ISSN 0971-4065

Vol 26, Supplement 1 - 2016

INDIAN JOURNAL OF NEPHROLOGY

Indian Society of Nephrology Guidelines for Vaccination in Chronic Kidney Disease

Official Publication of the Indian Society of Nephrology

Free full text at
www.indianjnephrol.org

PubMed

Medknow

Wolters Kluwer

Indian Society of Nephrology Guidelines for Vaccination in Chronic Kidney Disease

Work Group Membership

Convenor
Narayan Prasad,
Professor of Nephrology,
Sanjay Gandhi Postgraduate Institute of Medical Sciences,
Lucknow, Uttar Pradesh, India

Members
Arpita Roy Chaudhuri,
Professor of Nephrology,
N. R. S. Medical College and Hospital,
Kolkata, West Bengal, India

Basu Gopal,
Professor of Nephrology,
Christian Medical College,
Vellore, Tamil Nadu, India

Dharmendra Bhadauria,
Assistant Professor, Department of Nephrology,
Sanjay Gandhi Postgraduate Institute of Medical Sciences,
Lucknow, Uttar Pradesh, India

Manisha Sahay,
Professor and Head of Nephrology Department,
Osmania General Hospital,
Hyderabad, Telangana, India

Sidharth Sethi,
Department of Pediatric Nephrology,
Medanta the Medicity,
Gurgaon, Haryana, India

Tarun Jeloka,
Consultant Nephrologist,
Aditya Birla Hospital,
Pune, Maharashtra, India

The Indian Society of Nephrology gratefully acknowledges the support of Pfizer for an unrestricted educational grant that supported development of these guidelines.

In citing this document, the following format should be used: Indian Society of Nephrology Vaccination Work Group. Guidelines for Vaccination in Chronic Kidney Disease. Indian J Nephrol, 2016; Suppl. 1: S1-S30.

Indian Journal of Nephrology
Official Publication of the Indian Society of Nephrology
Volume 26 ❒ Supplement 1 - 2016

Table of Contents

Preface

Chronic kidney disease (CKD), no matter what is the cause, has a profound effect on both innate and adaptive immune system. This is specially exaggerated in dialysis patients and amongst kidney transplant recipients, leads to an increased risk of infections. Besides being the second leading cause of death in patients with CKD, infections also increase the risk for cardiovascular events and lead to catastrophic healthcare expenditure secondary to invasive diseases and hospitalizations.

Along with improved sanitation, immunisation is humanity's greatest advances in preventing sickness and death from infectious diseases. Vaccines have helped eliminate or significantly reduce the burden of more than a dozen illnesses. Recognising that childhood is the best time to provide lifelong protection against infections, most countries have pout in place universal immunisation programs.

Specific recommendations are available for adults as well, but these are less well implemented. Various factors may account for these low rates, including financial disincentives.

Overall, prevention through vaccination remains the best strategy to minimise the adverse consequences associated with these infectious diseases in patients with CKD. Protection against hepatitis B infection is a great success story. However, vaccine efficacy his suboptimal in this population, secondary to the same deficiencies in the immune response that increase infection risk. Getting around this barrier needs innovative approaches, such as use of nonspecific adjuvant compounds to enhance host response. by targeting important cellular elements of the vaccine response.

We need more research in this area, to better understand how vaccination in populations at risk for developing CKD might benefit from earlier vaccination, and to expand repertoire of vaccines available against particularly troublesome pathogens, particularly MRSA, Group A streptococcus and other bacteria. Next-generation vaccines offer the possibility of sustained immunological memory, which can substantially prevent chronic viral disease.

In addition, we need to change behaviour so that nephrologists become sensitised to the notion of prevention rather than treating infection after they become apparent. Nephrologists need to be steadfast proponents of vaccination.

Current guidelines recommend immunisations for all patients with CKD regardless of the disease stage, but they are recommended during the early stages of progressive renal disease to increase the likelihood of vaccine-induced immunity.

This document is intended to help the Indian physician community who take care of patients with kidney disease make informed decisions about this often overlooked aspect of care.

The document has been prepared by leading nephrology academics and clinicians who have examined all aspects of vaccination, culled evidence from CKD population and where this was not available, from the general population.

As usual, this document is intended to inform practice, rather than provide specific guidance about every single patient. Practitioners are encouraged to implement the suggestions and recommendations keeping in mind the specific clinical context of the patient.

Vivekanand Jha
Secretary, Indian Society of Nephrology

Overall immune profile and effect of chronic kidney disease on vaccination schedule

Infectious diseases are the second most common causes of morbidity and mortality (after cardiovascular disease) in patients with chronic kidney disease (CKD), contributing to 30–36% of deaths among patients on dialysis.[1-3] Uremic toxins, nutritional deficiencies, and immunosuppressive medications contribute to immune dysregulation, which are further complicated by renal replacement therapies.[4]

Vaccination prevents or attenuates infection risks. Live vaccines are contraindicated because of impaired cell-mediated and humoral immunity, and the inactivated vaccines produce suboptimal antibody responses.

Effect of Chronic Kidney Disease on Immune Systems

CKD affects both major immune systems: innate and adaptive responses.[5] The innate system is a rapid, effective, and universal form of defense against infections, driven by polymorphs, macrophages, and dendritic antigen-presenting cells (APC).[6] The adaptive immune system is antigen-specific, requires recognition of processed antigen, and is driven through activated T and B lymphocytes.[7] The summary of disturbances in immune system is shown in Table 1.

Table 1: Summary of altered innate and adaptive immune system in uremia

	Disturbances in ESRD
Innate immunity	
Pattern-recognition receptors	
Secreted	Up-regulated
Endocytic	Up-regulated
Signaling	Down-regulated
Cells	
Monocytes	Hyporeactive
Neutrophils	Decreased bactericidal abilities
Cytokines	Increased levels resulting from decreased renal clearance, production stimulated by recurrent infections, dialysis procedures, etc. Production inefficient to protect from infections
Complement	Activated
Adaptive immunity	
T lymphocytes	Impaired activation Increased Th1/Th2 ratio
B lymphocytes	Decreased cell count, preserved function
Antigen-presenting cells	Stimulated (function altered)

ESRD: End stage renal disease

Innate immune system

The innate immunity includes recognition, phagocytosis, digestion of pathogens, development of inflammation, and presentation of antigens. Innate immune recognition is characterized by specific pathogen-associated molecular pattern (PAMP).[8] PAMP receptors are expressed on effector cells–macrophages as well as dendritic APCs. Once the receptors identify a pattern, effector cells are triggered.[5]

These receptors are of three types: secreted, endocytic, and signaling.[8] The secreted pattern-recognition molecules function by opsonization, recognition by the mannose-binding lectin complement pathways and phagocytosis. Endocytic pattern-recognition receptors present on the surface of phagocytes recognize PAMPs on a microbial wall and mediate uptake of pathogens into lysosomes leading to destruction of pathogens. Signaling pattern recognition acts through expression of toll-like receptor family leading to cytokine release and inflammatory response.

Adaptive immune system

The adaptive immune system response begins with antigen presentation.[7] The processed antigens bind to the major histocompatibility complex (MHC) molecules on the APCs activate naive T cells, converting them into functional cells.

In addition to signaling by the peptide-MHC molecule complex, a costimulatory signal through CD80–CD86 interaction is also necessary.[8,9] After binding to specific foreign antigens, B lymphocytes are converted into plasmacytes that produce antibodies.

Even after successful pathogen elimination, certain lymphocytes retain a memory and exhibit an accelerated response in cases of repeat infection with the same pathogen.

Alterations of the immune system in end-stage renal disease

End-stage renal disease (ESRD) is associated with a variety of changes in the immune system: Both anti-inflammatory

interleukin (IL-10) and proinflammatory cytokines tumor necrosis factor-α (TNF-α, IL-6) are increased.[9-11] Cytokine accumulation occurs as a result of poor renal clearance and increased production. The latter may be affected by uremic toxins, oxidative stress, volume overload, and other comorbidities.

All three classes of PAMP receptors are affected by ESRD. Mannose-binding lectin levels[12] are increased.[13-15] The chronic inflammatory and oxidative stress induce chronic stimulation of macrophage scavenger receptors.[15] Monocyte from dialysis patients reacts poorly to lipopolysaccharide stimulation.[16] Monocytes and monocyte-derived dendritic cells show decreased endocytosis and impaired maturation in uremic serum.[17,18] The bactericidal capacities of polymorphs are reduced in hemodialysis patients, suggesting a role of dialyzable substances.[19] Some uremic toxins delay and others promote apoptosis.

T-cell proliferation is decreased in the uremia.[20,21] The proinflammatory Th1 cells produce TNF-α, IL-12, and interferon-γ whereas Th2 cells produce IL-4 and IL-5.[9] Th1 lymphocytes activate macrophages and neutrophils whereas Th2 cells are involved in promoting humoral immunity. Functional abnormalities of monocytes, neutrophils, and dendritic cells have been linked with infection risk.[9,16,22]

Vaccination and immunity in end-stage renal disease

The reduced response to vaccination in ESRD patients is generally related to alterations of T lymphocyte function.[23] Compared to general population, patients on dialysis have lower antibody titers.[24,25] The degree of renal failure correlates with antibody response.[26] Disturbances in T lymphocytes and APC function are thought to mediate this malfunction.[23,27,28] The association of dialysis adequacy and antibody response to vaccination is not well studied. However, indirect evidence suggests that increasing adequacy may be associated with better antibody response. In a study of 32 peritoneal dialysis (PD) patients who received hepatitis B vaccine, the weekly Kt/V was better in seroconverters than that in nonconverters (2.37 vs. 2.01).[29]

Hepatitis B Virus Vaccine

One of the most studied vaccines in CKD patients is hepatitis B. One of the most important factors for decrease in incidence of hepatitis B infection in CKD patients is hepatitis B vaccination.[30] Despite the reduced conversion rates, the decreased need for hepatitis B surface antigen surveillance and antibody status makes a case in favor of vaccination.[31] A case–control study found that hemodialysis patients vaccinated against hepatitis B had a 70% lesser risk for infection, compared to those who have not received this vaccine.[32] More than 90% patients without CKD develops anti-HBS protective antibodies following hepatitis B virus (HBV) vaccination as compared to only 50–60% of those with ESRD.[33,34] Antibody response also correlates with degree of renal failure. Patients not receiving dialysis have better antibody response.[35,36]

Vaccination and mode of dialysis

Data on effect of dialysis technique on response to vaccination are sparse. No difference in the serological response to HBV or influenza vaccines was noted in PD and hemodialysis (HD) patients, with response rate of 66–77.3% versus 66–78.7% in PD and HD patients, respectively.[37,38] Fabrizi *et al*. did not observe an impact of mode of dialysis on the seroconversion rate after HBV vaccine.[39] PD patients reached better protective antibody titers than that of patients on HD, but lower than those of patients without renal impairment following influenza vaccination.[40,41] The present evidence suggests that both PD and HD patients should receive the standard annual dose of all vaccines recommended in CKD.[42]

References

1. van Dijk PC, Jager KJ, de Charro F, Collart F, Cornet R, Dekker FW, *et al.* Renal replacement therapy in Europe: The results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. Nephrol Dial Transplant 2001;16:1120-9.
2. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis 1998;32 5 Suppl 3:S112-9.
3. Sarnak MJ, Jaber BL. Mortality caused by sepsis in patients with end-stage renal disease compared with the general population. Kidney Int 2000;58:1758-64.
4. Johnson DW, Fleming SJ. The use of vaccines in renal failure. Clin Pharmacokinet 1992;22:434-46.
5. Kato S, Chmielewski M, Honda H, Pecoits-Filho R, Matsuo S, Yuzawa Y, *et al.* Aspects of immune dysfunction in end-stage renal disease. Clin J Am Soc Nephrol 2008;3:1526-33.
6. Janeway CA Jr., Medzhitov R. Innate immune recognition. Annu Rev Immunol 2002;20:197-216.
7. Delves PJ, Roitt IM. The immune system. First of two parts. N Engl J Med 2000;343:37-49.
8. Medzhitov R, Janeway C Jr. Innate immunity. N Engl J Med 2000;343:338-44.
9. Stenvinkel P, Ketteler M, Johnson RJ, Lindholm B, Pecoits-Filho R, Riella M, *et al.* IL-10, IL-6, and TNF-alpha: Central factors in the altered cytokine network of uremia – The good, the bad, and the ugly. Kidney Int 2005;67:1216-33.
10. Stenvinkel P, Barany P, Heimbürger O, Pecoits-Filho R, Lindholm B. Mortality, malnutrition, and atherosclerosis in ESRD: What is the role of interleukin-6? Kidney Int Suppl 2002;80:103-8.

11. Pecoits-Filho R, Heimbürger O, Bárány P, Suliman M, Fehrman-Ekholm I, Lindholm B, *et al.* Associations between circulating inflammatory markers and residual renal function in CRF patients. Am J Kidney Dis 2003;41:1212-8.
12. Satomura A, Endo M, Ohi H, Sudo S, Ohsawa I, Fujita T, *et al.* Significant elevations in serum mannose-binding lectin levels in patients with chronic renal failure. Nephron 2002;92:702-4.
13. Ando M, Lundkvist I, Bergström J, Lindholm B. Enhanced scavenger receptor expression in monocyte-macrophages in dialysis patients. Kidney Int 1996;49:773-80.
14. Ando M, Gåfvels M, Bergström J, Lindholm B, Lundkvist I. Uremic serum enhances scavenger receptor expression and activity in the human monocytic cell line U937. Kidney Int 1997;51:785-92.
15. Chmielewski M, Bryl E, Marzec L, Aleksandrowicz E, Witkowski JM, Rutkowski B. Expression of scavenger receptor CD36 in chronic renal failure patients. Artif Organs 2005;29:608-14.
16. Ando M, Shibuya A, Yasuda M, Azuma N, Tsuchiya K, Akiba T, *et al.* Impairment of innate cellular response to *in vitro* stimuli in patients on continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 2005;20:2497-503.
17. Lim WH, Kireta S, Leedham E, Russ GR, Coates PT. Uremia impairs monocyte and monocyte-derived dendritic cell function in hemodialysis patients. Kidney Int 2007;72:1138-48.
18. Verkade MA, van Druningen CJ, Vaessen LM, Hesselink DA, Weimar W, Betjes MG. Functional impairment of monocyte-derived dendritic cells in patients with severe chronic kidney disease. Nephrol Dial Transplant 2007;22:128-38.
19. Anding K, Gross P, Rost JM, Allgaier D, Jacobs E. The influence of uraemia and haemodialysis on neutrophil phagocytosis and antimicrobial killing. Nephrol Dial Transplant 2003;18:2067-73.
20. Meuer SC, Hauer M, Kurz P, Meyer zum Büschenfelde KH, Köhler H. Selective blockade of the antigen-receptor-mediated pathway of T cell activation in patients with impaired primary immune responses. J Clin Invest 1987;80:743-9.
21. Stachowski J, Pollok M, Burrichter H, Spithaler C, Baldamus CA. Signalling via the TCR/CD3 antigen receptor complex in uremia is limited by the receptors number. Nephron 1993;64:369-75.
22. Cendoroglo M, Jaber BL, Balakrishnan VS, Perianayagam M, King AJ, Pereira BJ. Neutrophil apoptosis and dysfunction in uremia. J Am Soc Nephrol 1999;10:93-100.
23. Eleftheriadis T, Antoniadi G, Liakopoulos V, Kartsios C, Stefanidis I. Disturbances of acquired immunity in hemodialysis patients. Semin Dial 2007;20:440-51.
24. Rodby RA, Trenholme GM. Vaccination of the dialysis patient. Semin Dial 1991;4:102-5.
25. Dinits-Pensy M, Forrest GN, Cross AS, Hise MK. The use of vaccines in adult patients with renal disease. Am J Kidney Dis 2005;46:997-1011.
26. Kausz A, Pahari D. The value of vaccination in chronic kidney disease. Semin Dial 2004;17:9-11.
27. Litjens NH, Huisman M, van den Dorpel M, Betjes MG. Impaired immune responses and antigen-specific memory CD4+T cells in hemodialysis patients. J Am Soc Nephrol 2008;19:1483-90.
28. Agrawal S, Gollapudi P, Elahimehr R, Pahl MV, Vaziri ND. Effects of end-stage renal disease and haemodialysis on dendritic cell subsets and basal and LPS-stimulated cytokine production. Nephrol Dial Transplant 2010;25:737-46.
29. Dacko C, Holley JL. The influence of nutritional status, dialysis adequacy, and residual renal function on the response to hepatitis B vaccination in peritoneal dialysis patients. Adv Perit Dial 1996;12:315-7.
30. Finelli L, Miller JT, Tokars JI, Alter MJ, Arduino MJ. National surveillance of dialysis-associated diseases in the United States, 2002. Semin Dial 2005;18:52-61.
31. Favero MS, Alter MJ. The reemergence of hepatitis B virus infection in hemodialysis centers. Semin Dial 1996;9:373-4.
32. Miller ER, Alter MJ, Tokars JI. Protective effect of hepatitis B vaccine in chronic hemodialysis patients. Am J Kidney Dis 1999;33:356-60.
33. Stevens CE, Alter HJ, Taylor PE, Zang EA, Harley EJ, Szmuness W. Hepatitis B vaccine in patients receiving hemodialysis. Immunogenicity and efficacy. N Engl J Med 1984;311:496-501.
34. Buti M, Viladomiu L, Jardi R, Olmos A, Rodriguez JA, Bartolome J, *et al.* Long-term immunogenicity and efficacy of hepatitis B vaccine in hemodialysis patients. Am J Nephrol 1992;12:144-7.
35. Seaworth B, Drucker J, Starling J, Drucker R, Stevens C, Hamilton J. Hepatitis B vaccines in patients with chronic renal failure before dialysis. J Infect Dis 1988;157:332-7.
36. Dukes CS, Street AC, Starling JF, Hamilton JD. Hepatitis B vaccination and booster in predialysis patients: A 4-year analysis. Vaccine 1993;11:1229-32.
37. Liu YL, Kao MT, Huang CC. A comparison of responsiveness to hepatitis B vaccination in patients on hemodialysis and peritoneal dialysis. Vaccine 2005;23:3957-60.
38. Bel'eed K, Wright M, Eadington D, Farr M, Sellars L. Vaccination against hepatitis B infection in patients with end stage renal disease. Postgrad Med J 2002;78:538-40.
39. Fabrizi F, Dixit V, Bunnapradist S, Martin P. Meta-analysis: The dialysis mode and immunological response to hepatitis B virus vaccine in dialysis population. Aliment Pharmacol Ther 2006;23:1105-12.
40. Antonen JA, Hannula PM, Pyhälä R, Saha HH, Ala-Houhala IO, Pasternack AI. Adequate seroresponse to influenza vaccination in dialysis patients. Nephron 2000;86:56-61.
41. Cavdar C, Sayan M, Sifil A, Artuk C, Yilmaz N, Bahar H, *et al.* The comparison of antibody response to influenza vaccination in continuous ambulatory peritoneal dialysis, hemodialysis and renal transplantation patients. Scand J Urol Nephrol 2003;37:71-6.
42. Rangel MC, Coronado VG, Euler GL, Strikas RA. Vaccine recommendations for patients on chronic dialysis. The Advisory Committee on Immunization Practices and the American Academy of Pediatrics. Semin Dial 2000;13:101-7.

