7. Post-transplant Infection Considerations

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7.1 Viral

7.1.1 Cytomegalovirus

Manuel O, et al. (2024). Immune Monitoring-Guided Versus Fixed Duration of Antiviral Prophylaxis Against Cytomegalovirus in Solid-Organ Transplant Recipients: A Multicenter, Randomized Clinical Trial. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 78(2), 312–323. https://academic.oup.com/cid/article/78/2/312/7280465

- Randomized trial comparing CMV prophylaxis based on immune monitoring vs. fixed duration

Kleiboeker H, et al. (2024). Resource Use and Financial Impact of Oral Step-Down Therapy for Resistant Cytomegalovirus in Solid Organ Transplant Recipients. Transplantation proceedings, S0041-

1345(24)00061-7. Advance online publication. https://www.sciencedirect.com/science/article/abs/pii/S0041134524000617?via%3Dihub

- Case-series of patients receiving PO stepdown therapy to maribavir or letermovir from foscarnet

Kotton CN, et al. (2023). Slaying the "Troll of Transplantation"-new frontiers in cytomegalovirus management. A report from the CMV International Symposium 2023. Transplant infectious disease: an official journal of the Transplantation Society, e14183. Advance online publication. https://onlinelibrary.wiley.com/doi/10.1111/tid.14183

- A revitalized review article suggesting that current practices of CMV management is still complicated, despite new medications that have improved patient outcomes. Complicating factors include indirect effects of CMV, late onset viremia after prophylaxis, and CMV vaccination.

Walti CS, et al. (2023). New Treatment Options for Refractory/Resistant CMV Infection. Transplant international: official journal of the European Society for Organ Transplantation, 36, 11785. https://pubmed.ncbi.nlm.nih.gov/37901297/

- Review article looking at 30 published studies for novel treatment options for resistant/refractory CMV infection, primarily letermovir, maribavir, and T cell therapy.

Reischig T, et al. (2023). A Randomized Trial of Valganciclovir Prophylaxis Versus Preemptive Therapy in Kidney Transplant Recipients. Journal of the American Society of Nephrology: JASN, 34(5), 920–934. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10125645/

- Single center randomized trial comparing valganciclovir prophylaxis vs preemptive therapy in kidney transplant recipients. Incidence of acute rejection was lower in the valganciclovir group than with preemptive therapy (13% vs 23%) but was deemed not statistically significant. Preemptive therapy resulted in significantly higher incidences of CMV DNAemia (44% vs 75%, $p < 0.001$), but significantly lower rates of neutropenia

Limaye AP, et al (2023). Letermovir vs Valganciclovir for Prophylaxis of Cytomegalovirus in High-Risk Kidney Transplant Recipients: A Randomized Clinical Trial. JAMA, 330(1), 33–42. https://pubmed.ncbi.nlm.nih.gov/37279999/

- A randomized, double dummy non-inferiority phase 3 trial comparing the safety and efficacy of letermovir 480mg daily to valganciclovir 900 mg once daily for post-transplant CMV prophylaxis in kidney transplant recipients. Letermovir was found to be noninferior to valganciclovir through 52 weeks of follow up for the prevention of CMV viremia (10.4% vs 11.8%). Letermovir was also found to have a lower rate of leukopenia and neutropenia (26% vs 64%).

Doss KM, et al (2023). Real-world effectiveness of preemptive therapy (PET) for cytomegalovirus (CMV) disease prevention in CMV high-risk donor seropositive/recipient seronegative (D+R-) liver transplant recipients (LTxR). Transplant infectious disease: an official journal of the Transplantation Society, 25(2), e14015. https://pubmed.ncbi.nlm.nih.gov/36734631/

- Single center, real world retrospective analysis of 50 CMV D+/R- liver transplant recipients receiving preemptive therapy (PET) compared to 100 LTR receiving PET in the CAPSIL study. Prevention of CMV disease between both cohorts were similar, suggesting feasibility of PET in a real world setting.

Avery RK, et al. (2022). Maribavir for Refractory Cytomegalovirus Infections With or Without Resistance Post-Transplant: Results From a Phase 3 Randomized Clinical Trial. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 75(4), 690–701. https://academic.oup.com/cid/article/75/4/690/6448443

- Open-label study that looked at HSCT and SOT recipients receiving either maribavir 400mg BID or investigator-assigned therapy. Primary endpoint was clearance of CMV and symptom control by week 8, maintained through week 16. Maribavir was superior to investigator assigned therapy for clearance of CMV viremia and symptom control, alongside fewer treatment discontinuations.

Jorgenson MR, et al. (2022). Letermovir conversion after valganciclovir treatment in cytomegalovirus high-risk abdominal solid organ transplant recipients may promote development of cytomegalovirus-specific cell mediated immunity. Transpl Infect Dis. 2022 Feb;24(1):e13766. doi: 10.1111/tid.13766. https://pubmed.ncbi.nlm.nih.gov/34799964/

- Retrospective case series of kidney and liver transplant patients who were converted to letermovir 480 mg daily after treatment of symptomatic, high-level CMV viremia with ganciclovir-derivatives for a minimum of 4 weeks. Cell-mediated immunity (CMI) via ICS assay by flow cytometry found patients exhibited CMV-specific CMI after conversion to letermovir monotherapy. No patient had progressive replication or breakthrough disease while maintained on letermovir and three patients (42.9%) underwent antiviral withdrawal without recurrence at the last follow-up.

Jorgenson MR, et al. (2022). Cytomegalovirus antiviral stewardship in solid organ transplant recipients: A new gold standard. Transpl Infect Dis. 2022 Oct;24(5):e13864. https://pubmed.ncbi.nlm.nih.gov/35603982/

- Review article summarizing the growth of multidisciplinary cytomegalovirus antiviral stewardship initiatives, including quality improvement algorithms for implementation at other centers. Targeted CMV stewardship initiatives reduced the incidence of ganciclovir resistance and reduced CMV treatment rates (26% at initiation to 12% in the current state, p=0.012).

Kaminski H, et al. (2022). Incidence of cytomegalovirus infection in seropositive kidney transplant recipients treated with everolimus: A randomized, open-label, multicenter phase 4 trial. Am J Transplant. May;22(5):1430-1441. Epub 2022 Jan 19. https://pubmed.ncbi.nlm.nih.gov/34990047/

- A randomized, open-label, multicenter study comparing everolimus to mycophenolic acid to determine whether treatment with everolimus could decrease the incidence of CMV DNAemia and disease. At 6 months post transplant, 48% everolimus-treated patients met the composite endpoint (CMV DNAemia, CMV treatment, graft loss, death, discontinuation of study) versus 81% mycophenolate treated patients.

Linder, KA, et al. (2021). Letermovir treatment of cytomegalovirus infection or disease in solid organ and hematopoietic cell transplant recipients. Transplant infectious disease: an official journal of the Transplantation Society, 23(4), e13687. https://pubmed.ncbi.nlm.nih.gov/34251742/

- Retrospective, observational study of 47 patients (27 SOT, 21 HSCT, 1 received both SOT & HCT). 77% of patients reported intolerance to other agents.32% of patients had resistance to other agents. Among patients with VL >1000 IU/mL at time of letermovir initiation, success rates were lower.

Winstead RJ, et al. (2021). Letermovir Prophylaxis in Solid Organ transplant—Assessing CMV Breakthrough and Tacrolimus Drug Interaction. *Transpl Infect Dis*; 23(4). https://pubmed.ncbi.nlm.nih.gov/33469975

- Single center study comparing incidence of breakthrough CMV in transplant recipients while on letermovir prophylaxis vs valganciclovir prophylaxis. Also includes an evaluation of the drug interaction found with letermovir and tacrolimus.

Prakash K, et al. (2021). Utility of CMV-Specific Immune Monitoring for The Management of CMV In Solid Organ Transplant Recipients: A Clinical Update. *Diagnostics*. 11(5). https://pubmed.ncbi.nlm.nih.gov/34068377/

- Review of 20 studies published on utilization of CMV-specific cell mediated immunity in solid organ transplant recipients.

Boulay H, et al. (2021). Among CMV-Positive Renal Transplant Patients Receiving Non-T-Cell Depleting Induction, The Absence of CMV Disease Prevention Is a Safe Strategy: A Retrospective Cohort Of 372 Patients. *Transpl Infect Dis*, 23(3). https://pubmed.ncbi.nlm.nih.gov/33270341/

- Multicenter retrospective review including CMV-seropositive kidney transplant recipients who did not receive T-cell depleting induction therapy that compared outcomes among those who received valganciclovir prophylaxis and those who did not. No difference in incidence of CMV disease, rejection, graft survival, or patient survival was found between groups.

Hofmann E, et al. (2021). Emergence Of Letermovir Resistance in Solid Organ Transplant Recipients with Ganciclovir Resistant Cytomegalovirus Infection: A Case Series and Review of The Literature. *Transpl Infect Dis,* 23(3). https://pubmed.ncbi.nlm.nih.gov/33210830/

- Case series of two kidney transplant recipients with emergence of letermovir resistance when used for secondary prophylaxis of ganciclovir-resistant CMV.

Henry M, et al. (2020). Valganciclovir for the treatment of cytomegalovirus infections in pediatric intestinal transplant recipients: a case series. *Pediatric Transplantation* 2021;25:e14034. https://pubmed.ncbi.nlm.nih.gov/34081375/

- Retrospective review of pITR treated with valganciclovir evaluating the resolution of CMV viremia. 89% of patients had resolution of CMV viremia at an average dose of 14.3 mg/kg twice daily.

Singh N, et al. (2020). Effect of Preemptive Therapy vs Antiviral Prophylaxis on Cytomegalovirus Disease in Seronegative Liver Transplant Recipients with Seropositive Donors. JAMA; 323(14):1378-1387. https://jamanetwork.com/journals/jama/article-abstract/2764457

- Randomized clinical trial comparing the incidence of CMV disease in those high risk CMV liver transplant recipients who received preemptive therapy with valganciclovir 900mg twice daily to antiviral prophylaxis with valganciclovir 900mg daily.

Laub MR et al. (2020). Delayed versus initial cytomegalovirus prophylaxis after kidney transplantation. Clin Transplant. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/32163619

- Retrospective, single center study comparing early (< 72 hours post-transplant) versus delayed (> 72 hours post-transplant) initiation of CMV prophylaxis. Outcomes assessed included incidence of CMV infection, CMV disease, and cost analysis.

Razonable RR, et al. (2019). Cytomegalovirus in solid organ transplant recipients-Guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13512. Epub 2019 Mar 28. https://pubmed.ncbi.nlm.nih.gov/30817026/

- Most recent guidelines on the prevention and management of CMV in solid organ transplant recipients.

Phoompoung P, et al. (2019). Letermovir as salvage therapy for cytomegalovirus infection in transplant recipients. Transplantation;104;404-409. https://www.ncbi.nlm.nih.gov/pubmed/31107821

- Single-center, retrospective study of five stem cell and organ transplant recipients who received letermovir for the treatment of refractory or resistant CMV infections.

Turner N, et al. (2019). Use of letermovir as salvage therapy for drug-resistant cytomegalovirus. Antimicrob Agents Chemother. 63(3):e02337-18. https://www.ncbi.nlm.nih.gov/pubmed/30642941

- Case series of four patients with ganciclovir-resistant CMV retinitis treated with letermovir.

Westall G, et al. (2019). A Randomized Study of Quantiferon CMV-directed Versus Fixed-duration Valganciclovir Prophylaxis to Reduce Late CMV After Lung Transplantation. Transplantation;103(5):1005-13. https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/30247316

- Authors investigated utility of variable length valganciclovir prophylaxis as determined by the Quantiferon-CMV assay and found this method significantly reduced incidence of CMV infection

Maertens J, et al. (2019). Maribavir for Preemptive Treatment of Cytomegalovirus Reactivation. N Engl J Med; 381(12):1136-47. https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/31532960

- Phase II, open-label clinical trial comparing maribavir versus valganciclovir in recipients of hematopoietic-cell or solid organ transplants with CMV reactivation

Kotton CN, et al. (2018). The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation, 102(6), 900–931. https://pubmed.ncbi.nlm.nih.gov/29596116/

- A report summarizes the recommendations of an international panel of experts who convened in March 2017 to revise and expand evidence and expert opinion-based consensus guidelines on CMV management

Vincenti F, et al. (2018). A randomized, phase 2 study of ASP0113, a DNA-based vaccine, for the prevention of CMV in CMV-seronegative kidney transplant recipients receiving a kidney from a CMV-seropositive donor. Am J Transplant. 18(12):2945-54. https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29745007

- Phase II clinical trial comparing the efficacy, safety, and immunogenicity of ASP0113 (n=75) versus placebo (n=74); did not demonstrate efficacy in prevention of CMV viremia

Witzke O, et al. (2018). Valganciclovir prophylaxis versus preemptive therapy in cytomegalovirus-positive renal allograft recipients: long-term results after 7 years of a randomized clinical trial. Transplantation; 102(5):876-82. https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29166336

- Long-term follow-up (up to 84 months) of above study comparing valganciclovir as primary prophylaxis to preemptive therapy in kidney transplant recipients who were of intermediate risk

Hensler, et al. (2018). Impact of electronic health record-based, pharmacist-driven valganciclovir dose optimization in solid organ transplant recipients. Transpl Infect Dis. 2018 Apr;20(2):e12849. doi: 10.1111/tid.12849. Epub 2018 Feb 21. https://www.ncbi.nlm.nih.gov/pubmed/29360250

- This study reviews the impact of pharmacist intervention adjusting valganciclovir dosing for CMV prophylaxis. The primary endpoint was CMV infection and ganciclovir resistance in a pre-intervention vs post-intervention group.

Bruminhent J, et al. (2017). Epidemiology and outcome of ganciclovir-resistant cytomegalovirus infection after solid organ transplantation: a single transplant center experience in Thailand. Transplant Proceedings. 49(5):1048-1052. https://www.ncbi.nlm.nih.gov/pubmed/28369203

- Retrospective cohort of patients with CMV with U97 gene conferring ganciclovir resistance reviewing the treatment and clinical course patients experienced.

Fleming J, et al. (2017). Valganciclovir (VGCV) followed by cytomegalovirus (CMV) hyperimmune globulin compared to VGCV for 200 days in abdominal organ transplant recipients at high risk for CMV infection: A prospective, randomized pilot study. Transpl Infect Dis;19(6). https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/28921781

- Prospective, randomized, open-label pilot study comparing valganciclovir prophylaxis for 200 days vs VGCV for 100 days followed by CMV hyperimmue globulin in abdominal transplant recipients at high risk for CMV

Limaye AP, et al. (2016). Plasma IL-10 Levels to Guide Antiviral Prophylaxis Prevention of Late-Onset Cytomegalovirus Disease, in High Risk Solid Kidney and Liver Transplant Recipients. Transplantation,100(1):210-6. https://www.ncbi.nlm.nih.gov/pubmed/26680375

- A study that test the role of IL-10 being an indicator for the risk of development of CMV infection after prophylaxis, and hence guiding the needed length of prophylaxis in kidney and liver transplant recipients

Bradley D, et al. (2016). Pharmacokinetics and Safety of Valganciclovir in Pediatric Heart Transplant Recipients 4 Months of Age and Younger. Pediatr Infect Dis J, 35(12):1324-1328. https://www.ncbi.nlm.nih.gov/pubmed/27580058

- The pediatric dosing algorithm for VGCV (utilizing individuals' body surface area and renal function) provides systemic GCV exposures in patients younger than 4 months that are similar to those observed in older pediatric populations. The data indicate that this dosing algorithm is appropriate across the entire pediatric age range, including this youngest age group.

Durante-Mangoni E, et al. (2015). Effect of the immunosuppressive regimen on the incidence of cytomegalovirus infection in 378 heart transplant recipients: A single centre, prospective cohort study. J Clin Virol, 68:37-42. https://pubmed.ncbi.nlm.nih.gov/26071333/

- Use of everolimus was associated with a significantly lower rate of CMV infection compared to azathioprine or mycophenolate (OR 0.19, 95% C.I. 0.09-0.39; $p<0.0001$)

Gabardi S, et al. (2015). Evaluation of low-versus high-dose Valganciclovir for prevention of cytomegalovirus disease in high-risk renal transplant recipients. Transplantation. 99(7), 1499-1505. https://www.ncbi.nlm.nih.gov/pubmed/25643140

- A multicenter, retrospective study found that low-dose and high-dose valganciclovir regimens provide similar efficacy in preventing CMV disease in high-risk renal transplant recipients, Low-

dose valganciclovir group had reduced incidence of leukopenia associated and may provide a significant cost avoidance benefit

Witzke O, et al. Valganciclovir prophylaxis versus preemptive therapy in cytomegalovirus-positive renal allograft recipients: 1-year results of a randomized clinical trial. Transplantation. 2012 Jan 15;93(1):61-8. http://www.ncbi.nlm.nih.gov/pubmed/22094954

- The impact of valganciclovir as primary prophylaxis compared to preemptive therapy on rates of cytomegalovirus (CMV) infection and disease occurrence was evaluated in kidney transplant recipients who were of intermediate CMV risk.

Finlen Copeland CA, et al. Long-term efficacy and safety of 12 months of valganciclovir prophylaxis compared with 3 months after lung transplantation: A single-center, long-term follow-up analysis from a randomized, controlled cytomegalovirus prevention trial. J Heart Lung Transplant. 2011 Sep;30(9):990-6. Epub 2011 Apr 13. https://www.ncbi.nlm.nih.gov/pubmed/21489817

- A single-center study on a subset of patients who were initially enrolled in a prospective, randomized, placebo-controlled study of CMV prevention in lung transplantation. The study aimed to determine if extended prophylaxis conferred a sustained long-term benefit and to assess its hematologic safety. It showed that extending valganciclovir prophylaxis to 12 months provides a durable long-term CMV protective benefit compared with short-course therapy, without increasing adverse hematologic effects

Palmer SM, et al. Extended valganciclovir prophylaxis to prevent cytomegalovirus after lung transplantation: A randomized, controlled trial. Ann Intern Med. 2010 Jun 15;152(12):761-9. https://www.ncbi.nlm.nih.gov/pubmed/20547904

- Multicenter randomized, clinical trial involving 11 U.S. lung transplant centers, to determine whether extending prophylaxis with oral valganciclovir from the standard 3 months to 12 months after lung transplantation is efficacious. A beneficial effect with regard to prevention of CMV disease seems to extend at least through 18 months after transplantation.

Humar A, et al. (2010). The efficacy and safety of 200 days valganciclovir cytomegalovirus prophylaxis in high-risk kidney transplant recipients. Am J Transplant, 10(5), 1228-37. http://www.ncbi.nlm.nih.gov/pubmed/20353469

- CMV disease at 1 year was evaluated in high-risk kidney transplant recipients on valganciclovir prophylaxis for 100 days compared to 200 days.

Humar A, et al. (2010). Extended valganciclovir prophylaxis in D+/R- kidney transplant recipients is associated with long-term reduction in cytomegalovirus disease: two-year results of the IMPACT study. Transplantation. 90(12):1427-31. https://www.ncbi.nlm.nih.gov/pubmed/21197713

- International, randomized, prospective, double-blind study, compared 318 CMV D+/R- kidney transplant recipients receiving valganciclovir (900 mg) once daily for up to 200 days vs. 100 days. Long-term outcomes including CMV disease, acute rejection, graft loss, patient survival, and seroconversion were assessed

Avery RK, et al. (2010). Utility of leflunomide in the treatment of complex cytomegalovirus syndromes. Transplantation. 90(4):419-26. https://www.ncbi.nlm.nih.gov/pubmed/20683281

- Single-center, retrospective study that reports on its use in 17 transplant recipients with complex CMV syndromes who had failed or were intolerant to other therapies

Asberg A, et al. (2009). Long-term outcomes of CMV disease treatment with valganciclovir versus IV ganciclovir in solid organ transplant recipients. American journal of transplantation. 9(5):1205-13. https://www.ncbi.nlm.nih.gov/pubmed/19422345

- 1-year follow-up of VICTOR study, 321 SOT recipients with CMV disease were followed 1 year after treatment with either twice daily intravenous ganciclovir or oral valganciclovir (for 21 days) followed by once daily valganciclovir until day 49 in all patients

Bonaros N, et al. (2008). CMV-hyperimmune globulin for preventing cytomegalovirus infection and disease in solid organ transplant recipients: a meta-analysis. Clinical Transplantation, 22(1), 89-97. http://www.ncbi.nlm.nih.gov/pubmed/18217909

- Meta-analysis included 11 articles which evaluated the impact of cytomegalovirus (CMV) immune globulin on CMV disease prevention and rejection.

