*: Changes in tuberculosis risk after transplantation in the setting of decreased community tuberculosis incidence: a national population-based study, 2008–2020. *Ann. Clin. Microbiol. Antimicrob.* **23**, 1 (2024)
 44. Jang T.H., Park S.C., Yang J.H., Kim J.Y., Seok J.H., Park U.S., Choi C.W., Lee S.R., Han J.: Cryopreservation and its clinical applications. *Integr. Med. Res.* **6**, 12–18 (2017)
 45. Jing L., Yao L., Zhao M., Peng L.-P., Liu M.: Organ preservation: from the past to the future. *Acta Pharmacol. Sin.* **39**, 845–857 (2018)
 46. Jones G.L.A., Dekaris I., Hjortdal J., Pels E. European Eye Bank Association: past, present, and future. *Int. J. of Eye Bank.* **1**, 1–6 (2012) <https://eyebankingjournal.org/article/european-eye-bank-association-past-present-future/> <https://www.eeba.eu/home>
 47. Jones J.M., Kracalik I., Levi M.E., Bowman J.S., Berger J.J., Bixler D., Buchacz K., Moorman A., Brooks J.T., Basavaraju S.V.: Assessing solid organ donors and monitoring transplant recipients for Human Immunodeficiency Virus, Hepatitis B virus, and Hepatitis C virus infection – U.S. Public Health Service guideline, 2020. *MMWR Recomm. Rep.* **69**, 1–16 (2020)
 48. Kelly E.J., Oliver M.A., Carney B.C., Shupp J.W.: Infection and burn injury. *Eur. Burn J.* **3**, 165–179 (2022)
 49. Kieslichova E., Protus M., Nemcova D., Uchytlova E.: Single multidrug resistant *Enterobacteriaceae* donor-derived infection

- in four solid organ transplant recipients: a case report. *BMC Surgery*, **19**, 111 (2019)
50. Latchana N., Peck J.R., Whitson B.A., Henry M.L., Elkhammas E.A., Black S.M.: Preservation solutions used during abdominal transplantation: current status and outcomes. *World J. Transplant.* **5**, 154–164 (2015)
 51. Layer N., Cevallos V., Maxwell A.J., Hoover C., Keenan J.D., Jeng B.H.: Efficacy and safety of antifungal additives in Optisol-GS corneal storage medium. *JAMA Ophthalmol.* **132**, 832–837 (2014)
 52. Le Berre N., Ladrrière M., Corbel A., Remen T., Durin L., Frimat L., Thilly N., Pulcini C.: Antibiotic therapy in case of positive cultures of kidney transplant preservation fluid: a nationwide survey of prescribing practices. *Eur. J. Clin. Microbiol. Infect. Dis.* **39**, 915–921 (2020)
 53. Len O., Garzoni C., Lumberras C., Molina I., Meije Y., Pahissa A., Grossi P.: Recommendations for screening of donor and recipient prior to solid organ transplantation and to minimize transmission of donor-derived infections. *Clin. Microbiol. Infect.* **20**(Suppl. 7), 10–18 (2014)
 54. Levesque E., Paugam-Burtz C., Saliba F., Khoy-Ear L., Merle J.-C., Jung B., Stecken L., Ferrandiere M., Mihaila L., Botterel F.: Fungal complications after *Candida* preservation fluid contamination in liver transplant recipients. *Transpl. Int.* **28**, 1308–1316 (2015)
 55. Li G., Zhu H., Ji C., Zang X.: Microbiological contamination in donor corneas preserved for medium-term. *Cell Tissue Bank*, **20**, 379–387 (2019)
 56. Li J. & Wang C. *et al.*: The association of organ preservation fluid pathogens with early infection-related events after kidney transplantation. *Diagnostics*, **12**, 2248. (2022)
 57. Ling M.L.H., Wells M., Petsoglou C., Luo, K., Georges P., Devasahayam R., Hodge C., Trelloggen J., Sutton G., Zhu M.: Factors affecting corneal organ culture contamination: a 6-year study at the New South Wales Tissue Bank. *Cornea*, **38**, 829–835 (2019)