Guidelines for vaccinations of a normal child in India

The Expanded Program of Immunization (EPI) was introduced globally in 1974. The initial EPI program in India was limited to Bacillus Calmette Guerin (BCG), diphtheria, tetanus toxoids, whole cell pertussis (DTwP), oral poliomyelitis, and typhoid vaccines, and chiefly covered urban areas. The Universal Immunization Program (UIP), introduced in 1985, improved immunization coverage and extended the focus beyond infancy. Typhoid vaccine was excluded from the schedule, and measles vaccine was added. Vitamin A supplementation was added in 1990, and the Polio National Immunization Days introduced in 1995. Some states introduced hepatitis B vaccine in 2002 and a pentavalent vaccine (*Haemophilus influenzae* [b-HiB] and hepatitis B with DTwP) in 2011. UIP is an essential part of the Child Survival and Safe Motherhood Program since 1992, the Reproductive and Child Health Program (RCH-I) from 1997, and the RCH-II and National Rural Health Mission since 2005.[1]

Indian Academy of Pediatrics 2014 Guidelines

The Indian Academy of Pediatrics Advisory Committee on Vaccines and Immunization Practices recommended immunization of children until the age of 18 years based on the recent evidence of the licensed vaccines in the country [Table 2]. The major changes introduced in 2014 included[2] the following:

- Two doses of measles mumps rubella at 9 and 15 months of age, and no standalone measles vaccine at 9 months
- Single dose administration of live attenuated H2 strain hepatitis A vaccine, or two doses of inactivated (killed) hepatitis A vaccine
- New slot at 9–12 months for typhoid conjugate vaccine for primary immunization
- Two doses of human papillomavirus vaccines with a minimum interval of 6 months between doses of primary schedule of adolescent/preadolescent girls aged 9–14 years.

Special Circumstances

High-risk groups

The Indian Academy of Pediatrics recommends additional vaccines for children with high-risk conditions [Table 3].

Table 2: Comparison of vaccines included in the National Immunization Program and the 2014 recommendation of the Indian Academy of Pediatrics

Age	The National immunization schedule	2014 Indian Academy of Pediatrics
0 (at birth)	BCG, OPV0, HBV0*	BCG, OPV0, HBV1
6 weeks	DTwP1, OPV1, HBV1*, HiB1*	DTwP1, IPV1, HBV2, HiB1, Rotavirus 1, PCV1
10 weeks	DTwP2, OPV2, HBV2*, HiB2*	DTwP2, IPV2, HiB2, Rotavirus 2, PCV2
14 weeks	DTwP3, OPV3, HBV3*, HiB3*	DTwP3, IPV3, HiB3, Rotavirus 3, PCV3
6 months	-	OPV1, HBV3
9 months	Measles, Vitamin A	OPV2, MMR1 (9-12 months) typhoid conjugate vaccine
12 months	-	HAV1
15 months	MMR*	MMR2, varicella 1, PCV booster
16-24 months	DTwP B1, OPV B1, Vitamin A2, Japanese Encephalitis*	16-18 months DTwP B1/DTaP B1/IPV B1, HiB B1 (18 months) HAV2
2 years	-	Typhoid booster
5 years	DTwP B2	4-6 years DTwP B2/DTaP B2, OPV3, varicella 2, typhoid booster
10 years	TT	10-12 years Tdap/Td, HPV
16 years	TT	

*Implemented in selected states, districts, and cities. B1: First booster dose, B2: Second booster dose, BCG: Bacillus Calmette Guerin, DT: Diphtheria toxoid and tetanus toxoid, DTwP: Diphtheria, tetanus toxoid, whole cell pertussis, DTaP: Diphtheria, tetanus toxoid, acellular pertussis, HAV: Hepatitis A vaccine, Td: Tetanus toxoid with reduced diphtheria, Tdap: Reduced diphtheria toxoid and acellular pertussis vaccine, HBV: Hepatitis B vaccine, HiB: *Haemophilus influenzae* b, HPV: Human papillomavirus vaccine, MMR: Measles, mumps and rubella, OPV: Oral poliovirus vaccine, PCV: Pneumococcal conjugate vaccine, TT: Tetanus toxoid

Corticosteroids and immunosuppressive therapy

Children receiving high-dose (HD) steroids (prednisolone >2 mg/kg/day or for those more than 10 kg, 20 mg/day or equivalent) for >2 weeks should not receive live vaccines until the steroids have been discontinued for at least 1 month. Killed vaccines are safe but may be less efficacious.

Lapsed immunization

Table 4 outlines the suggested schedules for children who have missed routine immunizations. There is no need to restart a vaccine series regardless of the time that has relapsed between the individual doses due to the immune memory.

Solid Organ Transplantation

Children requiring transplantation require immunization due to the immunosuppressive nature of the underlying

Table 3: High-risk conditions where certain added vaccines may be necessary

High-risk clinical conditions	Vaccines that may be necessary
Congenital or acquired immunodeficiency (including HIV infection)	Influenza vaccine
Chronic cardiac, pulmonary (including asthma if treated with prolonged high dose steroids), hematologic, renal (*including nephrotic syndrome*) and liver disease	Meningococcal vaccine
Children on long-term steroids, salicylates, immunosuppressive or radiation therapy	Japanese encephalitis vaccine
Diabetes mellitus	Cholera vaccine
Cerebrospinal fluid leak	Rabies vaccine
Cochlear implant	Yellow fever vaccine
Malignancies	Pneumococcal polysaccharide vaccine 23
Children with functional/anatomic asplenia/hyposplenia	
During disease outbreaks; laboratory personnel and healthcare workers	
Travelers	
Children having pets at home	
Children perceived with increased threat of being bitten with dogs such as hostellers, risk of stray dog menace	

Clinical conditions relevant to kidney disorders have been made as italics

Table 4: Vaccinations in case of a previously unimmunized child

Visit	At first visit	After 1 month	After 2 months	After 6 months
Aged <7 years	BCG (if <5 years) Oral polio (if <5 years) DTwP/DTaP Hepatitis B	Oral polio DTwP/ DTaP Hepatitis B	MMR (preferred over measles) Typhoid	DTwP/ DTaP Hepatitis B
Aged >7 years	Tdap Hepatitis B	dT Hepatitis B	MMR Typhoid	Hepatitis B

BCG: Bacillus Calmette Guerin, DTwP: Diphtheria, tetanus toxoid, whole cell killed pertussis, DTaP: Diphtheria, tetanus toxoid, acellular pertussis, MMR: Measles, mumps, and rubella, Tdap: Reduced diphtheria toxoid and acellular pertussis vaccine, dT: Reduced dose diphtheria and tetanus toxoid

disease and the need for immunosuppression for the graft survival. In general, standard vaccination should be followed for such children. The recipients should complete all immunizations before the transplant in an accelerated schedule if needed. Live vaccines should be completed at least 2 weeks before the transplant. It will be desirable if the seroconversion is documented.

Table 5: Suggested vaccines before and after solid organ transplant in children

Vaccine	Pretransplant	Posttransplant
DTaP, Tdap	U	U, if not completed pretransplant
Hepatitis B	U: Age 1-18 years R: Age>18 years	R, if not completed pretransplant
Hepatitis A	U: Age 12-23 months R: >2 years	R, if not completed pretransplant
HiB	U	U
PCV	U: Age <5 years R: Age >6 years	U: Age 2-5 years R: Age >6 years if not received pretransplant
PPSV 23	R: Age >2 years	R: Age >2 years if not received pretransplant
Influenza	U	U*
Polio-IPV	U	U
HPV	U: Females 11-26 years	U: Females 11-26 years
MMR	R**: 6-11 months U**: Age >12 months	X
Varicella	R**	X
Rotavirus	U**	U**

*Inactivated influenza vaccine may be given to transplant recipients despite intensive immunosuppression, **Administer only if patient is more than 4 weeks before transplant and is not immunosuppressed. R: Recommended-administer if the patient has not received the vaccine; such patients are at risk of this vaccine-preventable disease, U: Usual - administer if the patient is not current with the IAP recommended schedule for immunocompetent individuals, X: Contraindicated, HiB: *Haemophilus influenzae* b, PCV: Pneumococcal conjugate vaccine, PPSV: Pneumococcal polysaccharide vaccine, MMR: Measles, mumps and rubella, DTaP: Diphtheria, tetanus toxoid, acellular pertussis, Tdap: reduced diphtheria toxoid and acellular pertussis vaccine, IPV: Inactivated polio vaccine, HPV: Human papillomavirus vaccine

Posttransplantation, all live vaccines are contraindicated. Vaccination with killed vaccines may be commenced 6 months posttransplantation when the immunosuppression is at the lowest possible. Table 5 summarizes vaccines before and after solid organ transplant in children.

References

1. Indian Academy of Pediatrics Committee on Immunization (IAPCOI). Consensus recommendations on immunization and IAP immunization timetable 2012. Indian Pediatr 2012;49:549-64.
2. Vashishtha VM, Choudhury P, Kalra A, Bose A, Thacker N, Yewale VN, *et al.* Indian Academy of Pediatrics (IAP) recommended immunization schedule for children aged 0 through 18 years – India, 2014 and updates on immunization. Indian Pediatr 2014;51:785-800.
3. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, *et al.* 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:309-18.

Guidelines for vaccination in normal adults in India

The immunization of an adult depends on the previous immunization received in childhood. Unlike the Pediatric Immunization Guidelines, given by the Indian Academy of Pediatrics and the National Immunization Programs,[1,2] the guidelines for vaccination in healthy adults vary from region to region.

The major guidelines are:

- The Advisory Committee on Immunization Practices (ACIP) guidelines from Centers for Disease Control and Prevention[3-5]
- WHO guidelines[6]
- Association of Physicians of India – Expert panel guidelines [Tables 6 and 7].[7]

Hepatitis B vaccine

Vaccine

Hepatitis B vaccine is a recombinant vaccine. Plasma- derived vaccine is not used due to risk of transmission of infections.

Schedule

Primary immunization at birth: In normal individuals, the dose is 10 μg in children given intramuscularly at 0, 1, and 6 months and a booster after 5 years. In adults, the dose is 20 μg. Booster is not needed in immunocompetent adults.[8-11]

Indications of hepatitis B vaccine in Indian adults

Adults at high risk, e.g., patients with percutaneous or mucosal exposure to blood and patients with sexual exposure should be vaccinated if not immunized in childhood. Percutaneous or mucosal exposure can occur in intravenous drug users; household contacts of persons with chronic hepatitis B virus (HBV) infection; inmates and staff of institutions for developmentally disabled persons in long-term care facilities; persons at risk for occupational exposure to HBV (such as dialysis staff, laboratory staff dealing with blood samples, blood bank staff, nurses working in intensive care units, operation theaters, and surgeons and other doctors at high-risk); patients who are human immunodeficiency virus (HIV)-seropositive, patients with chronic liver disease (CLD), chronic kidney disease (CKD); and diseases where blood products or multiple blood transfusions are required such as hemophilia, aplastic anemia, leukemia, hemoglobinopathies, and patients awaiting major surgeries. Sexual exposure is a risk factor for HBV infection in patients presenting to sexually transmitted disease clinics, homosexuals; promiscuous heterosexuals; commercial sex workers; and sex partners of hepatitis B surface antigen (HBsAg)-positive persons.

Prevaccination screening in general population has not been found to be cost-effective in India.

If the vaccination schedule is interrupted after the first dose, the second dose should be administered as soon as possible and the second and third doses should be separated by an interval of at least 8 weeks. If only the third dose has been delayed, it should be administered as soon as possible.

Postexposure screening is not indicated for most adults, except in immunocompromised persons, sex partners of HBsAg-positive persons, and health care workers at high risk for continued percutaneous or mucosal exposure to blood or body fluids. When indicated, postexposure screening should be performed 1–2 months after administration of the last dose of the vaccine series. The anti-HBs titer should be maintained above 10 mIU/ml in all healthy adults.

Nonresponders who are HBsAg and anti-HBc-negative should receive a further full course of vaccination as fourth, fifth, and sixth doses. Retesting should be done 1–2 months after the last dose. If there is no response, 40 μg of recombinant vaccine is administered at 0, 1,

Table 6: Vaccines recommended for all healthy adults

DPT
MMR
Influenza (>50 years)
Pneumococcal (>65 years)
Human papillomavirus (9-26 years)
Zoster (>60 years)

DPT: Diphtheria, pertussis, and tetanus, MMR: Measles, mumps, and rubella

Table 7: Vaccines recommended in high-risk individuals

Hepatitis B
Hepatitis A
Meningococcal
Varicella
HiB
Typhoid
Rabies
Cholera and Japanese encephalitis vaccines are routinely not indicated due to lack of adequate evidence

HiB: *Haemophilus influenzae* b

and 6 months. Retesting should be done 1–2 months after the last dose. If the person remains a nonresponder, alternative strategies for protection must be explored.

