Infection Transmission Through Organ Preservation Solutions
A Review

Shrey Sheladiya, MBBS, Shreya Patel, MBBS,* HariOm Vaja, MBBS,**
Ahan Banker, MBBS, and Sahil Patel, MD†*

Abstract: Organ preservation solutions have become vital for successful transplantation, and with the ever-rising number of transplantations yearly, pathogenic contamination poses a significant threat to the recipient, leading to posttransplant infections and complications. Microbial contamination in organ preservation solutions can result in severe infectious complications, increasing recipient mortality rates. Addressing this pressing concern is essential for patient safety and optimal transplant outcomes. Opportunistic infections posttransplantation underscore the need for effective antimicrobial prophylaxis. Among the multidrug-resistant pathogens, the ESKAPE bacteria (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* sp.) present grave challenges, as do fungal infections like candidiasis, aspergillosis, and cryptococcosis. Microbial contamination during organ transplantation significantly elevates infection risks and mortality rates. Maintaining vigilance, adhering to infection control measures, and swift intervention are critical to mitigating these threats and ensuring successful transplant outcomes. Ongoing research is combating antimicrobial resistance and biofilm formation in pathogens. The narrative review aims to bridge knowledge gaps by presenting recent updates and studies, thereby contributing to a comprehensive understanding of preventive strategies and enhanced patient outcomes. Databases, including PubMed and Scopus, were consulted for articles published from 1980 to 2024 in the preparation of this article.

Key Words: organ preservation, transplantation, pathogenic contamination, antimicrobial prophylaxis, ESKAPE bacteria

(*Infect Dis Clin Pract* 2025;33: e1508)

Organ preservation is crucial for transplantation success, allowing safe organ transport and minimizing contamination risks.[1] In 2024, over 48,000 transplants were performed,[2] yet a study by Zhang et al found that 64.5% of preservation solutions were contaminated, increasing transplant failure risks.[3]

Patients with terminal organ failure rely on transplantation for survival. Despite advancements, donor shortages, limited graft viability, and contamination persist as challenges.[4,5] Traditional preservation uses hypothermia, replacing blood with specialized solutions to sustain organ function.[1] The composition of these solutions is critical, driving research into optimal formulations.[1,5]

Posttransplant infections, especially in kidney recipients, pose significant risks due to surgical complications and immunosuppressive therapy. A study reported 77.8% contamination in preservation fluids, increasing infection risks.[6] Early posttransplant infections can originate from preservation fluids, with microbial contamination occurring during procurement or from the donor organ itself.[6]

Organ exchange networks improve donor-recipient matching and mitigate hypoxia-induced damage.[7] However, preservation solutions, intended to protect organs, may also introduce infections, which can impact patient safety and transplant outcomes. A critical review of this balance is essential for optimizing transplantation success. Databases, including PubMed and Scopus, were consulted for articles published from 1980 to 2024 in the preparation of this article.

From the *Civil Hospital, and †Department of Medicine, Civil Hospital, B.J. Medical College, Ahmedabad, Gujarat, India.
Correspondence to: HariOm Vaja, MBBS, Civil Hospital, Department of Medicine, B.J. Medical College, Ahmedabad, Gujarat, India 380016.
E-mail: hariomvajahuman@gmail.com.
The authors have no funding or conflicts of interest to disclose.

ISSN: 1056-9103

ORGAN PRESERVATION SOLUTIONS

Over the past 4 decades, organ preservation has become a cornerstone of modern transplantation, relying on sterile, regulatory-compliant synthetic solutions. These solutions support the preservation of solid organ grafts, including abdominal and cardiothoracic organs, in a standardized manner. The evolution of organ preservation solutions (OPSs) has been driven by a deeper understanding of postextraction organ changes.[8]

OPSs are now routine in organ transplantation but are vital "pseudo drugs." Like pharmaceutical agents, they require rigorous validation and adherence to regulatory standards. This quality assurance ensures the ongoing improvement of OPSs and strengthens their role in successful organ transplantation.[8]

TYPES AND CHARACTERISTICS OF ORGAN PRESERVATION SOLUTIONS (OPS)

Collins and EuroCollins Solutions

The introduction of Collins solution in 1969 marked a significant milestone as the first commercially available preservation solution. It was employed until 1980 to preserve vital organs, including the heart, liver, kidneys, and pulmonary tissues. Subsequent modifications led to the development of EuroCollins, which enhanced the solution by introducing impermeability to its composition, thereby fortifying its quality. This innovation was advantageous in affording superior protection against prolonged periods of cold ischemia, a critical factor in organ preservation.[9]

University of Wisconsin (UW) Solution

The UW solution is widely recognized as the standard for preserving abdominal organs.[10] It contains raffinose, hydroxyethyl starch to prevent edema, lactobionate as an antioxidant, and gluconate with low viscosity.[9] It is primarily used for abdominal organs like the pancreas, improving outcomes with cold storage.[11] A modified version, UW-gluconate, is used in experimental perfusion machines to support hepatic metabolism.[12] Although it has a higher incidence of biliary stenosis compared to solutions like IGL-1 and HTK, the UW solution excels in preserving organs during extended cold ischemia periods.[13]

IGL-1 (Institute George Lopez-1) Solution

The IGL-1 solution, composed of polyethylene glycol (PEG), inverted sodium/potassium content, and low viscosity, is a notable alternative to UW solution.[14] Studies show that it outperforms UW in preventing ATP loss and reducing proteolysis in hepatic tissue, making it an excellent choice for liver preservation. In

kidney preservation, IGL-1 delivers comparable results to UW in graft function, rejection rates, and patient survival.[14–16]

Histidine-Tryptophan-Ketoglutarate (HTK) Solution

Originally developed in the 1970s as a cardioplegic solution for open heart surgery,[17] the HTK solution has evolved to encompass preservation of the liver, kidney, and pancreas.[18,19] It comprises essential components such as histidine, tryptophan, and ketoglutarate, along with sodium chloride, potassium chloride, magnesium chloride, mannitol, and calcium chloride.[20] HTK solution has a multifaceted function with tryptophan acting as a stabilizer, ketoglutarate as an energy source, and histidine as a buffer against pH decline during cold ischemic conditions.[17]

Celsior Solution

Introduced in 1994, the Celsior solution represents an extracellular approach to preservation, effectively utilized for cardiac grafts, lungs, liver, pancreas, kidneys, and small bowel.[21,22] Combining elements from HTK and UW solutions, ie, mannitol and lactobionate, Celsior incorporates impermeants to prevent cellular edema and a free-radical scavenger to enhance preservation. Its unique composition confers a heightened capacity to buffer against acidosis while maintaining lower viscosity compared to UW.[23] Celsior is consisted of mannitol, lactobionate, glutamate, histidine, calcium chloride, potassium chloride, magnesium chloride, sodium hydroxide, and glutathione.[24]

