Vaccination in Transplant Recipients

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How does “Post-transplant” status matter ?

- Immunosuppressive regimens after solid-organ transplant include a combination of steroids and calcineurin inhibitors, such as cyclosporin and tacrolimus (FK506).
- In recipients, Both T- and B-cell responses are impaired through blockage of cellular proliferation after antigen stimulation.
- Recipients of solid-organ transplantation are at risk of severe infections due to their life-long immunosuppression.
- On immunosuppression, the immune system will not be able to mount a response as effective as in normal subjects
- Presence of post-transplantation hypogammaglobulinemia. (immunoglobulin G < 600 mg/dl), is associated with the development of recurrent infections ell as inhibition of cytokine production necessary for such stimulation

Post BMT …

- Entirely different recommendations
- All immune memory is cleared during mylo-ablative phase
- All vaccines are started as “Fresh” irrespective of Pre BMT status
- Unlike solid organ transplants, not on life-long immunosuppression
- Live vaccines- MMR, Varicella are used
- Cases which end up as GVHD and receive Prolonged immune suppression or blood products follow different schedule
- Refer to ICMR Guidelines

Concerns of vaccination in post transplant…

- The decision to administer vaccines to immunosuppressed children is a risk–benefit balance
- Qualitatively diminished immunological response
- Can develop diseases caused by the vaccine pathogen.
- Vaccination may cause a flare-up of disease activity or provocation of graft rejection
  - An enhanced lymphocyte proliferative response to donor-specific aortic endothelial cells following influenza vaccination has been reported in heart recipients by some groups
  - No reported case of rejection triggered by influenza vaccination in liver, kidney, and lung recipients.
  - Data suggest that the infectious agent, more commonly responsible for rejection, and effective immunizations may actually be more protective.

Concerns of vaccination in post transplant…

Cannot be assumed that a given antibody level provides the same protection in immunosuppressed (IS) children as in healthy ones

Immunity wanes faster in IS children than in healthy ones

Need to check antibody titers and consider re-vaccination

In contrast, live vaccines may lose their attenuated status in an IS host and cause disease due to uninhibited replication of the vaccine organism.

Vaccination considerations “Pre-Transplant”…

- Recollection of pretransplant immune memory, with one or more booster doses of a vaccine, is more effective than primary vaccination being done after transplant
- Primary immunizations should be given before transplantation, as early as possible during the course of disease - immune response to vaccines is decreased in patients with end-stage organ disease
- Vaccine to be initiated earlier with shortened intervals between the vaccine doses than routinely recommended.
- Antibody status, especially for live vaccines, should be measured before transplantation or immunosuppression therapy, and a revaccination if the levels are below the expected values
- Vaccination against hepatitis B, pneumococcus, and influenza are particularly recommended.

Vaccination considerations Post Transplant…

- First 6 months after transplantation - poorest response - receiving the highest doses of immunosuppression.
- First 6 months associated with a higher chance of graft dysfunction and rejection
- Post- pone immunizations until patients are taking maintenance immunosuppression, while some centres commence vaccination once steroid doses are minimized, which is usually achieved after 1 year.
- Avoid live vaccines in the immunosuppressed, i.e., patients receiving:
  - Prednisolone at ≥2 mg/kg or 20 mg, daily or alternate day, for >14 days.
  - Other immunosuppressants (CP, azathioprine, MMF, CSA, TAC, RTX etc.)

Vaccination considerations Post Transplant…

- If vaccination prior to transplant is incomplete or missed, inactivated vaccine counterparts (such as inactivated polio vaccine instead of live polio vaccine) should be used to complete the course. After transplant.
- Inactivated vaccines are generally safe in an IS patient.
- Vaccines, such as polio, influenza, typhoid and Japanese encephalitis are available both as inactivated and as live vaccines
- Live vaccines, such as oral polio (OPV), BCG, inhaled influenza and oral typhoid vaccines, are considered to be absolutely contra-indicated.