Booster doses of HBV vaccine are not indicated in persons with normal immune status. A booster dose may be administered when anti-HBs levels decline to <10 mIU ml and >65 years.

Pneumococcal vaccine

Pneumococcal vaccine is available in two forms:

- Polysaccharide vaccine consisting of polysaccharides from 23 serotypes. This vaccine is less immunogenic, does not affect carrier rates, promote herd immunity, or protect from respiratory tract infections as there is no mucosal immunity
- Conjugated Vaccine with 13 serotypes consists of capsular polysaccharides covalently bound to diphtheria toxoid, which is highly immunogenic but nontoxic. This combination results in mucosal immunity and lifelong immunity.[3-5,12,13]

Table 8 summarizes the key differences between Pneumococcal Polysaccharide Vaccine (PPSV23) and Pneumococcal Conjugate Vaccine (PCV13).[14]

PCV13 is approved in several countries worldwide, including the US, EU, and India, for use in adults aged >50 years for the prevention of pneumonia and/or invasive disease caused by *Streptococcus pneumonia* serotypes included in the vaccine.[14] In immunocompetent adults, PPSV23 is indicated in those over the age of 65. The vaccine is also indicated for those with CKD, chronic obstructive pulmonary disease (COPD), cirrhosis, diabetes, HIV, lupus, cancer and those on chemotherapy or radiotherapy, long-term steroid, asplenia, or splenectomy.

A single dose PPSV23 is recommended in immunocompetent adults. In those who have received primary immunization, vaccination is done with PPSV23 0.5 ml single dose IM. In those who have not received primary vaccination, PCV13 can be given followed by PPSV23 after a minimum interval of 8 weeks. If PPSV23 has been given earlier PCV can be given after 1 year.

Revaccination can be done with PPSV23 at least 5 years after the first dose. Revaccination with PPSV23 within 5 years leads to hyporesponsiveness. Monitoring for seroconversion is not needed.

In the year 2014, ACIP recommended routine use of PCV13 among adults aged ≥ 65 years.[15] This was based on the results of the CAPiTA trial that supported the evidence on the efficacy of PCV13 against noninvasive pneumococcal pneumonia among adults.[16] As per this recommendation, both PCV13 and PPV23 should be routinely administered in series to all adults aged ≥ 65 years. ACIP recommendations for use of PCV13 (high risk) in adults aged ≥ 19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants remain unchanged.

The recommendations for usage of both the vaccines is mentioned in Table 9.[14]

The ACIP recommendation was amended in 2015 to simplify the spacing between PCV13 and PPSV23 in

Table 8: Key differences between pneumococcal polysaccharide vaccine23 and pneumococcal conjugate vaccine13

Vaccine	Advantages	Disadvantages
PPSV23	Long experience (licensed in 1983) Not expensive At present, relatively high serotype coverage for IPD in elderly (60-70%) Considerable efficacy proven against IPD (50-70%) in immunocompetent elderly Cost-effective proven for elderly people even if it only prevents IPD	T-cell-independent immune response (IgM antibody produced, response declines in 3-5 years and no anamnestic response at revaccination) Decrease in memory B cell frequency after PPV23 Weak immunogenicity in some individuals Unclear (null to small) efficacy against nonbacteremic pneumococcal pneumonia No effect on nasopharyngeal carriage No efficacy demonstrated in reducing nasopharyngeal carriage No impact proven in reducing overall pneumococcal disease burden
PCV13	T cell-dependent immune response (larger duration and boosting effect at revaccination) High efficacy (80-90%) against vaccine type IPD proven in children Significant efficacy against pneumococcal pneumonia (CAPiTA study) Potential efficacy in reducing nasopharyngeal carriage Considerable impact in reducing all pneumococcal disease burden shown by prior PCV7	Short experience (approved in 2011) Expensive At present, relatively small serotype coverage for IPD in the elderly (30-40%) Future reduction of vaccination impact in adults/elderly (because of probable indirect effects from PCV13 pediatric use)

PPSV: Pneumococcal polysaccharide vaccine, PCV: Pneumococcal conjugate vaccine, IPD: Invasive pneumococcal disease

Table 9: Advisory Committee on Immunization Practice recommendations for the use of pneumococcal conjugate vaccine 13 and pneumococcal polysaccharide vaccine 23

Indications	Indications
Pneumococcal vaccine-naïve persons	One dose PCV13 followed by a dose of PPSV23
Adults aged ≥65 years who have not previously received pneumococcal vaccine or whose previous vaccination history is unknown	PPSV23 should be given 6-12 months after PCV13 If PPSV23 cannot be given during this time window, the dose of PPSV23 should be given during the next visit The two vaccines should not be co-administered, and the minimum acceptable interval between PCV13 and PPSV23 is 8 weeks
Previous vaccination with PPSV23	Should receive a dose of PCV13 if they have not yet received it
Adults aged ≥65 years who have previously received ≥1 doses of PPV23	A dose of PCV13 should be given ≥1 year after PPSV23 For those for whom an additional dose of PPSV23 is indicated, it should be given 6-12 months after PCV13 and ≥5 years after the most recent dose of PPSV23

PPSV: Pneumococcal polysaccharide vaccine, PCV: Pneumococcal conjugate vaccine

adults >65 years.[17] The old ACIP recommended that PPSV23 can be given after 6–12 months after PCV13. The new recommendation states that the recommended interval for adults receiving PCV13 and PPV23 to be at least 1 year apart, regardless of sequence. In summary, this means that PCV13 is given first followed by PPSV23 with spacing at least 1 year. If the adult above 65 years received PPSV23, he will receive PCV13 after 1 year as the older recommendation [Tables 10 and 11].

Influenza vaccine

The available vaccine in India is a killed virus vaccine to be given intramuscularly.[18,19] Other vaccines include nasal spray vaccines (containing live attenuated virus). As the influenza virus constantly mutates, a new batch is prepared every year. The vaccine becomes effective against influenza virus 2 weeks after administration. Since the peak influenza season begins in October and lasts till May, October–November are the best times to receive vaccination.[18,19]

A single dose of inactivated flu vaccine in dose of 0.5 ml is given intramuscularly into the deltoid muscle.

Vaccination is indicated in high-risk subjects, e.g., those with COPD, CKD, cardiac or lung diseases, hepatic, metabolic diseases (diabetes), hematological diseases, pregnancy, nursing homes, health care personnel, household contacts of children <5 years or adults >50 years, diseases which impair respiratory functions, and immunosuppressed individuals.

Side effects include allergic reactions, Guillain Barre syndrome. High-risk individuals (see above) should not receive nasal spray live flu vaccine. The vaccine provides adequate protection against HINI infection. Antibody monitoring is not required.

Meningococcal vaccine

The quadrivalent vaccines contain 50 μg of each of the antigens A, C, Y, and W135 whereas the bivalent vaccine has only A and C antigens. Two types of quadrivalent vaccines are available. The meningococcal polysaccharide vaccine (MPSV4) does not induce herd immunity, has no effect on nasopharyngeal carriage, and can be used only in those >2 years age. The meningococcal conjugate vaccine (MCV4) provides herd immunity, reduces nasopharyngeal carriage, provides long-lasting immunity after 28 days of vaccination, but cannot be used for people >55 years. These vaccines do not protect against meningococcus groups B or meningitis due to other organisms. MCV4 (conjugated) is preferred for adults who are aged 55 years or younger as well as for adults aged 56 years or older who (a) are vaccinated previously with MCV4 and are recommended for revaccination, or (b) for whom multiple doses are anticipated. MPSV4 is preferred for adults aged 56 years or older who have not received MCV4 previously and who require a single dose only (e.g., travelers).[20]

Vaccination is indicated in specific situations, such as during an outbreak. A single dose of vaccine (A + C) may be given to health care workers, laboratory workers, and close contacts of cases. Vaccination may be given to personnel living in dormitories, military recruits, jail inmates, immunocompromised individuals, such as those suffering from terminal complement component deficiency, splenectomy, active and passive smokers, systemic lupus erythematosus, HIV, and multiple myeloma (2 doses separated by 2 months for adult <55 years).

For travelers, a single dose is recommended 10-14 days before the scheduled visit depending on the prevalent serotype in the visiting country. As a national policy, the National Institute of Communicable Diseases, New Delhi, administers quadrivalent polysaccharide vaccine to the Haj pilgrims to fulfill the requirements of the Government of Saudi Arabia.

Rabies vaccine

The sheep brain-derived nerve tissue vaccine "semple vaccine" is no longer used. Tissue culture vaccines (TCV) such as human diploid cell vaccine, purified chicken embryo cell vaccine (PCECV), and newer and less expensive vero cell-purified rabies vaccines are now

Table 10: Immunization for all adults with normal immune status

		Immunized	Not immunized	Vaccine	Dose and route	brands
DPT	Universal except if contraindicated	18 to 64 years booster dose of Td vaccine once every 10 years till the age of 65 years	3 doses of Td vaccine; 2 doses are administered 4 weeks apart 3rd dose 6 to 12 months after the second dose	Td (one dose can be Tdap)	0.5 cc IM	Boostrix GSK Adacel –sanofi Triple Ag SI
MMR	Recommended in adults but contraindicated in pregnancy and immunosuppressed states	Not indicated	Single dose SC	Live vaccine	0.5 cc SC	Tresivac- SI GSK
Influenza	For all, esp high risk	Every year	Every year	Inactivated	0.5 cc IM	Fluvac
Pneumococcus	For all >65 years <65 years in those at risk	Single dose >65 years	Single dose >65 years		0.5 cc IM	Pneumococcal polysaccharide 23 Protein conjugate-13
Varicella	For all who are not immune	For those already immunized in childhood booster doses are not needed if titres are adequate	two doses administered 4 to 8 weeks apart	attenuated live VZV (Oka strain) in both	2 doses 0.5 ml in deltoid area SC	Varilrix (GlaxoSmithKline Biologicals) Okavax (Pasteur Mérieux) Varibed MSD Biovac chinese
Papilloma	For young adults	For adults who are already immunized, booster dose is not needed. For non immunized, 3 doses given	In age group 9-14 years 2 doses are recommended at an interval of 6 months. For 15-26 years at 0,1 and 6 months		dose is 0.5 ml intramuscularly	GSK Cervarix- bivalent MSD Guardasil -4 valent
Zoster	in>60 years	>60 years single dose	>60 years single dose	Live attenuated	0.65 ml subcutaneous in deltoid	

available. TCV are used for pre- and post-exposure prophylaxis. They are easy to administer, highly immunogenic, and have a good margin of safety.[7]

Pre-exposure schedule

Pre-exposure schedule for rabies vaccination is 3 doses at days 0, 7, and 28 and is recommended for high-risk groups such as veterinarians, laboratory personnel working with rabies virus, medical and paramedical personnel treating rabies patients, dog catchers, forest staff, zookeepers, postmen, policemen, courier boys, and schoolchildren in endemic countries. The human diploid cell culture vaccine [HDCV] and purified chick embryo cell culture PCECV (1 ml) or purified vero cell rabies vaccine (0.5 ml) are administered by intramuscular route in the deltoid region or the anterolateral thigh. The reconstituted tissue culture vaccines (0.1 ml) can be administered by the intradermal route over the deltoid region.

Antibody titers should be monitored every 6 months in persons working with live virus in diagnostic, research, and vaccine production laboratories. In other professions at permanent risk of exposure to rabies, such as veterinarians, animal handlers, and wildlife officers, antibody titers in the serum should be monitored annually. Booster dose should be administered when the titer falls below 0.5 IU/ml. The duration of immunity by two injection vaccination course is 2–3 years.

Postexposure prophylaxis

A person who is exposed and has never been vaccinated against rabies should get five doses of rabies vaccine at 0, 3, 7, 14, and 28 days. They should also get human rabies immune globulin (20 IU/kg body weight; up to a maximum of 1500 IU) at the same time as the first dose. A person who has been previously vaccinated should get 2 doses – 1 on 0 day and another on 3rd day.

When needed, the rabies immunoglobulin should be infiltrated as much as possible into and around the wounds and the remaining should be given intramuscularly at a site away from the site where vaccine has been administered.

Management of re-exposure

On reexposure, 2 booster doses should be administered on days 0 and 3 irrespective of category of exposure or time that has elapsed since previous vaccination. All subjects who have received incomplete vaccination should be treated as fresh cases.

If rabies immunoglobulin is not available, double dose of the first dose of vaccination may be administered

Table 11: Vaccination in special situation in adults

Insert vaccines	Risk groups	Immunized	Not immunized	Vaccine	Dose and route	Brands
Hepatitis B	At high risk	Not indicated	0, 1, and 6 months if not immunized in childhood	Recombinant and plasma-derived	Single dose	Shanta biotech
Hepatitis A	At risk	Single dose if high risk	2 doses 6 months if not immunized in childhood	Inactivated and live		Inactivated single antigen (HAV antigen) vaccine, e.g., havrix (GSK) and vaqta (merck and co); combination vaccine, e.g., Twinrix (HAV + HBV)(GSK)
Meningococcal	Not recommended routinely High risk Travelers and epidemic	Single dose	2 doses <16 years >16 years single dose	Meningococcal conjugate (not for<2 years or >55 years) Meningococcal polysaccharide	0.5 cc SC <55 years 2 doses 1 month apart >55 1 dose	
HiB	At risk	Single dose of HiB in high risk	Single dose of HiB in high risk	Ag is polyribose phosphate or outer membrane protein and carrier is tetanus toxoid conjugate or diphtheria CRM protein	0.5 ml IM	GSK
Rabies	Not routine as prophylaxis. Only for high-risk groups Indiacted postexposure	Preexposure for high risk For those immunized 0, 3rd days no immunoglobulin	Pre exposure 0, 7, and 28 days IM Postexposure 0.3, 7, 14, and 28 days (90 days optional) with RIg ID 0, 3, 7, and 28 days over deltoid	HDCS PCECV Verorab (not for pre exposure)	1 ml IM 0.1 ml ID 0.5 cc IM	
Cholera	High-risk patients Two currently available vaccines are not recommended in India	For high risk 2 separate doses, 1 to 6 weeks apart for those aged over 6 years	For high risk 2 separate doses, 1–6 weeks apart for those aged over 6 years	2 oral vaccines Dukoral (WC/rBS) Recombinant B-subunit	2 separate doses, 1 to 6 weeks apart 2 separate doses given 1 week apart	Dukoral (WC/rBS) Recombinant B-subunit (Vabiotech)
Typhoid	High-risk Travelers or outbreak	If immunized booster every 3 years	Three doses of typhoid 21a capsules/sachets are administered on alternate days Series repeated once in every 3 years as booster dose Vi vaccine single SC/IM dose of 0.5 ml. Revaccination every 3 years			Live oral typhoid 21a vaccine- suspension or capsule (not in India) Injectable Vi polysaccharide vaccine Typhoid conjugate – bharat biotech
Varicella	Those who did not have chickenpox	For those already immunized in childhood booster doses are not needed if titers are adequate	Two doses administered 4 to 8 weeks apart	Attenuated live VZV (Oka strain) in both	2 doses 0.5 ml in deltoid area SC	Varilrix (GSK Biologicals) Okavax (Pasteur Mérieux) Varibed MSD Biovac Chinese
Japanese encephalitis	Not routine	Single dose and booster dose may be given at 1 year		Mouse brain-derived inactivated vaccine (NA) cell-culture, live-attenuated vaccine	0.5 ml SC Booster at 1 year	
Polio	Adults traveling to polio infected countries	Single dose of IPV	3 doses of IPV/OPV spaced by 1 month	Oral sabin IM killed salk		Chiron - old protect Sanofi - immumax polio
Rotavirus	Not routinely recommended for adult immunization			Live vaccine		Rotarix GSK Rotatech MSD

ID: Intradermal, IM: Intramuscular, SC: Subcutaneous, GSK: GlaxoSmithKline, IPV: Inactivated polio vaccine, OPV: Oral poliomyelitis, NA: Not available, VZV: Varicella-zoster virus, PCECV: Purified chicken embryo cell vaccine, HDCS: Human diploid cell strains, HiB: *Haemophilus influenzae* b, HAV: Hepatitis A vaccine

in the following situations: (i) category III exposure, (ii) patients who are malnourished and patients receiving corticosteroids, anticancer drugs, and antimalarials, and (iii) patients with HIV/AIDS with CD4+ count <200/mm^3. If feasible, antibody titers should be monitored and boosters given if titer is less than 0.5 IU/ml.