HC-A and HC-A II Solutions

HC-A, a hyperosmolar citrate-based solution, promotes kidney function enhancement, and its high mannitol content serves as an impermeant to reduce cellular edema and mitigate oxidative stress.[14] HC-A II, an iteration of HC-A, incorporates citrate and phosphate buffers, a lower concentration of magnesium, and a higher concentration of adenosine, along with additional substances such as arginine, tryptophan, and ligustrazine to stabilize cell membranes and mitochondrial activity. These solutions have demonstrated effectiveness and safety in kidney preservation comparable to other established solutions such as HTK Solutions.[25]

In essence, although OPS compositions vary, their common goal is to rapidly lower graft temperature, preventing cellular swelling and acidification, thereby improving functionality during reperfusion.[26] These solutions offer distinct benefits and limitations, with some designed for specific organs or regions, whereas others show potential for broader use. For example, the UW solution is highly effective for preserving kidneys and livers, whereas solutions like Celsior, HTK, and Cardiosol, originally designed for thoracic organs, are now being explored for abdominal organ preservation.[27,28]

COMPLICATIONS AFTER TRANSPLANTATIONS

Postsolid organ transplantation, opportunistic infections are a leading cause of morbidity and mortality.[29] The use of potent immunosuppressive regimens has increased vulnerability to infections, particularly bacterial and fungal, often acquired nosocomially through routes like vascular access, drainage systems, endotracheal intubation, or surgical incisions. However, stringent antimicrobial prophylaxis has reduced the incidence of such infections. In a study, 98.4% of positive culture OPS showed no bacterial transmission to recipients who received antibacterial prophylaxis 48 hours posttransplantation.[29]

Infection Risks

Impurities in preservation solutions can significantly increase the risk of infections posttransplantation, raising illness and mortality rates among recipients.[30] Transplant patients are already more vulnerable due to factors like repeated hospitalizations, organ failure, extended pretransplant stays, and immunosuppressive treatments. Preservation solutions, although protecting grafts, can also promote microbial growth, becoming reservoirs of pathogens that may be transmitted to recipients. Contamination can lead to complications ranging from mild to life-threatening.[30] There can be multiple reservoirs of contamination (Fig. 1).

Bacterial Pathogens

Six nosocomial bacterial infections have emerged as particularly concerning due to their multidrug resistance and virulence:

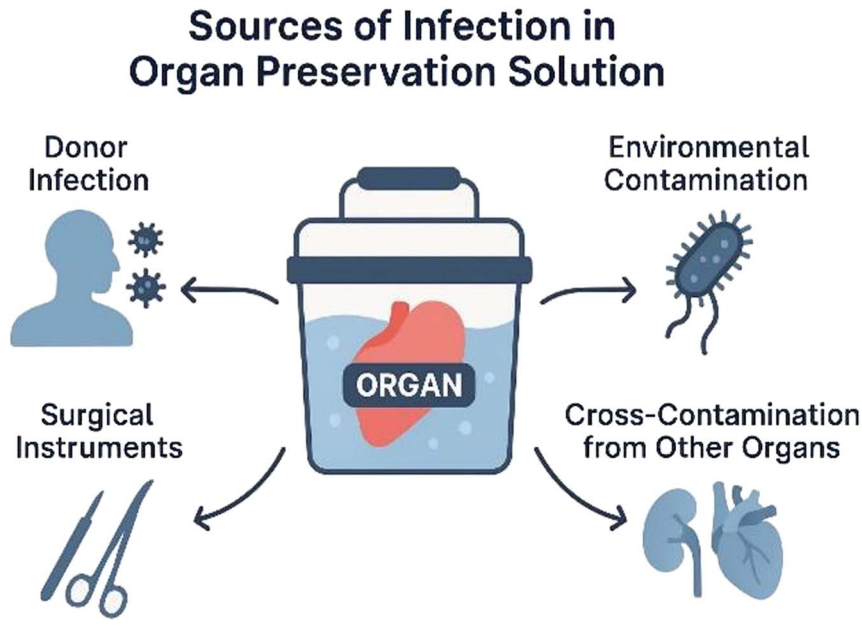

FIGURE 1. Major pathways through which organ preservation solution can become contaminated.

E. faecium, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *Enterobacter* sp. Collectively known by the acronym ESKAPE, these pathogens present a formidable challenge to treatment. The prolonged and widespread use of antibiotics has fueled the evolution of pathogens exhibiting both multidrug and wide drug resistance, rendering even the most potent antimicrobial agents ineffective. Notably, gram-negative bacteria that produce carbapenemase and extended-spectrum β-lactamases (ESBL) have emerged as a significant treatment hurdle.[31] For instance, *E. faecium*, a gram-positive organism normally residing in the human gastrointestinal tract, can cause various infections, including bacteremia, endocarditis, and neonatal meningitis. *S. aureus*, another gram-positive bacterium that colonizes human skin and the upper respiratory tract, can lead to a spectrum of infections ranging from pneumonia to sepsis.[32]

K. pneumoniae, a gram-negative member of the human microbiota found in the skin and digestive system, is associated with infections like respiratory and urinary tract infections, as well as bacteremia and liver abscesses. *A. baumannii*, a common gram-negative bacterium, can induce respiratory and urinary infections. *P. aeruginosa*, another gram-negative pathogen, is responsible for various illnesses, including lung infections (especially in cystic fibrosis patients), urinary tract infections, and skin infections (often in burn injury cases). *Enterobacter*, a genus of gram-negative bacteria that can be commensal in the human gastrointestinal system, has been linked to skin, lung, and urinary tract infections.[32]

Several other bacterial species known to contaminate preservation solutions include *Enterobacteriaceae*, *Propionibacterium*, *Corynebacterium*, *Lactobacillus*, *Streptococcus*, *Peptostreptococcus*, coagulase-negative staphylococci, *Clostridium difficile*, *Pseudomonas*, *Bacillus* sp. (especially *B. cereus*), *Micrococcus*, and more.[33]

Instances of infection demonstrated a marked increase in patients with microbial contamination compared to those in sterile environments.[34] Furthermore, the prevalence of potentially clinically significant donor-derived infections (p-DDIs) was significantly higher in cases where ESKAPE contamination was present, as opposed to other forms of bacterial contamination. Univariate analysis indicated that ESKAPE contamination was associated with an elevated risk of p-DDIs.[35] In recent times, the rise in cases of multidrug resistance (MDR), extensive drug resistance (XDR), and pan-drug resistance (PDR) among infections caused by ESKAPE pathogens has become a growing concern.[36]