Reischig T, et al. (2008). Valacyclovir prophylaxis versus preemptive valganciclovir therapy to prevent cytomegalovirus disease after renal transplantation. American Journal of Transplantation, 8(1), 69-77. http://www.ncbi.nlm.nih.gov/pubmed/17973956

- Preemptive valganciclovir therapy was compared to valacyclovir prophylaxis for their impact on cytomegalovirus disease and acute rejection at 12 months following kidney transplantation.

Asberg A, et al. (2007). Oral valganciclovir is noninferior to intravenous ganciclovir for the treatment of cytomegalovirus disease in solid organ transplant recipients. Am J Transplant. 7(9):2106-13. https://www.ncbi.nlm.nih.gov/pubmed/17640310

- A randomized, international trial (VICTOR study), recipients with cytomegalovirus disease were treated with either 900 mg oral valganciclovir or 5 mg/kg i.v. ganciclovir twice daily for 21 days, followed by 900 mg daily valganciclovir for 28 days. A total of 321 patients were evaluated. Oral valganciclovir shows comparable safety and is not inferior to i.v. ganciclovir for treatment of cytomegalovirus disease in organ transplant recipients and provides a simpler treatment strategy.

Khoury JA, et al. (2006). Prophylactic versus preemptive oral valganciclovir for the management of cytomegalovirus infection in adult renal transplant recipients. American Journal of Transplantation, 6(9), 2134-43. http://www.ncbi.nlm.nih.gov/pubmed/16780548

- Oral valganciclovir prophylaxis was compared to preemptive valganciclovir therapy for its pharmacoeconomic impact and occurrence of cytomegalovirus infection.

Paya C, et al. (2004). Efficacy and safety of valganciclovir vs. oral ganciclovir for prevention of cytomegalovirus disease in solid organ transplant recipients. American journal of transplantation. 4(4):611-20. https://www.ncbi.nlm.nih.gov/pubmed/15023154

- In this randomized, prospective, double-blind, double-dummy study, 364 CMV D+/R- patient received valganciclovir 900 mg once daily or oral ganciclovir 1000 mg three times a day (TID) within 10 days of transplant and continued through 100 days. It looked at development of CMV disease and CMV viremia during 6 & 12 months. Also, Time to onset of CMV disease and to viremia was compared.

Lowance D, et al. (1999). Valacyclovir for the prevention of cytomegalovirus disease after renal transplantation. International Valacyclovir Cytomegalovirus Prophylaxis Transplantation Study Group. N Engl J Med, 340(19), 1462-70. http://www.ncbi.nlm.nih.gov/pubmed/10320384

- A placebo-controlled trial evaluating valacyclovir prophylaxis for prevention of cytomegalovirus disease in kidney transplant recipients.

7.1.2 Epstein-Barr Virus and Lymphoproliferative disorder

Preiksaitis J, et al. (2024). The IPTA Nashville Consensus Conference on Post-Transplant lymphoproliferative disorders after solid organ transplantation in children: III - Consensus guidelines for Epstein-Barr virus load and other biomarker monitoring. Pediatric transplantation, 28(1), e14471. https://pubmed.ncbi.nlm.nih.gov/37294621/

- Consensus guidelines for EBV viral load monitoring in pediatric SOT

Green M, et al. (2024). The IPTA Nashville consensus conference on Post-Transplant lymphoproliferative disorders after solid organ transplantation in children: II-consensus guidelines for prevention. Pediatric transplantation, 28(1), e14350. https://pubmed.ncbi.nlm.nih.gov/36369745/

- Consensus guidelines for prevention of PTLD in pediatric SOT

Mahadeo KM, et al. (2024). Tabelecleucel for allogeneic haematopoietic stem-cell or solid organ transplant recipients with Epstein-Barr virus-positive post-transplant lymphoproliferative disease after failure of rituximab or rituximab and chemotherapy (ALLELE): a phase 3, multicentre, open-label trial. The Lancet. Oncology, S1470-2045(23)00649-6. Advance online publication. https://pubmed.ncbi.nlm.nih.gov/38309282/

- Multi-center, open-label, phase 3 trial of patients with biopsy-proven EBV-positive PTLD, relapsed or refractory to rituximab after HSCT and rituximab with or without chemotherapy after SOT

Franco A, et al., & en representación del grupo GREAT (2023). Lymphoproliferative disorders after renal transplantation along 2 decades: a large longitudinal study of 21,546 recipients. Nefrologia, 43(4), 427–434. https://pubmed.ncbi.nlm.nih.gov/37813738/

- Retrospective observational study assessing the incidence of PTLD and its relationship with EBV, alongside risk factors and outcomes in 21,546 patients across 21 transplant centers. Overall findings suggest PTLD has a low overall incidence in kidney transplant recipients, and can present in the absence of risk factors.

McKenna M, et al. (2023). Real-world evidence of the safety and survival with CD19 CAR-T cell therapy for relapsed/refractory solid organ transplant-related PTLD. British journal of haematology, 202(2), 248–255. https://pubmed.ncbi.nlm.nih.gov/37129856/

- Multicenter retrospective analysis of CD19 CAR-T therapy in relapsed PTLD in SOT recipients. Study results found safety and efficacy to be comparable to initial CAR-T trials, with 33% of patients achieving remission.

Asleh R, et al. (2022). Sirolimus-Based Immunosuppression Is Associated with Decreased Incidence of Post-Transplant Lymphoproliferative Disorder after Heart Transplantation: A Double-Center Study. J Clin Med. 2022;11(2):322. https://pubmed.ncbi.nlm.nih.gov/35054016/

- Retrospective analysis evaluating incidence of PTLD in heart transplant patients receiving sirolimus based immunosuppression. Conversion to sirolimus was found to be protective against development of PTLD in this population.

Liu J, et al. (2021). EBV-specific cytotoxic T lymphocytes for refractory EBV-associated post-transplant lymphoproliferative disorder in solid organ transplant recipients: a systematic review. Transpl Int. https://pubmed.ncbi.nlm.nih.gov/34510581/

- Review of 11 studies including a total of 76 solid organ transplant recipients who received treatment for PTLD with EBV-specific cytotoxic T lymphocytes. The review concluded that therapy with EBV-specific cytotoxic T lymphocytes is safe and effective in PTLD.

Allen U, et al. (2019). Post-transplant lymphoproliferative disorders, Epstein-Barr virus infection, and disease in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Am J Transplant;33e13652. https://pubmed.ncbi.nlm.nih.gov/31230381/

- The American Journal of transplantation guidelines for management of Epstein-Barr Virus and Posttransplant Lymphoproliferative Disorder in Solid Organ Transplantation

Dierickx D, et al. (2018). Post-transplantation lymphoproliferative disorders in adults. N Engl J Med. 378:549-62. https://www.nejm.org/doi/full/10.1056/NEJMra1702693

- Review article of epidemiology, presentation, diagnosis, and treatment of PTLD.

Pagano J, et al. Antiviral Drugs for EBV (2018). Cancers;10(6):197. https://www-ncbi-nlm-nih-gov.libproxy.usouthal.edu/pubmed/29899236

- Review article describing antiviral drugs used to inhibit EBV replication

Al Dabbagh MA, et al. (2017). The role of antiviral prophylaxis for the prevention of Epstein-Barr virus associated posttransplant lymphoproliferative disease in solid organ transplant recipients: a systematic review. Am J Transplant.17(3):770-781. https://www-ncbi-nlm-nihgov.ezproxy2.umc.edu/pubmed/27545492

- Systematic review and meta-analysis of antiviral prophylaxis for the prevention of PTLD in EBV seronegative patients receiving organs from EBV seropositive donors.

Yager J, et al. (2017). Valganciclovir for the Suppression of Epstein-Barr Virus Replication. J Infect Dis;216(2):198-202. https://pubmed.ncbi.nlm.nih.gov/28838145/

- Small randomized, double-blind, placebo-controlled study evaluating the effects of valganciclovir on oral EBV shedding

Mumtaz K, et al. (2015). Post-transplant lymphoproliferative disorder in liver recipients: Characteristics, management, and outcome from a single-center experience with >1000 liver transplantations. Canadian journal of gastroenterology & hepatology. 29(8):417-22. https://www.ncbi.nlm.nih.gov/pubmed/26076399

- A single, large-volume center assessed the incidence, predictors and outcomes of PTLD after liver transplantation. Suggested switching immunosuppression from calcineurin inhibitor to sirolimus may improve survival.

Evens AM, et al. (2010). A multicenter analysis of 80 solid organ transplantation recipients with post transplantation lymphoproliferative disease: outcomes and prognostic factors in the modern era. Journal of clinical oncology. 28(6):1038-46. https://www.ncbi.nlm.nih.gov/pubmed/20085936

- A multicenter retrospective study assessed the impact of rituximab on the outcome of PTLD. They examined the clinical features and outcomes among a large cohort of solid organ transplantation (SOT) patients with PTLD.

Opelz G, et al. (2007). Effect of cytomegalovirus prophylaxis with immunoglobulin or with antiviral drugs on post-transplantation-Hodgkin lymphoma: a multicentre retrospective analysis. The Lancet Oncology. 8(3):212-8. https://www.ncbi.nlm.nih.gov/pubmed/17329191

- A multicenter retrospective study analyzed the incidence of post-transplant non-Hodgkin lymphoma in 44 828 recipients of deceased-donor kidney transplants who were reported to the scientific registry of the Collaborative Transplant Study. Patients had received antiviral drugs (aciclovir or ganciclovir) or anti-CMV immunoglobulin to prevent CMV infection according to the transplant centers'' protocols, or no CMV prophylaxis

Humar A, et al. (2006). A randomized trial of ganciclovir versus ganciclovir plus immune globulin for prophylaxis against Epstein-Barr virus related posttransplant lymphoproliferative disorder. Transplantation. 81(6):856-61. https://www.ncbi.nlm.nih.gov/pubmed/16570008

- A multi-center trial assessing two different regimens and their effect on EBV replication. EBV D+/R- solid organ transplant recipients were randomized to receive either ganciclovir and placebo or ganciclovir and immunoglobulin (IG) for 3 months. No significant difference in EBV viral load suppression was observed when ganciclovir was compared with ganciclovir and IG in high-risk EBV D+/R- patients

Green M, et al. (2006). CMV-IVIG for prevention of Epstein Barr virus disease and posttransplant lymphoproliferative disease in pediatric liver transplant recipients. American Journal of Transplantation. 6(8):1906-12. https://www.ncbi.nlm.nih.gov/pubmed/16889546

- A randomized controlled trial of CMV-IVIG (cytomegalovirus-intravenous immunoglobulin) for prevention of Epstein Barr virus (EBV) posttransplant lymphoproliferative disease (PTLD) in pediatric liver transplantation (PLTx) recipients was begun in Pittsburgh and subsequently expanded to four additional sites. Patients were followed for 2 years post-LTx. No significant differences were seen in the adjusted 2-year EBV disease-free rate and PTLD-free rate between treatment and placebo groups at 2 years

7.1.3 Herpes Simplex and Varicella-Zoster virus

Reinhold I, et al. (2023). Donor-derived fulminant herpes simplex virus hepatitis after liver transplantation: Two cases and review of literature. Transplant infectious disease: an official journal of the Transplantation Society, 25(4), e14080. https://pubmed.ncbi.nlm.nih.gov/37247223/

- Two case reports about donor-derived HSV hepatitis in liver transplant recipients there were fatal. Neither patient received HSV or CMV prophylaxis and experienced significant hepatitis, and death was likely due to delayed diagnosis and treatment.

Heldman, MR et al. (2022). Assessing and restoring adaptive immunity to HSV, VZV, and HHV-6 in solid organ and hematopoietic cell transplant recipients. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 28(10), 1345–1350. https://pubmed.ncbi.nlm.nih.gov/35150885/

- Review article assessing available studies on cell mediated immunity to HSV and VZV and how it may be restored. Future considerations include T cell therapies and vaccines.

Laue T, et al. (2022). Long-Term Varicella Zoster Virus Immunity in Paediatric Liver Transplant Patients Can Be Achieved by Booster Vaccinations-A Single-Centre, Retrospective, Observational Analysis. Children (Basel). 2022;9(2):130. https://pubmed.ncbi.nlm.nih.gov/35204851/

- Retrospective, single center study of pediatric liver transplant recipients describing long term immunity over 10 years, including the influence of booster vaccinations.

Zeidan JH, et al. (2021). Donor-derived herpes simplex virus hepatitis in a kidney transplant recipient and review of the literature. *Transpl Infect Dis*, *23*(3). https://pubmed.ncbi.nlm.nih.gov/33432726/

- Case study of donor-derived herpes simplex virus hepatitis in a kidney transplant recipient and a review of eight previously published case studies.

Kwon DE, et al. (2021). Incidence of herpes zoster in adult solid organ transplant recipients: A meta-analysis and comprehensive review. *Transpl Infect Dis*, *23*(4). https://pubmed.ncbi.nlm.nih.gov/34153168/#:~:text=Results%3A%20The%20overall%20pooled%20crude,001).

- Review of 12 observational studies including 6560 solid organ transplant recipients that assessed the incidence of post-transplant herpes zoster infections across various organs.

Vink P, et al. (2020). Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in chronically immunosuppressed adults following renal transplant: a phase III, randomized clinical trial. Clin Infect Dis;70(2):181-190. https://www.ncbi.nlm.nih.gov/pubmed/30843046

- Randomized, observer-blind, multicenter trial of 234 renal transplant recipients comparing the immunogenicity and safety of recombinant zoster vaccine (RZV) to placebo.

Lee D, et al. (2019). Herpes simplex virus infections in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Am J Transplant;e13526. https://www.ncbi.nlm.nih.gov/pubmed/30859647

- The American Journal of Transplantation guidelines on the management of herpes simplex virus in solid organ transplantation

Pergam S, et al. (2019). Varicella zoster virus in solid organ transplantation. Am J Transplant; https://www.ncbi.nlm.nih.gov/pubmed/23465007

- The American Journal of Transplantation guidelines on the management of varicella zoster virus in solid organ transplantation

Lindahl J, et al. (2018) Long-term study showed that vaccination protected pediatric renal transplant recipients from life-threatening varicella zoster virus. Acta Paediatr;107:2185-92. https://www.ncbi.nlm.nih.gov/pubmed/29706010.

- Retrospective study of 85 children undergoing renal transplant assessing clinical outcomes in patients who had the VZV infection pre-transplant compared to those who received vaccination pre-transplant

Macesic N, et al. (2017). Herpes simplex virus-2 transmission following solid organ transplantation: donor-derived infection and transplantation from prior organ recipients. Transplant Infectious Disease. 19 (5):1-8. https://www.ncbi.nlm.nih.gov/pubmed/28618165

- Report detailing 5 clusters of donor-derived HSV-2 infection in donor positive, recipient negative solid organ transplant, the treatment of HSV and clinical outcomes of infection.

Arora A, et al. (2008). Double-blind study comparing 2 dosages of valacyclovir hydrochloride for the treatment of uncomplicated herpes zoster in immunocompromised patients 18 years of age and older. Journal of Infectious Diseases, 197, 1289-1295. http://www.ncbi.nlm.nih.gov/pubmed/18422441

- No differences in median time to full healing of HSV rash were detected among patients receiving valacyclovir 1 gram TID versus 2 grams TID

Boeckh M, et al. (2006) Long-term acyclovir for prevention of varicella zoster virus disease after allogeneic hematopoietic cell transplantation—a randomized double-blind placebo-controlled study. Blood. 107(5):1800-5. https://www.ncbi.nlm.nih.gov/pubmed/16282339

- A double-blind controlled trial, 77 hematopoietic cell transplant recipients at risk for VZV reactivation were randomized to acyclovir 800 mg twice daily or placebo given from 1 to 2 months until 1 year after transplantation. VZV disease at 1 year was the primary end point

Fiddian P, et al. (2002). Valacyclovir provides optimum acyclovir exposure for prevention of cytomegalovirus and related outcomes after organ transplantation. The Journal of infectious diseases. 186 Suppl 1:S110-5. https://www.ncbi.nlm.nih.gov/pubmed/12353195

- A meta-analysis of 12 randomized trials (1574 patients) examined herpesvirus (CMV, VZV, HSV) and related outcomes following organ transplantation over a range of acyclovir exposures (including valacyclovir)

Tyring S, et al. (2001). Collaborative Famciclovir Immunocompromised Study Group. A randomized, double-blind trial of famciclovir versus acyclovir for the treatment of localized dermatomal herpes zoster in immunocompromised patients. Cancer Investigation, 19, 13-22. http://www.ncbi.nlm.nih.gov/pubmed/11291551

- Famciclovir 500 mg three times a day was compared to acyclovir 800 mg five times a day showed no significant difference in new lesion formation, time to healing or duration of pain were observed

Shepp DH, et al. (1986). Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. New England Journal of Medicine, 314, 208-212. http://www.ncbi.nlm.nih.gov/pubmed/3001523

- Acyclovir limited cutaneous dissemination as well as abbreviated duration of positive cultures, pain associated with lesions, postulation of lesions, crusting of lesions and complete healing of lesions.

7.1.4 Adenovirus infection

Grasa C, et al. (2023). Adenovirus infection in hematopoietic and solid organ paediatric transplant recipients: treatment, outcomes, and use of cidofovir. *Microorganisms*, *11*(7), 1750. https://pubmed.ncbi.nlm.nih.gov/37512922/

- Retrospective study of adenovirus in 38 episodes in pediatric HSCT and 11 episodes in SOT recipients. Cidofovir was used as treatment in 49% of patients with limited benefit and associated lymphopenia ICU admission, and high viral load.

Verga S, et al. (2023). Adenovirus Infection in Lung Transplant Recipients: Treatment & Outcomes. The Journal of Heart and Lung Transplantation, 42(4), S303-S304. https://www.jhltonline.org/article/S1053-2498(23)00741-6/fulltext

- Case series of 4 lung transplant recipients who received and were successfully treated with cidofovir for adenovirus. All patients were dosed 1mg/kg every other day, tolerated treatment with limited bone marrow suppression, and no relapses.

Florescu D, et al. (2019). Adenovirus in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Am J Transplant;33e13527.

https://pubmed.ncbi.nlm.nih.gov/30859626/#:~:text=The%20current%20update%20of%20the,therapy%20in%20a%20symptomatic%20patient.

- The American Journal of Transplantation guidelines for the diagnosis and management of Adenovirus in solid organ transplantation

Gonzalez-Vicent, et al. (2019). Current practices in the management of adenovirus infection in allogeneic hematopoietic stem cell transplant recipients in Europe: The AdVance study. Eur J Haematol;102(3):210-217. https://www.ncbi.nlm.nih.gov/pubmed/30418684

- Physician surveys conducted to determine current adenovirus screening and treatment practices at their center

Grimley M, et al. (2017) Brincidofovir for Asymptomatic Adenovirus Viremia in Pediatric and Adult Allogeneic Hematopoietic Cell Transplant Recipients: A Randomized Placebo-Controlled Phase II Trial. Biol Blood Marrow Transplant;23(3):512-21. https://www.ncbi.nlm.nih.gov/pubmed/28063938

- Randomized, placebo-controlled phase II trial evaluating preemptive treatment with brincidofovir for the prevention of adenovirus disease in pediatric and adult allogeneic HCT recipients with asymptomatic adenovirus viremia

Wy Ip W, et al. (2013). Management of adenovirus in children after allogeneic hematopoietic stem cell transplantation. Advances in hematology. 176418. Epub 2013 Oct 28. https://www.ncbi.nlm.nih.gov/pubmed/24288536

- A review on the management of pediatric patients with adenovirus infection post-transplant pediatric patients.