Immunosuppressed patients should avoid activities for which rabies preexposure prophylaxis is indicated. Antibody titer is checked after immunization in an immunosuppressed person. Sera should be collected around day 14 of vaccine series and at the time of completing prophylaxis.

Human papillomavirus vaccine

The vaccine protects against human papillomavirus (HPV) types responsible for most cervical cancers and genital warts. It is most effective when administered before onset of sexual activity.[21]

It can be given to young males and females between the ages of 9 and 26 years. In age group 9-14 years, 2 doses are recommended at an interval of 6 months. For >15 years, the dose is 0.5 ml intramuscularly at 0, 1, and 6 months.

Tetanus, diphtheria, and pertussis vaccine

Full dose diphtheria, tetanus, and pertussis are used in children (DPT). Acellular pertussis vaccine (DTaP) should be used for older children instead of whole cell vaccine (DTwP) because it is associated with less neurological complications. Two new tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines (Tdap) are available for use in those who are more than 10 years of age.[22,23]

The vaccination schedule varies with status of primary immunization. The dose is 0.5 ml given IM preferably in deltoid. DTaP (acellular pertussis) or DTwP (whole cell pertussis) vaccine should be used for first booster at 18 months while Tdap (low dose diphtheria and acellular pertussis) may be used for the second booster at 5 years and 10–15 years.

For adults between 18 and 64 years who have completed their primary vaccination schedule, a booster dose of Td vaccine is indicated once every 10 years till the age of 65; one dose of Tdap vaccine may be administered in place of Td vaccine. For adults >18 years who have not received prior vaccination against diphtheria, pertussis and tetanus, three doses of Td vaccine are indicated; two doses are administered at least 4 weeks apart, and the third dose is given 6–12 months after the second dose. The Tdap vaccine can substitute any one of the Td doses.

For adults who have not received Tdap vaccine and are likely to come in contact with infants suffering from diphtheria or pertussis, a single dose of Tdap vaccine should be given 2 weeks before the contact with the infant if 2 years or more have elapsed since the last dose of Td vaccination. Health care personnel, especially those in direct contact with the patients, who have not received Tdap vaccine should receive a single dose of Tdap vaccine if 2 years or more have elapsed since the last dose of Td vaccination. Women planning pregnancy should receive one dose of Tdap vaccine if they did not receive it previously. Pregnant women who have received the Td vaccination more than 10 years ago should receive one dose of Td vaccine in the second or third trimester of pregnancy. Pregnant women who have received Td vaccination during the preceding 10 years should receive one dose of Tdap in the immediate postpartum period if the last dose of Td was administered more than 2 years ago. For pregnant women who have never received previous vaccination, three doses of Td vaccine are indicated; in the second or third trimester of pregnancy, two doses are administered at least 4 weeks apart, and the third dose is given 6–12 months after the second dose. Following minor trauma in non immunized individual or those immunized more than 10 years if major wound both Td/Tdap and TIG should be given; if immunized >5 years and <10 years ago only Td/Tdap is given and TIG is not required. Modified dose vaccine is not effective post transplant and full dose is needed.

Precautions

Tdap/Td vaccines are contraindicated for persons with a history of anaphylaxis to any component. The Tdap vaccine is contraindicated in adults with a history of encephalopathy not attributable to an identifiable cause within 7 days of administration of a vaccine with pertussis component; these persons should receive Td vaccine. In adults with moderate or severe acute illness and those with unstable neurologic conditions (e.g., stroke, acute encephalopathies), Tdap vaccination is to be deferred until the acute illness resolves. In adults with a history of Arthus reaction with the previous dose of tetanus/diphtheria containing vaccine, Tdap/Td is administered only after 10 years since the last dose.

Haemophilus influenzae

The vaccine antigen is polyribose phosphate or outer membrane protein (OMP), and carrier is tetanus toxoid conjugate or diphtheria CRM protein.[7]

Vaccination is a part of primary immunization. Adults at high risk such as patients with asplenia, HIV, hematological

malignancies, corticosteroid use, CSF leak, trauma, diabetes, pregnancy, alcoholism, immunosuppression due to bone marrow or kidney transplant, cancer, radiation, or chemotherapy should be vaccinated.

A single 0.5 ml dose of haemophilus influenza b (HiB) conjugate vaccine is administered intramuscularly.[7]

Hepatitis A

Vaccines against hepatitis A virus (HAV) include inactivated vaccines as single antigen (HAV antigen) vaccines or combined with HBV antigens.

Universal immunization for hepatitis A is not recommended. The following groups of adults are considered at high risk for acquiring hepatitis A: persons who use illicit drugs; persons who work with HAV-infected primates or with HAV in a laboratory; people who receive clotting factor concentrates; persons infected with other hepatitis viruses; persons with CLD who are not already immune to HAV; persons who have received, or are awaiting a liver transplant; food handlers; and men who have sex with men. Hepatitis A vaccine is indicated for all transplant candidates with CLD or those patients of end-stage renal disease (ESRD) who have chronic hepatitis B or C because of increased risk of fulminant hepatic failure.[9,10]

Typhoid vaccine

The available vaccines for typhoid fever include inactivated whole cell vaccine, live oral Ty21a vaccine, injectable Vi polysaccharide vaccine, and Vi-rEPA vaccine. The lyophilized oral Ty21a vaccine is available in two formulations: A liquid suspension (in sachets) or enteric coated capsules. The Vi polysaccharide vaccine is a subunit vaccine composed of purified Vi capsular polysaccharide.[7]

Three doses of Ty21a capsules/sachets are administered on alternate days. This series should be repeated once in every 3 years as a booster dose. The capsule formulation should be taken orally with safe water. The sachet should be given with 100 ml of safe water with buffer to protect the B-subunit against gastric acidity. The Vi vaccine is given as a single subcutaneous or intramuscular dose of 0.5 ml, with revaccination every 3 years. Typbar conjugate vaccine is now recommended between 9 and 12 months.

Entire community at risk should be vaccinated during an outbreak. If immunization of the entire community is not possible, individuals aged 2–19 years should be specifically targeted. Ty21a should not be used during pregnancy. Vaccination policy for renal disease patients is same as for normal population. Live oral typhoid is contraindicated in transplant recipient.

Cholera

Vaccines for cholera are available as injectable killed whole cell vaccine; and oral cholera vaccine. The injectable killed whole cell vaccine has a poor efficacy with short-lasting protection and is not recommended.

Among the oral cholera vaccines, Dukoral (WC/rBS) is approved for use in persons aged over 2 years. Dukoral is administered in three separate doses, 1–6 weeks apart for 2–6-year-old children and as two separate doses, 1–6 weeks apart for those aged over 6 years. It confers 85–90% protection for 6 months among all age groups which declines over 6 months to 2 years.[7]

Japanese encephalitis

The vaccines used for immunization against Japanese encephalitis (JE) are mouse brain-derived inactivated vaccine and cell-cultured, live-attenuated vaccine. With effect from 2007, the production of the mouse brain-derived inactivated vaccine has been stopped. The live attenuated vaccine is currently in use in India. It is administered subcutaneously as a single 0.5 ml dose, with a booster dose at 1 year.[7]

The JE vaccine is primarily useful in the pediatric age. The issue of adult immunization against JE in case of major outbreaks needs to be reviewed.

Varicella vaccine

Two vaccines, both containing an attenuated live VZV are currently available in India.[20]

All adults who have never had chickenpox should receive 2 doses 0.5 ml in deltoid area subcutaneously. For <13 years of age, the first dose is administered at 12–15 months and the second dose at age 4–6 years. For people older than 13 years, the two doses are administered 4–8 weeks apart. For those already immunized, booster doses are not needed if titers are adequate. In resource-limited countries at least the females in reproductive age group, people at high risk for exposure to varicella, i.e., health care workers, household contacts, etc., should be vaccinated.[20]

Varicella vaccines should not be administered to persons receiving HD systemic immunosuppressive therapy, including oral corticosteroids >2 mg/kg of body weight or a total of more than 20 mg/day of prednisone or its equivalent for persons who weigh >10 kg, when administered for >2 weeks; HIV-seropositive adult or adolescent with CD4 + T-lymphocytes count <200 cells/μL; persons with a family history of

congenital or hereditary immunodeficiency in first-degree relatives (e.g. parents, siblings). It is also contraindicated in those with gelatin allergy, neomycin allergy, people on radiotherapy or chemotherapy, people who have received blood products or transfusions during past 5 months. Varicella vaccination has been shown to be effective in patients with nephrotic syndrome and should be given to all patients with negative varicella titers. It is ideally administered when in remission or on low-dose alternative days or off corticosteroid therapy. It is recommended for all CKD patients and those on dialysis.

Patient groups at risk for severe disease and complications from varicella can receive varicella zoster immunoglobulin (VZIG). These include those with immune-deficiency disorders; neoplastic diseases; on immunosuppressive treatment and pregnant women. VZIG should be administered within 96 h of the exposure at a dose of 125 units/10 kg body weight, up to a maximum of 625 units. Patients should be monitored for varicella for 28 days after exposure as VZIG prolongs incubation period.[24]

Rotavirus

The vaccine can be given after the age of 6 weeks–2 doses at 10 weeks and 14 weeks. It is not routinely recommended for adult immunization. The vaccine is recommended for pediatric solid organ transplant candidates before transplantation.[1-3]

References

1. Vashishtha VM, Choudhury P, Kalra A, Bose A, Thacker N, Yewale VN, *et al.* Indian Academy of Pediatrics (IAP) recommended immunization schedule for children aged 0 through 18 years – India, 2014 and updates on immunization. Indian Pediatr 2014;51:785-800.
2. Yewale V, Choudhury P, editors. IAP Guidebook on Immunization. Gwalior: Naveen Thacker Published by Indian Academy of Pediatrics; 2009. p. 1-177.
3. CDC Guidelines Centers for Disease Control and Prevention. Recommended adult immunization schedule – United States, 2012. MMWR Morb Mortal Wkly Rep 2012;61:1.
4. Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of vaccines and immune globulins for persons with altered immunocompetence. MMWR Recomm Rep 1993;42:1-18
5. National Center for Immunization and Respiratory Diseases. General recommendations on immunization --- recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2011;60:1.
6. WHO Recommendations for Routine Immunization. Available from: http://www.who.int/immunization/policy/immunization_tables/en/. [Last accessed on 2016 Jan 25 at 1300 hours].
7. Muruganathan A, Mathai D, Sharma SK, editors. Adult Immunization. J Assoc Physicians India; 2014. p. 1-270.
8. Guidelines for Vaccinating Dialysis Patients and Patients with Chronic Kidney Disease. Summarized from Recommendations of the Advisory Committee on Immunization Practices (ACIP); December, 2012.
9. Guidelines for the Management of CKD. Indian J Nephrol 2005;15 Suppl 1:S72-4.
10. Danzinger-Isakov L, Kumar D; AST Infectious Diseases Community of Practice. Guidelines for vaccination of solid organ transplant candidates and recipients. Am J Transplant 2009;9 Suppl 4:S258-62.
11. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Inter 2013;Suppl 3:1-150.
12. Nuorti JP, Whitney CG; Centers for Disease Control and Prevention (CDC). Prevention of pneumococcal disease among infants and children – Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine – Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2010;59:1-18.
13. Kumar D, Welsh B, Siegal D, Chen MH, Humar A. Immunogenicity of pneumococcal vaccine in renal transplant recipients – Three year follow-up of a randomized trial. Am J Transplant 2007;7:633-8.
14. Swaminathan S, Balajee G. Pneumococcal vaccines. A real world perspective. Special issue on the remaining challenge of pneumococcal disease in older adults. J Assoc Physicians India 2015;63:25-8.
15. Tomczyk S, Bennett NM, Stoecker C, Gierke R, Moore MR, Whitney CG, *et al.* Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged >65 years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2014;63:822-5.
16. Bonten MJ, Huijts SM, Bolkenbaas M, Webber C, Patterson S, Gault S, *et al.* Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 2015;372:1114-25.
17. Nuorti JP, Whitney CG; Centers for Disease Control and Prevention (CDC). Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2010;59:1-18.
18. Beyer WE, Versluis DJ, Kramer P, Diderich PP, Weimar W, Masurel N. Trivalent influenza vaccine in patients on haemodialysis: Impaired seroresponse with differences for A-H3N2 and A-H1N1 vaccine components. Vaccine 1987;5:43-8.
19. Scharpé J, Evenepoel P, Maes B, Bammens B, Claes K, Osterhaus AD, *et al.* Influenza vaccination is efficacious and safe in renal transplant recipients. Am J Transplant 2008;8:332-7.
20. Centers for Disease Control and Prevention (CDC). Licensure of a meningococcal conjugate vaccine (Menveo) and guidance for use - Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Morb Mortal Wkly Rep 2010;59:273.
21. Kwak EJ, Julian K; AST Infectious Diseases Community of Practice. Human papillomavirus infection in solid organ transplant recipients. Am J Transplant 2009;9 Suppl 4:S151-60.
22. Centers for Disease Control and Prevention (CDC). Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. MMWR Morb Mortal Wkly Rep 2011;60:13-5.
23. Centers for Disease Control and Prevention (CDC). Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine in adults aged 65 years and older - Advisory Committee on Immunization Practices (ACIP), 2012. MMWR Morb Mortal Wkly Rep 2012;61:468-70.
24. Sahay M. Post-transplant varicella infection. J Assoc Physicians India 2008;56:869.

Guidelines for vaccination in patients with chronic kidney disease

By virtue of their immunosuppressive state, chronic kidney disease (CKD) patients are at risk for many infections, some of which are vaccine preventable. Knowledge of vaccination is imperative to treat CKD patients effectively.[1] Table 12 summarizes the vaccine schedule for CKD patients.[1-7]

Discussed in this section are special issues related to vaccination in subjects with CKD.

Hepatitis B Vaccine

Hepatitis B vaccination is recommended for all CKD patients.[1,2,8,10,11] Patients with uremia who were vaccinated before they required dialysis have higher seroprotection rates and antibody titers. The response to vaccination is also better in children.[12]

Dosage and schedule

Higher vaccine dosages or an increased number of doses are recommended for subjects with CKD (eGFR <30 ml/min).

- Patients should receive four doses of hepatitis B vaccine as early in the course of disease as possible
- Recombinant hepatitis B vaccine is recommended
- Use special formulations of vaccine (40 mcg/ml) or two 1 ml 20 mcg doses given at one site. Dose schedule should be 0, 1, 2, and 6 months
- Vaccine should be given intramuscular in deltoid regions
- Assess antibody titer to hep B surface antigen (anti-HBs). First titer should be done 1–2 months after the primary course is completed and annually thereafter
- Booster dose should be given if anti-HBs titer falls below 10 mU/ml
- Revaccination with full doses is recommended for persons who do not develop protective antibody titer after primary course.

If an adult patient begins the vaccine series with a standard dose before beginning hemodialysis treatment, then moves to hemodialysis treatment before completing the series, completing the series using the higher dose is recommended for hemodialysis patients. No specific recommendations have been made for higher doses for pediatric hemodialysis patients. If a lower than recommended vaccine dose is administered to adults or children, the dose should be repeated.

Rationale

The prevalence and incidence of the hepatitis B infections are high, at about 7.6% and 3.2%, respectively among dialysis patients in India.[13] Vaccine provides effective protection against the infection. Vaccination in early stages of CKD has better seroconversion rate than late vaccination.

There is no difference in seroconversion rate in recombinant and plasma-derived vaccine but recombinant vaccine is preferred due to fear of disease communication with plasma.

Double dose (40 mcg) and four doses give better seroprotection rate (73–92%) compared to 45–67% with conventional 3 dose schedule.