In a comprehensive study conducted by Li et al, encompassing data from the years 2015 to 2020 (n = 1395), the prevalence of different pathogens was determined as follows: *Staphylococcus* sp., 35.6%; *Enterococcus* sp., 14.5%; *Klebsiella* sp., 8.4%; *Candida* sp., 8.1%; *Pseudomonas* sp., 6.5%; *Acinetobacter* sp., 4.7%; and *Enterobacteriaceae* sp., 5.3%.[36]

E. faecium

E. faecium, a member of the facultative gram-positive cocci family, commonly resides in the gastrointestinal tract of humans, serving as commensals.[37]

Vancomycin-resistant *Enterococcus* (VRE) stands out as a significant multidrug-resistant nosocomial infection in South India, with prevalence escalating from 6.12% to 19.2% over a period of 3 years.[38] VRE colonization denotes the presence of VRE bacteria within the body without causing an active infection, often preceding a VRE infection. Once established, VRE colonization can persist for extended durations, spanning from months to years.[5,39,40]

VRE infection manifests with diverse clinical presentations, varying in frequency and organ-specific occurrences.[41] Infections attributed to VRE can take on several forms, with surgical site infections and organ/space infections being the most frequently encountered. In the context of solid organ transplant recipients, such as liver, kidney, or thoracic transplants, VRE infections can lead to specific complications:

- Liver transplant recipients may experience VRE-related biliary tract infections and intra-abdominal abscesses.
- Kidney transplant recipients often present with VRE-induced pyelonephritis.
- Thoracic transplant recipients may develop mediastinitis due to VRE infection.

It is noteworthy that surgical site infections associated with VRE can escalate to bloodstream infections.[42]

VRE-induced complications have the potential to seriously impact the transplant procedure's success. Swift identification, appropriate treatment strategies, and unwavering adherence to infection prevention protocols are pivotal in effectively managing VRE infections within these vulnerable patient populations.[43]

S. aureus

S. aureus causes severe infections due to its virulence and toxin production.[44] It colonizes the skin and nares in ~30% of healthy adults but can become invasive if barriers are breached. Its biofilm-forming ability associates it with intravascular catheters, urinary catheters, and endotracheal tubes.[45] Infections range from skin and soft tissue infections to pneumonia, bacteremia, endocarditis, and osteomyelitis.[44]

A meta-analysis revealed that patients colonized with MRSA before transplantation had a 6-fold higher risk of posttransplant MRSA infections, whereas those colonized afterward faced an 11-fold increase. In the pretransplant phase, approximately 8.5% of patients were MRSA-colonized, a prevalence comparable to other high-risk groups like hemodialysis patients.[46] Comparative analysis between individuals infected with methicillin-susceptible *S. aureus* (MSSA) and MRSA has associated MRSA bloodstream infections (BSIs) and surgical site infections (SSIs) with longer median hospital stays, increased hospital expenses, and elevated fatality rates. The exclusion of MRSA from the respiratory system has been linked to decreased survival in cystic fibrosis patients awaiting lung transplants. The impact of this phenomenon, however, can vary based on specific centers, organ types, and the site of infection.[47]

K. pneumoniae

K. pneumoniae is a major cause of healthcare-acquired gram-negative bacteremia, with multidrug-resistant strains at 34.37% prevalence and an overall pooled prevalence of 2%.[48] Antimicrobial resistance, especially in ESBL-producing strains, has risen sharply. High-risk groups include solid-organ transplant (SOT) recipients, chronic liver disease patients, dialysis patients, and cancer patients.[49] SOT recipients, due to organ failure, major surgery, and lifelong immunosuppression, are particularly vulnerable to multidrug-resistant *K. pneumoniae* infections.[50]

Carbapenem-resistant *K. pneumoniae* (CR-Kp) bacteremia can manifest among intestinal and liver transplant recipients.[51] In these cases, CR-Kp infections are frequently associated with various intra-abdominal complications such as abscesses, peritonitis, or biliary infections.

The emergence of carbapenem-resistant strains of *K. pneumoniae* is especially concerning due to their resistance to multiple antibiotics, including carbapenems, which are considered a last-resort treatment option for severe bacterial infections.[51]

The spectrum of infections caused by *K. pneumoniae* is broad, encompassing bacteremia, urinary tract infections, pneumonia, and surgical site infections. Compounding the challenge of managing these infections is their multidrug resistance.[52]

Acinetobacter baumanii

A. baumannii has become a significant concern in recent years due to its resistance to multiple antibiotics.[53,54] *A. baumannii* is known for its ability to persist in the hospital environment and is considered an opportunistic pathogen. It has inherent resistance to certain β-lactam antibiotics. It can also acquire resistance to virtually all available antimicrobial agents.[55]

Carbapenem-resistant *A. baumannii* (categorized as extensively drug-resistant [XDR]) is responsible for an increasing number of nosocomial (hospital-acquired) infections in the United States. They are resistant to all antimicrobial agents except for polymyxins, such as colistin, and tigecycline.[56]

P. aeruginosa

P. aeruginosa, classified as a non–lactose-fermenting gram-negative bacillus, is highly virulent, inherently resistant to certain commonly employed antibiotics, and possesses the capacity to evolve resistance across multiple antibiotic classes.[57–59] Consequently, it gives rise to both acute and chronic infections that can prove fatal, particularly in immunocompromised individuals.

P. aeruginosa holds significant implications for liver transplantation. Among bacteremia liver transplant (LT) recipients, the abdominal/biliary tract and intravascular catheters have emerged as primary portals for *P. aeruginosa* infections. Multiple studies have consistently identified these sources.[59–61] Intra-abdominal infections, including abscesses or peritonitis, can provide a conduit for *P. aeruginosa* to infiltrate the bloodstream, sparking bacteremia in LT recipients. Similarly, the biliary tract, encompassing the bile ducts, stands as another potential wellspring of *P. aeruginosa* infection.