 58. Louart B., Charles C., Nguyen T.-L., Builles N., Roger C., Lefrant J.-Y., Vachieri-Lahaye F., De Vos J., Couderc G., Muller L.: Microbial contamination and tissue procurement location: A conventional operating room is not mandatory. An observational study. *PLoS ONE* **14**, e0210140 (2019)
 59. Malinis M., Boucher H.W.: Screening of donor and candidate prior to solid organ transplantation – guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin. Transplant.* **33**, e13548 (2019)
 60. Malinis M., Koff A.: *Mycobacterium tuberculosis* in solid organ transplant donors and recipients. *Curr. Opin. Organ Transplant.* **26**, 432–439 (2021)
 61. Manuel O., Van den Bogaart L., Mueller N.J., Neofytos D.: Which trial do we need? Culture of preservation fluid in abdominal organ transplant recipients. *Clin. Microbiol. Infect.* **29**, 832–834 (2023)
 62. Manzarbeitia C., Arvelakis A.: Liver transplantation. *Mescape*, April (2022) <https://emedicine.medscape.com/article/431783>
 63. Mathes K.J., Tran K.D., Mayko Z.M., Stoeger C.G., Straiko M.D., Terry M.A.: Reports of post-keratoplasty infections for eye bank prepared and non-eye bank-prepared corneas. *Cornea*, **38**, 263–267 (2019)
 64. Mattner F., Kola A., Fischer S., Becker T., Haverich A., Simon A., Suerbaum S., Gastmeier P., Weissbrodt H., Strüber M.: Impact of bacterial and fungal donor organ contamination in lung, heart-lung, heart and liver transplantation. *Infection*, **36**, 207–212 (2008)
 65. Meier R.P.H. & Berney T. *et al.*: Pancreas preservation fluid microbial contamination is associated with poor islet isolation outcomes – a multi-centre cohort study. *Transpl. Int.* **31**, 917–929 (2018)
 66. Merrill JP, Murray JE, Harrison JH, Guild WR. Successful homotransplantation of the human kidney between identical twins. *JAMA*. **160**, 277–282 (1956)
 67. Mistò R., Giurgola L., Pateri F., Limongelli A., Ragazzi E., D'Amato Tóthová J.: A new storage medium containing amphotericin B versus Optisol-GS for preservation of human donor corneas. *British J. Ophthalmol.* **106**, 184–189 (2020)
 68. Mullane K.M., Dubberke E.R.: AST ID Community of Practice: Management of *Clostridioides* (formerly *Clostridium*) *difficile* infection (CDI) in solid organ transplant recipients: Guidelines from the American Society of Transplantation Community of Practice. *Clin. Transplant.* **33**, e13564 (2019)
 69. Nguyen Van R. & Tattevin P. *et al.*: Characteristics, management, and outcome of tuberculosis after liver transplant: a case series and literature review. *Infect. Dis. Now*, **54**, 104869 (2024)
 70. Oli A.N., Babajide Rowaiye A., Adejumo S.A., Anazodo F.I., Ahmad R., Sinha S., Haque M., Adnan N.: Classic and current opinions in human organ and tissue transplantation. *Cureus*, **14**, e30982 (2022)
 71. ONT-WHO Global Observatory on Donation and Transplantation. <https://www.transplant-observatory.org/summary/>
 72. Oriol I., Lladó L., Vila M., Baliellas C., Tubau F., Sabé N., Fabregat J., Carratalà J.: The etiology, incidence, and impact of preservation fluid contamination during liver transplantation. *PLoS ONE*, **11**, e0160701 (2016)
 73. Oriol I., Sabé N., Tebé C., Veroux M., Boin F.S.F., Carratalà J.: Clinical impact of culture-positive preservation fluid on solid organ transplantation: a systematic review and meta-analysis. *Transplant. Rev.* **32**, 85–91 (2018)
 74. Oriol I. & Carratalà J. *et al.*: The impact of culturing the organ preservation fluid on solid organ transplantation: a prospective multicenter cohort study. *Open Forum Infect. Dis.* **6**, ofz180 (2019)