7.1.5 HBV prophylaxis and treatment

Yin S, et al. (2023). Incidence, risk factors, and clinical outcomes of HBV reactivation in non-liver solid organ transplant recipients with resolved HBV infection: A systematic review and meta-analysis. PLoS medicine, 20(3), e1004196. https://pubmed.ncbi.nlm.nih.gov/36920988/

- Meta-analysis looking at non-liver transplant recipients with resolved HBV and reactivation outcomes. Overall HBV reactivation rate was 2.5%, with higher rates in patients with negative anti-HBs. Suggested risk factors include use of rituximab, thymoglobulin, anti-HBs status, acute rejection, and ABO blood type incompatible.

Tilley MS, et al. Hepatitis B prophylaxis among recipients of a hepatitis B core antibody positive liver transplant. J Am Pharm Assoc (2023). 2023 Jul-Aug;63(4S):S69-S72. 2023.01.009. https://pubmed.ncbi.nlm.nih.gov/36759305/

- Retrospective, single-center cohort analysis of adult liver transplant recipients in the first 12 months post-transplant comparing incidence of breakthrough HBV infection between recipients of an HBcAb+ organ and recipients of an HBcAb- organ. Secondary outcomes included graft survival, patient survival, and allograft rejection. There were no documented cases of breakthrough HBV infection, suggesting current strategies for HBV post exposure prophylaxis are effective. Patient and graft survival was similar between both groups.

Shaikh SA, et al. (2022). A multicenter evaluation of hepatitis B reactivation with and without antiviral prophylaxis after kidney transplantation. Transpl Infect Dis. 2022;24(1):e13751. https://onlinelibrary.wiley.com/doi/abs/10.1111/tid.13751

- Multicenter, retrospective study evaluating prevalence of HBV reactivation in HBsAg negative, anti-HBc-positive kidney transplants who did or did not receive HBV prophylaxis. Study suggests that prevalence of HBV reactivation in this cohort is low regardless of prophylaxis.

Song Z, et al. (2021). Prophylactic strategy against de novo hepatitis B virus infection for pediatric recipients who receive hepatitis B core antibody-positive liver grafts. Liver Transpl 2021;27:96-105. https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/lt.25813

- Prospective trial evaluating a perioperative Hepatitis B virus (HBV) prophylaxis regimen in pediatric liver transplant patients receiving a HBV core antibody positive (HBcAb) graft. Patients needed a HbsAb serum titer of 1000 IU/L or more pre-transplant (were vaccinated if not) and needed to maintain a HbsAb titer of 200 IU/L post-transplant (would receive Hepatitis B immunoglobulin if not). Graft and survival rates were not significantly different between patients who received an HBcAb+ versus a HBcAb- graft. Patients who met pre- and/or post-operative HBsAb criteria had a lesser incidence of de novo Hepatitis B infection post-transplant. Infection rate in those meeting both criteria was 1.3%, those with only pre-operative criteria was 4.2%, those with only post-operative criteria was 1.9%, and those meeting neither criteria was 43.8%. Authors concluded that their prophylactic strategy was effective at preventing de novo Hepatitis B infection in HbcAb+ liver graft recipients.

Srisuwarn P, et al. (2021). Kidney transplant from donors with hepatitis B: A challenging treatment option. World J Hepatol, 13(8);853–67. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8422915/

- A review of current practices for kidney transplants using hepatitis B positive donors including a summary of long-term outcomes.

Te H, et al. (2019). Viral hepatitis: Guidelines by the American Society of Transplantation Infectious Disease Community of Practice. Am J Transplant;33:e13514. https://pubmed.ncbi.nlm.nih.gov/30817047/

- The American Society of Transplantation's practice guidelines for preventing and treating viral hepatitis in solid organ transplant recipients.

Wong T, et al. (2019). Liver transplantation using Hepatitis B core positive grafts with antiviral monotherapy prophylaxis. J Hepatol;70(6):1114-1122. https://pubmed.ncbi.nlm.nih.gov/30871981/

- Retrospective study describing impact of hepatitis B core antibody positive liver grafts on survival and risk of de novo HBV infection

Terrault NA, et al. (2018). Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology (Baltimore, Md.), 67(4), 1560–1599. https://pubmed.ncbi.nlm.nih.gov/29405329/

- AASLD guidlines on chronic hepatitis B

Choi H, et al. (2017) A multicenter phase III study to evaluate the efficacy and safety of Hepabulin, a new Hepatitis B Immunoglobulin, in liver transplantation recipients with Hepatitis B. Ann Transplant;22:740-748. https://www.ncbi.nlm.nih.gov/pubmed/29229898

- Phase III, open-label, single arm study evaluating Hepabulin HBIG and its effect on preventing Hepatitis B seroconversion in naïve liver transplant recipients.

Malik M, et al. (2017). Prophylaxis among Hepatitis B core antibody-positive deceased-donor liver transplant recipients: Hepatitis B Immunoglobulin plus oral antiviral agents versus antiviral agents alone:

a single-center experience. Exp Clin Transplant;15(2):183-188.
https://pubmed.ncbi.nlm.nih.gov/27212251/

- Retrospective review of hepatitis B core antibody positive liver transplant recipients comparing use of hepatitis B immunoglobulin, antivirals, or combination

Fung J, et al. (2017). Long-term outcomes of entecavir monotherapy for chronic hepatitis B after liver transplantation: Results up to 8 years. Hepatology;66(4):1036-44.
https://pubmed.ncbi.nlm.nih.gov/28370215/

- Described long-term outcomes of 265 consecutive chronic hepatitis B liver transplant recipients treated with entecavir monotherapy.

Terrault NA, et al. (2016). AASLD guidelines for treatment of chronic hepatitis B. Hepatology, 63(1), 261-283. https://www.ncbi.nlm.nih.gov/pubmed/26566064

- The American Association for the Study of Liver Diseases (AASLD) recommendations on the treatment of chronic hepatitis B virus infection in adults and children in compliance with the Institute of Medicine standards for trustworthy practice guidelines

Huprikar S, et al. (2015). Solid organ transplantation from hepatitis B virus-positive donors: consensus guidelines for recipient management. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 15(5), 1162–1172.
https://pubmed.ncbi.nlm.nih.gov/25707744/

- Consensus guidelines for recipient management of HBV positive donors

Yap DY, et al. (2010). Long-term outcome of renal transplant recipients with chronic hepatitis B infection-impact of antiviral treatments. Transplantation, 90(3), 325-30.
http://www.ncbi.nlm.nih.gov/pubmed/20562676

- The impact of entecavir, adefovir, and lamivudine therapy on virologic and biologic responses in hepatitis B surface antigen positive kidney transplant recipients is evaluated.

Tse KC, et al. (2010). Response to adefovir or entecavir in renal allograft recipients with hepatitis flare due to lamivudine-resistant hepatitis B. Clinical Transplantation, 24(2), 207-12.
http://www.ncbi.nlm.nih.gov/pubmed/19758269

- Case series evaluating the use of entecavir or adefovir in kidney transplant recipients with hepatitis B virus infection resistant to lamivudine.

Potthoff A, et al. (2006). Improved outcome of chronic hepatitis B after heart transplantation by long-term antiviral therapy. Journal of Viral Hepatitis, 13(11), 734-41.
http://www.ncbi.nlm.nih.gov/pubmed/17052272

- The impact of long term antiviral therapies (lamivudine, tenofovir, adefovir) on hepatitis B virologic response and liver disease was evaluated in heart transplant recipients.

Buti M, et al. (2003). A randomized study comparing lamivudine monotherapy after a short course of hepatitis B immune globulin (HBIg) and lamivudine with long-term lamivudine plus HBIg in the prevention of hepatitis B virus recurrence after liver transplantation. Journal of Hepatology, 38(6), 811-7.
http://www.ncbi.nlm.nih.gov/pubmed/12763375

- The prospective, open-label trial evaluates the strategies for preventing hepatitis B virus recurrence following liver transplantation. Patients received lamivudine in addition to hepatitis B

immune globulin as combination therapy for the first month following transplant and were then randomized to receive either combination therapy for 17 months or lamivudine monotherapy for 17 months.

Schiff ER, et al. (2003). Adefovir dipivoxil therapy for lamivudine-resistant hepatitis B in pre- and post-liver transplantation patients. Hepatology, 38(6), 1419-27. http://www.ncbi.nlm.nih.gov/pubmed/14647053

- An open-label, multicenter, international study that evaluated the impact of adefovir in pre- and post- liver transplant recipients on hepatitis B viral load was evaluated in patients with lamivudine-resistant hepatitis B.

7.1.6 Arenavirus and West Nile virus (WNV)

Kasule SN, et al. (2023). Neuroinvasive West Nile virus infection in solid organ transplant recipients. Transplant infectious disease: an official journal of the Transplantation Society, 25(1), e14004. https://pubmed.ncbi.nlm.nih.gov/36573623/

- Single-center experience of neuroinvasive West Nile Virus in kidney transplant recipients in the setting of a 2021 outbreak in Arizona. Neuroinvasive West Nile Virus is associated with significant morbidity and mortality in solid organ transplant patients, with flaccid paralysis being an indicator of poor prognosis.

Abbas A, et al. (2022). Neuroinvasive West Nile virus infections after solid organ transplantation: Single center experience and systematic review. Transplant infectious disease: an official journal of the Transplantation Society, 24(6), e13929. https://pubmed.ncbi.nlm.nih.gov/35980220/

- Systematic review and single-center study reviewing outcomes of neuroinvasive West Nile Virus in kidney transplant recipients. Authors concluded that WNV infections were more commonly community-acquired and infections were more severe in patients who underwent organ transplantation.

Aziz F, et al. (2020). Epidemiology, management, and graft outcomes after West Nile virus encephalitis in kidney transplant recipients. Transplant infectious disease: an official journal of the Transplantation Society, 22(4), e13317. https://pubmed.ncbi.nlm.nih.gov/32386074/

- Single-center observational cohort study reviewing the management of WNL and associated morbidity and mortality outcomes in kidney transplant recipients. None of the 11 WNV infections within the study population were donor-derived. Authors concluded the majority of patients who were treated with immunosuppression reduction and IVIG recovered fully. WNV infection was associated with relatively small reduction in eGFR at year one.

Lauterio A, et al. (2023). The role of intravenous immunoglobulin in the treatment of community - Acquired West Nile virus encephalitis after liver transplantation. Transplant infectious disease: an official journal of the Transplantation Society, 25(3), e14025. https://pubmed.ncbi.nlm.nih.gov/36715644/

- Letter to the editor discussing the role of IVIG in treatment for WNV post-liver transplantation.

Anesi J, et al. (2019). Arenaviruses and West Nile Virus in solid organ transplant recipients. Am J Transplant;33(9):e13576. https://pubmed.ncbi.nlm.nih.gov/31022306/

- American Society of Transplantation’s guidelines on Arenaviruses and West Nile viruses in the pre- and post-transplant period

Yango AF, et al. (2014). West Nile virus infection in kidney and pancreas transplant recipients in the Dallas-Fort Worth Metroplex during the 2012 Texas epidemic. Transplantation, 97(9), 953-957. www.ncbi.nlm.nih.gov/pubmed/24406451

- Case series of WNV infection in kidney and pancreas transplant recipients that compared their outcomes with the general population and discussed the utility of U.S. plasma-derived IVIG as an adjuvant therapy for immunocompromised patients with complicated WNV infection. Arenavirus is mainly managed with supportive care with meticulous fluid balance and electrolyte infection Intravenous ribavirin is the drug of choice for Lassa fever and should be considered for the treatment of Argentine and Bolivian hemorrhagic fever

Winston DJ, et al. (2014). Donor-derived West Nile virus infection in solid organ transplant recipients: report of four additional cases and review of clinical, diagnostic, and therapeutic features. Transplantation, 97(9), 881-889. https://www.ncbi.nlm.nih.gov/pubmed/24827763.

- Therapeutic strategies of donor-derived WNV infection based on these 4 cases included supportive care, reduction of immunosuppression, and frequent intravenous immunoglobulin and interferon

Ravindra KV, et al. (2004). West Nile Virus—Associated Encephalitis in Recipients of Renal and Pancreas Transplants: Case Series and Literature Review. Clinical infectious diseases, 38(9), 1257-1260. www.ncbi.nlm.nih.gov/pubmed/15127337

- A review of 3 cases of kidney or pancreas transplants recipients who developed West Nile fever and had meningoencephalitis and review the literature on West Nile fever in organ transplant recipients

Iwamoto M, et al. (2003). Transmission of West Nile virus from an organ donor to four transplant recipients. New England Journal of Medicine, 348(22), 2196-2203. www.ncbi.nlm.nih.gov/pubmed/12773646

- Report two recipients of cadaveric kidneys from a single donor showed that organ recipients receiving immunosuppressive drugs may be at high risk for severe disease after WNV infection and blood transfusion was the probable source of the West Nile virus viremia in the organ donor

7.1.7 BK Polyomavirus

Lorant C, et al. (2024). The risk factors associated with post-transplantation BKPyV nephropathy and BKPyV DNAemia: a prospective study in kidney transplant recipients. *BMC infectious diseases*, *24*(1), 245. https://doi.org/10.1186/s12879-024-09093-7

- Prospective, single center cohort study assessing incidence of BKPyVAN post implementation of BKPyV screening strategy. Authors concluded male gender and advanced age are associated with increased risk of BKPyVAN or high level BKPyV viremia.

Seifert ME, et al. (2024). A multicenter prospective study to define the natural history of BK viral infections in kidney transplantation. *Transplant infectious disease: an official journal of the Transplantation Society*, e14237. Advance online publication. https://doi.org/10.1111/tid.14237

- Prospective, multicenter observational study to define natural history of BK virus in kidney transplantation. Authors concluded that male donor sex was associated with lower risk, black race associated with increased risk, and female sex associated with faster clearance BK viremia. Additionally, persistent BK viremia associated with worse allograft function at 24 months post transplant.

Kodama H, et al. (2024). Incidence of postoperative cytomegalovirus and BK-polyoma virus infections and graft loss in ABO-incompatible renal transplant recipients: a multicenter retrospective study. *International urology and nephrology*, 10.1007/s11255-023-03934-1. Advance online publication. https://doi.org/10.1007/s11255-023-03934-1

- Retrospective, multicenter case-control study evaluating incidence of CMV and BK virus infections, graft loss-free survival, and overall survival in ABO compatible versus ABO incompatible kidney transplant patients. Authors concluded that the ABO incompatibility was associated with higher incidence of both viral infections but no difference in graft loss or overall survival.

Hod-Dvorai R, et al. (2023). Development of de novo donor-specific antibodies in renal transplant recipients with BK viremia managed with immunosuppression reduction. Transplant infectious disease: an official journal of the Transplantation Society, 25(1), e13993. https://doi.org/10.1111/tid.13993

- Retrospective case-control study assessing the frequency of de novo DSA in the setting of reduced immunosuppression as treatment for BK virus in renal transplant recipients. Authors concluded that patients with confirmed BKV viremia had higher incidence of dDSA. AMR was similar between cases and controls and rejection was more common in the BKV cases.

Gras J, et al. (2023). BK virus genotypes and humoral response in kidney transplant recipients with BKV associated nephropathy. Transplant infectious disease: an official journal of the Transplantation Society, 25(2), e14012. https://doi.org/10.1111/tid.14012

- Retrospective, single-center observational study evaluating 32 cases of biopsy-proven BKV nephropathy to assess if BKV replication and genetic evolution following transplantation. Authors concluded that BKV genotype from donor are likely not responsible for BKVN pathogenesis.

Yaghobi R, et al. (2023). Host and viral RNA dysregulation during BK polyomavirus infection in kidney transplant recipients. Wiley interdisciplinary reviews. RNA, 14(4), e1769. https://doi.org/10.1002/wrna.1769

- This article aims to recognize complicated facts regarding the impact of BKPyV infection on the distribution of miRNAs and mRNAs within the host cell and the virus.

Hirsch HH, et al (2022). BK Polyomavirus Consensus. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 75(11), 2046–2047. https://doi.org/10.1093/cid/ciac594

- Letter to the editor for the IDSA onsensus on of BKPyV.

Imlay H, et al. (2022). Consensus Definitions of BK Polyomavirus Nephropathy in Renal Transplant Recipients for Clinical Trials. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 75(7), 1210–1216. https://doi.org/10.1093/cid/ciac071

- Consensus definition for BKV to establish consistent end points in clinical trials for future clinical research.

van Doesum WB, et al. (2022). Longitudinal monitoring of BKPyV miRNA levels in kidney transplant recipients with BKPyV-related pathology reflects viral DNA levels and remain high in viremia patients after clearance of viral DNA. Transplant infectious disease: an official journal of the Transplantation Society, 24(6), e13927. https://doi.org/10.1111/tid.13927

- Retrospective, longitudinal study was conducted to assess if BKV miRNA measurements has additional diagnostic and predictive value in kidney transplant recipines compared to current

methods of monitoring with PKV DNA loads. Authors were unable to demonstrate any additional value to miRNA monitoring in the early phase post-transplantation. Further studies are warranted.

Myint TM, et al. (2022) Polyoma BK Virus in Kidney Transplant Recipients: Screening, Monitoring, and Management. Transplantation; 106(1):e76-e89. https://pubmed.ncbi.nlm.nih.gov/33908382/

- Review of epidemiology of BKPyV infections in kidney transplant recipients and current evidence that supports screening and management strategies

Funahashi Y. (2021). BK virus-associated nephropathy after renal transplantation. Pathogens; 10(2):1-14. https://doi.org/10.3390/pathogens10020150

- Review of BK-associated nephropathy after kidney transplant including risk factors, screening and diagnostic criteria, and treatment.

Shen CL, et al. (2021). BK polyomavirus nephropathy in kidney transplantation: Balancing rejection and infection. Viruses; 13(3). https://doi.org/10.3390/v13030487

- Review of BK polyomavirus nephropathy after kidney transplant and the optimization of immunosuppression in this patient population

Ahlenstiel-Grunow T, et al. (2020). Diagnostics, treatment, and immune response in BK polyomavirus infection after pediatric kidney transplantation. Pediatr Nephrol 2020;35:375-382. https://link.springer.com/article/10.1007%2Fs00467-018-4164-3

- Review of the diagnosis and treatment of BK virus associated nephropathy. Includes summary of differences seen in pediatric patients as well as a treatment algorithm.

Hirsch, et al. (2019). BK polyomavirus in solid organ transplantation – Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl;e13528. https://doi.org/10.1111/ctr.13528

- The American Society of Transplantation's practice guidelines for preventing and treating BKV in solid organ transplant recipients.