Immunization of contacts …

- Vaccination strategy should include vaccination of household contacts/ siblings **and health care workers at transplant centers** unless contraindicated.
- Should receive all standard immunizations including non-transmissible live vaccines (MMR, varicella).
- Immunization with varicella vaccine in unprotected (seronegative) contacts/health care workers poses a low risk to IS patients, but this risk is greatly outweighed by the benefits.
- **SHOULD NOT use transmissible live vaccines** (oral polio, rota virus vaccine).
  - Transplant Recipients should avoid handling diapers of infants who have been vaccinated with rotavirus vaccine or OPV for 4 weeks after these vaccinations.
- Influenza vaccine is strongly recommended annually for all health care workers and household contacts

Vaccination before traveling

Infectious diseases are endemic in certain geographical regions, and an IS patient traveling to these areas is at a greater risk.

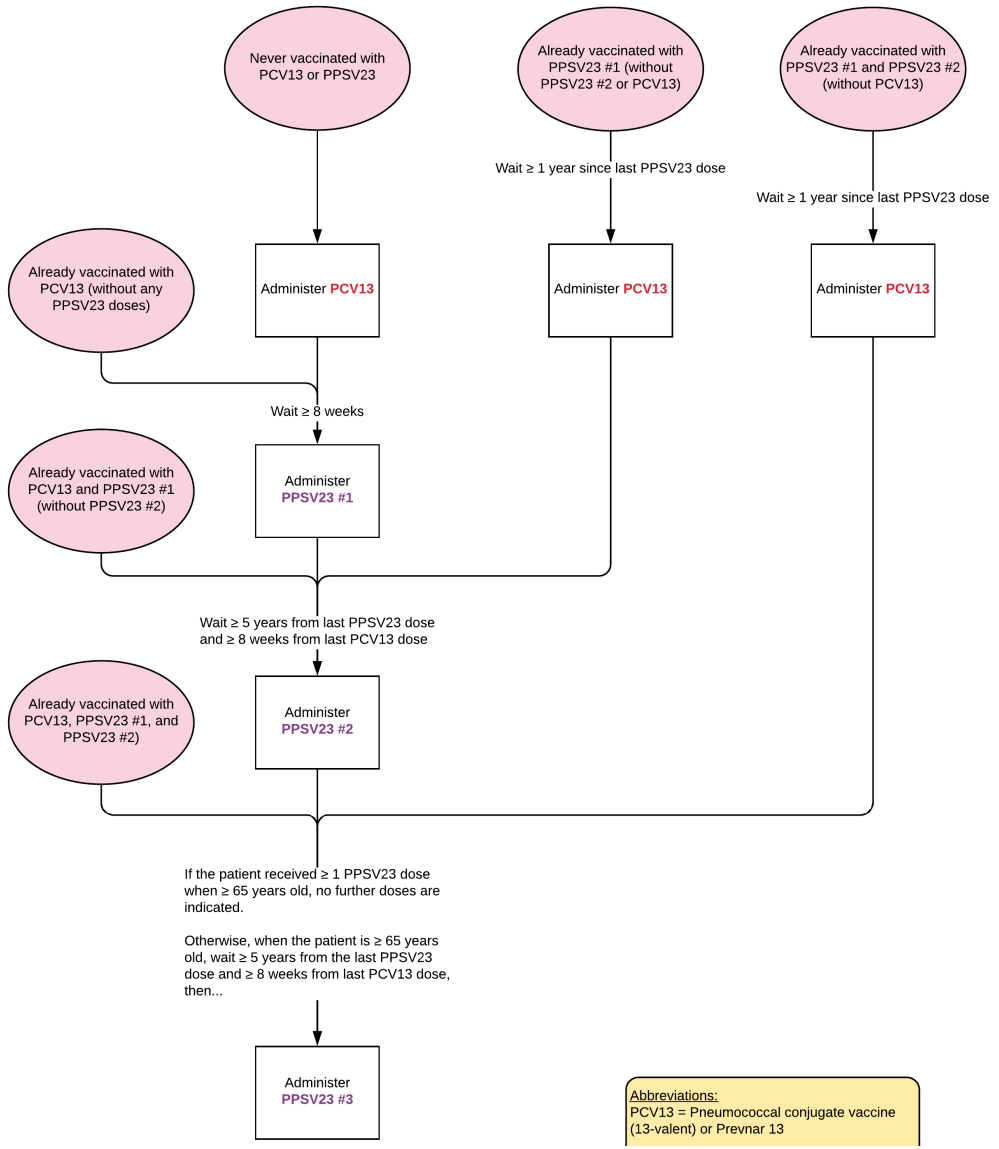
Immunization should be arranged before travel and may include inactivated vaccines for typhoid, Japanese encephalitis, and cholera.