Intravascular catheters, such as central venous catheters or other vascular access devices, can serve as entry points for *P. aeruginosa*. These catheters are routinely employed in LT recipients for a spectrum of purposes, including monitoring, fluid administration, and medication delivery.[59]

Enterobacter Species

In recent times, the emergence of carbapenem-resistant *Enterobacteriaceae* (CRE) has escalated into a public health concern.[62] This development poses a challenge for solid organ transplantation. Being a transplant recipient stands as an independent risk factor for contracting CRE infections.[63] The transplant population embodies several established risk factors for colonization and infection by drug-resistant pathogens, including repeated exposure to broad-spectrum antimicrobials, extensive engagement with healthcare facilities, prolonged hospitalization, intensive care unit exposure, and renal impairment.[64,65]

Infections mainly occur early posttransplantation, with sites varying by organ type.[66] Lung transplants, for instance, are linked to pneumonia, whereas liver transplants are associated with intra-abdominal infections and bacteremia. Similarly, kidney transplant recipients may experience urinary tract infections as a primary source of infection.[67,68]

Fungal Infections

Invasive mycotic infections present a formidable challenge for individuals who have undergone solid organ transplantation (SOT).[69] Predominantly, candidiasis is the most common invasive fungal infection (IFI) in transplanted patients, accounting for 50% to 60% of infections. The second most common IFI is aspergillosis, accounting for 20% to 25% of cases. However, in lung transplant recipients, it accounts for most cases of IFIs. *Cryptococcus* species (6%–7%), the endemic fungi (5%), and many other rare and emerging mycoses cause the remaining infections.[70]

The contamination of preservation fluids by *Candida* species has been linked to significantly elevated mortality. Stern et al investigated 2521 preservation solutions (PSs) and identified fungal contamination in 1.2% (15/1,248) of liver grafts and 0.86% (11/1,273) of renal grafts.[71] Additionally, one patient underwent a combined liver and kidney transplant, where only the liver graft's PS was contaminated. *Candida* species were the most commonly detected fungi in the evaluated PSs.[72] Complications such as mycotic aneurysms and anastomotic rupture have been observed in both kidney and liver grafts.[73,74]

Human skin, the respiratory tract, reproductive organs, and the gastrointestinal system often harbor *Candida* species, particularly *Candida albicans*. Invasive candidiasis typically originates from an endogenous source, commonly the skin or gastrointestinal tract.[75]

Candida parapsilosis has emerged as a pathogen in SOT and is frequently associated with infections related to medical devices. Noteworthy infections among SOT recipients also include *Candida glabrata* (30%) and *Candida krusei* (5%), particularly in individuals with a history of antifungal medication.[75,76]

Aspergillosis can arise as a reactivation of a dormant process, such as colonization or subclinical infection, or as a de novo infection resulting from inhalation of this common mold after transplantation.

Reactivation of latent infection is a central mechanism in diseases like cryptococcosis, histoplasmosis, and coccidioidomycosis. Chronic fungal carriage is a significant concern in cystic fibrosis patients and in unilateral lung transplant recipients before transplantation. These individuals may retain residual lung tissue, aberrant sinuses, and atypical upper respiratory tracts, serving as reservoirs for potentially harmful fungi that can eventually develop into invasive infections.[75,77]

Transplanted organs have been identified as potential reservoirs for various pathogenic fungi. Transmission of a range of pathogenic fungi, such as species of *Histoplasma capsulatum*, *Coccidioides immitis*, and *Scedosporium apiospermum*, in addition to *Candida*, *Aspergillus*, and *Cryptococcus* have been documented.[78–80]

The mortality rate at the 12-month mark stands at approximately 40% for aspergillosis, roughly 34% for candidiasis, and about 27% for cryptococcosis in patients affected by invasive fungal infections attributed to preservation solutions.[69]

Candidiasis

Invasive candidiasis typically follows colonization,[81] with risk factors including colonization intensity, broad-spectrum antibiotics, corticosteroids, diabetes, prolonged ICU stays, and urinary catheters.[82–84] Although colonization precedes infection, it does not always lead to invasive disease, which depends on pathogen virulence and host immune status.

Disruptions in mucosal barriers from catheters, surgery, and immunosuppression contribute to infection.[85] Most cases involve candidemia or intra-abdominal infections, common in abdominal organ transplant recipients.[86,87] Candidemia stems from intestinal translocation or central catheter sites, whereas intra-abdominal candidiasis affects the peritoneum, kidneys, and bile ducts. Candida species appear in ~10% of postoperative liver transplant infections.[88]

Aspergillosis

Aspergillosis can manifest clinically as asymptomatic colonization or as invasive conditions such as sinusitis, tracheobronchitis, invasive pulmonary aspergillosis (IPA), and empyema. Most IPA cases present clinical signs like cough, fever, or pleuritic chest discomfort, rarely leading to acute respiratory collapse.

Tracheobronchial aspergillosis (TBA) affects about 4% to 6% of lung transplant recipients, leading to airway obstruction,

bronchial ulcerations, and pseudomembrane development.[89,90] When bronchial anastomotic infection leads to dehiscence, aggressive coordination of medical and surgical treatments is required.[91,92]

Aside from respiratory conditions, aspergillosis can also result in musculoskeletal disorders, thyroidal diseases, dermal diseases, mediastinitis, rhino cerebral disease, ocular conditions, organ-specific infections, endocarditis, CNS disorders, and disseminated forms. The latter is associated with poor outcomes, with liver transplant recipients being particularly susceptible to widespread illness and CNS involvement.[93,94] Among recipients of liver transplants, disseminated illness prevalence is the highest at 55%.[93] Aspergillosis of the urinary tract has also been linked to transmission via the renal graft.[95,96]

Cryptococcus

Cryptococcosis primarily presents with neurotrophic tendencies, often manifesting as CNS disease such as meningitis or pneumonia.[97] Nonetheless, its impact extends across a spectrum of anatomical domains, including the integumentary system (skin and soft tissues), the prostate gland, hepatic parenchyma, renal parenchyma, osseous structures, and articulating joints.[98] Pulmonary involvement spans from inconspicuous colonization or infection to severe pneumonia resulting in respiratory insufficiency.[99] Radiographic assessments reveal nonspecific findings, such as nodular opacities, masses, and sporadic consolidation or pleural effusions. Isolated pulmonary engagement is observed in about 33% of solid organ transplant (SOT) recipients. The lungs and central nervous system are the primary targets of the disease. In three-quarters of cases, it spreads beyond the lungs, with 61% developing into a systemic form. Mortality rises significantly when the central nervous system is affected, ranging from 17% to 50%.[99,100]

Disseminated disease has been noted in 61% of SOT recipients, with 54% showing pulmonary implications and 8.1% displaying cutaneous, subcutaneous, or osteoarticular manifestations.[98] Liver allograft recipients particularly exhibit a 6-fold increase in susceptibility to disseminated infection compared to other SOT recipients. Fungemia occurs in up to 33% of SOT recipients with cryptococcosis. Patients with CNS involvement have a higher propensity for fungemic status.[98,99,101–103]