Patel S, et al. (2019). Ciprofloxacin for BK viremia prophylaxis in kidney transplant recipients: Results of a prospective, double-blind, randomized, placebo-controlled trial. Am J Transplant;19(6):1831-1837. https://pubmed.ncbi.nlm.nih.gov/30811872/

- A 3-month course of ciprofloxacin early following transplantation did not prevent BK viremia but was associated with increased rate of fluoroquinolone-resistant infections

Bischof, et al. (2019). Reducing calcineurin inhibitor first for treating BK polyomavirus replication after kidney transplantation:long-term outcomes. Nephrol Dial Transplant;34(7):1240-50. https://pubmed.ncbi.nlm.nih.gov/30476254/

- Retrospective single-center study assessing long-term outcomes using standard operating procedure of treating BK polyomavirus based on first reducing calcineurin inhibitor

Hocker B, et al. (2019). Epidemiology and risk factors for BK polyomavirus replication and nephropathy in pediatric renal transplant recipients: an international CERTAIN Registry Study. Transplantation;103(6):1224-1233. https://pubmed.ncbi.nlm.nih.gov/30130322/

- Analysis of Cooperative European Pediatric Renal Transplant Initiative Registry describing the epidemiology and risk factors for BK polyomavirus in pediatric renal transplant recipients

Keller N, et al. (2019). Clinical utility of leflunomide for BK polyomavirus associated nephropathy in kidney transplant recipients: A multicenter retrospective study. Transpl Infect Dis;21(2):e13058. https://pubmed.ncbi.nlm.nih.gov/30730102/

- Observational retrospective study evaluating the impact of leflunomide treatment for BK polyomavirus associated nephropathy

Bicalho C, et al. (2018). Determination of viremia cut-off for risk to develop BKPyV-associated nephropathy among kidney transplant recipients. Transpl Infect Dis;20(5):e12969. https://pubmed.ncbi.nlm.nih.gov/30074295/

- Single-center study assessing cut-off value of viremia that best discriminates the risk of progression to nephropathy

Nickeleit V, et al. (2018). The Banff Working Group classification of definitive polyomavirus nephropathy: morphologic definitions and clinical correlations. J Am Soc Nephrol;29(2):680-693. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5791071/

- A morphologic classification scheme for definitive PVN is described by the Banff Working Group on Polyomavirus Nephropathy

Verghese P, et al. (2017). The impact of recipient BKV shedding before transplant on BKV viruria, DNAemia, and nephropathy post-transplant: A prospective study. Pediatr Transplant;21(5). https://pubmed.ncbi.nlm.nih.gov/28557148/

- This prospective study found that recipient BKV viruria prior to transplant predicts post-transplant viruria but not viremia or BKV nephropathy

Simard-Meilleur M, et al. (2017). Stabilization of renal function after the first year of follow up in kidney transplant recipients for significant BK polyomavirus infection or BK polyomavirus-associated nephropathy. Transpl Infect Dis;19(3). https://pubmed.ncbi.nlm.nih.gov/28207975/

- Retrospective analysis of BK polyomavirus screening and immunosuppression reduction demonstrating short-term decline in renal function but long-term benefits for graph function with early detection, prompt diagnosis, and reduction in immunosuppression

Mallat, et al. (2017) CMV and BKPyV infections in renal transplant recipients receiving an mTOR inhibitor-based regimen versus a CNI-based regimen: a systematic review and meta-analysis of randomized, controlled trials. Clin J Am Soc Nephrol; 12(8):1321-1336. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5544521/

- Meta-analysis comparing incidences of cytomegalovirus and BK polyoma virus infections in renal transplant recipients receiving a mTOR inhibitor based regimen compared with a calcineurin inhibitor-based regimen

Arroyo D, et al. (2014). Adjuvant ciprofloxacin for persistent BK polyomavirus infection in kidney transplant recipients. Journal of transplantation, 2014. https://www.hindawi.com/journals/jtrans/2014/107459/

- A retrospective evaluation of kidney transplant recipients diagnosed with BK viruria treated with ciprofloxacin course following the initial reduction in immunosuppression showed that ciprofloxacin may be a useful therapeutic tool for BKV infection refractory to conventional treatment.

Humar A , et al. (2014). Levofloxacin for BK Virus Prophylaxis Following Kidney Transplantation. https://www.ncbi.nlm.nih.gov/pubmed/25399012

- A 3-month course of levofloxacin early following transplantation did not prevent BK viruria, but was associated with an increased risk of adverse events such as bacterial resistance

Jung YH, et al. (2013). Leflunomide therapy for BK virus allograft nephropathy after pediatric kidney transplantation. Pediatric transplantation, 17(2), E50-E54. www.ncbi.nlm.nih.gov/pubmed/23210794

- Leflunomide therapy in addition to a reduction of the immunosuppressive therapies resulted in a significant decline in the BK viral load without further deterioration of renal function

Cibrik D et al. (2013). Randomized trial of everolimus-facilitated calcineurin inhibitor minimization over 24 months in renal transplantation. Transplantation. 95(7), 933-42. http://www.ncbi.nlm.nih.gov/pubmed/23422495

- The use of everolimus to minimize calcineurin inhibitors was investigated in kidney transplant recipients. Over two years, a higher rate of CMV (infection, disease, and syndrome) and BKV was found in groups not receiving everolimus.

Dharnidharka VR et al. (2010). Retransplantation after BK nephropathy in prior kidney transplant: an OPTN database analysis. American Journal of Transplantation.10 (5), 1312-5. http://www.ncbi.nlm.nih.gov/pubmed/20353461

- From June 2004 – December 2008, 823 patients were retransplanted following BK nephropathy in prior kidney. Of these patients, 17.5% required treatment for BKV after retransplant.
- The 1 and 3 year Kaplan–Meier graft survival rates and median GFR were 98.5%, 93.6%, 65.5 and 68.4mL/min, respectively.

Gabardi S et al. (2010). Evaluation of fluoroquinolones for the prevention of BK viremia after renal transplantation. Clinical Journal of the American Society of Nephrology. 5(7), 1298-304. http://www.ncbi.nlm.nih.gov/pubmed/20507960

- Patients taking fluoroquinolones for one month after kidney transplant to prevent UTIs was associated with lower rates of BK viremia within 1-year post-transplant.

Johnston O et al. (2010). Treatment of polyomavirus infection in kidney transplant recipients: a systemic review. Transplantation. 37(8), 3546-8. http://www.ncbi.nlm.nih.gov/pubmed/20090569

- A systemic review evaluated 40 studies looking at immunosuppression reduction and antivirals for the management of BKV. There is no graft survival benefit to adding leflunomide or cidofovir to immunosuppression reduction for the management of BKV.

Kuypers DRJ et al. (2009). A single-centre study of adjuvant cidofovir therapy for BK virus interstitial nephritis (BKVIN) in renal allograft recipients. Journal of Antimicrobial Chemotherapy. 63(2), 417-9. http://www.ncbi.nlm.nih.gov/pubmed/19056749

- Kidney transplant patients with BKV were managed with immunosuppression reduction with or without cidofovir 1.0 mg/kg weekly for up to 10 weeks without probenecid. The Kaplan-Meier graft survival at 6 years was significantly improved in patients who received cidofovir.

Schold JD et al. (2009). Treatment for BK virus: incidence, risk factors and outcomes for kidney transplant recipients in the United States. Transplant International. 22(6), 626-34. http://www.ncbi.nlm.nih.gov/pubmed/19207187

- From 2004 - 2006, 34, 937 kidney transplant patients were reviewed for the diagnosis of treated BK virus (TBKV) and risk factors. TBKV was found in 1.6% and 2.6% of patients at 6 months 1 year after transplant respectively.
- Risk factors for TBKV included advanced donor age, pediatric, African American and male recipients, HLA-mismatching, tacrolimus maintenance and Thymoglobulin induction as baseline immunosuppression.

Josephson MA et al. (2006). Treatment of renal allograft polyoma BK virus infection with leflunomide. Transplantation. 81(5), 704-10. http://www.ncbi.nlm.nih.gov/pubmed/16534472

- Treating BKV in kidney transplant recipients with leflunomide alone or leflunomide plus cidofovir resulted in graft loss of 15% with a follow-up time of 6-40 months.
- The target leflunomide metabolite (A77 1726) trough was 50 – 100 mcg/mL; leflunomide trough values of < 40 mcg/mL did not clear the virus until cidofovir was added or adequate leflunomide drug levels were attained.

Sener A et al. (2006). Intravenous immunoglobulin as a treatment for BK virus associated nephropathy: one-year follow-up of renal allograft recipients. Transplantation.81 (1), 117-20. http://www.ncbi.nlm.nih.gov/pubmed/16421486

- Kidney transplant patients received immunosuppression reduction and 2 g/kg of IVIG. After a mean follow-up of 15 months, 88% of patients still had functioning grafts.

Brennan DC et al. (2005). Incidence of BK with tacrolimus versus cyclosporine and impact of preemptive immunosuppression reduction. American Journal of Transplantation. 5(3), 582-94. http://www.ncbi.nlm.nih.gov/pubmed/15707414

- The use of BK viral monitoring and immunosuppression reduction kidney transplant recipients following the identification of viremia was associated with resolution of viremia and absence of BK nephropathy.
- BKV plasma PCR was collected pre-transplant, weekly for 16 weeks, and then at months 5, 6, 9, and 12.
- At the time of BKV identification, the antiproliferative was discontinued. If viremia did not clear within 4 weeks, the calcineurin inhibitor dose was decreased by 20-25%.

Kuypers DRJ et al. (2005). Adjuvant low-dose cidofovir therapy for BK polyomavirus interstitial nephritis in renal transplant recipients. American Journal of Transplantation. 5(8), 1997-2004. http://www.ncbi.nlm.nih.gov/pubmed/15996251

- Treating BKV in kidney transplant recipients with cidofovir 0.5–1.0 mg/kg weekly for 4-10 weeks with probenecid in addition to immunosuppression reduction resulted in renal function stabilization and no graft loss with a follow-up time of 8–41 months (median 24.8).

Nickeleit V et al. (2000). Testing for polyomavirus type BK DNA in plasma to identify renal-allograft recipients with viral nephropathy. New England Journal of Medicine. 342(18), 1309-15. http://www.ncbi.nlm.nih.gov/pubmed/10793163

- Checking BKV DNA PCR in plasma from kidney transplant recipients is a sensitive (100%) and specific (88%) method for identifying viral nephropathy.

7.1.8 Human Parvovirus

Ersal T, et al. (2024). Two Cases of Kidney Transplant Recipients With Multiple Relapsing Pure Red Cell Aplasia Due to Parvovirus B19 Infection. *Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation*, *22*(1), 75–79. https://doi.org/10.6002/ect.2022.0145

- Two case reports assessing parvovirus B19 infection with pure red cell aplasia in kidney transplant recipients. Both patients tested negative for parvovirus IgG and IgM, whilst parvovirus PCR was positive. Immunosuppression was reduced and patients received IVIG for 4 weeks. Authors suggest parvovirus B19 infection should be in differential of posttransplant anemia.

Bertazza Partigiani N, et al. (2023). Pre-Existing Intrarenal Parvovirus B19 Infection May Relate to Antibody-Mediated Rejection in Pediatric Kidney Transplant Patients. International journal of molecular sciences, 24(11), 9147. https://doi.org/10.3390/ijms24119147

- Retrospective analysis of 106 pediatric kidney transplant recipients. RT-PCR was preformed on renal biopsies. Authors concluded intrarenal parvovirus B19 infection was associated with higher rates of AMR.

Yaghoubi F, et al. (2023). Relapsing anemia associated with parvovirus B19 infection in a kidney transplant recipient: A case report and review of the literature. Clinical case reports, 11(9), e7906. https://doi.org/10.1002/ccr3.7906

- Case report and literature review evaluating the rare incidence of relapsing anemia in kidney transplant recipients. Authors suggest modification of immunosuppression regimens and treatment with IVIG.

Zhong Q, et al. (2022). The detection, treatment of parvovirus B19 infection induced anemia in solid organ transplants: A case series and literature review of 194 patients [published online ahead of print, 2022 Jan 8]. Transfus Clin Biol;S1246-7820(21)00530-9. https://pubmed.ncbi.nlm.nih.gov/35007720/

- Retrospective analysis of solid organ transplant recipients with parvovirus B19 infection to determine association with anemia and treatment modalities and literature review

Eid A et al. (2019). Human Parvovirus B19 in solid organ transplantation: Guidelines from the American society of transplantaton infectious diseases community of practice. Clin Transplant;33:e13535. https://doi.org/10.1111/ctr.13535

- The American society of transplantation guidelines for management of Parvovirus in solid organ transplantation

Baek C et al. (2017). Risk factors and long-term outcomes of parvovirus B19 infection in kidney transplant patients. Transpl Infect Dis;19(5). https://pubmed.ncbi.nlm.nih.gov/28741797/

- Multivariate analyses to identify risk factors of positive parvovirus B19 PCR results

Razonable RR et al. (2016). Not the Usual Viral Suspects: Parvovirus B19, West Nile Virus, and Human T-Cell Lymphotrophic Virus Infections After Kidney Transplantation. Seminars in nephrology. 36(5):428-434. https://www.ncbi.nlm.nih.gov/pubmed/27772627

- A review article that discusses the epidemiology, clinical manifestations, diagnosis and treatment of less common viruses (e.g.: West Nile virus, Parvovirus and human T-cell lymphotrophic virus) in the setting of kidney transplantation

Eid AJ et al. (2006). Parvovirus B19 infection after transplantation: a review of 98 cases. Clinical infectious diseases. 1;43(1):40-8. https://www.ncbi.nlm.nih.gov/pubmed/16758416

- A review of 91 cases describing the epidemiology and clinical spectrum of posttransplant PVB19 infection over 16 years period, with literature review

7.1.9 RNA Respiratory Viruses

Trubin P, et al. (2024). The respiratory syncytial virus vaccines are here: Implications for solid organ transplantation. *American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, S1600-6135(24)00129-1. Advance online publication. https://doi.org/10.1016/j.ajt.2024.02.003

- Review of RSV vaccine in solid organ transplant patients

Ramírez-Sánchez IC, et al. (2024). Invasive pulmonary aspergillosis following human metapneumovirus infection in solid-organ transplant recipients: Another virus to add to the list. *Transplant infectious disease: an official journal of the Transplantation Society*, *26*(1), e14188. https://doi.org/10.1111/tid.14188

- Case report of a 63 year old female kidney transplant recipient with invasive pulmonary aspergillosis infection after metapneumovirus. Authors suggest that metapneumovirus may be a risk factor of fungal pulmonary co-infection

Bazemore K, et al (2022). Elevated cell-free DNA in respiratory viral infection and associated lung allograft dysfunction. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 22(11), 2560–2570. https://doi.org/10.1111/ajt.17125

- Multicenter prospective cohort study of lung transplant recipients enrolled in GRAfT (Genomic Research Alliance for Transplantation) to evaluating elevated cell-free DNA in respiratory viral infections and associated risk of CLAD and allograft dysfunction. Authors found that cell-free DNA associated with RVI predicted decline in lung function, CLAD progression, and allograft dysfunction.

Stevaert A, et al. (2022). Nucleoside analogs for management of respiratory virus infections: mechanism of action and clinical efficacy. Current opinion in virology, 57, 101279. https://doi.org/10.1016/j.coviro.2022.101279

- Review of current use of nucleoside analogs for various RNA following use of remdesivir in COVID-19 infections.

Bitterman R, et al. (2021). Respiratory Viruses in Solid Organ Transplant Recipients. *Viruses*, *13*(11);2146. https://doi.org/10.3390/v13112146

- Review of the epidemiology, clinical manifestations, prevention, and treatment of RNA and DNA respiratory viruses, excluding SARS-CoV-2.

Danziger-Isakov L, et al. (2021). Impact of COVID-19 in solid organ transplant recipients. *Am J Transplant,* 21(3);925-37. https://doi.org/10.1111/ajt.16449

- Review of the impact of COVID-19 on solid organ transplantation, including epidemiology, outcomes, diagnosis, and treatment of COVID-19 in this population.

Azzi Y, et al. (2021). COVID-19 and Solid Organ Transplantation: A Review Article. *Transplantation*, 105(1);37–55. https://doi.org/10.1097/TP.0000000000003523

- Review of the immune response to SARS-CoV-2, diagnostics, treatment, and clinical outcomes in solid organ transplant recipients as well as transplant activity during the COVID-19 pandemic.

Raja MA, et al. (2021). COVID-19 in solid organ transplant recipients: A systematic review and meta-analysis of current literature. *Transplant Rev*, 35(1). https://doi.org/10.1016/j.trre.2020.100588

- Systematic review including 215 studies and 2772 solid organ transplant recipients (and meta-analysis including 60 studies) evaluating treatment strategies and outcomes related to SARS-CoV-2 infection.

Daoud A, et al. (2021). Immunosuppression in kidney transplant recipients with COVID-19 infection–where do we stand and where are we heading? *Renal Failure;* 43(1);273-80. https://doi.org/10.1080/0886022X.2021.1876730

- Review of maintenance immunosuppression strategies in the setting of COVID-19 infection in kidney transplant recipients.

Giannella M, et al. (2021). SARS-CoV-2 vaccination in solid-organ transplant recipients: What the clinician needs to know. *Transplant Int,* 34(10);1776-88. https://doi.org/10.1111/tri.14029

- Review of data for SARS-CoV-2 vaccines in solid organ transplant recipients including humoral and cellular immune response and proposed alternative immunization schemes.

Phadke VK, et al. (2021). Immune Responses to SARS-CoV-2 in Solid Organ Transplant Recipients. *Curr Transpl Rep,* 8(2);127-39. https://doi.org/10.1007/s40472-021-00322-5

- Review of immune response to SARS-CoV-2 infection in solid organ transplant recipients, including some comparisons to non-transplant patients.

Karruli A, et al. (2021). Effect of immunosuppression maintenance in solid organ transplant recipients with COVID-19: Systematic review and meta-analysis. *Transpl Infect Dis*, 23(4). https://doi.org/10.1111/tid.13595

- Systematic review and meta-analysis including 202 solid organ transplant recipients evaluating maintenance immunosuppression strategies in the setting of COVID-19 disease.

Hall VG, et al. (2021). Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. *N Eng J Med*, *385*(13);1244–6. https://doi.org/10.1056/nejmc2111462

- Randomized, placebo-controlled trial for a third dose of mRNA-1273 vaccine in solid organ transplant recipients. Patients receiving a third dose had significantly higher immunogenicity than those receiving placebo.

Qin J et al. (2020). Perioperative Presentation of COVID-19 Disease in a Liver Transplant Recipient. Hepatology. 2020 March 27. https://www.ncbi.nlm.nih.gov/pubmed/32220017

- This case report summarizes perioperative presentation to aid clinicians in identifying potential COVID-19 cases in patients prior to transplantation.

Kumar D et al. (2020). COVID-19: A Global Transplant Perspective on Successfully Navagating a Pandemic. Am J Transplant. 2020 March 23. https://www.ncbi.nlm.nih.gov/pubmed/32202064

- A summarization of collective viewpoints on the emerging COVID-19 pandemic, including mitigation strategies and impact on organ transplantation.

Guillen E et al. (2020). Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation? Am J Transplant. 2020 March 20. https://www.ncbi.nlm.nih.gov/pubmed/32198834

- This case report describes an atypical intial presentation of novel COVID-19 in a solid organ transplant recipient.