BCG vaccine

- Tuberculosis (TB) infection can be devastating in an IS child
- Every effort should be taken to immunize the child before the immunosuppressive therapy
- In those whose vaccination status is unknown, the current guide-lines recommend a tuberculin skin test or the QuantiFERON GOLD test to diagnose latent TB infection or previous vaccination.
- Vaccination is indicated for children who produce negative results with the above tests

Pneumococcal Vaccine….

- Solid-organ transplant recipients may develop severe infection with Streptococcus pneumoniae.
- Vaccination has been recommended in heart, renal and liver recipients.
- Higher immune response seen where primary doses given pre transplant (preferable 1 month) compared to those who were vaccinated for the first time post transplant.
- All recipients should be vaccinated against pneumococcus – Priming with PCV13 and PPSV23 as booster.
- At least one dose of PCV vaccine pre transplant , preferably 1 month prior and PPSV as booster post transplant


Never vaccinated with PCV13 or PPSV23
Already vaccinated with PPSV23 #1 (without PPSV23 #2 or PCV13)
Already vaccinated with PPSV23 #1 and PPSV23 #2 (without PCV13)
Wait ≥ 1 year since last PPSV23 dose
Wait ≥ 1 year since last PPSV23 dose
Already vaccinated with PCV13 (without any PPSV23 doses)
Administer PCV13
Administer PCV13
Administer PCV13
Wait ≥ 8 weeks
Already vaccinated with PCV13 and PPSV23 #1 (without PPSV23 #2)
Administer PPSV23 #1
Wait ≥ 5 years from last PPSV23 dose and ≥ 8 weeks from last PCV13 dose
Already vaccinated with PCV13, PPSV23 #1, and PPSV23 #2)
Administer PPSV23 #2
If the patient received ≥ 1 PPSV23 dose when ≥ 65 years old, no further doses are indicated.
Otherwise, when the patient is ≥ 65 years old, wait ≥ 5 years from the last PPSV23 dose and ≥ 8 weeks from last PCV13 dose, then...
Administer PPSV23 #3
Abbreviations:
PCV13 = Pneumococcal conjugate vaccine (13-valent) or Prevnar 13

INFUENZA....

Side effects and risks of the vaccination are minimal,

No challenges with Cost and availability

Strongly recommend vaccination in patients, household contacts, and all personnel of transplant centers

Influenza vaccination can begin as early as 1 month after transplant if there is significant local influenza activity.

Hepatitis B

All solid-organ recipients may have a more rapid and severe progression of hepatitis B as well as reactivation of latent infection due to immunosuppression.

Protection against hepatitis B may increase the safety of a transplant of a non-hepatic graft from a donor who is hepatitis B surface antigen negative and core antibody positive.

Vaccination for hepatitis B has been specifically recommended before liver transplantation to prevent de novo graft infection and in renal transplant recipients because of the increased risk of exposure(dialysis)

The vaccine should be given as early as possible in the course of the disease to obtain the best response.

Current recommended dose of recombinant hepatitis B vaccine in patients with end-stage liver and renal disease waiting transplantation is 40 µg in at least three repeated doses.

Monitoring of titers can be useful - antibodies levels lower than 10 mIU/ml

Additional booster doses and revaccination at intervals of 2 to 3 years has been proposed

No Strong recommendations for Meningococcal, Hepatitis A, Typhoid Vaccine

Should follow Local Guidelines as per disease endemicity.

Thank you

References

- Vaccinations for Adult Solid-Organ Transplant Recipients: Current Recommendations and Protocols Clin Microbiol Rev. 2003 Jul
- Vaccinations in children on immunosuppressive medications for renal disease Sushmita Banerjee1 & Pathum Vindana Dissanayake2 & Asiri Samantha Abeyagunawardena . Pediatr Nephrol, Oct 2015
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Thanks for contributions….

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