Cutaneous cryptococcosis can present as papular, nodular, or ulcerative lesions to cellulitis-like manifestations, often appearing in the lower extremities and commonly coinciding with CNS comorbidities.[104,105] Although cutaneous lesions typically signify hematogenous dissemination, the integumentary environment is recognized as both a potential route of *Cryptococcus* entry and a plausible site for the subsequent dissemination of disease in SOT recipients.[106]

Prevention and Mitigation Strategies

Biofilm-forming ESKAPE pathogens, resistant to antimicrobial treatments, present significant challenges, with biofilms being up to 1000 times less susceptible to antibiotics than planktonic forms.[32] The growing antimicrobial resistance among these pathogens remains a global threat. To combat biofilms, strategies such as antimicrobial peptides, peptoids, bacteriophages, and biofilm growth inhibitors are being explored, although bacterial resistance remains a concern. Combining these with traditional antibiotics, such as using essential oils to enhance antimicrobial effectiveness, shows promise. Phages can also help dismantle biofilm matrices, making them more susceptible to antibiotics. Novel combinations of these approaches are crucial to tackling ESKAPE-biofilm infections.[32]

Fungal infections in transplantation, often due to digestive tract rupture or donor exposure to broad-spectrum antibiotics, are managed with prophylactic fluconazole. For azole-resistant *Candida* infections, liposomal amphotericin B or echinocandins are recommended.[13,14] Early detection through CT scans for endovascular complications like hepatic artery aneurysms is also vital.[74,107,108]

These strategies reflect ongoing efforts to address biofilm-related and fungal infections in organ transplantation. The current standard prevention strategies are depicted in Fig. 2.[109]

CONCLUSIONS

In the realm of organ preservation solutions (OPS), continuous progress is being made to enhance the outcomes of transplantation. The future of OPS lies in innovative strategies such as leveraging cryogenic agents and exploiting hypometabolic pathways found in cold-tolerant organisms. This involves formulating solutions with optimal pharmacokinetics and hormone distribution to effectively mitigate ischemic reperfusion damage.

Another approach involves using hormones as nanocarriers, offering controlled release, stability, and precise targeting. This strategy holds the potential for refining OPS precision and performance. Additionally, integrating micronutrients into preservation fluids offers a unique way to tailor OPS composition, influencing posttransplant organ functionality.

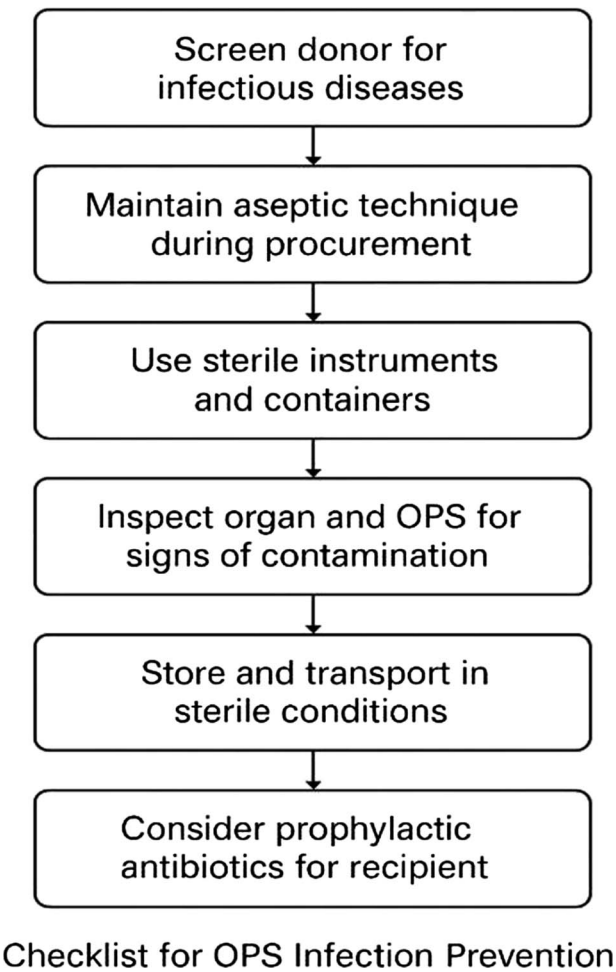

FIGURE 2. Flow chart depicting stepwise preventive strategies for infection prevention in organ preservation solutions.

In conclusion, the future of OPS is dependent on advancements in cryogenic agents, hormone nanocarriers, and micronutrient integration. These avenues offer hope for reducing ischemic reperfusion injury and revolutionizing organ transplantation. As research progresses, these approaches could reshape the landscape of OPS, optimizing the success of organ transplantation.