Manuek O et al. (2019). RNA respiratory viral infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl;33:e13511. https://doi.org/10.1111/ctr.13511

- American Society of Transplantations's guidelines on RNA respiratory viral infections in solid organ transplant recipients

Trang T et al. (2018). Comparative effectiveness of aerosolized versus oral ribavirin for the treatment of respiratory syncytial virus infections: a single center retrospective cohort study and review of the literature. Transpl Infect Dis;20(2):e12844. https://pubmed.ncbi.nlm.nih.gov/29360277/

- Retrospective cohort analysis of adult patients diagnosed with RSV infection and treated with ribavirin

Natori Y et al. (2018). A double-blind randomized trial of high-dose vs standard-dose influenza vaccine in adult solid organ transplant recipients. Clin Infect Dis;66(11):1698-1704. https://pubmed.ncbi.nlm.nih.gov/29253089/

- Randomized, double-blind trial comparing the safety and immunogenicity of the 2016-2017 high dose vs standard dose influenza vaccine in adult transplant recipients

Burrows et al. (2015). Oral ribavirin for respiratory syncytial virus infection after lung transplantation: Efficacy and cost-efficiency. J Heart Lung Transplant;34(7):958-62. https://pubmed.ncbi.nlm.nih.gov/25753833/

- Series of 56 episodes of RSV are described to evaluate the efficacy, safety, and cost-effectiveness of oral ribavirin for the treatment of RSV infection after lung transplant

Ison M et al. (2014). Outcome of influenza infection managed with oseltamivir in lung transplant recipients. J Heart Lung Transplant;27(3):282-288. https://pubmed.ncbi.nlm.nih.gov/18342750/

- Analysis of 9 lung transplant recipients treated with oseltamivir for influenza infection

Li L et al. (2012). Oral versus inhaled ribavirin therapy for respiratory syncytial virus lower respiratory tract infection. J Heart Lung Transplant;28(1):67-71. https://pubmed.ncbi.nlm.nih.gov/22621746/

- Retrospective study investigating outcomes of oral versus inhaled ribavirin therapy

Kumar et al. (2011). Influenza vaccination in the organ transplant recipient: review and summary recommendations. Am J Transplant;11(10):2020-2030. https://pubmed.ncbi.nlm.nih.gov/21957936/

- Review article describing influenza vaccines in transplant recipients

Vu D et al. (2011) Respiratory viruses in lung transplant recipients: a critical review and pooled analysis of clinical studies. Am J Transplant;11(5):1071-1078. https://pubmed.ncbi.nlm.nih.gov/21521473/

- Review of the literature examining viral respiratory infections in lung transplant recipients and their effect on graft complications

Kumar et al. (2010). Outcomes from pandemic influenza A H1N1 infection in recipients of solid organ transplants: a multicentre cohort study. Lancet Infect Dis;10(8):521-526. https://pubmed.ncbi.nlm.nih.gov/20620116/

- Multicenter cohort study of adults and children who received organ transplants with confirmation of influenza A infection to assess morbidity and mortality

Palaez A et al. (2009). Efficacy of oral ribavirin in lung transplant patients with respiratory syncytial virus lower respiratory tract infection. J Heart Lung Transplant;28(1):67-71. https://pubmed.ncbi.nlm.nih.gov/19134533/

- Use of oral ribavirin in five lung transplant recipients with RSV is described

Hopkins, P.et al. (2008). Human metapneumovirus in lung transplant recipients and comparison to respiratory syncytial virus. American journal of respiratory and critical care medicine, 178(8), 876-881. www.ncbi.nlm.nih.gov/pubmed/18658110

- The mainstay of treatment of human metapneumovirus consist of intravenous ribavirin at a starting dose of 33 mg/kg/day for the first 24 hours, then 20 mg/kg/day thereafter. Duration of therapy was determined by resolution of clinical symptoms and sustained improvements in respiratory function

Boeckh M et al. (2007). Randomized controlled multi-center trial of aerosolized ribavirin for respiratory syncytial virus upper respiratory tract infections in hematopoietic cell transplant recipients. Clin Infect Dis 44: 245–249. https://www.ncbi.nlm.nih.gov/pubmed/17173225

- A multicenter prospective trial on hematopoietic cell transplant recipients with respiratory syncytial virus infection of the upper airways investigates the safety and efficacy of aerosolized ribavirin in preventing disease progression.

Glanville AR et al. (2005). Intravenous ribavirin is a safe and cost-effective treatment for respiratory syncytial virus infection after lung transplantation. J Heart Lung Transplant 24: 2114–2119. https://www.ncbi.nlm.nih.gov/pubmed/16364859

- A study that investigated the utility of intravenous (IV) ribavirin with steroids for the treatment of RSV infection after LTx. In 18 symptomatic patients

Vilchez R et al. (2003). Parainfluenza virus infection in adult lung transplant recipients: an emergent clinical syndrome with implications on allograft function. Am J Transplant;3(2):116-120. https://pubmed.ncbi.nlm.nih.gov/12603206/

- Review article describing parainfluenza virus infection in adult lung transplant recipients

7.1.10 Measles

Keutler A, et al. (2024). Live-attenuated vaccination for measles, mumps, and rubella in pediatric liver transplantation. *Pediatric transplantation*, *28*(1), e14687. https://doi.org/10.1111/petr.14687

- A literature review including 9 prospective observational studies and 3 retrospective case series with the aim of assessing appropriateness of live-attenuated MMR vaccine administration after transplant in pediatric liver transplantation. The authors conclude MMR vaccine may be administered to liver transplant recipients who receive individualized risk assessment safetly.

Liu Y, et al. (2015). Measles Virus Infection in Pediatric Liver Transplantation Recipients. Transplantation proceedings (Vol. 47, No. 9, pp. 2715-2718). https://www.ncbi.nlm.nih.gov/pubmed/26680079

- Broad-spectrum anti-infective drugs combined with IVIG should be given for Measles infection in pediatric liver transplant recipients.

Centers for Disease Control and Prevention (CDC). (2007) Multistate measles outbreak associated with an international youth sporting event--Pennsylvania, Michigan, and Texas, August-September, Morbidity and Mortality Weekly Report, 57, 169-173. http://www.ncbi.nlm.nih.gov/pubmed/18288074

- This report summarizes exposure to measles through international travel and illustrates the potential for immunocompromised patients to encounter the virus despite common coverage with effective vaccine in the US.

Danerseau AM, et al. (2008). Efficacy and safety of measles, mumps, rubella and varicella live viral vaccines in transplant recipients receiving immunosuppressive drugs. World journal of pediatrics. 4(4):254-8. https://www.ncbi.nlm.nih.gov/pubmed/19104888

- A review of published data on the efficacy and safety of live viral vaccines for measles, mumps, rubella, or varicella in post-transplant patients currently on immunosuppression

Warmington L, et al. (2005). Loss of antibodies to measles and varicella following solid organ transplantation in children. Pediatric Transplantation, 9, 311-314. http://www.ncbi.nlm.nih.gov/pubmed/15910386

- Serologies of 18 children were reviewed 6 months post-transplant. Four of 18 (22.2%) and 2/18 (11.1%) lost immunity to measles and varicella, respectively.

7.2 Bacterial

7.2.1 Central venous catheter infections and treatment options

Walker, LW et al. (2023). Outcomes in Pediatric Central Line–associated Bloodstream Infections Treated With Antimicrobial Locks: A 14-Year Retrospective Analysis. *The Pediatric Infectious Disease Journal*, *42*(6), 473-478. https://pubmed.ncbi.nlm.nih.gov/36854127/

- Single center retrospective study looking at 1,188 CLASBI treated with antimicrobial lock therapy with small subgroup of SOT recipients

Kovács R, et al. (2022). Antifungal lock therapy: an eternal promise or an effective alternative therapeutic approach? Lett Appl Microbiol10.1111/lam.13653. https://sfamjournals.onlinelibrary.wiley.com/doi/full/10.1111/lam.13653

- Review of Candida-related in vitro, in vivo data, and case studies related to antifungal lock therapy

Böll B, et al. (2020). Central venous catheter-related infections in hematology and oncology: 2020 updated guidelines on diagnosis, management, and prevention by the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). Ann Hematol;100(1):239-259. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7782365/

- Updated guidelines for the management of CVC infections, including recommended antibiotic therapies with duration for catheter-related infections

Arechabala MC, et al. (2018). Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis. Cochrane Database Syst Rev.4:CD010597. https://www.ncbi.nlm.nih.gov/pubmed/29611180

- Cochrane review of 30 studies comparing antimicrobial (antibiotic and non-antibiotic) lock solutions to standard sealing solutions (usually heparin) of the CVC for HD. Authors concluded that antibiotic antimicrobial and combined (antibiotic-non antibiotic) lock solutions decreased infections compared to control lock solutions, whereas non-antibiotic lock solutions reduced infections only for tunneled CVC. The level of confidence of the conclusions is low.

Kritikos, A., et al. (2016). Bloodstream infections after solid-organ transplantation. Virulence, 7(3), 329–340. https://doi.org/10.1080/21505594.2016.1139279

- Review article of blood stream infections as a whole within transplant, with risk factors including central venous catheters

Hentrich, M et al. (2014). Central venous catheter-related infections in hematology and oncology: 2012 updated guidelines on diagnosis, management and prevention by the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology. Annals of Oncology, 00, 1-12. http://www.ncbi.nlm.nih.gov/pubmed/24399078

- Guidelines for management of CVC infections, including recommended antibiotic therapies for specific pathogens.

O'Grady, N et al. (2011) Guidelines for the prevention of intravascular catheter-related infections. Clinical Infectious Diseases, 52(9), e162-e193. http://www.ncbi.nlm.nih.gov/pubmed/21460264

- IDSA guidelines for prevention of catheter- related infections.

Bouza, E, et al. (2011). Managing intravascular catheter-related infections in heart transplant patients: how far can we apply IDSA guidelines for immunocompromised patients? Current Opinion in Infectious Disease, 24(4), 302-308. http://www.ncbi.nlm.nih.gov/pubmed/21666455

- Recommendations for management of catheter-related bloodstream infections in heart transplant patients. Recommends empiric coverage of Gram-positive and Gram-negative bacteria as well as Candida spp., and antimicrobial therapy for durations longer than would be used in other patients.

Soothill, J et al. (2009). A fall in bloodstream infections followed a change to 2% chlorhexidine in 70% isopropanol for catheter connection antisepsis: a pediatric single center before/after study on a hemopoietic stem cell transplant ward. American Journal of Infection Control, 37(8), 626-630. http://www.ncbi.nlm.nih.gov/pubmed/19616869

- An observational study in stem cell transplant patients showed a significant decrease in rates of catheter-related bloodstream infections after switching from isopropanol to chlorhexidine for disinfection of catheter connections.

Vokurka S, et al. (2009). Antimicrobial chlorhexidine/ silver sulfadiazine-coated central venous catheters versus those uncoated in patients undergoing allogeneic stem cell transplantation. Support Care Cancer, 17, 145–151. http://www.ncbi.nlm.nih.gov/pubmed/18449570

- Prospective non-randomized study of antimicrobial-coated CVCs (n= 58) compared with uncoated (n= 49) uncoated CVCs. Significantly fewer fever days per 1,000 catheter days and positive blood cultures were observed in the antimicrobial-covered CVC group.

7.2.2 Clostridium Difficile

Rodig, NM et al. (2023). Fecal Microbiota Transplant in Pediatric Solid Organ Transplant Recipients. Transplantation, 107(9), 2073–2077. https://pubmed.ncbi.nlm.nih.gov/37211643/

- Single center retrospective study of 6 SOT recipients ages 4-18 who received FMT a median of 5.3 years post-transplant

Cheng YW, et al. (2019). Fecal microbiota transplantation for the treatment of recurrent and severe Clostridium difficile infection in solid organ transplant recipients: A multicenter experience. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 19(2), 501–511.https://pubmed.ncbi.nlm.nih.gov/30085388/

- Multi-center, retrospective study of 94 SOT recipients who underwent FMT (78% for recurrent CDI & 22% for severe or fulminant CDI)
- At 3 months, primary cure was 58.7% and overall cure was 91.3%
- Predictors of failing a single FMT: inpatient status, severe and fulminant CDI, presence of pseudomembranous colitis & use of non-CDI antibiotics at time of FMT

Mullane KM, et al. (2019). Management of Clostridioides (formerly Clostridium) difficile infection (CDI) in solid organ transplant recipients: Guidelines from the American Society of Transplantation Community of Practice. Clinical transplantation, 33(9), e13564. https://pubmed.ncbi.nlm.nih.gov/31002420/

- AST Transplant COP guidelines for management of CDI in SOT

7.2.3 Mycobacterium tuberculosis

Gadde, AB et al. (2023). Renal Transplantation in Patients With Tuberculosis: A Single-center Experience From an Endemic Region. Transplantation direct, 9(11), e1541. https://doi.org/10.1097/TXD.0000000000001541

- Retrospective single center study of kidney transplant recipients transplanted while on anti-tubercular therapy vs. matched control group without tuberculosis at the time of transplant
- No patients had recurrence of TB at follow-up
- Death censored graft surivval and biopsy proven rejection rates not statistically significant between groups

Yahav, D., et al. (2023). Screening for Latent Tuberculosis Infection in Solid Organ transplant recipients to predict active disease: a systematic review and meta-analysis of diagnostic studies. In *Open forum infectious diseases* (Vol. 10, No. 8, p. ofad324). US: Oxford University Press. https://pubmed.ncbi.nlm.nih.gov/37559757

- Systematic review of diagnostic tests screening for active and latent tuberculosis in solid organ transplant candidates and their predictive value

Abad, CLR et al. (2023). Multi-drug resistant and rifampin-resistant tuberculosis in transplant recipients. *Transplant Infectious Disease*, e14088.https://pubmed.ncbi.nlm.nih.gov/37335213/

- Review article on the management of MDR mycobacterium tuberculosis in transplant recipients

Katrak, S., et al. (2023). Solid organ transplant recipients with tuberculosis disease in California, 2010 to 2020. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 23(3), 401–407. https://doi.org/10.1016/j.ajt.2022.11.019

- Utilizes the California Tuberculosis Registry data and matched patients to UNOS registry to compare outcomes of patients with TB to SOT patients with TB

Radisic, MV et al. (2022). Tuberculosis treatment without rifampin in kidney/kidney-pancreas transplantation: A case series report. Transplant infectious disease : an official journal of the Transplantation Society, 24(6), e13949. https://doi.org/10.1111/tid.13949

- A case series about 57 kidney/kidney-pancreas transplant recipients with confirmed TB and management of disease without the use of rifampin

Malinis M, et al. (2022). Donor-derived tuberculosis among solid organ transplant recipients in the United States-2008 to 2018. Transpl Infect Dis;e13800. https://onlinelibrary.wiley.com/doi/abs/10.1111/tid.13800

- Review of OPTN reports of donor derived tuberculosis to evaluate outcomes and better understand donor derived tuberculosis

Malinis M, Koff A (2021). Mycobacterium tuberculosis in solid organ transplant donors and recipients. Curr Opin Organ Transplant;26(4):432-439. https://pubmed.ncbi.nlm.nih.gov/34074939/

- Review of current approaches to diagnosis and treatment options of latent TB infections (LTBI) and TB disease in solid organ transplant donors and recipients

Nahid, P., et al. (2019). Treatment of Drug-Resistant Tuberculosis. An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline. American journal of respiratory and critical care medicine, 200(10), e93–e142. https://doi.org/10.1164/rccm.201909-1874ST

- ATS/CDC/ERS/IDSA Guidelines for drug-resistant TB

Subramanian AK, et al., and the Infectious Diseases Community of Practice of the American Society of Transplantation. Mycobacterium tuberculosis infections in solid organ transplantation: Guidelines from the infectious diseases community of practice of the American Society of Transplantation (2019). Clin Transplant. 33(9):e13513. https://www.ncbi.nlm.nih.gov/pubmed/30817030

- AST IDCOP 2019 Guidelines on Mycobacterium Tuberculosis in Solid Organ Transplantation

Abad CL, et al. (2019). Treatment of latent TB infection and the risk of tuberculosis after solid organ transplantation: comprehensive review. Transplant Infect Dis.21:e13178. https://onlinelibrary.wiley.com/doi/full/10.1111/tid.13178

- Literature review of cohort and RCTs regarding treatment agents for latent TB infections in SOT patients

Simkins J, et al. (2017). Twelve-Week Rifapentine Plus Isoniazid Versus 9-Month Isoniazid for the Treatment of Latent Tuberculosis in Renal Transplant Candidates. Transplantation.101(6):1468-1472. https://www.ncbi.nlm.nih.gov/pubmed/27548035

- RCT illustrating 12 weeks of RPT/INH as an alternative to 9 months of INH for latent TB

Nahid P, et al. (2016). Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis.63.147-95. https://academic.oup.com/cid/article/63/7/e147/2196792

- IDSA guidelines for drug-susceptible TB

Sun HY, et al. (2013). Mycobacterium tuberculosis-associated immune reconstitution syndrome in solid-organ transplant recipients. Transplantation. 95:1173-81. https://www.ncbi.nlm.nih.gov/pubmed/23435454

- Retrospective, observational study that attempted to identify risk factors for immune reconstitution syndrome in transplant patients being treated for TB.

Morris MI, et al. (2012). Diagnosis and management of tuberculosis in transplant donors: a donor-derived infections consensus conference report. Am J Transplant.12:2288-300. http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6143.2012.04205.x/full

- Consensus report on the potential for donor-derived TB and how to manage recipients with potential donor exposure.

Currie AC, et al. (2010). Tuberculosis in renal transplant recipients: the evidence for prophylaxis. Transplantation.90(7):695-704. https://www.ncbi.nlm.nih.gov/pubmed/20647975

- A literature review on the use of TB prophylaxis in kidney transplant recipients

Torre-cisneros J, et al. (2009). Tuberculosis after solid-organ transplant: incidence, risk factors, and clinical characteristics in the RESITRA (Spanish Network of Infection in Transplantation) cohort. Clin Infect Dis.48(12):1657-65. https://www.ncbi.nlm.nih.gov/pubmed?term=19445585

- A multicenter study that identified the incidence and risk factors for developing TB in solid organ transplant recipients.

7.2.4 Nontuberculosis Mycobacterium

Marty PK, et al (2023). Risk factors and outcomes of non-tuberculous mycobacteria infection in lung transplant recipients: A systematic review and meta-analysis. The Journal of heart and lung transplantation: the official publication of the International Society for Heart Transplantation, 42(2), 264–274. https://doi.org/10.1016/j.healun.2022.10.004

- Systematic review of 11 studies (n = 3,371), of which 10 studies underwent meta-analysis of risk factors & outcomes of non-tuberculous mycobacteria infection in lung transplant recipients

Friedland AE, et al. (2023). Epidemiology, management, and clinical outcomes of extrapulmonary Mycobacterium abscessus complex infections in heart transplant and ventricular assist device recipients. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 23(7), 1048–1057. https://doi.org/10.1016/j.ajt.2023.04.009

- Case series of 10 OHT & 6 VAD patients with extrapulmonary M. abscessus subspecies abscessus infection

Dedrick RM, et al. (2023). Phage Therapy of Mycobacterium Infections: Compassionate Use of Phages in 20 Patients With Drug-Resistant Mycobacterial Disease. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 76(1), 103–112. https://doi.org/10.1093/cid/ciac453

- Phage therapy for compassionate use intravenously or by aerosolization to 20 patients with nontuberculous Mycobacterium infections
- No adverse reactions attributed to therapy were seen
- Favorable clinical or microbiological responses were observed in 11 patients

van Gemert JP, et al. (2023). Non-tuberculous mycobacteria disease pre-lung transplantation: A systematic review of the treatment regimens and duration pre- and post-transplant. Transplantation reviews (Orlando, Fla.), 37(4), 100800. https://doi.org/10.1016/j.trre.2023.100800

- Review article looking at treatment for pre and post-transplant recipients with non-mycobacterium tuberculosis

Asif H, et al. (2023). Management of nontuberculous mycobacteria in lung transplant cases: an international Delphi study. ERJ open research, 9(2), 00377-2022. https://doi.org/10.1183/23120541.00377-2022

- Consensus recommendations for the management of non-tuberculosis mycobacterium in lung transplant recipients

Ebisu Y, et al. (2022). Mycobacterium abscessus Infections in Solid Organ Transplant Recipients: Single-Center Experience in the United States, 2013-2018. Open forum infectious diseases, 9(7), ofac254. https://doi.org/10.1093/ofid/ofac254

- Single center retrospective cohort study of SOT recipients with a positive culture for M. abscessus

Park Y, et al. (2022). Nontuberculous mycobacterial infection after lung transplantation: A single-center experience in South Korea. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi, 55(1), 123–129. https://doi.org/10.1016/j.jmii.2020.08.021

- Single center study in South Korea assessing 14 patients diagnosed with non-tuberculosis mycobacterium finding no difference in all cause mortality at 12 months post transplant

Poon YK, et al. (2021). Tedizolid vs linezolid for the treatment of nontuberculous mycobacteria infections in solid organ transplant recipients. Open Forum Infect Dis;8(4):ofab093. https://pubmed.ncbi.nlm.nih.gov/33884276/

- Single-center, retrospective review of tedizolid and linezolid for the treatment of nontuberculous mycobacteria infections demonstrating a potential benefit in symptoms and microbiological improvement without significant adverse events

Daley CL, et al. (2020). Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. The European respiratory journal, 56(1), 2000535. https://doi.org/10.1183/13993003.00535-2020

- ATS/ERS/ESCMID/IDSA 2020 Guidelines on non-tuberculous mycobacterium

Longworth SA, et al. (2019); AST Infectious Diseases Community of Practice. Management of infections due to nontuberculous mycobacteria in solid organ transplant recipients- Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 33(9):e13588. https://onlinelibrary.wiley.com/doi/full/10.1111/ctr.13588

- AST IDCOP 2019 Update of Management of non-tuberculous mycobacterium

Friedman DZP, et al. K (2019). Non-tuberculous mycobacteria in lung transplant recipients: prevalence, risk factors, and impact on survival and chronic lung allograft dysfunction. Transpl Infect Dis.00:e13229. https://www.ncbi.nlm.nih.gov/pubmed/31794120

- Retrospective review of non-tuberculous mycobacteria impact on lung transplant survival and chronic lung allograft dysfunction.

