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Fecal microbiota transplantation in transplant patients for C. difficile infection and beyond

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Solid organ transplantation (SOT) is an important treatment for a large number of patients with end-stage liver disease or end-stage renal disease. Although improved surgical techniques, potent immunosuppressive drugs, and anti-infective prophylaxis substantially improved transplant outcome, SOT recipients still suffer from rejections, infections, and immunosuppressive-specific adverse effects. Recently, increasing evidence has suggested that human microbiome contributes to the pathophysiology and treatment outcome of a variety of diseases. Gut microbiome has been known to be associated with the survival of patients undergoing hematopoietic stem cell transplantation (HCT). However, changes in gut microbiota populations, the resulting physiologic impact and associated outcomes in SOT recipients has not yet been extensively studied. The microbiome in SOT recipients are characterized by a low microbial diversity, viral infections, *Clostridioides difficile* infections (CDI), as well as by increased colonization by multidrug-resistant bacteria. The risk of developing CDI in SOT recipients is five times higher compared to the general population with an estimated annual incidence of CDI after SOT to range from 2.5% to 22.9%. Treatment guidelines published in 2018 recommend using oral vancomycin or fidaxomicin for an initial episode of CDI, with metronidazole as an option for patients unable to obtain the former options. However, there are no specific recommendations for CDI treatment in immunocompromised patients, likely due to rarity of data. Fecal microbiota transplantations (FMTs) are increasingly being performed in clinical practice to restore the physiological composition of the gut microbiota. FMT has become a standard treatment for recurrent CDI and it is associated with a cure rate of >90%. In addition, FMT could be an option in immunocompromised patients who fail to respond to standard antibiotic treatment, based on limited published studies. However, larger studies are required to evaluate the short and long-term safety, especially in terms of the possibility of infectious exposures. Beyond CDIs, FMT is currently investigated in many other diseases associated with gut dysbiosis. Analyses of fecal specimens taken from recipients of allogenic HCT around the time of engraftment have shown that reduced microbial diversity is associated with significantly worse survival outcomes such as acute graft-versus-host disease (GVHD) and disease relapse. Based on these recent advances in the field, several interventional studies are ongoing that will alter

microbiota by means of diet and prebiotics, antibiotics, probiotics, microbial metabolites, and FMT. Although the evidence to support the effectiveness of FMT in treating GVHD is very limited and to this date is comprised of only case series, preliminary reports and studies of FMT in allogenic HCT recipients suggest that it is safe, feasible, and associated with promising efficacy in multiple clinical settings. However, there are many unanswered questions regarding FMT, including identification of the best FMT donors, appropriate donor screening before FMT in immunocompromised patients, long-term safety, and regulatory issues. In addition, more research is needed to elucidate the multiple mechanisms by which FMT can reset the intestinal microenvironment after allogenic HCT and to provide clarity regarding the appropriate clinical indications for FMT in this specific population.