 75. Ozgur O.S., Namsrai B.-E., Pruett T.L., Bischof J.C., Toner M., Finger E.B., Uygun K.: Current practice and novel approaches in organ preservation. *Front. Transplant.* **2**, 1156845 (2023)
 76. Paolin A., Montagner G., Petit P., Trojan D.: Contamination profile in allografts retrieved from multi tissue donors: longitudinal analysis. *Cell Tissue Bank*, **19**, 809–817 (2018)
 77. Parasuraman R., Julian K., AST Infectious Diseases Community of Practice: Urinary tract infections in solid organ transplantation. *Am. J. Transplant.* **13**(Suppl. 4), 327–336 (2013)
 78. Peghin M., Graziano E., Grossi P.A.: Skin and soft tissue infections in solid organ transplants. *Cur. Opin. Infect. Dis.* **37**, 112–120 (2024)
 79. Petrenko A., Carnevale M., Somov A., Osorio J., Rodríguez J., Guibert E., Fuller B., Froghi F.: Organ preservation into the 2020s: the era of dynamic intervention. *Transfus. Med. Hemother.* **46**, 151–172 (2019)
 80. Pilmis B., Weiss E., Scemla A., Le Monnier A., Grossi P.A., Slavin M.A., Van Delden C., Lortholary O., Paugam-Burtz C., Zahar J.-R.: Multidrug-resistant *Enterobacterales* infections in abdominal solid organ transplantation. *Clin. Microbiol. Infect.* **29**, 38–43 (2023)
 81. Ranghino A., Diena D., Simonato F., Messina M., Burdese M., Piraina V., Fop F., Segoloni G.P., Biancone L.: Clinical impact of bacterial contamination of perfusion fluid in kidney transplantation. *SpringerPlus* **5**, 7 (2016)
 82. Rao J.S., Finger E.B.: Pancreas transplantation. *Mescape* April (2022) <https://emedicine.medscape.com/article/429408>
 83. Reimondez S., Chamorro M.L., Alcaraz A., Segade E.G., Pereyra R., Marari M., Maraschio M.A.: Preservation fluids cultures, clinical significance in liver transplantation. *Medicina (Buenos Aires)*, **81**, 555–558 (2021)

84. Reticker A., Lichvar A., Walsh M., Gross A.E., Patel S.: Research the significance and impact of screening preservation fluid cultures in renal transplant recipients. *Prog. Transplant.* **31**, 40–46 (2021)
85. Röck D., Wude J., Bartz-Schmidt K.U., Yoeruek E., Thaler S., Röck T.: Factors influencing the contamination rate of human organ-cultured corneas. *Acta Ophthalmol.* **95**, e706–e712 (2017)
86. Ruiz P., Gastaca M., Gonzalez J., Hernandez M.J., Ventoso A., Valdivieso A., Montejo M., Ortiz de Urbina J.: Incidence and clinical relevance of bacterial contamination in preservation solution for liver transplantation. *Transplant. Proc.* **41**, 2169–2171 (2009)
87. Saad E.J. & de la Fuente J. *et al.*: Infections in the first year after renal transplant. *Medicina (Buenos Aires)*, **80**, 611–621 (2020)
88. Salehi S., Tran K., Grayson W.L.: Advances in perfusion systems for solid organ preservation. *Yale J. Biol. Med.* **91**, 301–312 (2018)
89. Sauget M., Verdy S., Slekovec C., Bertrand X., Talon D.: Bacterial contamination of organ graft preservation solution and infection after transplantation. *Transpl. Infect. Dis.* **13**, 331–334 (2011)
90. Sawinski D. and Blumberg E.A.: 40 – Infection in renal transplant recipients. (in) *Chronic Kidney Disease, Dialysis, and Transplantation* Ed. J. Himmelfarb, T. Alp Ikizler, Elsevier, 2019, 621–638.e6
91. Sidhu A., Verma G., Humar A., Kumar D.: Outcome of latent tuberculosis infection in solid organ transplant recipients over a 10-year period. *Transplantation*, **98**, 671–675 (2014)
92. Sotiropoulos G.C., Steinmann J., Stern S., Raduenz S., Machairas N., Rath P.M., Saner F.H., Paul A., Gallinat A.: Donor leucocytosis predicts bacterial and fungal contamination of the preservation solution in visceral organ transplantation. *Prog. Transplant.* **28**, 24–28 (2018)