Griffith DE, et al. (2018). Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by Mycobacterium avium Complex (CONVERT). A Prospective, Open-Label, Randomized Study. Am J Respir Crit Care Med.15;198(12):1559-1569. https://www.ncbi.nlm.nih.gov/pubmed/30216086

- Data to support the use of inhaled amikacin in refractory cases

Doucette K, et al. (2004). Nontuberculous mycobacterial infection in hematopoietic stem cell and solid organ transplant recipients. Clinical Infectious Diseases. 38(10):1428-1439. https://www.ncbi.nlm.nih.gov/pubmed/15156482

- Review of literature summarizing case reports of NTM infections in stem cell and solid organ transplant recipients.

Vanermarliere A, et al. (2003). Mycobacterial infection in renal transplantation in Western population. Transplant Infectious Disease. 5(1):9-15. https://www.ncbi.nlm.nih.gov/pubmed/12791069.

- Review of 19 cases of NTM infection in renal transplant patients including treatment and outcomes.

Queipo JA, et al. (2003). Mycobacterial infection in a series of 1261 renal transplant recipients. Clinical microbiology and infection. 9(6):518-525. http://onlinelibrary.wiley.com/doi/10.1046/j.1469-0691.2003.00532.x/full.

- Retrospective study of 27 cases of mycobacterial infection after renal transplant of a total of 1261 transplants. Seven patients were found to have infection with NTM organisms. The article includes description of clinical manifestations, treatment and outcomes.

7.2.5 Nocardia

Passerini M, et al. (2024). Trimethoprim-sulfamethoxazole significantly reduces the risk of nocardiosis in solid organ transplant recipients: systematic review and individual patient data meta-analysis. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 30(2), 170–177. https://doi-org.proxy.lib.umich.edu/10.1016/j.cmi.2023.10.008

- Systematic review of TMP-SMX prophylaxis on risk of nocardia in SOT recipients

Yetmar ZA, et al. (2023). Outcomes of transplant recipients with pretransplant Nocardia colonization or infection. Transplant infectious disease: an official journal of the Transplantation Society, 25(5), e14097. https://doi.org/10.1111/tid.14097

- Retrospective chart review looking at outcomes of transplant recipients (HSCT/SOT) with nocardia infection or colonization. Two patients were infected, 7 were colonized, finding no incidence of post-transplant nocardia and suggesting bactrim prophylaxis is adequate after transplantation.

Xu Y, et al. (2023). Clinical characteristics and treatment strategy of nocardiosis in lung transplant recipients: A single-center experience. IDCases, 32, e01758. https://doi.org/10.1016/j.idcr.2023.e01758

- Retrospective analysis assessing lung transplant recipients with nocardiosis in South China. They found an incidence rate of 4.2% in their population, of which most patients responded appropriately to combination antibiotic therapy.

Yetmar ZA, et al. (2023). Risk factors and prophylaxis for nocardiosis in solid organ transplant recipients: A nested case-control study. Clinical transplantation, 37(9), e15016. https://doi.org/10.1111/ctr.15016

- Multicenter case control study looking at 123 SOT transplant recipients with confirmed nocardiosis assessing risk factors for nocardia; including but not limited to multimodal immunosuppression and lack of bactrim prophylaxis

Ghandour M, et al. (2021). Disseminated Nocardiosis in a Renal Transplant Recipient. Cureus. -13(1):e12497. https://pubmed.ncbi.nlm.nih.gov/33564506/

- Case report of a kidney transplant recipient with cutaneous and pulmonary nocardiosis, treated with high-dose trimethoprim/sulfamethoxazole and linezolid in combination with reduced immunosuppression.

Yetmar ZA, et al. (2021). Recurrent nocardiosis in solid organ transplant recipients: An evaluation of secondary prophylaxis. Transpl Infect Dis.;23(6):e13753. https://pubmed.ncbi.nlm.nih.gov/34724316/

- A retrospective cohort study evaluating Nocardia recurrence in solid organ transplant recipients, specifically with forms of secondary prophylaxis.

Goodlet KJ, et al. (2021). Nocardia prophylaxis, treatment, and outcomes of infection in lung transplant recipients: A matched case-control study. Transpl Infect Dis;23(2):e13478. https://pubmed.ncbi.nlm.nih.gov/32989873/

- Case-control study of nocardia after lung transplant in 586 recipients assessing incidence, risk factors, efficacy of trimethoprim/sulfamethoxazole prophylaxis

Restrepo A, et al. (2019). Infectious Diseases Community of Practice of the American Society of Transplantation. Nocardia infections in solid organ transplantation: Guidelines from the Infectious Diseases Community of Practice of the American Society of Transplantation. Clin Transplant. 33(9):e13509. https://www.ncbi.nlm.nih.gov/pubmed/30817024

- AST IDCOP 2019 guideline

Hemmersbach-Miller M, et al. (2018). Nocardia infections in the transplanted host.Transpl Infect Dis.20(4):e12902. https://www.ncbi.nlm.nih.gov/pubmed/29668123

- Epidemiologic and outcome data describing Nocardia infections in SOT and HCT recipients.

Coussement J, et al. (2016). Nocardia Infection in Solid Organ Transplant Recipients: A Multicenter European Case-control Study. Clin Infect Dis.63(3):338-45. https://www.ncbi.nlm.nih.gov/pubmed/27090987

- Case-control study which identified 5 risk factors for nocardiosis after SOT which included a high calcineurin level in the month prior to diagnosis, use of tacrolimus at the time of diagnosis, corticosteroid dose at diagnosis, patient age, and length of stay in ICU after transplant.

Peleg AY, et al. (2007). Risk factors, clinical characteristics, and outcome of Nocardia infection in organ transplant recipients: a matched case-control study. Clin Infect Dis. 15;44(10):1307-14. https://www.ncbi.nlm.nih.gov/pubmed/17443467

- Case control identifying risk factor for nocardiosis found recipient of high-dose steroids, history of CMV disease, and high levels of CNI as risk factor for nocardia in organ transplant recipients.

7.3 Fungal

7.3.1 PJP

Zhu X, et al. (2024). Clinical characteristics and risk factors for late-onset pneumocystis jirovecii pneumonia in kidney transplantation recipients. Mycoses, 67(1), e13688. https://doi.org/10.1111/myc.13688

- Retrospective analysis of kidney transplant recipients and characteristics of developing early-onset versus late-onset PJP. Authors identified that ABO-incompatibility is highest risk for acute

onset, while late-onset risk most closely associated with CMV viremia, T cell subset percentages, and serum albumin in patients on tacrolimus.

Cheng NC, et al (2023). High mortality risk of type III monomicrobial gram-negative necrotizing fasciitis: The role of extraintestinal pathogenic Escherichia coli (ExPEC) and Klebsiella pneumoniae. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases, 132, 64–71. https://doi.org/10.1016/j.ijid.2023.04.390

- Retrospective case-control study that matched each patient with four controls and analyzed the risk factors for late-onset PCP in liver transplant recipients. Authors identified that patients ≥ 65 years at time of LT, cytomegalovirus infection, steroid pulse therapy, hepatocellular carcinoma recurrence, and lymphocytopenia were independently associated with PJP.

Yetmar ZA, et al. (2023). Risk factors and outcomes of Pneumocystis pneumonia in solid organ transplant recipients: Impact of posttransplant lymphoproliferative disorder. Clinical transplantation, 37(9), e15021. https://doi.org/10.1111/ctr.15021

- Nested case-controlled study evaluating the association between post-transplant lymphoproliferative disorder (PTLD) and *Pneumocystis jirovecii* pneumonia (PJP). Authors concluded that incidence of PTLD was independently associated with PJP after adjustment for known risk factors.

Hedvat J, et al. (2021). An evaluation of PJP prophylaxis and anemia among renal transplant recipients. Transpl Infect Dis. 23(3):e13543. https://pubmed.ncbi.nlm.nih.gov/33280205/

- A retrospective analysis of adult renal transplant recipients receiving PJP prophylaxis evaluating anemia as an adverse effect of dapsone-treated patients compared to a control group of atovaquone-treated patients. All patients receiving dapsone had normal G6PD function. Dapsone was associated with a significantly greater decrease in hemoglobin from baseline. Median time to nadir hemoglobin from dapsone initiation was 30.5 days.

Lum J, et al. (2021). Alternative pneumocystis prophylaxis in solid organ transplant recipients at two large transplant centers. Transpl Infect Dis, 23(1):e13461. https://pubmed.ncbi.nlm.nih.gov/32894607/

- A multicenter, retrospective study describing the incidence, reasons for, and outcomes of using alternative prophylactic agents (APA) for PJP. APA use was possibly unwarranted in many cases, increasing the risk for APA-related side effects or preventable opportunistic infections.

Permpalung N, et al. (2021). A Comprehensive Evaluation of Risk Factors for Pneumocystis jirovecii Pneumonia in Adult Solid Organ Transplant Recipients: A Systematic Review and Meta-analysis. Transplantation,105(10):2291-2306. https://pubmed.ncbi.nlm.nih.gov/33323766/

- A meta-analysis determining the pooled effect of potential risk factors on post-transplant PJP in solid organ transplant recipients. In addition to the risk factors discussed in the AST Infectious Diseases Community of Practice guidelines, this study identified that recipients with lymphopenia, BK virus infections, and rituximab exposure should be considered for PJP prophylaxis.

Ji J, et al. (2021). Efficacy of low-dose trimethoprim/sulfamethoxazole for the treatment of *Pneumocystis jirovecii* pneumonia in deceased donor kidney recipients. Infect Drug Resist;14:4913-4920. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8628180/

- Retrospective, single-center study of using low-dose trimethoprim/sulfamethoxazole (10mg/kg/day) for the treatment of pneumocystis jirovecii pneumonia in deceased donor kidney transplant recipients demonstrated reduced adverse events without compromising efficacy.

Park SY, et al. (2020). Epidemiology and risk factors associated with Pneumocystis jirovecii pneumonia in kidney transplant recipients after 6-month trimethoprim-sulfamethoxazole prophylaxis: a case-control study. Transpl Infect Dis. E13245. https://www.ncbi.nlm.nih.gov/pubmed/31943590

- Case-control study of 3,941 kidney and kidney-pancreas transplant patients who received 6 months of PCP prophylaxis with sulfamethoxazole-trimethoprim. Rejection and CMV infection were found to be independently associated with PCP development after completion of prophylaxis.

Fishman JA, et al. (2019); AST Infectious Diseases Community of Practice. Pneumocystis jiroveci in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant.33(9):e13587. https://www.ncbi.nlm.nih.gov/pubmed/31077616

- AST IDCOP 2019 Updates to Management of PCP

Hosseini-Moghaddam SM, et al. (2019). A Multicenter Case-control Study of the Effect of Acute Rejection and Cytomegalovirus Infection on Pneumocystis Pneumonia in Solid Organ Transplant Recipients. Clin Infect Dis.68(8):1320-1326. https://www.ncbi.nlm.nih.gov/pubmed/30107568

- Multicenter study looking at PCP incidence with acute rejection (AR) and CMV infection found to PCP mostly as a late-onset disease occurring after completing course of prophylaxis, particularly among pts w/ AR or CMV infection.

Gabardi S, et al. (2012). Atovaquone versus trimethoprim-sulfamethoxazole as Pneumocystis jirovecii pneumonia prophylaxis following renal transplantation. Clinical Transplantation, 26(3), E184-90. https://www.ncbi.nlm.nih.gov/pubmed/22487221

- A retrospective analysis evaluating atovaquone 1500mg daily (N=25) compared to trimethoprim-sulfamethoxazole single-strength daily (N=160) for preventing pneumocystis carinii pneumonia within one year following kidney transplantation. No cases of pneumocystis carinii pneumonia were seen in either study group.

Wang EH, et al. (2012). Pneumocystis pneumonia in solid organ transplant recipients: not yet an infection of the past. Transplant Infectious Disease, 14(5):519-25. http://www.ncbi.nlm.nih.gov/pubmed/22571389

- Retrospective review evaluating pneumocystis jirovecii pneumonia (PCP) occurrence in kidney (N=657), kidney/pancreas (N=44), liver (N=436), lung or heart/lung (N=104) transplant recipients receiving trimethoprim-sulfamethoxazole for PCP prophylaxis for 6 months in kidney/pancreas, 12 months in lung, and no prophylaxis in liver transplant recipients. The overall incidence of PCP was low with the highest frequency seen in lung transplant recipients and all episodes occurring more than two years following transplant.

Anand S, et al. (2011). Pneumocystis jirovecii pneumonia is rare in renal transplant recipients receiving only one month of prophylaxis. Transplant Infectious Disease, 13(6):570-4. http://www.ncbi.nlm.nih.gov/pubmed/22093215

- Retrospective review evaluating pneumocystis jirovecii pneumonia (PCP) and Nocardia occurrence in 1352 kidney transplant recipients receiving trimethoprim-sulfamethoxazole prophylaxis for one month following transplant. The incidence of PCP and Nocardia was low in this patient population.

El-Sadr WM, et al. (1998). Atovaquone compared with dapsone for the prevention of Pneumocystis carinii pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. Community Program for Clinical Research on AIDS and the AIDS Clinical Trials Group. New England Journal of Medicine, 339(26):1889-95. http://www.ncbi.nlm.nih.gov/pubmed/9862944

- Multicenter, open-label trial that evaluated atovaquone daily (N=536) compared to dapsone daily (N=521) as prophylaxis for the development of pneumocystis carinii pneumonia in human immunodeficiency virus-positive patients who were intolerant to sulfamethoxazole-trimethoprim. The incidence of pneumocystis carinii pneumonia was similar among both study groups.

Ioannidis JP, et al. (1996). A meta-analysis of the relative efficacy and toxicity of Pneumocystis carinii prophylactic regimens. Archives of Internal Medicine, 156(2), 177-88. http://www.ncbi.nlm.nih.gov/pubmed/8546551

- Thirty-five clinical trials including those that compared prophylactic regimens to placebo, different doses of prophylactic agents, and different prophylactic regimens were analyzed to identify ideal medications and their respective doses to prevent pneumocystis carinii pneumonia.

Barber BA, et al. (1996). Clindamycin/primaquine as prophylaxis for Pneumocystis carinii pneumonia. Clinical Infectious Disease, 23(4),718-22. http://www.ncbi.nlm.nih.gov/pubmed/8909833

- A retrospective analysis evaluating clindamycin/primaquine, trimethoprim-sulfamethoxazole, and dapsone prophylaxis for preventing pneumocystis carinii pneumonia in 206 patients with advanced human immunodeficiency virus infection. The rate of pneumocystis carinii pneumonia was lowest in patients receiving trimethoprim-sulfamethoxazole, followed by dapsone, then clindamycin/primaquine.

Sistek CJ, et al. (1992). Adjuvant corticosteroid therapy for Pneumocystis carinii pneumonia in AIDS patients. Ann Pharmacother.26(9):1127-33. https://www.ncbi.nlm.nih.gov/pubmed/1421680

- Systematic review on the use of adjunctive corticosteroid therapy in AIDS patients with PCP pneumonia. Identified that steroid therapy was most beneficial in patients with arterial O2 pressures < 70 mmHg, alveolar-arterial gradient > 35 mmHg on room air, and when started with 72 hr of PCP treatment.

7.3.2 Aspergillus

Giacinta A, et al. (2024). *Aspergillus granulosus* femoral osteomyelitis in a cardiac transplant patient: first reported case and literature review. *Therapeutic advances in infectious disease*, *11*, 20499361241231482. https://doi.org/10.1177/20499361241231482

- First case report of Aspergillus granulosus femoral osteomyelitis in a heart transplant recipient successfully treated with isavuconazole

Pennington KM, et al. (2024). Risk Factors for Early Fungal Disease in Solid Organ Transplant Recipients: A Systematic Review and Meta-analysis. Transplantation, 108(4), 970–984. https://doi.org/10.1097/TP.0000000000004871

- Review and analysis that pertained to the risk factors for development of invasive fungal infections in SOT. Authors concluded three variables with high certainty of evidence and strong associations to early fungal infections across all SOT groups were reoperation, post-transplant CRRT, and CMV disease.

Fernández-Ruiz M, et al. (2023). Isavuconazole for the Treatment of Invasive Mold Disease in Solid Organ Transplant Recipients: A Multicenter Study on Efficacy and Safety in Real-life Clinical Practice. *Transplantation*, *107*(3), 762–773. https://doi.org/10.1097/TP.0000000000004312

- Retrospective study including all adult SOT recipients with proven or probable invasive mold disease (IMD) that received isavuconazole for ≥24 h as first-line or salvage therapy at 10 Spanish centers between September 2017 and November 202. Authors concluded clinical response by weeks 6 and 12 was achieved in 53.1% of isavuconazole as first-line and 54.3% of patients used as salvage therapy.

Boutin CA, et al. (2023). Utility of deceased donor cultures in solid organ transplantation in preventing donor-derived bacterial and fungal infectious diseases transmission. Transplant infectious disease: an official journal of the Transplantation Society, 25(2), e14032. https://doi.org/10.1111/tid.14032

- Guidance on interpretation, management, and treatment of donor-derived bacterial and fungal infections.

Gueneau R, et al. (2023). Aspergillus spp. renal arteritis after kidney transplantation: A reappraisal. Transplant infectious disease: an official journal of the Transplantation Society, 25(5), e14108. https://doi.org/10.1111/tid.14108

- Case report of renal transplant recipient 10 months prior to presentation with asymptomatic transplant renal artery pseudoaneurysm. Most common cause of renal arteritis is Candida spp. Graft was emergently removed and Aspergillus flavus grew.

Melenotte C, et al. (2023). Invasive aspergillosis in liver transplant recipients. Transplant infectious disease : an official journal of the Transplantation Society, 25(3), e14049. https://doi.org/10.1111/tid.14049

- Systematic review of invasive aspergillus (IA) in liver transplant recipients. Authors determined while incidence of IA is low, mortality is high. Infection typically occurs within 3 months post-transplant and identified risk factors depending on relation to transplant, including: before - steroids, renal or hepatic failure, during - massive transfusion and duration of procedure, after - ICU stay, re-transplantation or operation.

Marinelli T, et al. (2022). Antifungal prophylaxis in adult lung transplant recipients: Uncertainty despite 30 years of experience. A systematic review of the literature and network meta-analysis. Transplant infectious disease: an official journal of the Transplantation Society, 24(3), e13832. https://doi.org/10.1111/tid.13832

- Systematic review and meta-analysis of 13 studies of a total 1515 lung transplant recipients and 12 different prophylaxis strategies and antifungal complications. The top three ranked treatments were inhaled liposomal amphotericin B (L-AmB), inhaled amphotericin deoxycholate (AmBd), and itraconazole plus inhaled amphotericin B (AmB). Among the azoles, isavuconazole ranked highest.

Phoompoung P, et al. (2022). Risk factors of invasive fungal infections in liver transplant recipients: A systematic review and meta-analysis. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 22(4), 1213–1229. https://doi.org/10.1111/ajt.16935

- Systematic review and meta analysis of published studies to determine which risk factors are associated with invasive fungal infections (IFI) in liver transplant recipients. Authors identified most relevant independent risk factors being vascular complications, renal failure, and fungal

colonization. Post-transplant renal replacement therapy was associated with the highest risk of invasive aspergillus infection in liver transplant recipients.

Thompson GR 3rd, et al. (2021). Aspergillus Infections. N Engl J Med, 385(16):1496-1509. https://pubmed.ncbi.nlm.nih.gov/34644473/

- Review article of aspergillus infections, including: immune response, risk factors, epidemiology, diagnosis, prophylaxis, treatment, resistance, etc.

Amin A, et al. (2021). Liver Transplantation in Patients With Pretransplant Aspergillus Colonization: Is It Safe to Proceed? Transplantation, 105(3):586-592. https://pubmed.ncbi.nlm.nih.gov/32301905/

- A retrospective review of liver transplant recipients who were colonized with *Aspergillus* pre-transplantation. It was concluded that prior colonization should not withhold or delay liver transplantation for otherwise acceptable candidates and can be managed with appropriate antifungal prophylaxis.