REFERENCES

1. Southard JH, Belzer FO. Organ preservation. *Annu Rev Med*. 1995;46: 235–247.
2. HRSA. Organ donation statistics. Health Resources & Service Administration. March 2023. Available at: https://www.organdonor.gov/learn/organ-donation-statistics. Accessed July 6, 2023.
3. Zhang F, Wang W, Zhong J, et al. Effect of preservation fluid contamination and associated possible donor-derived infections on early postoperative prognosis in kidney transplant recipients. *BMC Microbiol*. 2024;24(1):189.
4. Grinyó JM. Why is organ transplantation clinically important? *Cold Spring Harb Perspect Med*. 2013;3(6):a014985.
5. Ostróżka-Cieślik A, Dolińska B. Pharmacological benefits and risk of using hormones in organ perfusion and preservation solutions in the aspect of minimizing hepatic ischemia-reperfusion injury during storage. *Biomed Res Int*. 2019;2019:1–16.
6. Yahav D, Manuel O. Clinical relevance of preservation-fluid contamination in solid-organ transplantation: a call for mounting the evidence. *Clin Microbiol Infect*. 2019;25(5):536–537.
7. Guibert EE, Petrenko AY, Balaban CL, et al. Organ preservation: current concepts and new strategies for the next decade. *Transfus Med Hemother*. 2011;38(2):125–142.
8. Fuller B, Froghi F, Davidson B. Organ preservation solutions: linking pharmacology to survival for the donor organ pathway. *Curr Opin Organ Transplant*. 2018;23(3):361–368.
9. Jing L, Yao L, Zhao M, et al. Organ preservation: from the past to the future. *Acta Pharmacol Sin*. 2018;39(5):845–857.
10. Dholakia S, Royston E, Sharples EJ, et al. Preserving and perfusing the allograft pancreas: past, present, and future. *Transplant Rev (Orlando)*. 2018;32(3):127–131.
11. Hamada E, Ebi N, Miyagi-Shiohira C, et al. Comparison between modified extracellular-type trehalose-containing Kyoto solution and University of Wisconsin solution in 18-hour pancreas preservation for islet transplantation. *Pancreas*. 2018;47(7):e46–e47.
12. Burra P, Zanetto A, Russo F, et al. Organ preservation in liver transplantation. *Semin Liver Dis*. 2018;38(03):260–269.
13. Mangus RS, Schroering JR, Hathaway TJ, et al. Comparison of histidine-tryptophan-ketoglutarate and University of Wisconsin preservation solutions in pediatric liver transplantation. *Pediatr Transplant*. 2018;e13252. Published online June 15, 2018. doi:10.1111/petr.13252.
14. Chen Y, Shi J, Xia TC, et al. Preservation solutions for kidney transplantation: history, advances and mechanisms. *Cell Transplant*. 2019;28(12):1472–1489.
15. Zaouali MA, Panisello-Roselló A, Lopez A, et al. Relevance of proteolysis and proteasome activation in fatty liver graft preservation: an Institut Georges Lopez-1 vs University of Wisconsin appraisal. *World J Gastroenterol*. 2017;23(23):4211–4221.
16. Giraud S, Thuillier R, Codas R, et al. The optimal PEG for kidney preservation: a preclinical porcine study. *Int J Mol Sci*. 2018;19(2):454.
17. Bretschneider H. Myocardial protection. *Thorac Cardiovasc Surg*. 1980; 28(05):295–302.
18. Gubernatis G, Pichlmayr R, Lamesch P, et al. HTK-solution (Bretschneider) for human liver transplantation. *Langenbecks Arch Chir*. 1990;375(2):66–70.
19. Lindell SL, Gandolph D, Southard JH, et al. Comparison of PBS, HTK, and UW solutions for kidney preservation. *Transplant Proc*. 1991;23(5): 2399–2401.
20. Sakwa M. Custodiol-HTK (Histidine-Tryptophan-Ketoglutarate) Solution as a Cardioplegic Agent. Full Text View. ClinicalTrials.gov. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT01681095. Accessed January 1, 2023.
21. Karam G, Compagnon P, Hourmant M, et al. A single solution for multiple organ procurement and preservation. *Transpl Int*. 2005;18(6):657–663.
22. Jovine E, Di Benedetto F, Quintini C, et al. Procurement technique for isolated small bowel, pancreas, and liver from multiorgan cadaveric donor. *Transplant Proc*. 2002;34(3):904–905.
23. Menasche P, Termignon JL, Pradier F, et al. Experimental evaluation of Celsior, a new heart preservation solution. *Eur J Cardiothorac Surg*. 1994; 8(4):207–213.
24. Thatte HS, Rousou L, Hussaini BE, et al. Development and evaluation of a novel solution, Somah, for the procurement and preservation of beating and nonbeating donor hearts for transplantation. *Circulation*. 2009; 120(17):1704–1713.
25. Zhu Y. A new HC-A II solution for kidney preservation: a multi-center randomized controlled trial in China. *Ann Transplant*. 2014;19: 614–620.
26. Schreinemachers MCJM, Doorschodt BM, Florquin S, et al. Comparison of preservation solutions for washout of kidney grafts: an experimental study. *Transplant Proc*. 2009;41(10):4072–4079.
27. Voigt MR, DeLario GT. Perspectives on abdominal organ preservation solutions: a comparative literature review. *Prog Transplant*. 2013;23(4): 383–391.
28. Taylor MJ, Baicu SC. Current state of hypothermic machine perfusion preservation of organs: the clinical perspective. *Cryobiology*. 2010;60(3): S20–S35.
29. Ruiz P, Gastaca M, Gonzalez J, et al. Incidence and clinical relevance of bacterial contamination in preservation solution for liver transplantation. *Transplant Proc*. 2009;41(6):2169–2171.
30. Sotiropoulos GC, Kostakis ID, Prodromidou A, et al. Contamination of the preservation solution in solid organ transplantation. *Transplant Proc*. 2019;51(2):392–395.
31. Mulani MS, Kamble EE, Kumkar SN, et al. Emerging strategies to combat ESKAPE pathogens in the era of antimicrobial resistance: a review. *Front Microbiol*. 2019;10:539.
32. Panda SK, Buroni S, Swain SS, et al. Recent advances to combat ESKAPE pathogens with special reference to essential oils. *Front Microbiol*. 2022;13:1029098.
33. Sauget M, Verdy S, Slekovec C, et al. Bacterial contamination of organ graft preservation solution and infection after transplantation. *Transpl Infect Dis*. 2011;13(4):331–334.
34. Wendt JM, Kaul D, Limbago BM, et al. Transmission of methicillin-resistant *Staphylococcus aureus* infection through solid organ transplantation: confirmation via whole genome sequencing. *Am J Transplant*. 2014;14(11):2633–2639.
35. Yu X, Wang R, Peng W, et al. Incidence, distribution and clinical r elevance of microbial contamination of preservation solution in deceased kidney transplant recipients: a retrospective cohort study from China. *Clin Microbiol Infect*. 2019;25(5):595–600.
36. Li J, Su X, Li J, et al. The association of organ preservation fluid pathogens with early infection-related events after kidney transplantation. *Diagnostics (Basel)*. 2022;12(9):2248.
37. Krawczyk B, Wityk P, Gałęcka M, et al. The many faces of *Enterococcus* spp.—commensal, probiotic and opportunistic pathogen. *Microorganisms*. 2021;9(9):1900.
38. Gunalan A, Sivaradjy M, Priyadarshi K, et al. Increasing trend of vancomycin-resistant enterococci bacteremia in a tertiary care hospital

of South India: a three-year prospective study. *Indian J Crit Care Med*. 2021;25(8):881–885.