Table 12: Recommendations for all vaccines in chronic kidney disease patients

Vaccine	Age	Dose	Vaccination schedule/ route of administration	Booster doses
Hepatitis B, Engerix B®	≥20 years	40 mcg	0, 1, 2, and 6 months/IM	Yes, when anti-HBs <10 UI/l
	<20 years	10 mcg	0, 1, and 6 months/IM	Yes, when anti-HBs <10 UI/l
Pneumococcal	.....	.....	.....Refer Table 13.....	.....
Influenza	3-8 years	15 µg	Each year/IM	No
	9-12 years	15 µg	Each year/IM	No
	>12 years	15 µg	Each year/IM	No
Varicella	1-12 years	0.5 ml	One single dose/SC	No
Hepatitis A, Havrix®	>17 years	1440 U	0, 6–12 months/IM	No
Measles, mumps, and rubella	>18 years	0.5 ml	One single dose/SC	No
Inactivated poliovirus	<18 years	0.5 ml	Three doses with an interval of 1-2 months	No (revaccination 1 year after the third dose)
Diphtheria and tetanus toxoids	7 years	0.5 ml	Three doses/IM	No

IM: Intramuscular, SC: Subcutaneous

Deltoid region is preferred to ensure intramuscular administration. Intradermal administration has no advantage over intramuscular administration.

Antibody titer falls with time in patients on dialysis, necessitating annual monitoring.

Vaccine has been shown to be safe for patients on dialysis with only minor local reactions including pain, redness, or swelling at the vaccination site.

An increase in anti-HBs response with coadministration of zinc, erythropoietin, or immunomodulators such as alpha and gamma interferon, thymopentine, interleukin-2, and granulocyte macrophage colony stimulating factor have been reported. Such approaches should be reserved for patients in whom it is difficult to achieve seroconversion with at least two courses of the vaccine.

Pneumococcal Vaccine

The recommendations for administering pneumococcal conjugate vaccine-13 (PCV13) and valent pneumococcal polysaccharide vaccine 23 (PPSV23) in patients with CKD are shown in Table 13.[1,3,4,5,6,7] CKD patients over the age of 19 should receive a dose of PCV13 first, followed by a dose of PPSV23 at least 8 weeks later. Subsequent doses of PPSV23 should follow current PPSV23 recommendations for adults at high risk. Specifically, the second PPSV23 dose is recommended 5 years after the first PPSV23 dose for persons aged 19–64 years.

The burden of pneumococcal infections in CKD patients is high, the cost of pneumococcal vaccination is low as compared with the global health costs in this population, and there are no data indicating potential disadvantages. Thus, pneumococcal vaccination should be administered to all patients with CKD as early in the disease as possible.[14] The ACIP schedule recommends a PCV13 prime vaccination followed by a PPV23 vaccination as mentioned in Table 13.

Influenza vaccine

Influenza vaccine should be given annually before the beginning of the influenza season for persons 6 months of age or older on dialysis.[15] Household contacts and health care workers should also be vaccinated annually to decrease the transmission to high-risk CKD patients.

The vaccine dose is 0.25 ml by intramuscular route for those between the ages of 6 and 35 months, and 0.5 ml thereafter. To those <9 years of age, 2 doses of influenza vaccine are administered at least 1 month apart and at 9–12 years, one dose of split virus vaccine should be given. After the age of 12 years, one dose of whole or split virus vaccine should be given.

Rationale

Dialysis patients are at increased risk of influenza-related mortality. Four-fold increase in serum antibody titer against influenza antigens have been observed in 50% of dialysis patients compared to 40% healthy controls, and no systemic reactions have been reported following influenza vaccination in dialysis patients.

Recommendations regarding other routine vaccines

Live attenuated vaccines

Live vaccines are contraindicated in immunocompromised patients due to risk of vaccine-induced infections. Even though the limited number of studies in CKD patients has not shown any adverse reactions, these vaccines should be avoided, with the exception of varicella and MMR vaccines.[1]

Children 1 year of age or older should receive 1 dose of subcutaneous varicella vaccine as recommended for healthy children of 13 years of age and younger who do not had chicken pox previously. Adolescents and adults should receive 2 doses of 0.5 ml subcutaneously, with second injection at least 4 weeks after the first. MMR vaccine should be given to all children including those on dialysis between 12 and 15 months of age with a booster dose between 4 and 6 years of age.

Rationale

There is high risk of complications and death associated with chicken pox infection in adulthood. About 85% of children on dialysis develop protective antibody levels within 6 months following single dose of vaccine. Varicella vaccine has been reported to be safe for children on dialysis.

Seroconversion rate following MMR vaccine for all 3 antigens is approximately 30%, for mumps alone 50%, and for measles and rubella combined 80%. Patients on dialysis should be tested for seroconversion.

Use of inactivated vaccines and toxoids in chronic kidney disease

All inactivated vaccine and toxoids are safe and effective when used in dialysis patients and should be administered to children and adults on chronic dialysis using the same doses and schedules recommended for immunocompetent persons.[16]

Haemophilus influenzae Type B conjugate vaccine (HiB) HiB vaccine is safe and should be given to children

Table 13: Recommendation for administering PCV13 and PPSV23 vaccines for patients with chronic kidney disease

Infants and children (ages 0-18)			
Vaccine history	**Recommended regimen**		
Never vaccinated with PCV7 or PCV13 up to age	Routine vaccination for PCV13 (4 dose series)	Administer 1 dose of PPSV23 at age ≥2 years and ≥8 weeks after last indicated dose of PCV13	Administer 1 dose of PPSV23 after 5 years
Completed all recommended doses of PCV7	Administer 1 dose of PCV13 ≥8 weeks later	Administer 1 dose of PPSV23 at age ≥2 years and ≥8 weeks after last indicated dose of PCV13	Administer 1 dose of PPSV23 after 5 years
Children aged 24-71 months who received <3 doses of PCV7 before age 24 months	Administer 2 doses of PCV13 now	Administer 1 dose of PPSV23 ≥8 weeks later after last indicated dose of PCV13	Administer 1 dose of PPSV23 after 5 years
Children aged 24-71 months who received any incomplete schedule of 3 doses of PCV7 before age 24 months	Administer 1 dose of PCV13 now	Administer 1 dose of PPSV23 ≥8 weeks later	Administer 1 dose of PPSV23 5 year after
Completed all recommended doses of PCV13	Administer 1 dose of PPSV23 at age ≥2 years and ≥8 weeks after last indicated dose of PCV13	Administer 1 dose of PPSV23 after 5 years	
Children aged 6-18 years who have not received PCV13	Administer 1 dose of PCV13 now		
Age 19-64 year			
Never vaccinated with PCV13 or PPSV23	Administer 1 dose of PCV13 now	Administer 1 dose of PPSV23 ≥8 weeks later	Administer 1 dose of PPSV23 ≥5 years later
Previously vaccinated with 1 dose PPSV23 ≥1 year ago; never vaccinated with PCV13	Administer 1 dose of PCV13 now	Administer 1 dose of PPSV23 ≥8 weeks after PCV13, which must be ≥5 years after first dose of PPSV23	
Previously vaccinated with 2 doses of PPSV23 (last dose was ≥1 year ago); never vaccinated with PCV13	Administer 1 dose of PCV13 now		
Previously vaccinated with ≥1 dose PCV13 (≥8 weeks ago); never vaccinated with PPSV23	Administer 1 dose of PCV13 now	Administer 1 dose of PPSV23 ≥5 years later	
Previously vaccinated with ≥1 dose PCV13 (≥8 weeks ago) and 1 dose PPSV23	Administer 1 dose of PPSV23 ≥5 years after first PPSV23 dose		
Age 65 year and over			
Never vaccinated with PCV13	Administer 1 dose of PCV13 now	Administer 1 dose of PPSV23 ≥8 weeks after PCV13, which must be ≥5 years after last dose of PPSV23	
Previously vaccinated with ≥1 dose PCV13 (≥8 weeks ago)	Administer 1 dose of PPSV23 now		

beginning at 2 months to 5 years of age using same dosage and schedule used for healthy children and adults. A study of children on chronic ambulatory peritoneal disease (CAPD) has shown seroconversion rate of 90%.

Children on dialysis should receive diphtheria and tetanus toxoids and pertussis vaccine as recommended for healthy children. The vaccine is well tolerated by dialysis patients. The persistence of immunity in patients on dialysis is comparable to that among healthy persons.

Hepatitis A vaccine is highly immunogenic in children, adolescents, and adults, with up to 100% of recipients develop protective level of antibodies > 20 mU/ml persisting for up 48 months. CKD patients at increased risk of infections such as travelers to countries to intermediate or high endemicity of infection, children 2 years of age and older living in areas rate of hepatitis A are at least twice the national average, drug users, men who have sex with men, persons with CLD or clotting disorders and persons working with nonprimates should receive the vaccine as recommended for normal adults.

Staphylococcus aureus vaccine

Patients on dialysis are at high-risk of *S. aureus* infection.[17] ESRD patients had an impaired immunological response to *S. aureus* vaccination, in comparison to that of the healthy controls, and showed 50% reduction of IgG levels 6 months after a 25-μg vaccination with a monovalent conjugated *S. aureus* type 5 capsular polysaccharide.[18] In another study, a single injection of a bivalent conjugate vaccine containing *S. aureus* type 5 and 8 capsular polysaccharide 25 μg of each capsular polysaccharide also showed only partial and short-lived protection in ESRD patients. The study was declared as failure study as the decrease in vaccine efficacy occurred after 40 weeks.[19]

To prolong the efficacy of the vaccine, a higher dose of the same vaccine (100 μg of each capsular polysaccharide) was tested in ESRD patients in comparison to placebo. The vaccine was efficient and well tolerated in comparison to placebo during the study period. However, the incidence of *S. aureus* bacteremias was not statistically different from placebo after 50 weeks.[20] With limited data on *S. aureus* vaccination in these patients, this vaccine is presently not recommended. It appears that there is need of multicomponent vaccines incorporating several surface proteins, toxoids, and surface polysaccharides to overcome multiple and redundant virulence factors of staph aureus.[21]

References

1. Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of vaccines and immune globulins for persons with altered immunocompetence. MMWR Recomm Rep 1993;42:1-18.
2. Johnson DW, Fleming SJ. The use of vaccines in renal failure. Clin Pharmacokinet 1992;22:434-46.
3. Centers for Disease Control and Prevention (CDC). Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012;61:816-9.
4. Nuorti JP, Whitney CG; Centers for Disease Control and Prevention (CDC). Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2010;59:1-18.
5. Nuorti JP, Whitney CG. Updated recommendations for prevention of invasive pneumococcal disease among adults using the 23-valent pneumococcal polysaccharide vaccine (PPSV23). MMWR Morb Mortal Wkly Rep 2010;59:1102-6.
6. Tomczyk S, Bennett NM, Stoecker C, Gierke R, Moore MR, Whitney CG, *et al*. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged >65 years: Recommendations of the advisory committee on immunization practices (ACIP). Morb Mortal Wkly Rep (MMWR) 2014;63:822-5.
7. Available from: http://www.cdc.gov/vaccines/vpd-vac/pneumo/vac-PCV13-adults.htm. [Last accessed on 2016 Jan 25 at 1300 hrs].
8. Centers for Disease Control and Prevention (CDC). Outbreaks of hepatitis B virus infection among hemodialysis patients- California, Nebraska, and Texas, 1994. MMWR Morb Mortal Wkly Rep 1996;45:285-9.
9. Buti M, Viladomiu L, Jardi R, Olmos A, Rodriguez JA, Bartolome J, *et al*. Long-term immunogenicity and efficacy of hepatitis B vaccine in hemodialysis patients. Am J Nephrol 1992;12:144-7.
10. Miller ER, Alter MJ, Tokars JI. Protective effect of hepatitis B vaccine in chronic hemodialysis patients. Am J Kidney Dis 1999;33:356-60.
11. Mitwalli A. Responsiveness to hepatitis B vaccine in immunocompromised patients by doubling the dose scheduling. Nephron 1996;73:417-20.
12. Fivush BA, Neu AM. Immunization guidelines for pediatric renal disease. Semin Nephrol 1998;18:256-63.
13. Vaccine recommendations for patients of chronic kidney disease. Indian J Nephrol 2005;15 Suppl 1:S72-4.
14. Vandecasteele SJ, Ombelet S, Blumental S, Peetermans WE. The ABC of pneumococcal infections and vaccination in patients with chronic kidney disease. Clin Kidney J 2015;8:318-24.
15. Centre for Disease Control and Prevention: Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practice (AICP). Morb Mortal Wkly Rep 1999;48:1-28.
16. Rangel MC, Coronado VG, Euler GL, Strikas RA. Vaccine recommendations for patients on chronic dialysis. The Advisory Committee on Immunization Practices and the American Academy of Pediatrics. Semin Dial 2000;13:101-7.
17. Kessler M, Hoen B, Mayeux D, Hestin D, Fontenaille C. Bacteremia in patients on chronic hemodialysis. A multicenter prospective survey. Nephron 1993;64:95-100.
18. Welch PG, Fattom A, Moore J Jr., Schneerson R, Shiloach J, Bryla DA, *et al*. Safety and immunogenicity of *Staphylococcus aureus* type 5 capsular polysaccharide-Pseudomonas aeruginosa recombinant exoprotein A conjugate vaccine in patients on hemodialysis. J Am Soc Nephrol 1996;7:247-53.
19. Fattom A, Fuller S, Propst M, Winston S, Muenz L, He D, *et al*. Safety and immunogenicity of a booster dose of *Staphylococcus aureus* types 5 and 8 capsular polysaccharide conjugate vaccine (StaphVAX) in hemodialysis patients. Vaccine 2004;23:656-63.
20. Shinefield H, Black S, Fattom A, Horwith G, Rasgon S, Ordonez J, *et al*. Use of a *Staphylococcus aureus* conjugate vaccine in patients receiving hemodialysis. N Engl J Med 2002;346:491-6.
21. Schaffer AC, Lee JC. Staphylococcal vaccines and immunotherapies. Infect Dis Clin North Am 2009;23:153-71.

Guidelines for vaccination in kidney transplant recipients

Kidney transplant recipients are at increased risk of developing infections, including vaccine-preventable diseases.[1] However, some of these vaccines may not be beneficial whereas others could even be harmful to kidney transplant recipients.[2] Under immunosuppression not only could live vaccine strains proliferate unchecked causing vaccine-induced diseases but also the immune response of recipients to the vaccines could be suboptimal, rendering vaccination ineffective, or even futile in certain situations.

The Kidney Disease Improving Global Outcomes (KDIGO) in 2009 brought out comprehensive, evidence-based guidelines for care of kidney transplant recipients including vaccination.[3] This chapter would attempt to endorse those guidelines with comments on the same or modify them if required, based on current literature to suit Indian scenario, with supporting rationale and evidence where available. For most of the supporting evidence for those guidelines adopted from the KDIGO guidelines, the readers are requested to refer to the original document.

1. Kidney transplant recipients should receive age-appropriate inactivated vaccinations as recommended for general population
    a. Hepatitis B Vaccination should be guided by anti-HBS titers, (measured at least 3 months after completion of vaccination and annually thereafter).
2. Kidney transplant recipients should not receive live vaccines. If a patient has received a live vaccine, the transplant should be delayed by at least 4 weeks since the time of administration
3. In general, it is best to wait until the first 3–6 months after kidney transplantation, the period of intense immunosuppression, before attempting vaccination. However, inactivated influenza vaccination can be administered as early as 1 month after kidney transplant to time it before onset of the flu season
4. Kidney transplant patients should receive ancillary inactivated vaccines based on the risk factors for the respective disease and the propensity to develop these rare infections, especially for vaccines that are neither routinely recommended for general population nor specifically in transplant recipients.

Rationale and Supporting Evidence

Response to vaccination has been shown to be suboptimal in transplant recipients.[1] The pretransplant vaccination history and the seroprotective status would affect the posttransplant vaccination strategies. Hence, detailed vaccination history should be obtained in all kidney transplant recipients at the first visit after kidney transplantation to plan the vaccination schedule if it is not already available.

Timing of vaccination after kidney transplant

Immune responses are suboptimal during the period of intense immunosuppression. The greater the degree of immunosuppression, the poorer is the response to vaccination. In this context, the degree of immunosuppression is best considered from the net state of immunosuppression rather than by the immunosuppressive drug doses and concentrations alone. Considering that the initial 3-6 months are a period of intense immunosuppression after kidney transplantation, it is preferable to avoid vaccinations during this time.[2] After 3–6 months, once maintenance immunosuppressive levels are reached, immunization could be undertaken.