Hoenigl M, et al. (2021). Global guideline for the diagnosis and management of rare mould infections: an initiative of the European Confederation of Medical Mycology in cooperation with the International Society for Human and Animal Mycology and the American Society for Microbiology. Lancet Infect Dis, 21(8):e246-e257. https://pubmed.ncbi.nlm.nih.gov/33606997/

- ECMM guidelines on mycological infections

Neofytos D, et al. (2021). Invasive aspergillosis in solid organ transplant patients: diagnosis, prophylaxis, treatment, and assessment of response. BMC Infect Dis. 2021 Mar 24;21(1):296. https://pubmed.ncbi.nlm.nih.gov/33761875/

- Review of diagnosis, prophylaxis, treatment, and assessment of response in invasive aspergillosis in solid organ transplant patients

Bernardo V, et al. (2020). Initial posaconazole dosing to achieve therapeutic serum posaconazole concentrations among children, adolescents, and young adults receiving delayed-release tablet and intravenous Posaconazole. Pediatr Transplant;24(6):e13777. https://onlinelibrary.wiley.com/doi/abs/10.1111/petr.13777.

- Single-center study describing experience with posaconazole, including dosing, plasma trough concentrations, safety, and tolerability with observations showing that DRT and IV formulations are both safe and effective in immunocompromised children, adolescents, and young adults. Higher dosing per body weight of DRT and IV Posaconazole may be required in patients < 13 years of age compared with patients 13 years of age and older to achieve therapeutic plasma concentrations.

Husain S, et al. (2019). Invasive Aspergillosis in solid-organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 33(9):e13544. https://www.ncbi.nlm.nih.gov/pubmed/30900296

- AST IDCOP 2019 updates for aspergillosis

Ullmann AJ, et al. (2018). Diagnosis and management of Aspergillus diseases: executive summary of the 2017 ESCMID-ECMM-ERS guideline. Clin Microbiol Infect. 2018 May;24 Suppl 1:e1-e38. https://www.ncbi.nlm.nih.gov/pubmed/29544767

- European guidelines for the management of Aspergillus. Comments on various Aspergillus strains, resistance, combination therapy, and TDM.

Patterson, et al. (2016). Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 63(4), e1–e60. https://doi.org/10.1093/cid/ciw326

- IDSA guidelines for aspergillosis

Maertens JA, et al. (2016). Isavuconazole versus voriconazole for primary treatment of invasive mould disease caused by Aspergillus and other filamentous fungi (SECURE): a phase 3, randomised-controlled, non-inferiority trial. Lancet.387:760-9. https://www.ncbi.nlm.nih.gov/pubmed/26684607

- Non-inferiority trial comparing the efficacy of isavuconazole to voriconazole for the treatment of invasive mold infections. Majority of the study population had hematological malignancies and had infections caused by Aspergillus. Isavuconazole was found to be non-inferior to voriconazole for the treatment of invasive mould infections and was associated with decreased adverse effects. However, therapeutic drug monitoring for voriconazole was not utilized.

Marr KA, et al. (2015). Combination antifungal therapy for invasive aspergillosis: a randomized trial. Ann Intern Med.162:81-9. https://www.ncbi.nlm.nih.gov/pubmed/25599346

- Randomized trial in patients with hematological malignancies with invasive aspergillosis infections treatment with voriconazole monotherapy or combination therapy with voriconazole and anidulafungin. Combination antifungal therapy was found to have a survival benefit compared to monotherapy, but this trial was not powered to make superiority claims.

Pascual A, et al. (2012). Challenging recommended oral and intravenous voriconazole doses for improved efficacy and safety: population pharmacokinetics-based analysis of adult patients with invasive fungal infections. Clin Infect Dis.55(3):381-90. https://www.ncbi.nlm.nih.gov/pubmed/22610925

- Study looking at use of oral vs IV use of voriconazole for treatment and found the need for higher oral than IV doses.

Pfeiffer CD, et al. (2006). Diagnosis of invasive aspergillosis using a galactomannan assay: a meta-analysis. Clin Infect Dis. 42:1417-27. https://www.ncbi.nlm.nih.gov/pubmed/16619154

- Meta-analysis to determine the accuracy of serum galactomannan assays for diagnosing aspergillosis infections in immunocompromised patients. For solid organ transplant recipients, galactomannan assays were found to have a sensitivity of 0.22 and specificity of 0.84.

Gavalda J, et al. (2005). Risk factors for invasive aspergillosis in solid-organ transplant recipients: a case-control study. Clin Infect Dis.41:52-9. https://academic.oup.com/cid/article/41/1/52/325103

- Retrospective, case control series that identified risk factors for developing aspergillosis infections in solid organ transplant recipients. Risk factors included use of vasoactive agents, prolonged ICU stay post-transplant, renal failure requiring HD, CMV disease, or one episode of bacterial infection.

Drew RH, et al. (2004). Comparative safety of amphotericin B lipid complex and amphotericin B deoxycholate as aerosolized antifungal prophylaxis in lung-transplant recipients. Transplantation.77:232-7. https://www.ncbi.nlm.nih.gov/pubmed/14742987.

- A prospective, randomized trial comparing amphotericin B lipid complex and amphotericin B deoxycholate inhalations for prophylaxis of aspergillosis in lung transplant recipients. Both agents

were associated with low rates of invasive fungal infections, but the lipid formulation was associated with decreased adverse effects.

Helmi M, et al. (2003). Aspergillus infection in lung transplant recipients with cystic fibrosis: risk factors and outcomes comparison to other types of transplant recipients. Chest.123:800-8. https://www.ncbi.nlm.nih.gov/pubmed/12628881.

- A retrospective study that aimed to characterize Aspergillus infections in lung transplant recipients. Patients that are pre-colonized with Aspergillus infections prior to lung transplant may benefit from systemic antifungal prophylaxis after transplant.

Herbrecht R, et al. (2002). Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Engl J Med.347(6):408-15. https://www.ncbi.nlm.nih.gov/pubmed/12167683

- RCT of voriconazole vs amphotericin which established voriconazole as a first-line agent for the treatment of aspergillosis with improved response and survival rates. TDM not used for voriconazole.

7.3.3 Cryptococcus

Pennington KM, et al. (2024). Risk Factors for Early Fungal Disease in Solid Organ Transplant Recipients: A Systematic Review and Meta-analysis. Transplantation, 108(4), 970–984. https://doi.org/10.1097/TP.0000000000004871

- Review and analysis that pertained to the risk factors for development of invasive fungal infections in SOT. Authors concluded three variables with high certainty of evidence and strong associations to early fungal infections across all SOT groups were reoperation, post-transplant CRRT, and CMV disease.

Jayaprakash V, et al. (2023). Cryptococcal myositis and monoarthritis in a failed renal allograft recipient. Transplant infectious disease: an official journal of the Transplantation Society, 25(4), e14092. https://doi.org/10.1111/tid.14092

- Case report of 38-yo living-related renal transplant recipient with hepatitis B, post-transplant diabetes with failing allograft due to chronic allograft nephropathy. Presented with a painful knee with swelling, synovial fluid grew Crypococcus neoformans and was treated with amphotericin and fluconazole with complete resolution of infection.

Zhao PJ, et al. (2022). Cryptococcosis after heart transplantation: A literature review and case report. Transplant infectious disease: an official journal of the Transplantation Society, 24(6), e13990. https://doi.org/10.1111/tid.13990

- Letter to the editor addressing a literature review and case report of the incidence of Cryptococcal infections following heart transplantation.

Natarajan P, et al. (2021). Donor-derived Cryptococcus gattii sensu stricto infection in two kidney transplant recipients, southeastern United States. Am J Transplant, 21(11):3780-3784. https://pubmed.ncbi.nlm.nih.gov/34173328/

- Case report of an organ transplant-associated outbreak of *C. gattii* infection involving an HIV-negative immunosuppressed donor. 2 of the 3 recipients from this donor developed severe *C. gattii* infections following transplantation.

Baddley JW, et al. (2019); AST Infectious Diseases Community of Practice. Cryptococcosis in solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 33(9):e13543. https://www.ncbi.nlm.nih.gov/pubmed/30900315

- AST IDCOP 2019 updates for cryptococcosis

Marinelli T, et al. (2019). Very early onset of Cryptococcus neoformans disease following liver transplantation: report of two cases and a review of the literature. Transpl Infect Dis.22;e13227. https://www.ncbi.nlm.nih.gov/pubmed/31785187

- Two case reports of cryptococcosis infection early after liver transplantation and review of literature in SOT.

Perfect JR, et al. (2010). Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis, 50(3):291-322. https://academic.oup.com/cid/article/50/3/291/392360

- Treatment guidelines for cryptococcal disease in HIV-infected individuals, organ transplant recipients, and non-HIV-infected nontransplant hosts. Includes recommendations for other unique populations and those with Cryptococcus gattii infection.

Sun H, et al. (2009). Lipid Formulations of Amphotericin B Significantly Improve Outcome in Solid Organ Transplant Recipients with Central Nervous System Cryptococcosis. Clin Infect Dis, 49(11):1721-1728. https://doi.org/10.1086/647948.

- In 79 patients with central nervous system cryptococcosis, lipid formulations of amphotericin B were associated with lower mortality when compared to amphotericin B deoxycholate.

Dromer F, et al. (2008). Major role for amphotericin B–flucytosine combination in severe cryptococcosis. PLoS ONE. 3(8):e2870. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0002870.

- Prospective, cohort study of patients with C. neoformans showed that lack of flucytosine induction is an independent risk factor for mycotic failure at two weeks.

7.3.4 Invasive Candidiasis

Pennington KM, et al. (2024). Risk Factors for Early Fungal Disease in Solid Organ Transplant Recipients: A Systematic Review and Meta-analysis. Transplantation, 108(4), 970–984. https://doi.org/10.1097/TP.0000000000004871

- Systematic review and meta-analysis of transplant recipients as risk for early fungal diseases.

Yang Q, et al. (2022). In vitro synergistic antifungal activities of caspofungin in combination with fluconazole or voriconazole against Candida species determined by the Etest method. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases, 122, 982–990. https://doi.org/10.1016/j.ijid.2022.07.056

- Prospective study evaluating in vitro synergy of caspofungin in combination with fluconazole or voriconazole for treatment of resistant Candida spp. from 28 isolates at a single center.

Phoompoung P, et al. (2022). Risk factors of invasive fungal infections in liver transplant recipients: A systematic review and meta-analysis. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 22(4), 1213–1229. https://doi.org/10.1111/ajt.16935

- Systematic review and meta analysis of published studies to determine which risk factors are associated with invasive fungal infections (IFI) in liver transplant recipients. Authors identified most relevant independent risk factors being vascular complications, renal failure, and fungal colonization. Post-transplant renal replacement therapy was associated with the highest risk of invasive aspergillus infection in liver transplant recipients.

Sartain E, et al. (2021). Perioperative anidulafungin combined with triazole prophylaxis for the prevention of early invasive candidiasis in lung transplant recipients. Transpl Infect Dis, 23(4):e13692. https://pubmed.ncbi.nlm.nih.gov/34270137/

- A retrospective analysis of lung transplant recipients evaluating the effectiveness of perioperative anidulafungin for early invasive candidiasis prevention in addition to long-term triazole antifungal prophylaxis compared to triazole prophylaxis alone. There was no statistically significant difference in incidence of invasive candidiasis between cohorts (6% vs 13%, p=0.16).

Boonstra JM, et al. (2021). Optimization of fluconazole dosing for the prevention and treatment of invasive candidiasis based on the pharmacokinetics of fluconazole in critically ill patients. Antimicrob Agents Chemother;65(3):e01554-20. https://pubmed.ncbi.nlm.nih.gov/33361296/6/

- Pharmacokinetic study of fluconazole dosing for the prevention and treatment of invasive candidiasis in critically ill patients including solid organ transplant recipients

Leitheiser S, et al. (2020). Risk factors associated with invasive fungal infections in kidney transplant patients. Am J Med Sci. 3599(2):108-116. https://www.ncbi.nlm.nih.gov/pubmed/31836132.

- Review of USRDS data to identify risk factors for invasive fungal infections (Candida, Histoplasmosis, Aspergillosis, cryptococcosis, other mycoses) in kidney transplant recipients. Identified risk factors include age > 65 years, diabetes, bacterial pneumonia and UTI.

Kullberg BJ, et al. (2019). Isavuconazole Versus Caspofungin in the Treatment of Candidemia and Other Invasive Candida Infections: The ACTIVE Trial. Clin Infect Dis. 68(12):1981-1989. https://www.ncbi.nlm.nih.gov/pubmed/30289478

- Non-inferiority of isavuconazole to caspofungin was not shown

Aslam S, et al. (2019). Candida infections in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant, 33(9):e13623. https://www.ncbi.nlm.nih.gov/pubmed/31155770

- AST IDCOP 2019 updates to management of candida in SOT

Bidaud AL, et al. (2018). Candida auris: An emerging drug resistant yeast - A mini-review. J Mycol Med. 28(3):568-573. https://www.ncbi.nlm.nih.gov/pubmed/30030072

- Updated review on Candida auris

Pappas PG, et al (2016). Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 62(4), e1–e50. https://doi.org/10.1093/cid/civ933

- IDSA 2016 guidelines for treatment of candidiasis.

Eschenauer GA, et al. (2015). Targeted versus universal antifungal prophylaxis among liver transplant recipients. Am J Transplant.15(1):180-189. https://onlinelibrary.wiley.com/doi/10.1111/ajt.12993

- Retrospective review of liver transplant recipients to assess the feasibility and efficacy of tiered, targeted fungal prophylaxis. Intra-abdominal candidiasis was the most common fungal infection (73%); invasive fungal infections occurred in 6% of high-risk transplants who received prophylaxis versus 4% in low risk transplant who did not receive prophylaxis.

Gavalda J, et al. (2014). Invasive fungal infections in solid organ transplant recipients. Clin Microbiol Infect 20(7):27–48. https://www.sciencedirect.com/science/article/pii/S1198743X14605000?via%3Dihub

- Review of risk factors, prevention, diagnosis, and treatment of invasive fungal infections in SOT recipients (focus on candidiasis and aspergillosis).

Singh N, et al. (2012). Donor-derived fungal infections in organ transplant recipients: guidelines of the American Society of Transplantation, infectious diseases community of practice. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 12(9), 2414–2428. https://doi.org/10.1111/j.1600-6143.2012.04100.x

- The American Society of Transplantation guidelines for management of donor-derived fungal infections in solid organ transplant recipients.

Reboli AC, Rotstein C, et al. (2007). Anidulafungin versus fluconazole for invasive candidiasis. N Engl J Med. 356(24):2472-82. https://www.ncbi.nlm.nih.gov/pubmed/17568028

- Andidafungin was non-inferior to fluconazole with a favorable response in the andidafungin arm.

Mora-Duarte J, Betts R, et al. (2002); Caspofungin Invasive Candidiasis Study Group. Comparison of caspofungin and amphotericin B for invasive candidiasis. N Engl J Med. 347(25):2020-9. https://www.ncbi.nlm.nih.gov/pubmed/12490683

- Caspofungin was as effective as amphotericin B who had candidemia with a favorable response in the caspofungin arm.

7.3.5 Histoplasmosis

Abad CL, et al. (2024). Donor-derived endemic mycoses after solid organ transplantation: A review of reported cases. *Clinical transplantation*, *38*(1), e15199. https://doi.org/10.1111/ctr.15199

- Review of 18 donor-derived endemic mycoses case reports (16 coccidioidomycosis, 7 histoplasmosis, and 1 talaromycosis). Author reports about half of these cases were probable infections, a majority of infectious cases were disseminated, and mortality was reported in about half of patients. Additionally, a majority of donors had exposure to coccidioidomycosis and histoplasmosis.

Siegrist EA, et al. (2023). Disseminated histoplasmosis after alemtuzumab. Transplant infectious disease: an official journal of the Transplantation Society, 25(6), e14089. https://doi.org/10.1111/tid.14089

- Case report of two patients (kidney, pancreas) who received alemtuzumab found to have histoplasmosis.

Shikarwar T, et al. (2023). Disseminated histoplasmosis with refractory thrombocytopenia in a renal transplant patient. Transplant infectious disease: an official journal of the Transplantation Society, 25(6), e14163. https://doi.org/10.1111/tid.14163

- Case report reviewing a renal transplant recipient with idiopathic thrombocytopenic purpura following histoplasmosis infection.

Hernandez A, et al. (2023). Disseminated histoplasmosis with central nervous system involvement in a kidney transplant recipient. Transplant infectious disease: an official journal of the Transplantation Society, 25(4), e14033. https://doi.org/10.1111/tid.14033

- Case report reviewing a renal transplant recipient who presented with non-specific CNS infection symptoms and found to have CNS histoplasmosis infection.

Rodríguez-Echeverri C, et al. (2023). Histoplasma capsulatum modulates the immune response, affects proliferation and differentiation, and induces apoptosis of mesenchymal stromal cells. Mycoses, 66(2), 157–167. https://doi.org/10.1111/myc.13537

- Article reviewing the effect of histoplasma on the immune system and immunomodulatory properties.

Benchbani H, et al. 2022). Histoplasma osteomyelitis in a 15-year-old kidney transplant patient. Transplant infectious disease: an official journal of the Transplantation Society, 24(6), e13953. https://doi.org/10.1111/tid.13953

- Case report of 15-yo boy with history of kidney transplant on immunosuppressive therapy found to have histoplasma osteomyelitis.

Miller R, et al. (2019). AST Infectious Diseases Community of Practice. Endemic fungal infections in solid organ transplant recipients-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant;33(9):e13553. https://www.ncbi.nlm.nih.gov/pubmed/30924967

- AST IDCOP 2019 updates on managements of endemic fungal infections

Thompson GR III, et al. (2016). Isavuconazole treatment of Cryptococcosis and dimorphic mycoses. Clin Infect Dis.63(3):356-362. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946023/

- “VITAL” study: Open-label nonrandomized phase 3 trial evaluating efficacy and safety of isavuconazole in treatment of rare invasive fungal diseases. Seven of the patients were treated for histoplasmosis, with 1 having complete success, 3 with partial success, 1 with stable disease, and 2 with progression of disease. Median isavuconazole levels ranged from 3.2 ng/mL to 4.01 ng/mL and it was overall well tolerated.

Kauffman CA, et al. (2015). Histoplasmosis and Blastomycosis in Solid Organ Transplant Recipients. J Fungi. 1(2):84-106. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5753102/

- Review of the epidemiology, clinical presentation, and treatment strategies for Histoplasmosis and Blastomycosis in SOT recipients.

Kauffman CA, et al. (2014). Endemic fungal infections in solid organ and hematopoeitic cell transplant recipients enrolled in TRANSNET. Transpl Infect Dis.16(2):213-224. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5664161/

- Prospective surveillance study of 70 patients (64 SOT recipients) across 15 centers to characterize endemic infections in these patients.

Assi M, et al. (2013). Histoplasmosis after solid organ transplant. Clin Infect Disease.57(11):1542-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3814825/

- Retrospective review of 152 cases of histoplasmosis across 24 centers to identify risk factors and characterize infections. The average time to onset was 27 months, with the first year being the highest risk time frame. Ten percent of patients died, usually within the first month. In patients

that survived one month after diagnosis, amphotericin followed by 12 months of an azole was usually successful.

Wheat JL, Freifeld AG, Kleiman MB, Baddley JW, McKinsey DS, Loyd JE, Kauffman CA. Clinical practice guidelines for the management of patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2007; 45:807–25.
https://academic.oup.com/cid/article/45/7/807/541502

- IDSA 2007 guidelines for treatment of histoplasmosis.