39. Hayden MK. Insights into the epidemiology and control of infection with vancomycin-resistant enterococci. *Clin Infect Dis*. 2000;31(4): 1058–1065.
40. Ziakas PD, Pliakos EE, Zervou FN, et al. MRSA and VRE colonization in solid organ transplantation: a Meta-analysis of published studies. *Am J Transplant*. 2014;14(8):1887–1894.
41. O'Driscoll T, Crank CW. Vancomycin-resistant enterococcal infections: epidemiology, clinical manifestations, and optimal management. *Infect Drug Resist*. 2015;8:217–230.
42. Gold HS. Vancomycin-resistant enterococci: mechanisms and clinical observations. *Clin Infect Dis*. 2001;33(2):210–219.
43. Contreras GA, Munita JM, Arias CA. Novel strategies for the management of vancomycin-resistant enterococcal infections. *Curr Infect Dis Rep*. 2019;21(7):22.
44. Bennett J, Dolin R, Blaser M. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. *In: Seventh Elsevier*. 2020;2564.
45. Lee AS, De Lencastre H, Garau J, et al. Methicillin-resistant *Staphylococcus aureus*. *Nat Rev Dis Primers*. 2018;4:18033.
46. Pereira MR, Rana MM, AST ID Community of Practice. Methicillin-resistant *Staphylococcus aureus* in solid organ transplantation—Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33(9):e13611.
47. Dasenbrook EC. Association between respiratory tract methicillin-resistant *Staphylococcus aureus* and survival in cystic fibrosis. *JAMA*. 2010;303(23):2386–2392.
48. Bhattacharya C, Das-Mondal M, Gupta D, et al. Infection in cirrhosis: a prospective study. *Ann Hepatol*. 2019;18(6):862–868.
49. Meng F, Zhu C, Zhu C, et al. Epidemiology and pathogen characteristics of infections following solid organ transplantation. *J Appl Microbiol*. 2024;135(12):lxae292.
50. Linares L, Cervera C, Cofán F, et al. Epidemiology and outcomes of multiple antibiotic–resistant bacterial infection in renal transplantation. *Transplant Proc*. 2007;39(7):2222–2224.
51. Clancy CJ, Chen L, Shields RK, et al. Epidemiology and molecular characterization of bacteremia due to carbapenem-resistant *Klebsiella pneumoniae* in transplant recipients. *Am J Transplant*. 2013;13(10): 2619–2633.
52. Wu D, Huang X, Jia C, et al. Clinical manifestation, distribution, and drug resistance of pathogens among abdominal solid organ transplant recipients with *Klebsiella pneumoniae* infections. *Transplant Proc*. 2020; 52(1):289–294.
53. Falagas ME, Karveli EA, Siempos II, et al. *Acinetobacter* infections: a growing threat for critically ill patients. *Epidemiol Infect*. 2008;136(8): 1009–1019.
54. Giamarellou H, Antoniadou A, Kanellakopoulou K. *Acinetobacter baumannii*: a universal threat to public health? *Int J Antimicrob Agents*. 2008;32(2):106–119.
55. Mak JK, Kim MJ, Pham J, et al. Antibiotic resistance determinants in nosocomial strains of multidrug-resistant *Acinetobacter baumannii*. *J Antimicrob Chemother*. 2009;63(1):47–54.
56. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48(1):1–12.
57. McGowan JE Jr. Resistance in nonfermenting gram-negative bacteria: multidrug resistance to the maximum. *Am J Med*. 2006;119(6 Suppl 1): S29–S70.
58. Bonomo RA, Szabo D. Mechanisms of multidrug resistance in *Acinetobacter* species and *Pseudomonas aeruginosa*. *Clin Infect Dis*. 2006;43(Suppl 2):S49–S56.
59. Liu T, Zhang Y, Wan Q. Pseudomonas aeruginosa bacteremia among liver transplant recipients. *Infect Drug Resist*. 2018;11:2345–2356.
60. Kim HK, Park YK, Wang HJ, et al. Epidemiology and clinical features of post-transplant bloodstream infection: an analysis of 222 consecutive liver transplant recipients. *Infect Chemother*. 2013;45(3):315–324.
61. Hashimoto M, Sugawara Y, Tamura S, et al. Bloodstream infection after living donor liver transplantation. *Scand J Infect Dis*. 2008;40(6–7): 509–516.
62. Pilmis B, Weiss E, Scemla A, et al. Multidrug-resistant Enterobacterales infections in abdominal solid organ transplantation. *Clin Microbiol Infect*. 2023;29(1):38–43.
63. Patel G, Huprikar S, Factor SH, et al. Outcomes of carbapenem-resistant *Klebsiella pneumoniae* infection and the impact of antimicrobial and adjunctive therapies. *Infect Control Hosp Epidemiol*. 2008;29(12): 1099–1106.
64. Moreno Camacho A, Ruiz Camps I. Infección nosocomial en el paciente receptor de un trasplante de órgano sólido o de precursores hematopoyéticos. *Enferm Infecc Microbiol Clin*. 2014;32(6):386–395.
65. Schwaber MJ, Klarfeld-Lidji S, Navon-Venezia S, et al. Predictors of Carbapenem-resistant *Klebsiella pneumoniae* acquisition among hospitalized adults and effect of acquisition on mortality. *Antimicrob Agents Chemother*. 2008;52(3):1028–1033.
66. Lanini S, Costa AN, Puro V, et al. Incidence of carbapenem-resistant gram negatives in Italian transplant recipients: a nationwide surveillance study. *PLoS ONE*. 2015;10(4):e0123706.
67. Aguado JM, Silva JT, Fernández-Ruiz M, et al. Management of multidrug resistant gram-negative bacilli infections in solid organ transplant recipients: SET/GESITRA-SEIMC/REIPI recommendations. *Transplant Rev*. 2018;32(1):36–57.
68. Satlin MJ, Jenkins SG, Walsh TJ. The global challenge of Carbapenem-resistant *Enterobacteriaceae* in transplant recipients and patients with hematologic malignancies. *Clin Infect Dis*. 2014;58(9):1274–1283.
69. Shoham S, Marr KA. Invasive fungal infections in solid organ transplant recipients. *Future Microbiol*. 2012;7(5):639–655.
70. Senoner T, Breitkopf R, Treml B, et al. Invasive fungal infections after liver transplantation. *J Clin Med*. 2023;12(9):3238.
71. Stern S, Bezinover D, Rath PM, et al. *Candida* contamination in kidney and liver organ preservation solution: does it matter? *J Clin Med*. 2021; 10(9):2022.
72. Cerutti E, Stratta C, Romagnoli R, et al. Bacterial- and fungal-positive cultures in organ donors: clinical impact in liver transplantation. *Liver Transpl*. 2006;12(8):1253–1259.
73. Mai H, Champion L, Ouali N, et al. *Candida albicans* arteritis transmitted by conservative liquid after renal transplantation: a report of four cases and review of the literature. *Transplantation*. 2006;82(9):1163–1167.
74. Levesque E, Suet G, Merle JC, et al. Candida vascular complication in a liver transplant recipient due to yeast contamination of preservation solution. *Transpl Infect Dis*. 2014;16(5):827–829.
75. Neofytos D, Fishman JA, Horn D, et al. Epidemiology and outcome of invasive fungal infections in solid organ transplant recipients. *Transpl Infect Dis*. 2010;12(3):220–229.
76. Lockhart SR, Wagner D, Iqbal N, et al. Comparison of in vitro susceptibility characteristics of *Candida* species from cases of invasive candidiasis in solid organ and stem cell transplant recipients: Transplant-Associated Infections Surveillance Network (TRANSNET), 2001 to 2006. *J Clin Microbiol*. 2011;49(7):2404–2410.
77. Pappas PG, Alexander BD, Andes DR, et al. Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). *Clin Infect Dis*. 2010; 50(8):1101–1111.
78. Wong SY, Allen DM. Transmission of disseminated histoplasmosis via cadaveric renal transplantation: case report. *Clin Infect Dis*. 1992;14(1): 232–234.
79. Wright PW, Pappagianis D, Wilson M, et al. Donor-related coccidioidomycosis in organ transplant recipients. *Clin Infect Dis*. 2003; 37(9):1265–1269.