If needed, some vaccines can be given after 2 months of kidney transplantation although the immune response is likely to be muted.[3,4]

Type of vaccine

Live attenuated vaccines pose considerable risk of unchecked vaccine strain proliferation and vaccine induced diseases in transplant recipients. Live virus vaccines should be administered as early in the course of chronic kidney disease (CKD) as possible. After administration of a live attenuated vaccine, a mandatory minimum waiting period of 4 weeks is necessary before using immunosuppression.[2]

Monitoring immune response to vaccination

Wherever possible, seroconversion should be documented after 4 weeks of completing the course of immunization to ascertain adequacy of protection, and determine need or additional boosters. While on ongoing immunosuppression, it may be prudent to monitor protective antibody levels to time booster doses appropriately.

Monitoring cellular immunity for protection against infections is under research.

Vaccination of health care workers and household contacts

Prevention of infections in kidney transplant should also involve a strategy to vaccinate household contacts and pets with vaccines for preventable diseases.

Vaccine-preventable diseases such as Hepatitis B, pneumococcal disease, and especially influenza vaccine should be offered to household contacts of transplant recipients. In general, inactivated vaccines are preferred for vaccination of household contacts.

Administration of live vaccines to household contacts can result in viral shedding, which can potentially result in vaccine-induced infectious disease in the transplant recipient. Hence, care should be taken to avoid live vaccines for household contacts of transplant recipients. Of importance to India is the administration of oral polio vaccine to children in the recipient's household, which can result in virus shedding and potentially result in virus-induced disease in the kidney transplant recipient. However, so far, there have been no documented reports of vaccine-induced poliomyelitis among transplant recipients, possibly due to preexisting immunity against polio among the recipients.

In case only a live attenuated vaccine is available, viral shedding should be considered and preferably the household contacts who have received them should exercise precaution as well as infection prevention measures such as frequent hand-washing and limit contact with the transplant recipient for the first 2 weeks, when viral shedding is likely to be at its peak.

Vaccines of special interest in transplantation

A summary of the various vaccines used in kidney transplant recipients is given in Table 14.

Hepatitis B Vaccination

The ideal time to administer Hepatitis B vaccine is before the onset of End stage renal disease. However, many patients do not receive the complete course of vaccination before kidney transplantation.

Kidney transplant recipients who lack protective antibody titers (>10 IU/ml) should receive hepatitis B vaccination.[5-8] It is preferable that the vaccination be administered at a time of less intense immunosuppression, which is after the first 3 months of kidney transplantation. Protective response to hepatitis B vaccination post solid organ transplant varies widely from 17 to 89%.[9,10] In view of low immunogenic response, there has been interest in accelerated vaccination schedules[11,12] although they have not been studied in kidney transplant recipients.

Protective antibody titres against Hepatitis B (Anti HBS) show a rapid decline post kidney transplantation. Hence, Anti HBS titres should be checked every 6-12 months and booster doses should be administered either when the titres fall below 10IU/ml or when it is expected to fall below that level in the next 3-6 months. In addition, it is important to note that the response to booster doses in transplant recipients will be less intense than with general population.

Pneumococcal vaccination

Vaccination with both 23 valent polysaccharide vaccine (PPSV23) and 13 valent conjugate vaccine (PCV13) are safe in kidney transplant recipients.[13-15] The schedule of immunization with the vaccines is as per the recommended schedule for general adults. The ACIP guidelines suggest the following comprehensive approach for optimal vaccine efficacy among immunocompromised adults:[16]

- If a patient receives the first dose of PCV13, it should be followed by PPSV23 at about 8 weeks later
- If patient had received PPSV23 in the past, a PCV13 dose should be administered after at least a year only
- If a patient who has received PPSV23 requires further doses of PPSV23, it should be administered at least 5 years after the last dose of PPSV23.

For immunocompromised children:[17]

- Between 2 and 5 years age: Two doses of PCV13 administered 8 weeks apart, followed by the additional dose of PPSV23 should be administered at least 8 weeks after the last dose of PCV13
- 6–18 years age:
  a. The first dose of PCV13 should be followed by 8 weeks later a dose of PPSV23
  b. If patient had been administered PPSV23, PCV13 should be administered after 8 weeks later.

In the year 2014, ACIP recommended routine use of PCV13 among adults aged ≥65 years.[18] As per this recommendation, both PCV13 and PPV23 should be routinely administered in series to all adults aged ≥65 years. ACIP recommendations for use of PCV13 (high risk) in adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants remain unchanged. The ACIP recommendation was amended in 2015 to simplify the spacing between PCV13 and PPSV23 in adults >65 years.[19] The new recommendation states that the recommended interval for adults receiving PCV13 and PPV23 to be at least 1 year apart, regardless of sequence.

Influenza vaccination

Among the various flu vaccines, the injectable inactivated vaccine is safe in kidney transplant recipients whereas the nasal live attenuated vaccine is contraindicated in the immunocompromised.[20] If an ESRD patient received a live attenuated influenza vaccine, he/she should not be

immunosuppressed preferably for the next 4-6 weeks, and at least for not <2 weeks.[20]

After kidney transplantation, routine annual inactivated influenza vaccine administration is recommended in all transplant recipients.[20-30] Immunogenicity of the influenza vaccine in kidney transplant recipients varies widely.[31,32] This variation could be attributed to the vaccine strain, the time after transplantation, the immunosuppressive regimen, as well as the net state of immunosuppression of the recipient.[1,31,33] For example, patients on MMF have a lower seroprotective rate.[31,32]

Concerns about influenza vaccine triggering an immune response and increase the risk of acute rejections[34,35] were not substantiated in large scale studies that demonstrated no increase in acute rejection episodes when influenza vaccine was used.[36,37] In large registry data, influenza vaccine use in transplant recipients was associated with lower rates of allograft loss and death.[27] However, use of adjuvanted Influenza vaccines has been shown to cause a rise in anti-HLA antibodies but not acute rejection episodes.[38,39] It is, therefore, advisable not to use adjuvanted influenza vaccines in kidney transplant recipients.[20]

Varicella vaccines

Being a live vaccine, this vaccine is contraindicated in kidney transplant recipients. It should be administered at least 4-6 weeks before kidney transplantation.[40] If transplant is emergently indicated in a patient who has received a varicella vaccine recently, he/she should receive peri-transplant prophylaxis with intravenous acyclovir or oral valacyclovir.[2] The *Zoster vaccine,* composed of a stronger dose of the live attenuated strain, is also contraindicated in kidney transplant recipients.[41]

Human papillomavirus vaccination

HPV vaccination should be completed prior to kidney transplantation. If the vaccination has been initiated pretransplant and could not be completed, additional doses could be administered after 3 months of kidney transplantation when the intensity of immunosuppression is less.[42] Serconversion after kidney transplant is around 50–70%. Unvaccinated kidney transplant recipients who satisfy the following criteria must receive HPV vaccination[43-45]

- 9–13 years age girls should be primary target of vaccination. Similar age boys could also be vaccinated
- Catch-up vaccination can be administered to those men and women between 11-26 years of age who have not been vaccinated previously.

The role of HPV vaccination among male and female kidney transplant recipients may expand in future.[46]

Hepatitis A vaccination

Hepatitis A vaccine is an inactivated subunit vaccine that can be administered in high-risk individuals or a potential to contract the viral infection from food, water, and body fluids of infected individuals. One study has shown reasonable seroprotective rates with the two-dose regimen among solid organ transplant recipient including kidney transplant recipients.[47]

***Haemophilus influenzae* vaccine**

Pediatric transplant recipients are significantly susceptible to haemophilus influenza pneumonia. A study of the *Haemophilus influenzae* b (HiB) vaccine in adult kidney transplant recipients demonstrated 71% immunogenicity.[48]

Considering that splenectomized individuals and sickle cell disease (SCD) are at high risk of this infection,[45] it is reasonable to consider immunizing CKD patients with SCD and in those undergoing desensitization protocol or ABO incompatible transplantation.

In contrast, children should receive the vaccine as per routine schedule and the immunogenicity can be assessed by a follow up HiB antibody titer after 4 weeks of the vaccination.[2]

Meningococcal vaccine

Kidney transplant recipients at risk of developing meningococcal infection and those who undergo a desensitization protocol transplantation or ABO incompatible transplantation may be reasonably administered the vaccine.[2]

Tetanus vaccine

Among adults, immunization against tetanus with the inactivated tetanus toxoid vaccine should be kept updated. Following the general principles of immunization, adult kidney transplant recipients should undergo a similar updating of their vaccination status based on routine indications and recommendations as for adults.[2] The immunogenicity of tetanus vaccine and its safety in kidney transplant recipients have been supported by several studies.[39-51] Pediatric kidney transplant recipients should be vaccinated according to the regular pediatric schedule of immunization.[2]

Rabies vaccine

Rabies cell culture vaccines are safe in immunocompromised individuals, and kidney transplant recipients should

receive rabies vaccine as per recommendations for general population.[2] Although kidney recipients can potentially acquire rabies from the organ donor through donation,[52,53] currently there is no evidence to recommend vaccination for all potential deceased donor kidney transplant wait-listed patients. While kidney transplant patients who have been bitten by a rabid dog must receive vaccination according to international guidelines, the protective effect may be inadequate[54] and it is prudent to monitor protective immunoglobulin levels and administer additional vaccine doses when indicated.[55,56]

Polio vaccine

Oral polio vaccine is contraindicated in kidney transplant recipients.[2] Pediatric transplant recipients below the age of 5 years should not participate in the pulse polio campaign to avoid oral polio vaccine strain induced poliomyelitis due to their immunocompromised state. Vaccine strain transmission has been documented from household contacts of immunocompromised individuals; therefore, household contacts of transplant recipients should also not receive oral polio vaccine.[57,58] Injectable inactive polio vaccine is safe and effective and pediatric kidney transplant recipients should be vaccinated according to the regular schedule of immunization for polio.[57]

Typhoid vaccine

Live oral typhoid vaccine Ty21a is contraindicated in transplant recipients and their household contacts.[4,59] Instead, killed Vi polysaccharide vaccine can be administered when indicated.[33] Typhoid vaccine is recommended as per routine indications in the country.

Cholera vaccine

Oral live cholera vaccine is contraindicated in kidney transplant recipients.[4,58] The new indigenous vaccine from India (VA 1.4) developed by the National Institute of Cholera and Enteric Diseases in Kolkata is a live oral vaccine that should not be used in transplant recipients.[60,61] The killed and subunit vaccine is considered safe in immunocompromised patients

Table 14: Vaccines in kidney transplantation

Vaccine	Type (LA/ inactivated - I)	Permitted for children		Permitted for adult		Monitor immune response	References
		Before Tx.	After Tx.	Before Tx.	After Tx.		
Hepatitis B	I	Yes (R)	Yes (R)	Yes (R)	Yes (R)	Monitor anti-HBs. Give booster if titre <10 IU/ml; consider when titre <100 IU/ml	[5-8]
Pneumococcus	I	Yes (R)	Yes (R)	Yes (R)	Yes (R)	Can be measured	[13-15]
Influenza inactivated	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	No	[20-30]
Influenza live attenuated	LA	No	No	No	No	No	[4,20]
Meningococcus	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	No	[34]
Human papillomavirus	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	No	[41,65]
Varicella (chicken pox - Varivax)	LA	Yes (R)	No	Yes (R)	No	Can be measured	[39,66-69]
Varicella (Zoster - Zostavax)	LA	-	-	Yes (R)	No	No	[70,71]
Hepatitis A	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	Can be measured	[47,72]
Diphtheria	I	Yes (U)	Yes (U)	-	-	No	[49,73,74]
Pertussis	I	Yes (U)	Yes (U)	-	-	No	[2,4]
Tetanus	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	Can be measured	[49,73,74]
Injectable polio vaccine	I	Yes (U)	Yes (U)	-	-	No	[49,73,74]
Oral polio vaccine	LA	Yes (U)	No	-	No	No	[75]
Haemophilus influenzae	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	Can be measured	[49]
Measles	LA	Yes (U)	No	-	No	No	[76,77]
Mumps	LA	Yes (U)	No	-	No	No	[76]
Rubella	LA	Yes (U)	No	-	No	No	[76]
BCG	LA	Yes (U)	No	-	No	No	[78]
Rotavirus	LA	Yes (U)	No	-	No	No	[2,4]
Rabies	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	Can be measured	[55,79]
Salmonella typhi oral typhoid 21a	LA	Yes (U)	No	Yes (U)	No	No	[80-82]
Parenteral typhim (V1 polysac) vaccine	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	No	[80-82]
Cholera - oral live cholera vaccine	LA	Yes (U)	No	Yes (U)	No	No	[2,60,62]
Oral killed cholera vaccine (Dukoral/Shanchol)	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	No	[2,61,62]
Japanese encephalitis	I	Yes (U)	Yes (U)	Yes (U)	Yes (U)	No	[83,84]
Yellow fever	LA	Yes (U)	No	Yes (U)	No	No	[2,4,63]
Smallpox	LA	No	No	No	No	No	[4,85]

U: Usual indication and dose as per standard recommendation for general population, R: Recommended specifically in the transplant context, No: Contraindicated/ not advisable to use in most cases, LA: Live attenuated, Tx: Transplant

although its immunogenicity of the vaccine in transplant recipients in unclear.[62]

Yellow fever vaccine

The live attenuated Yellow fever vaccine is contraindicated in kidney transplant recipients.[2,4] Although a case series has suggested that there was no important side effects in that cohort of solid organ transplanted patients.[63] Travel to endemic regions is best avoided. If unavoidable, travelers should take precautionary measures and carry a letter from physician stating the contraindication to vaccination with the stamp of an approved yellow fever immunization center.[64] However, some countries may deny entry without immunization.