7.4 Other

7.4.1 Timing of post-transplant infections (including donor-derived infections)

Khedr L, et al. (2023). Infections in the first year of living related kidney transplantation in a young transplant cohort. BMC nephrology, 24(1), 328. https://doi.org/10.1186/s12882-023-03379-9

- Prospective observational study exploring infections within 1 year after living donor kidney transplant recipients

Boutin CA, et al. (2023). Utility of deceased donor cultures in solid organ transplantation in preventing donor-derived bacterial and fungal infectious diseases transmission. Transplant infectious disease: an official journal of the Transplantation Society, 25(2), e14032. https://doi.org/10.1111/tid.14032

- Review with guidance on deceased donor culture results based upon organ transplanted

Anesi JA, et al., & CDC Prevention Epicenters Program (2022). Impact of donor multidrug-resistant organisms on solid organ transplant recipient outcomes. Transplant infectious disease: an official journal of the Transplantation Society, 24(1), e13783. https://doi.org/10.1111/tid.13783

- Multicenter retrospective cohort study that show that multi-drug resistant organisms on donor culture increase risk of early post-transplant infection, but do not appear to affect long-term graft or recipient survival

Kaul DR, et al. (2021). Ten years of donor-derived disease: A report of the disease transmission advisory committee. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 21(2), 689–702. https://doi.org/10.1111/ajt.16178

- Report with proven and probable transmission of donor-derived infection by organ type

Wolfe CR, et al. (2019). AST Infectious Diseases Community of Practice. Donor-derived infections: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant;33(9):e13547. https://www.ncbi.nlm.nih.gov/pubmed/30903670

- AST IDCOP 2019 Guidelines on donor-derived infections

Malinis M, et al. (2019). Screening of donor and candidate prior to solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clinical transplantation, 33(9), e13548. https://doi.org/10.1111/ctr.13548

- AST ID COP 2019 guidlines on screening of donor and candidate prior to SOT

Fishman JA (2017). Infection in Organ Transplantation. American Journal of Transplantation.17:856-879. https://www.ncbi.nlm.nih.gov/pubmed/28117944

- Review of risk factors contributing to infections in transplant patients and timing of infections post-transplant.

Green M (2013). Introduction: Infections in Solid Organ Transplantation. American Journal of Transplantation; 13: 3–8. http://www.ncbi.nlm.nih.gov/pubmed/23464993

- This article examines risk factors that contribute to infections in transplant patients as well as the timing of infections post-transplant.

Sun HY, et al. (2010). Unrecognized pretransplant and donor-derived cryptococcal disease in organ transplant recipients. Clinical Infectious Diseases, 51(9):1062-1069. https://academic.oup.com/cid/article/51/9/1062/292746.

- Retrospective review of solid organ transplant recipients who developed cryptococcosis post-transplant, including nine who developed infection within 30 days which could indicate unrecognized pretransplant or donor-derived cryptococcosis.

Humar A, et al. (2006). American Society of Transplantation Recommendations for Screening, Monitoring and Reporting of Infectious Complications in Immunosuppression Trials in Recipients of Organ Transplantation. American Journal of Transplantation, 6: 262–274. http://www.ncbi.nlm.nih.gov/pubmed/16426310

- This article provides definitions for infections in transplant patients to be used during clinical trials assessing immunosuppressive therapy and also provides recommendations for monitoring for infections.

Snydman DR, et al. (2001). Epidemiology of Infections after Solid-Organ Transplantation. Clinical Infectious Diseases, 33 (Suppl 1), S5–8. http://www.ncbi.nlm.nih.gov/pubmed/11389515

- This is a review article focusing on the epidemiology of infections after transplant categorized into three time frames- the first month, second through sixth month, and greater than six months.

Freeman RB, et al. (1999). Outcome of transplantation of organs procured from bacteremic donors. Transplantation, 68(8):1107-1111. https://pubmed.ncbi.nlm.nih.gov/10551637/

- Retrospective review analyzing the transmission rates and 30-day graft and patient survival outcomes for recipients of organs procured from bacteremic donors.

7.4.2 Infectious exposure management

7.4.2.1 Measles

Statler, VA et al. (2023). Spotting a potential threat: Measles among pediatric solid organ transplantation recipients. Pediatric transplantation, 27(4), e14502. https://doi.org/10.1111/petr.14502

- Review article assessing the reemergence of measles due to a decrease in vaccination rates and how to optimize prevention in the pediatric transplant population

Kreiger-Benson E, et al. (2021). Measles outbreak risk assessment for transplant candidates and recipients. Am J Transplant. 21(1):338-343. https://pubmed.ncbi.nlm.nih.gov/32808470/

- A review of the implementation of a systematic risk assessment during a large measles outbreak in the New York City area, with a total of 649 cases reported from 2018-2019.

Seckin ZI, et al. (2021). Serologic screening and infectious diseases consultation in renal transplant candidates for measles, mumps, rubella and varicella. Rom J Intern Med;59(2):159-165. https://pubmed.ncbi.nlm.nih.gov/33565307/

- A retrospective study of kidney transplant patients to investigate the number of recipients who were evaluated for serologic status again MMR and varicella. It was found that the screening rate for MMR serologies was lower than varicella and pre-transplant infectious disease consult increased vaccination rate.

Kreiger-Benson E, et al. (2021). Measles outbreak risk assessment for transplant candidates and recipients. Am J Transplant;21(1):338-343. https://pubmed.ncbi.nlm.nih.gov/32808470/

- The systematic risk assessment approach to identify and protect at-risk solid organ transplant recipients during the large measles outbreak in late 2018-summer of 2019 in the New York City area

Centers for Disease Control and Prevention (CDC). (2007) Multistate measles outbreak associated with an international youth sporting event--Pennsylvania, Michigan, and Texas, August-September, Morbidity and Mortality Weekly Report, 57, 169-173. http://www.ncbi.nlm.nih.gov/pubmed/18288074

- This report summarizes exposure to measles through international travel and illustrates the potential for immunocompromised patients to encounter the virus despite common coverage with effective vaccines in the US.

Warmington L, et al. (2005). Loss of antibodies to measles and varicella following solid organ transplantation in children. Pediatric Transplantation, 9, 311-314. http://www.ncbi.nlm.nih.gov/pubmed/15910386

- Serologies of 18 children were reviewed 6 months post-transplant. Four of 18 (22.2%) and 2/18 (11.1%) lost immunity to measles and varicella.

7.4.2.2 Varicella

Sarı N, et al. (2023). Herpes Zoster Infections in Solid-Organ Transplant Recipients. Experimental and clinical transplantation: official journal of the Middle East Society for Organ Transplantation, 21(9), 764–771. https://doi.org/10.6002/ect.2023.0185

- Retrospective review of herpes zoster infections in transplant recipients, with an emphasis on early supportive measures and prophylaxis regimens

Suarez-Zdunek MA, et al. (2023). Herpesvirus immunology in solid organ transplant recipients - liver transplant study (HISTORY): a retrospective and prospective observational cohort study. BMC infectious diseases, 23(1), 214. https://doi.org/10.1186/s12879-023-08153-8

- Observational cohort study assessing the cellular response against CMV and VZV infections in liver transplant recipients, useful for predicting patients at a higher risk for infection post transplant

Tamura D, et al. (2021). Lack of persisting antibody in a post-transplant patient after vaccine-strain varicella. Pediatr Transplant. 25(7):e14070. https://pubmed.ncbi.nlm.nih.gov/34120389/

- Case report of a female child received live attenuated varicella vaccine 30 months after a living donor liver transplant at the age of 2 months. 2 years later however the antibody titer decreased to undetectable levels.

Crouch A, et al. (2021). Evaluation of low dose famciclovir as herpes simplex virus and varicella zoster virus prophylaxis in cytomegalovirus low-risk solid organ transplant recipients. Transpl Infect Dist;23(5):e13711. https://pubmed.ncbi.nlm.nih.gov/34379876/

- Low-risk CMV solid organ transplant recipients receiving once-daily famciclovir experienced no HSV/VZV/CMV infection while on prophylaxis for a duration of 3 months.

Bobrowski AE, et al. (2020). Varicella infection following vaccination in a pediatric kidney transplant recipient. Pediatr Transplant. 24(4):e13667. https://pubmed.ncbi.nlm.nih.gov/32068320/

- Case report of a 4-year-old boy who received the live attenuated MMR-varicella vaccine 16 months after receiving a living donor kidney transplant. He developed documented disseminated varicella infection 5 weeks later.

Pergam SA, et al. (2013). Varicella zoster virus in solid organ transplantation. Am J Transplant.13 Suppl 4:138-46. https://www.ncbi.nlm.nih.gov/pubmed/20070670

- Review article on the management of varicella zoster in solid organ transplant recipients.

Arora A, et al. (2008). Double-blind study comparing 2 dosages of valacyclovir hydrochloride for the treatment of uncomplicated herpes zoster in immunocompromised patients 18 years of age and older. Journal of Infectious Diseases, 197, 1289-1295.http://www.ncbi.nlm.nih.gov/pubmed/18422441

- No differences in median time to full healing of HSV rash were detected among patients receiving valacyclovir 1 gram TID versus 2 grams TID.

Tyring S, et al. (2001). A randomized, double-blind trial of famciclovir versus acyclovir for the treatment of localized dermatomal herpes zoster in immunocompromised patients. Cancer Investigation, 19, 13-22. http://www.ncbi.nlm.nih.gov/pubmed/11291551

- Famciclovir 500 mg three times a day was compared to acyclovir 800 mg five times a day and no significant differences in new lesion formation, time to healing or duration of pain were observed

Shepp DH, et al. (1986). Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. New England Journal of Medicine, 314, 208-212. http://www.ncbi.nlm.nih.gov/pubmed/3001523

- Acyclovir limited cutaneous dissemination as well as abbreviated duration of positive cultures, pain associated with lesions, postulation of lesions, crusting of lesions and complete healing of lesions.

7.4.2.3 Influenza

Arentoft NS et al. (2023). Influenza in Liver and Kidney Transplant Recipients: Incidence and Outcomes. Microbiology spectrum, 11(2), e0322622. Advance online publication. https://doi.org/10.1128/spectrum.03226-22

- Retrospective study assessing the MiBa database, a nationwide database in Denmark, finding no differences in vaccination, sex, age, or comorbidities in kidney and liver transplant recipients

Yue MC, et al. (2017). Successful use of oseltamivir prophylaxis in managing a nosocomial outbreak of influenza A in a hematology and allogeneic stem cell transplant unit. Asia Pac J Clin Oncol.13(1):37-43. https://www.ncbi.nlm.nih.gov/pubmed/27730741

- Description of infection control and oseltamivir prophylaxis in an outbreak of 12 patients in a group of immunocompromised patients.

7.4.2.4 Tuberculosis

CDC MMWR: Guidelines for the investigation of contacts of persons with infectious tuberculosis. 2005;54(RR15):1-37. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

- CDC guidelines for evaluating patients at risk for developing TB after an exposure. Includes a section specifically regarding immunocompromised hosts that suggests considering them as "high priority" when evaluating potential contacts of a TB infected person.

7.4.2.5 Bacterial meningitis

CDC Guidance for the evaluation and public health management of suspected outbreaks of meningococcal disease. https://www.cdc.gov/meningococcal/downloads/meningococcal-outbreak-guidance.pdf

- Guidelines for management of meningococcal outbreaks. There are no specific recommendations for immunocompromised patients.

7.4.3 Immunizations

Dadhania, DM et al. (2023). Age-related decline in anti-HBV antibodies in vaccinated kidney transplant recipients. Transplant infectious disease: an official journal of the Transplantation Society, 25(4), e14090. https://doi.org/10.1111/tid.14090

- Single center retrospective study of kidney transplant recipients who had HBsAb measured pretransplant and 1 year post transplant. Findings suggest that HBsAb levels significantly decline post kidney transplant, and place recipients, specifically older patients, at higher risk of HBV infection.

Berman MA, et al. (2023). Disseminated vaccine-induced varicella infection in a kidney transplant recipient. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 23(11), 1806–1810. https://doi.org/10.1016/j.ajt.2023.05.034

- Case report of 33-yo kidney transplant recipient with disseminated vaccine-induced varicella infection.

Dadhania DM, et al. (2023). Age-related decline in anti-HBV antibodies in vaccinated kidney transplant recipients. Transplant infectious disease: an official journal of the Transplantation Society, 25(4), e14090. https://doi.org/10.1111/tid.14090

- Single-center, retrospective study of 96 kidney transplant recipients who had hepatitis B surface antibody (HBsAb) levels measured pre-transplant and 1-year post and stratified according to age. Authors found that HBsAg IgG levels decreased significantly at 1-year post-transplant, were significantly lower in the older cohort and if patients received antithymocyte globulin.

ACIP Altered Immunocompetence Guidelines for Immunizations. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html (Aug 2023).

- Most recently updated CDC/ACIP vaccinations in immunocompromised patients.

Kitano T, et al. (2023). Immunogenicity of a quadrivalent human papillomavirus vaccine in pediatric kidney and liver transplant recipients. Pediatric transplantation, 27(3), e14476. https://doi.org/10.1111/petr.14476

- Prospective, observational study including females aged 12-19 who received either kidney or liver transplants and healthy participants to evaluate the immunogenicity of quadrivalent HPV vaccine. Authors concluded that though not statistically significant, the HPV titers were 25-50% lower in transplant recipients compared to 100% in healthy subjects.

Felzer JR, et al. (2023). Disparities in vaccination rates in solid organ transplant patients. Transplant infectious disease: an official journal of the Transplantation Society, 25(2), e14010. https://doi.org/10.1111/tid.14010

- Retrospective, observational study of 468 SOT recipients to assess socioeconomic and demographic factors associated with influenza and pneumococcal vaccination rates in four counties in southern Minnesota. Authors concluded there was an overall vaccination rate of 57-63% for influenza and 56% for pneumococcal. Among organs, liver and lung recipients were least vaccinated for influenza, and heart recipients were least up-to-date on pneumococcal vaccines.

Schneider S, et al. (2022). Serologic evaluation of vaccine preventable infections and vaccination rates in kidney transplant candidates. Transplant infectious disease: an official journal of the Transplantation Society, 24(6), e13973. https://doi.org/10.1111/tid.13973

- Retrospective, descriptive study examining serologic status and rates of live vaccination in 672 patients listed for kidney transplant. Authors found a large portion of candidates had immunity gaps that were not resolved prior to transplant.

Newman AM, et al. (2022). Live virus vaccination following pediatric liver transplantation: Outcomes from two academic children's hospitals. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 22(4), 1201–1212. https://doi.org/10.1111/ajt.16937

- Retrospective, cohort study of 204 pediatric liver transplant recipients at 2 children's hospitals of which 97 received at least one LVV after transplant. Authors concluded 6 patients who did not receive the vaccine had evidence of vaccine-preventable illness; 1 patient who received LVV after transplant developed a diffuse VZV-related rash; similar rejection rates and no serious ADEs caused by LVV after transplant.

Danziger-Isakov L, et al; AST ID Community of Practice (2019). Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice. Clin Transplant, 33(9):e13563. https://www.ncbi.nlm.nih.gov/pubmed/31002409

- AST IDCOP 2019 updates on vaccinations

Buchan CA, et al.; AST Infectious Diseases Community of Practice (2019). Travel medicine, transplant tourism, and the solid organ transplant recipient-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant, 33(9):e13529. https://www.ncbi.nlm.nih.gov/pubmed/30859623

- AST ICDOP 2019 updates on travel medicine where a column for immunocompromised conditions and recommended vaccinations can be found

Vink P, et al. (2019). Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: a Phase III, Randomized Clinical Trial. Clin Infect Dis. https://www.ncbi.nlm.nih.gov/pubmed/30843046

- Initial studies on use of Shingrix in transplant recipients, additional trials currently underway.

Natori Y, et al. (2018). A Double-Blind, Randomized Trial of High-Dose vs Standard-Dose Influenza Vaccine in Adult Solid-Organ Transplant Recipients. Clin Infect Dis. 66(11):1698-1704. https://www.ncbi.nlm.nih.gov/pubmed/29253089

- RCT which demonstrated that high dose vaccine may improve immunogenicity, study did not look at rates of disease.

Cordero E, et al. (2017). Two Doses of Inactivated Influenza Vaccine Improve Immune Response in Solid Organ Transplant Recipients: Results of TRANSGRIPE 1-2, a Randomized Controlled Clinical Trial. Clin Infect Dis.64(7):829-838. https://www.ncbi.nlm.nih.gov/pubmed/28362949

- Booster dose 5 weeks after initial flu vaccination induces an increased antibody response.

7.4.4 Toxoplasmosis prophylaxis and treatment

Francí EV, et al. (2023). Complex considerations - Fever and pancytopenia after solid organ transplantation. Transplant infectious disease: an official journal of the Transplantation Society, 25(4), e14079. https://doi.org/10.1111/tid.14079

- Case report of 42-yo man who underwent kidney transplant and had pancytopenia with acute hepatic failure. He was found to have donor-derived toxoplasmosis.

Kilduff S, et al. (2024). Pet safety guidelines for pediatric transplant recipients. Pediatric transplantation, 28(1), e14527. https://doi.org/10.1111/petr.14527

- Guidelines for pet safety in pediatric solid organ transplant recipients.

Cohen A, et al. (2022). Isolated cerebral toxoplasmosis 17 years post renal transplant. Transplant infectious disease: an official journal of the Transplantation Society, 24(4), e13880. https://doi.org/10.1111/tid.13880

- Case report of 59-yo female 17 years post-transplant who presented with recurrent falls, visual changes, headaches, and confusion who was found to have cerebral toxoplasmosis.

Adekunle RO, et al. (2021). Clinical characteristics and outcomes of toxoplasmosis among transplant recipients at two US academic medical centers. Transpl Infect Dis;23(4):e13636. https://pubmed.ncbi.nlm.nih.gov/33993599/

- A retrospective review of SOT and HSCT recipients with toxoplasmosis between 2002 and 2018 at two large transplant centers in the United States.

Ramanan P, et al. (2020). Toxoplasmosis in non-cardiac solid organ transplant recipients: a case series and review of literature. Transpl Infect Dis. 22e13218. https://www.ncbi.nlm.nih.gov/pubmed/31769583

- Case series of 3 patients (two liver, one lung) who developed post-transplant donor-derived toxoplasmosis. All patients were not on TMP-SMX prophylaxis at diagnosis, and two patients died with disseminated infection.

Hoz R, et al. (2019). Tissue and blood protozoa including toxoplasmosis, Chagas disease, leishmaniasis, Babesia, Acanthamoeba, Balamuthia, and Naegleria in solid organ transplant recipients – Guidelines

from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl;33:e13546. https://www.ncbi.nlm.nih.gov/pubmed/30900295

- American Society of Transplantation's guidelines on the diagnosis, prevention, and management of toxoplasmosis in the pre- and post-transplant period

Cherhrazi-Raffle A, et al. (2015). Toxoplasma gondii serology and outcomes after heart transplantation: contention in the literature. Transplant Proceedings.47(6):1949-1953. https://www.ncbi.nlm.nih.gov/pubmed/26293079

- Single center study of the effect of T. gondii donor and recipient serostatus on heart transplant outcomes, including 5 year mortality and rates of CAV comparing results to previous studies of association of toxoplasmosis serostatus to outcomes.

Fernandez-Sabe N, et al. (2012). Risk factors, clinical features and outcomes of toxoplasmosis in solid-organ transplant recipients: a matched case-control study. Clin Inf Dis. 54(3):355-361. https://pubmed.ncbi.nlm.nih.gov/22075795/

- Multicenter study of cases of toxoplasmosis with details including diagnosis, manifestations and outcomes.

Derouin F, et al.(2008). Prevention of toxoplasmosis in transplant patients. Clin Microbio Infect. 2008; 14:1089-1101. https://www.ncbi.nlm.nih.gov/pubmed/19018809

- Review article discussing the relative risk of toxoplasmosis infection, timing of infection and prophylaxis options in solid organ and hematopoietic stem cell transplant recipients.

Wreghitt TG, et al. (1995). Antibiotic prophylaxis for the prevention of donor-acquired toxoplasma gondii infection in transplant patients. Journal of Infection. 31(3):253-254. https://www.ncbi.nlm.nih.gov/pubmed/8586854

- Summary of literature discussing chemoprophylaxis of toxoplasmosis infection.