93. Sotiropoulos G.C., Kostakis I.D., Prodromidou A., Garoufalia Z., Stamopoulos P., Machairas N.: Contamination of the preservation solution in solid organ. *Transplant. Proc.* **51**, 392–395 (2019)
94. Southard J.H., Belzer F.O.: Organ preservation. *Annu. Rev. Med.* **46**, 235–247 (1995)
95. Stern S., Bezinover D., Rath P.-M., Paul A., Saner F.H.: *Candida* contamination in kidney and liver organ preservation solution: does it matter? *J. Clin. Med.* **10**, 2022 (2021)
96. Šuca H. & Gál P. *et al.*: Current approaches to wound repair in burns: how far have we come from cover to close? A narrative review. *J. Surg. Res.* **296**, 383–403 (2024)
97. Thareja T., Kowalski R., Kamyar R., Dhaliwal D., Jeng B.H., Tu E.: Fungal infection after keratoplasty and the role of antifungal supplementation to storage solution: a review. *British J. Ophthalmol.* **104**, 1036 (2020)
98. The Nobel Prize in Physiology or Medicine 1990. <https://www.nobelprize.org/prizes/medicine/1990/press-release/>
99. Tran-Dinh A. & Montravers P.: Impact of culture-positive preservation fluid on early morbidity and mortality after lung transplantation. *Transpl. Int.* **36**, 10826 (2023)
100. Tu E.Y.: The rush to supplement: the current case against anti-fungal supplementation of hypothermic corneal storage media. *Cornea*, **40**, 1091–1092 (2021)
101. UK Standards for Microbiology Investigations, Abdominal organ transport fluid testing. Technical, B62, Issue 1, 2020. NIS, PHE. <https://www.rcpath.org/profession/publications/standards-for-microbiology-investigations/bacteriology.html>
102. Veroux M. & Veroux P.: Contamination of preservation fluid in kidney transplantation: single-center analysis. *Transplant. Proc.* **42**, 1043–1045 (2010)
103. Weissenbacher A., Vrakas G., Nasralla D., Ceresa C.D.L.: The future of organ perfusion and re-conditioning. *Transpl. Int.* **32**, 586–597 (2019)
104. Whaley D., Damyar K., Witek R.P., Mendoza A., Alexander M., Lakey J.R., Cryopreservation: an overview of principles and cell-specific considerations. *Cell Transplant.* **30**, 963689721999617 (2021)
105. Whitson, B.A. Lung transplantation. *Mescape*. **April**, 2022. <https://emedicine.medscape.com/article/429499>
106. WHO Fact Sheet, Burns, 2023 <https://www.who.int/news-room/fact-sheets/detail/burns>
107. Yahav D., Manuel O.: Clinical relevance of preservation-fluid contamination in solid-organ transplantation: a call for mounting the evidence. *Clin. Microbiol. Infect.* **25**, 536–537 (2019)
108. Yansouni C.P., Dendukuri N., Liu G., Fernandez M., Frenette C., Paraskevas S., Sheppard D.C.: Positive cultures of organ preservation fluid predict postoperative infections in solid organ transplantation recipients. *Control Hosp. Epidemiol.* **33**, 672–680 (2012)
109. Yong L. & Cai C.-J. *et al.*: Clinical impacts and outcomes with possible donor-derived infection in infected donor liver transplantation: a single-center retrospective study in China. *J. Infect. Dis.* **221**(Suppl. 2), S164–S173 (2020)
110. Yu X. & Chen J. *et al.*: Incidence, distribution and clinical relevance of microbial contamination of preservation solution in deceased kidney transplant recipients: a retrospective cohort study from China. *Clin. Microbiol. Infect.* **25**, 595–600 (2019)
111. Zhang F., Zhong J., Ding H., Liao G.: Effects of preservative fluid associated possible donor-derived carbapenem-resistant *Klebsiella pneumoniae* infection on kidney transplantation recipients. *BMC Nephrology*, **23**, 101 (2022)