References

1. Gangappa S, Kokko KE, Carlson LM, Gourley T, Newell KA, Pearson TC, *et al.* Immune responsiveness and protective immunity after transplantation. Transpl Int 2008;21:293-303.
2. Danziger-Isakov L, Kumar D; AST Infectious Diseases Community of Practice. Vaccination in solid organ transplantation. Am J Transplant 2013;13 Suppl 4:311-7.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant 2009;9 Suppl 3:S1-155.
4. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, *et al.* 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:e44-100.
5. Jacobson IM, Jaffers G, Dienstag JL, Tolkoff-Rubin NE, Cosimi AB, Delmonico F, *et al.* Immunogenicity of hepatitis B vaccine in renal transplant recipients. Transplantation 1985;39:393-5.
6. Krishnamurthy G, Kher V, Naik S. Immunogenicity and efficacy of hepatitis B vaccination in Indian chronic renal failure patients on hemodialysis and after renal transplantation. Nephron 1996;74:424-5.
7. Krishnamurthy K, John GT, Abraham P, Jacob CK. Granulocyte macrophage colony stimulating factor augmented hepatitis B vaccine protocol for rapid seroprotection in voluntary kidney donors. Indian J Med Res 2004;119:162-4.
8. Lefebure AF, Verpooten GA, Couttenye MM, De Broe ME. Immunogenicity of a recombinant DNA hepatitis B vaccine in renal transplant patients. Vaccine 1993;11:397-9.
9. Grob PJ, Binswanger U, Zaruba K, Joller-Jemelka HI, Schmid M, Häcki W, *et al.* Immunogenicity of a hepatitis B subunit vaccine in hemodialysis and in renal transplant recipients. Antiviral Res 1983;3:43-52.
10. Serrano B, Bayas JM, Bruni L, Díez C. Solid organ transplantation and response to vaccination. Vaccine 2007;25:7331-8.
11. Domínguez M, Bárcena R, García M, López-Sanroman A, Nuño J. Vaccination against hepatitis B virus in cirrhotic patients on liver transplant waiting list. Liver Transpl 2000;6:440-2.
12. Villeneuve E, Vincelette J, Villeneuve JP. Ineffectiveness of hepatitis B vaccination in cirrhotic patients waiting for liver transplantation. Can J Gastroenterol 2000;14 Suppl B: 59B-62B.
13. Kumar D, Rotstein C, Miyata G, Arlen D, Humar A. Randomized, double-blind, controlled trial of pneumococcal vaccination in renal transplant recipients. J Infect Dis 2003;187:1639-45.
14. Kumar D, Chen MH, Wong G, Cobos I, Welsh B, Siegal D, *et al.* A randomized, double-blind, placebo-controlled trial to evaluate the prime-boost strategy for pneumococcal vaccination in adult liver transplant recipients. Clin Infect Dis 2008;47:885-92.
15. Kumar D, Welsh B, Siegal D, Chen MH, Humar A. Immunogenicity of pneumococcal vaccine in renal transplant recipients – Three year follow-up of a randomized trial. Am J Transplant 2007;7:633-8.
16. Centers for Disease Control and Prevention (CDC). Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012;61:816-9.
17. Centers for Disease Control and Prevention (CDC). Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among children aged 6-18 years with immunocompromising conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2013;62:521-4.
18. Tomczyk S, Bennett NM, Stoecker C, Gierke R, Moore MR, Whitney CG, *et al.* Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged >65 years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2014;63:822-5.
19. Available from: http://www.cdc.gov/vaccines/vpd-vac/pneumo/vac-PCV13-adults.htm. [Last accessed on 2016 Jan 25 at 1300 hrs].
20. Kumar D, Blumberg EA, Danziger-Isakov L, Kotton CN, Halasa NB, Ison MG, *et al.* Influenza vaccination in the organ transplant recipient: Review and summary recommendations. Am J Transplant 2011;11:2020-30.
21. Azevedo LS, Gerhard J, Miraglia JL, Precioso AR, Tavares Timenetsky MD, Agena F, *et al.* Seroconversion of 2009 pandemic influenza A (H1N1) vaccination in kidney transplant patients and the influence of different risk factors. Transpl Infect Dis 2013;15:612-8.
22. Birdwell KA, Ikizler MR, Sannella EC, Wang L, Byrne DW, Ikizler TA, *et al.* Decreased antibody response to influenza vaccination in kidney transplant recipients: A prospective cohort study. Am J Kidney Dis 2009;54:112-21.
23. Cowan M, Chon WJ, Desai A, Andrews S, Bai Y, Veguilla V, *et al.* Impact of immunosuppression on recall immune responses to influenza vaccination in stable renal transplant recipients. Transplantation 2014;97:846-53.
24. Crespo M, Collado S, Mir M, Cao H, Barbosa F, Serra C, *et al.* Efficacy of influenza A H1N1/2009 vaccine in hemodialysis and kidney transplant patients. Clin J Am Soc Nephrol 2011;6:2208-14.
25. Fairhead T, Hendren E, Tinckam K, Rose C, Sherlock CH, Shi L, *et al.* Poor seroprotection but allosensitization after adjuvanted pandemic influenza H1N1 vaccine in kidney transplant recipients. Transpl Infect Dis 2012;14:575-83.
26. Fernández-Ruiz M, Lumbreras C, Arrazola MP, López-Medrano F, Andrés A, Morales JM, *et al.* Impact of squalene-based adjuvanted influenza vaccination on graft outcome in kidney transplant recipients. Transpl Infect Dis 2015;17:314-21.
27. Hurst FP, Lee JJ, Jindal RM, Agodoa LY, Abbott KC. Outcomes associated with influenza vaccination in the first year after kidney transplantation. Clin J Am Soc Nephrol 2011;6:1192-7.
28. Nailescu C, Xu X, Zhou H, Hall H, Wilson AC, Leiser JD, *et al.* Influenza vaccine after pediatric kidney transplant: A Midwest Pediatric Nephrology Consortium study. Pediatr Nephrol 2011;26:459-67.
29. Ott U, Sauerbrei A, Lange J, Schäfler A, Walther M, Wolf G, *et al.* Serological response to influenza A H1N1 vaccine (Pandemrix®) and seasonal influenza vaccine 2009/2010 in renal transplant recipients and in hemodialysis patients. Med Microbiol Immunol 2012;201:297-302.
30. Zand MS. Safety and efficacy of influenza vaccination in renal transplant recipients. Nat Clin Pract Nephrol 2008;4:358-9.
31. Scharpé J, Evenepoel P, Maes B, Bammens B, Claes K,

Osterhaus AD, *et al.* Influenza vaccination is efficacious and safe in renal transplant recipients. Am J Transplant 2008;8:332-7.
32. Sanchez-Fructuoso AI, Prats D, Naranjo P, Fernández-Pérez C, González MJ, Mariano A, *et al.* Influenza virus immunization effectivity in kidney transplant patients subjected to two different triple-drug therapy immunosuppression protocols: Mycophenolate versus azathioprine. Transplantation 2000;69:436-9.
33. Blumberg EA, Albano C, Pruett T, Isaacs R, Fitzpatrick J, Bergin J, *et al.* The immunogenicity of influenza virus vaccine in solid organ transplant recipients. Clin Infect Dis 1996;22:295-302.
34. Avery RK, Michaels M. Update on immunizations in solid organ transplant recipients: What clinicians need to know. Am J Transplant 2008;8:9-14.
35. Blumberg EA, Fitzpatrick J, Stutman PC, Hayden FG, Brozena SC. Safety of influenza vaccine in heart transplant recipients. J Heart Lung Transplant 1998;17:1075-80.
36. Kimball P, Verbeke S, Flattery M, Rhodes C, Tolman D. Influenza vaccination does not promote cellular or humoral activation among heart transplant recipients. Transplantation 2000;69:2449-51.
37. Candon S, Thervet E, Lebon P, Suberbielle C, Zuber J, Lima C, *et al.* Humoral and cellular immune responses after influenza vaccination in kidney transplant recipients. Am J Transplant 2009;9:2346-54.
38. Brakemeier S, Schweiger B, Lachmann N, Glander P, Schönemann C, Diekmann F, *et al.* Immune response to an adjuvanted influenza A H1N1 vaccine (Pandemrix(®)) in renal transplant recipients. Nephrol Dial Transplant 2012;27:423-8.
39. Katerinis I, Hadaya K, Duquesnoy R, Ferrari-Lacraz S, Meier S, van Delden C, *et al. De novo* anti-HLA antibody after pandemic H1N1 and seasonal influenza immunization in kidney transplant recipients. Am J Transplant 2011;11:1727-33.
40. Geel A, Zuidema W, van Gelder T, van Doornum G, Weimar W. Successful vaccination against varicella zoster virus prior to kidney transplantation. Transplant Proc 2005;37:952-3.
41. Pergam SA, Limaye AP; AST Infectious Diseases Community of Practice. Varicella zoster virus in solid organ transplantation. Am J Transplant 2013;13 Suppl 4:138-46.
42. Chin-Hong PV, Kwak EJ; AST Infectious Diseases Community of Practice. Human papillomavirus in solid organ transplantation. Am J Transplant 2013;13 Suppl 4:189-200.
43. Markowitz LE, Dunne EF, Saraiya M, Chesson HW, Curtis CR, Gee J, *et al.* Human papillomavirus vaccination: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2014;63:1-30.
44. Petrosky E, Bocchini JA Jr, Hariri S, Chesson H, Curtis CR, Saraiya M, *et al.* Use of 9-valent human papillomavirus (HPV) vaccine: Updated HPV vaccination recommendations of the advisory committee on immunization practices. MMWR Morb Mortal Wkly Rep 2015;64:300-4.
45. Centers for Disease Control. Advisory Committee on Immunization Practices (ACIP) recommended immunization schedules for persons aged 0 through 18 years and adults aged 19 years and older – United States, 2013. Morb Mortal Wkly Rep Surveill Summ 2013;62 Suppl 1:1.
46. Kwak EJ, Julian K; AST Infectious Diseases Community of Practice. Human papillomavirus infection in solid organ transplant recipients. Am J Transplant 2009;9 Suppl 4:S151-60.
47. Stark K, Günther M, Neuhaus R, Reinke P, Schröder K, Linnig S, *et al.* Immunogenicity and safety of hepatitis A vaccine in liver and renal transplant recipients. J Infect Dis 1999;180:2014-7.
48. Sever MS, Yildiz A, Eraksoy H, Badur S, Yüksel-Onel D, Görçin B, *et al.* Immune response to *Haemophilus influenzae* type B vaccination in renal transplant recipients with well-functioning allografts. Nephron 1999;81:55-9.
49. Enke BU, Bökenkamp A, Offner G, Bartmann P, Brodehl J. Response to diphtheria and tetanus booster vaccination in pediatric renal transplant recipients. Transplantation 1997;64:237-41.
50. Girndt M, Pietsch M, Köhler H. Tetanus immunization and its association to hepatitis B vaccination in patients with chronic renal failure. Am J Kidney Dis 1995;26:454-60.
51. Krüger S, Müller-Steinhardt M, Kirchner H, Kreft B. A 5-year follow-up on antibody response after diphtheria and tetanus vaccination in hemodialysis patients. Am J Kidney Dis 2001;38:1264-70.
52. Bronnert J, Wilde H, Tepsumethanon V, Lumlertdacha B, Hemachudha T. Organ transplantations and rabies transmission. J Travel Med 2007;14:177-80.
53. Srinivasan A, Burton EC, Kuehnert MJ, Rupprecht C, Sutker WL, Ksiazek TG, *et al.* Transmission of rabies virus from an organ donor to four transplant recipients. N Engl J Med 2005;352:1103-11.
54. Kopel E, Oren G, Sidi Y, David D. Inadequate antibody response to rabies vaccine in immunocompromised patient. Emerg Infect Dis 2012;18:1493-5.
55. Rodríguez-Romo R, Morales-Buenrostro LE, Lecuona L, Escalante-Santillán N, Velasco-Villa A, Kuzmin I, *et al.* Immune response after rabies vaccine in a kidney transplant recipient. Transpl Infect Dis 2011;13:492-5.
56. WHO Publication. Rabies vaccines: WHO position paper – Recommendations. Vaccine 2010;28:7140-2.
57. Burroughs M, Moscona A. Immunization of pediatric solid organ transplant candidates and recipients. Clin Infect Dis 2000;30:857-69.
58. Duchini A, Goss JA, Karpen S, Pockros PJ. Vaccinations for adult solid-organ transplant recipients: Current recommendations and protocols. Clin Microbiol Rev 2003;16:357-64.
59. Pirofski LA, Casadevall A. Use of licensed vaccines for active immunization of the immunocompromised host. Clin Microbiol Rev 1998;11:1-26.
60. Kanungo S, Sen B, Ramamurthy T, Sur D, Manna B, Pazhani GP, *et al.* Safety and immunogenicity of a live oral recombinant cholera vaccine VA1.4: A randomized, placebo controlled trial in healthy adults in a cholera endemic area in Kolkata, India. PLoS One 2014;9:e99381.
61. Mahalanabis D, Lopez AL, Sur D, Deen J, Manna B, Kanungo S, *et al.* A randomized, placebo-controlled trial of the bivalent killed, whole-cell, oral cholera vaccine in adults and children in a cholera endemic area in Kolkata, India. PLoS One 2008;3:e2323.
62. Jelinek T, Kollaritsch H. Vaccination with Dukoral against travelers' diarrhea (ETEC) and cholera. Expert Rev Vaccines 2008;7:561-7.
63. Azevedo LS, Lasmar EP, Contieri FL, Boin I, Percegona L, Saber LT, *et al.* Yellow fever vaccination in organ transplanted patients: Is it safe? A multicenter study. Transpl Infect Dis 2012;14:237-41.
64. Gershman M, Staples J. Yellow fever. In: Centers for Disease Control and Prevention, editor. Health Information for International Travel. New York: Oxford University Press, The Yellow Book 2014.
65. Gomez-Lobo V, Whyte T, Kaufman S, Torres C, Moudgil A. Immunogenicity of a prophylactic quadrivalent human papillomavirus L1 virus-like particle vaccine in male and female adolescent transplant recipients. Pediatr Transplant 2014;18:310-5.
66. Broyer M, Tete MJ, Guest G, Gagnadoux MF, Rouzioux C. Varicella and zoster in children after kidney transplantation: Long-term results of vaccination. Pediatrics 1997;99:35-9.
67. Furth SL, Hogg RJ, Tarver J, Moulton LH, Chan C, Fivush BA; Southwest Pediatric Nephrology Study Group. Varicella vaccination in children with chronic renal failure. A report of the Southwest Pediatric Nephrology Study Group. Pediatr Nephrol 2003;18:33-8.
68. Webb NJ, Fitzpatrick MM, Hughes DA, Brocklebank TJ, Judd BA, Lewis MA, *et al.* Immunisation against varicella in end stage and pre-end stage renal failure. Trans-Pennine Paediatric Nephrology Study Group. Arch Dis Child 2000;82:141-3.

69. Chaves Tdo S, Lopes MH, de Souza VA, Dos Santos Sde S, Pereira LM, Reis AD, *et al.* Seroprevalence of antibodies against varicella-zoster virus and response to the varicella vaccine in pediatric renal transplant patients. Pediatr Transplant 2005;9:192-6.
70. Zostavax in Renal Transplant Patients. ClinicalTrials.gov Identifier NCT01137669. Available from: https://www.clinicaltrials.gov/ct2/show/NCT01137669 [Last accessed on 2015 Oct 25].
71. Safety and Immunogenicity of Zostavax Vaccine in Patients Undergoing Living Donor Kidney Transplantation. ClinicalTrials.gov Identifier: NCT00940940. Available from: https://www.clinicaltrials.gov/ct2/show/NCT00940940 [Last accessed on 2015 Oct 25].
72. Günther M, Stark K, Neuhaus R, Reinke P, Schröder K, Bienzle U. Rapid decline of antibodies after hepatitis A immunization in liver and renal transplant recipients. Transplantation 2001;71:477-9.
73. Balloni A, Assael BM, Ghio L, Pedrazzi C, Nebbia G, Gridelli B, *et al.* Immunity to poliomyelitis, diphtheria and tetanus in pediatric patients before and after renal or liver transplantation. Vaccine 1999;17:2507-11.
74. Pedrazzi C, Ghio L, Balloni A, Panuccio A, Foti M, Edefonti A, *et al.* Duration of immunity to diphtheria and tetanus in young kidney transplant patients. Pediatr Transplant 1999;3:109-14.
75. Nkowane BM, Wassilak SG, Orenstein WA, Bart KJ, Schonberger LB, Hinman AR, *et al.* Vaccine-associated paralytic poliomyelitis. United States: 1973 through 1984. JAMA 1987;257:1335-40.
76. Flynn JT, Frisch K, Kershaw DB, Sedman AB, Bunchman TE. Response to early measles-mumps-rubella vaccination in infants with chronic renal failure and/or receiving peritoneal dialysis. Adv Perit Dial 1999;15:269-72.
77. Turner A, Jeyaratnam D, Haworth F, Sinha MD, Hughes E, Cohen B, *et al.* Measles-associated encephalopathy in children with renal transplants. Am J Transplant 2006;6:1459-65.
78. Grange JM. Complications of bacille Calmette-Guérin (BCG) vaccination and immunotherapy and their management. Commun Dis Public Health 1998;1:84-8.
79. Cramer CH nd, Shieck V, Thomas SE, Kershaw DB, Magee JC, Lopez MJ. Immune response to rabies vaccination in pediatric transplant patients. Pediatr Transplant 2008;12:874-7.
80. Recommendations of the Advisory Committee on Immunization Practices (ACIP): Use of vaccines and immune globulins for persons with altered immunocompetence. MMWR Recomm Rep 1993;42:1-18.
81. National Center for Immunization and Respiratory Diseases. General recommendations on immunization – Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2011;60:1-64.
82. Engels EA, Bennish ML, Falagas ME, Lau J. Typhoid fever vaccines. Vaccine 2000;18:1433-4.
83. Takahashi H, Pool V, Tsai TF, Chen RT Adverse events after Japanese encephalitis vaccination: Review of post-marketing surveillance data from Japan and the United States. The VAERS Working Group. Vaccine 2000;18:2963-9.
84. Kurane I, Takasaki T. Immunogenicity and protective efficacy of the current inactivated Japanese encephalitis vaccine against different Japanese encephalitis virus strains. Vaccine 2000;18 Suppl 2:33-5.
85. Dropulic LK, Rubin RH, Bartlett JG. Smallpox vaccination and the patient with an organ transplant. Clin Infect Dis 2003;36:786-8.