80. Van Der Vliet JA, Tidow G, Kootstra G, et al. Transplantation of contaminated organs. *Br J Surg*. 1980;67(8):596–598.
81. Tavanti A, Lupetti A, Ghelardi E, et al. Molecular monitoring of *Candida albicans* infections in liver transplant recipients. *Eur J Clin Microbiol Infect Dis*. 2001;20(8):544–553.
82. Bendel CM, Wiesner SM, Garni RM, et al. Cecal colonization and systemic spread of *Candida albicans* in mice treated with antibiotics and dexamethasone. *Pediatr Res*. 2002;51(3):290–295.
83. Charles PE, Dalle F, Aube H, et al. *Candida* spp. colonization significance in critically ill medical patients: a prospective study. *Intensive Care Med*. 2005;31(3):393–400.
84. Bartholomew GA, Rodu B, Bell DS. Oral candidiasis in patients with diabetes mellitus: a thorough analysis. *Diabetes Care*. 1987;10(5):607–612.
85. Shoham S, Marwaha S. Invasive fungal infections in the ICU. *J Intensive Care Med*. 2010;25(2):78–92.
86. Florescu DF, Islam KM, Grant W, et al. Incidence and outcome of fungal infections in pediatric small bowel transplant recipients. *Transpl Infect Dis*. 2010;12(6):497–504.
87. Gladdy RA, Richardson SE, Davies HD, et al. Candida infection in pediatric liver transplant recipients. *Liver Transpl*. 1999;5(1):16–24.
88. Reid GE, Grim SA, Sankary H, et al. Early intra-abdominal infections associated with orthotopic liver transplantation. *Transplantation*. 2009; 87(11):1706–1711.
89. Fernández-Ruiz M, Silva JT, San-Juan R, et al. *Aspergillus* tracheobronchitis: report of 8 cases and review of the literature. *Medicine (Baltimore)*. 2012;91(5):261–273.
90. Kramer MR, Denning DW, Marshall SE, et al. Ulcerative tracheobronchitis after lung transplantation: a new form of invasive aspergillosis. *Am Rev Respir Dis*. 1991;144(3 Pt 1):552–556.
91. Segal BH. Aspergillosis. *N Engl J Med*. 2009;360(18):1870–1884.
92. Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;63(4):e1–e60.
93. Husain S, Silveira FP, Azie N, et al. Epidemiological features of invasive mold infections among solid organ transplant recipients: PATH Alliance® registry analysis. *Med Mycol*. 2017;55(3):269–277.
94. Gavalda J, Len O, San Juan R, et al. Risk factors for invasive aspergillosis in solid-organ transplant recipients: a case-control study. *Clin Infect Dis*. 2005;41(1):52–59.
95. Keating MR, Guerrero MA, Daly RC, et al. Transmission of invasive aspergillosis from a subclinically infected donor to three different organ transplant recipients. *Chest*. 1996;109(4):1119–1124.
96. Mueller NJ, Weisser M, Fehr T, et al. Donor-derived aspergillosis from use of a solid organ recipient as a multiorgan donor. *Transpl Infect Dis*. 2010; 12(1):54–59.
97. Mueller NJ, Fishman JA. Asymptomatic pulmonary cryptococcosis in solid organ transplantation: report of four cases and review of the literature. *Transpl Infect Dis*. 2003;5(3):140–143.
98. Paterson DL, Singh N, Gayowski T, et al. Pulmonary nodules in liver transplant recipients. *Medicine (Baltimore)*. 1998;77(1):50–58.
99. Singh N, Alexander BD, Lortholary O, et al. Pulmonary cryptococcosis in solid organ transplant recipients: clinical relevance of serum cryptococcal antigen. *Clin Infect Dis*. 2008;46(2):e12–e18.
100. Díaz-Ramírez GS, Martínez-Casas OY, Marín-Zuluaga JI, et al. Disseminated cryptococcosis after liver transplant: a case report. *Exp Clin Transplant*. 2020;18(3):402–406.
101. Husain S, Wagener MM, Singh N. *Cryptococcus neoformans* infection in organ transplant recipients: variables influencing clinical characteristics and outcome. *Emerg Infect Dis*. 2001;7(3):375–381.
102. Wu G, Vilchez RA, Eidelman B, et al. Cryptococcal meningitis: an analysis among 5521 consecutive organ transplant recipients. *Transpl Infect Dis*. 2002; 4(4):183–188.
103. Singh N, Lortholary O, Dromer F, et al. Central nervous system cryptococcosis in solid organ transplant recipients: clinical relevance of abnormal neuroimaging findings. *Transplantation*. 2008;86(5): 647–651.
104. Sun HY, Alexander BD, Lortholary O, et al. Cutaneous cryptococcosis in solid organ transplant recipients. *Med Mycol*. 2010;48(6):785–791.
105. Horrevorts AM, Huysmans FTM, Koopman RJJ, et al. Cellulitis as first clinical presentation of disseminated cryptococcosis in renal transplant recipients. *Scand J Infect Dis*. 1994;26(5):623–626.
106. Neuville S, Dromer F, Morin O, et al. Primary cutaneous cryptococcosis: a distinct clinical entity. *Clin Infect Dis*. 2003;36(3):337–347.
107. Singh N, Huprikar S, Burdette SD, et al. Donor-derived fungal infections in organ transplant recipients: guidelines of the American Society of Transplantation, Infectious Diseases Community of Practice. *Am J Transplant*. 2012;12(9):2414–2428.
108. Albano L, Bretagne S, Mamzer-Bruneel M, et al. Evidence that graft-site candidiasis after kidney transplantation is acquired during organ recovery: a multicenter study in France. *Clin Infect Dis*. 2009;48(2): 194–202.
109. Pergam SA. Infection prevention in transplantation. *Curr Infect Dis Rep*. 2016;18(2):7.