Vaccination guidelines in patients with chronic kidney disease and renal transplant recipients travelling abroad

The number of people traveling internationally has continued to grow in the past decade. Patients with chronic kidney disease (CKD) and transplant recipients are no exception. International travel takes many forms, including tourism, business, study abroad, research, visiting relatives and friends, ecotourism, adventure, medical tourism, mission work, and responding to international disaster. Travelers are as unique as they cover all ages and having a variety of health concerns and conditions. The infectious disease risks that a traveler faces are also dynamic, some destinations have become safer while in other areas, new diseases, such as Zika, have emerged and others have reemerged.

The risk of becoming ill during international travel depends on many factors such as the place visited, traveler's age, severity of kidney disease and transplant status, duration of stay, and diversity of planned activities.[1] The Centers for Disease Control and prevention (CDC) provides international health information to address the health risks that a traveler may face through their website www.nc.cdc.gov/travel.[2] Table 15 summarizes the vaccines

Table 15: Vaccines to update or consider during pretravel consultations

Routine vaccines	
Haemophilus influenzae type b	No report of travel-related infection, although organism is ubiquitous
Hepatitis	Recommended for travelers visiting countries where HBsAg prevalence is >2% vaccination may be considered for all international travelers, regardless of destination, depending on the traveler's behavioral risk as determined by the provider and traveler
Human papillomavirus	No report of travel-acquired infection although causal relationship is difficult to establish
Influenza	Outbreaks have occurred on cruise ships, and 2009 influenza A (H1N1) illustrated the rapidity of spread via travel
Measles, mumps, and rubella	Infections are common in countries that do not immunize children routinely, including Europe. Outbreaks have occurred in the United States as a result of travel
Meningococcal	Outbreaks occurred with Hajj pilgrimage, and the Kingdom of Saudi Arabia requires the quadrivalent vaccine for pilgrims
Pneumococcal	Organism is ubiquitous and causal relationship to travel is difficult to establish
Polio	Unimmunized or underimmunized travelers can acquire poliovirus as occurred in a case reported in association with a stay with a host family in Latin America that had been declared polio-free
Rotavirus	Common in developing countries, although not a common cause of travelers' diarrhea in adults. The vaccine is only recommended in young children
Tetanus, diphtheria, and pertussis	Rare cases of diphtheria have been attributed to travel. Pertussis has occurred in travelers, recently in adults whose immunity has waned
Varicella	Infections are common in countries that do not immunize children routinely as in most developing countries. Naturally occurring disease also occurs later in tropical countries
Zoster	Travel (a form of stress) may trigger herpes zoster, but causal relationship is difficult to establish
Travel vaccines	
Cholera	Cases in travelers have occurred recently in association with travel to the Dominican Republic and Haiti
Hepatitis A	Prevaccination incidence was 3-20 cases/1000 person-months of travel, but recent surveillance indicated a decline to 3-11 cases/100,000 person-months of travel. Prevalence patterns of HAV infection may vary among regions within a country, and missing or obsolete data present a challenge. Some expert travel clinicians advise people traveling outside the United States to consider hepatitis A vaccination regardless of their country of destination
Japanese encephalitis	Rare cases have occurred, estimated at <1 case/1 million travelers to endemic countries
Rabies	Rabies preexposure immunization simplifies postexposure immunoprophylaxis
Tickborne encephalitis	Cases have been identified in travelers with an estimated risk of 1/10,000 person-months in travelers. Endemic areas are expanding in Europe
Typhoid	UK surveillance found the highest risk to be travel to India (6 cases/100,000 visits), Pakistan (9 cases/100,000 visits), and Bangladesh (21 cases/100,000 visits)
Yellow fever	Risk occurs mainly in defined areas of sub-Saharan Africa and the Amazon drainage of South America. Some countries require proof of vaccination for entry. For travelers visiting multiple countries, order of travel may make a difference in the requirements

Table adapted from CDC Yellow book and modified. HAV: Hepatitis A vaccine, CDC: Centers for Disease Control and Prevention

recommended for travelers and Table 16 for renal failure and transplant recipients who are traveling.[3-14]

The Pretravel Consultation

Immunizations are a crucial component of pre-travel consultations, and the risk assessment forms the basis of recommendations for travel vaccines. At the same time, the pre-travel consultation presents an opportunity to update routine vaccines [Table 15] In considering travel immunizations, the approach to address "aggregate travel" or cumulative risk over years of travel, rather than risk associated with a single trip, allows travelers to prepare for multiple trips. Travelers should receive a record of immunizations administered.

The pre-travel consultation also provides the ideal setting to review wellness strategies with travelers and to remind them of healthy practices during travel. Topics to be explored are numerous and could be organized into a checklist, placing priority on the most serious and frequently encountered issues . General issues such as preventing injury and sunburn also deserve mention. Written information is essential to supplement the oral advice and enable travelers to review the abundant instructions from their clinic visits. Advice on self-treatable conditions may minimize the need for travelers to seek medical care while abroad and possibly lead to faster return to good health.

Table 16: Travel vaccines indicated in renal failure and posttransplant patients

Vaccine	Renal failure	Posttransplant	Monitor titers	Quality of evidence
Live vaccines				
BCG	Yes	No	No	III
Influenza (LAIV)	Yes	No	No	III
MMR	Yes	No	Yes	II-I
Varicella	Yes	No	Yes	II-2
Yellow fever	Yes	No	No	III
V. cholerae	Yes	No	No	
Zoster	Yes	No	No	
Typhoid 21a (oral)	Yes	No	No	III
Inactivated vaccines				
Haemophilus influenzae	Yes	Yes	No	II-2
Inactivated influenza	Yes	Yes	No	II-2
Hepatitis A	Yes	Yes	Yes	II-1
Hepatitis B	Yes	Yes	Yes	II-2
Tetanus	Yes	Yes	No	II-2
Pertussis	Yes	Yes	No	III
Inactivated polio	Yes	Yes	No	III
Pneumococcal	Yes	Yes	Yes	I
Meningococcal	Yes	Yes	Yes	III
Rabies	Yes	Yes	No	III
Human papillomavirus	Yes	Yes	No	III
Japanese encephalitis	Yes	Yes	No	III
Traveler's diarrhea and cholera vaccine (dukoral)	Yes	Yes	No	III

Parenteral cholera vaccine is poorly immunogenic highly reactogenic. Live attenuated vaccine should be avoided in immunosuppressed patients. Oral killed whole cell recombinant B subunit vaccine should pose no risk to immunocompromised patient. Cholera and enterotoxigenic *Escherichia coli* vaccine provides short-term protection. BCG: Bacillus Calmette Guerin, LAIV: Live attenuated influenza vaccine

Despite providers' best efforts, some travelers will become ill. Obtaining reliable and timely medical care during travel can be problematic in many destinations. As a result, prescribing certain medications in advance can empower the traveler to self-diagnose and treat common health problems. With some activities in remote settings, such as trekking, the only alternative to self-treatment would be no treatment. Pre-travel counseling may actually result in a more accurate self-diagnosis and treatment than relying on local medical care in some areas.In sum, travelers should be encouraged to carry a travel health kit with prescription and nonprescription medications. Typical medications include malaria chemoprophylaxis, self-management of travelers' diarrhea, and prophylaxis or treatment for acute mountain sickness. If a traveler anticipates the need to treat motion sickness, jet lag, or severe allergic reactions, consider medications for self-management, such as motion sickness therapy, a sleep aid, and epinephrine. Prescribing multiple medications, particularly for travelers already taking medications, warrants a review for possible drug interactions, particularly relevant for post transplant patients

For renal failure and post transplant patients it is important to emphasize food and water precautions, plan for self management of dehydration which can worsen renal function, arrange dialysis abroad if such situation arises. For chronic renal failure 3 vaccines are must to be updated: influenza, pneumococcal and hepatitis B.

Immunocompromised travelers to malaria-endemic areas should be prescribed drugs for malaria chemoprophylaxis and receive counseling about mosquito bite avoidance—the same as for immunocompetent travelers. Special concerns for immunocompromised travelers include any of the following possibilities:

Drugs used for malaria chemoprophylaxis may interact with drugs in the traveler's maintenance regimen, including leading to prolongation of the cardiac QTc interval, arrhythmia, and death.

The underlying medical condition or immunosuppressive regimen may predispose the immunocompromised traveler to more serious disease from malaria infection.

A malaria infection and the drugs used to treat the malaria infection may exacerbate the underlying disease.

The severity of malaria is increased in HIV-infected people: malaria infection increases HIV viral load and thus may exacerbate disease progression. All CKD patients and transplant recipients should seek pretravel advice to determine potential health hazards involved in the trip plan, understand anticipated risks, and methods of prevention; receive immunizations for vaccine-preventable diseases and medications for prophylaxis and/or self-treatment and to help the traveler to manage his/her health throughout the trip. Immunization history particularly becomes important in these patients. Overall consideration for vaccine recommendation such as destination and the likely risk for disease exposure are the same for immunocompromised travelers as for other travelers. The risk of severe outcome of a vaccine preventable disease must be weighed against potential adverse events from administering a live vaccine to the immunocompromised patient. Some complex cases where the traveler cannot tolerate recommended immunizations and prophylaxis, or where no prophylaxis is available, traveler should consider changing itineraries, altering the activities during travel, or deferring the trip.

The important issues regarding travel plan are:

- Whether the medical condition of the patient is stable for example, it is preferable for a post renal transplant recipient to avoid travel to a place which involves significant health hazard risk in the 1st year after transplantation
- The disease prevention measures as requirement for a live vaccine may destabilize a stable clinical course.

Yellow fever vaccine may be required for travel to some countries of Africa and South America but should be waived if travelers are immunosuppressed. Severely immunosuppressed should be strongly discouraged from traveling to destinations that pose true risk of yellow fever.

References

1. Danzinger-Isakov L, Kumar D; AST Infectious Diseases Community of Practice. Guidelines for vaccination of solid organ transplant candidates and recipients. Am J Transplant 2009;9 Suppl 4:S258-62.
2. CDC Yellow Book. Available from: http://www.nc.cdc.gov/travel/yellowbook/2016/table-of-contents. [Last accessed on 2016 Jan 24].
3. Avery RK, Michaels M. Update on immunizations in solid organ transplant recipients: What clinicians need to know. Am J Transplant 2008;8:9-14.
4. Scharpé J, Evenepoel P, Maes B, Bammens B, Claes K, Osterhaus AD, *et al.* Influenza vaccination is efficacious and safe in renal transplant recipients. Am J Transplant 2008;8:332-7.
5. Arslan M, Wiesner RH, Sievers C, Egan K, Zein NN. Double-dose accelerated hepatitis B vaccine in patients with end-stage liver disease. Liver Transpl 2001;7:314-20.
6. Are booster immunisations needed for lifelong hepatitis B immunity? European Consensus Group on Hepatitis B Immunity. Lancet 2000;355:561-5.
7. Stark K, Günther M, Neuhaus R, Reinke P, Schröder K, Linnig S, *et al.* Immunogenicity and safety of hepatitis A vaccine in liver and renal transplant recipients. J Infect Dis 1999;180:2014-7.
8. Günther M, Stark K, Neuhaus R, Reinke P, Schröder K, Bienzle U. Rapid decline of antibodies after hepatitis A immunization in liver and renal transplant recipients. Transplantation 2001;71:477-9.
9. Balloni A, Assael BM, Ghio L, Pedrazzi C, Nebbia G, Gridelli B, *et al.* Immunity to poliomyelitis, diphtheria and tetanus in pediatric patients before and after renal or liver transplantation. Vaccine 1999;17:2507-11.
10. Sever MS, Yildiz A, Eraksoy H, Badur S, Yüksel-Onel D, Görçin B, *et al.* Immune response to *Haemophilus influenzae* type B vaccination in renal transplant recipients with well-functioning allografts. Nephron 1999;81:55-9.
11. Kumar D, Rotstein C, Miyata G, Arlen D, Humar A. Randomized, double-blind, controlled trial of pneumococcal vaccination in renal transplant recipients. J Infect Dis 2003;187:1639-45.
12. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Report from the Advisory Committee on Immunization Practices (ACIP): Decision not to recommend routine vaccination of all children aged 2-10 years with quadrivalent meningococcal conjugate vaccine (MCV4). MMWR Morb Mortal Wkly Rep 2008;57:462-5.
13. Engels EA, Bennish ML, Falagas ME, Lau J. Typhoid fever vaccines. Vaccine 2000;18:1433-4.
14. Jelinek T, Kollaritsch H. Vaccination with Dukoral against travelers' diarrhea (ETEC) and cholera. Expert Rev Vaccines 2008;7:561-7.

Technical aspects of vaccine administration

Vaccination is an important aspect of prevention of several infections but at times, it may lead to complications by virtue of technical mishaps. Before recommending vaccine to anyone, practitioner must ensure the technical aspects of vaccine administration. One should ensure following points:

1. Right patient
2. Right vaccine/diluents
3. Right time
4. Right dose
5. Right route
6. Right site
7. Right technique
8. Right documentation
9. Right storage and handling– maintain correct temperature.

The schedule, dosing, route, and site have already been discussed previously. Here, we will focus on the technical aspect of vaccine administration.

Administration of vaccines:

a. Occupational health and safety issues – Utmost care should be practiced while administering vaccine so as to minimize the risk of needle stick injury and exposure to blood and body fluids. A new, sterile, disposable syringe and needle must be used for each injection. Used items must be discarded into a clearly labeled container as per biomedical waste management protocol. Vaccine providers should be aware of disposal and handling sharp containers
b. Equipment for vaccination – Appropriate equipment required for vaccination, such as appropriate size, gauge of needle should be used [Table 17]. Correct vaccines should be selected, maintained at correct temperature, and prepared as per requirement of the said vaccine (for example, reconstituted or prefilled vaccine). Vaccines should never be mixed in one syringe, and local anesthetic should not be mixed with a vaccine. Multidose vials should not be used. If unavoidable, extra precautions must be utilized to avoid contamination and maintain sterility
c. Preparation for vaccine administration – The receiver should be made comfortable and in adequate position. There is a potential of syncope after the vaccination and appropriate measures should be taken to prevent it. Hence, receiver should be adequately seated or lying. One may clean the skin using alcohol swab. Topical anesthetic may be used, if required, in children who are apprehensive, but at recommended time before the procedure
d. Recommended injection sites are anterolateral thigh (for infants) and the deltoid (for adults). Ventrogluteal region is an alternative site for all ages [Figure 1]
e. Vaccination injection technique – Hand washing with soap and water or alcohol-based waterless antiseptic is recommended before vaccine preparation. For multiple injections, the most painful dose should be given as last vaccine. The correct route of administration should be ensured for individual vaccine
    - Intramuscular injection – use appropriate needle, position the limb, pierce the needle at 90°

Table 17: Description of vaccine administration site and route

	Injection site and needle size	
Age	**Needle length**	**Injection site**
Subcutaneous (sc) injection		
Use a 23-25 gauge needle. Choose the injection site appropriate to the person's age and body mass		
Infants (1-12 months)	5/8 "	Fatty tissue over antero-lateral thigh muscle
Children 12 months or older, adolescents, and adults	5/8 "	Fatty tissue over antero-lateral thigh muscle or over triceps
Intramuscular (im) injection		
Use a 22-25 gauge needle. Choose the injection site and needle length appropriate to the person's age and body mass		
Newborn (up to 28 days)	5/8 "	Antero-lateral thigh muscle
Infants (1-12 months)	1"	Antero-lateral thigh muscle
Toddlers (1-2 years)	1-11/4 " 5/8-1"	Antero-lateral thigh muscle or Deltoid muscle of arm
Children and teens (3-18 years)	5/8-1" 1-11/4 "	Deltoid muscle of arm or Antero-lateral thigh muscle
Adult (19 years or older)		
Male or female <58.5 kg	5/8-1"	Deltoid muscle of arm
Female 58.5 - 90 kg Male 58.5 - 117 kg	1-11/2"	Deltoid muscle of arm

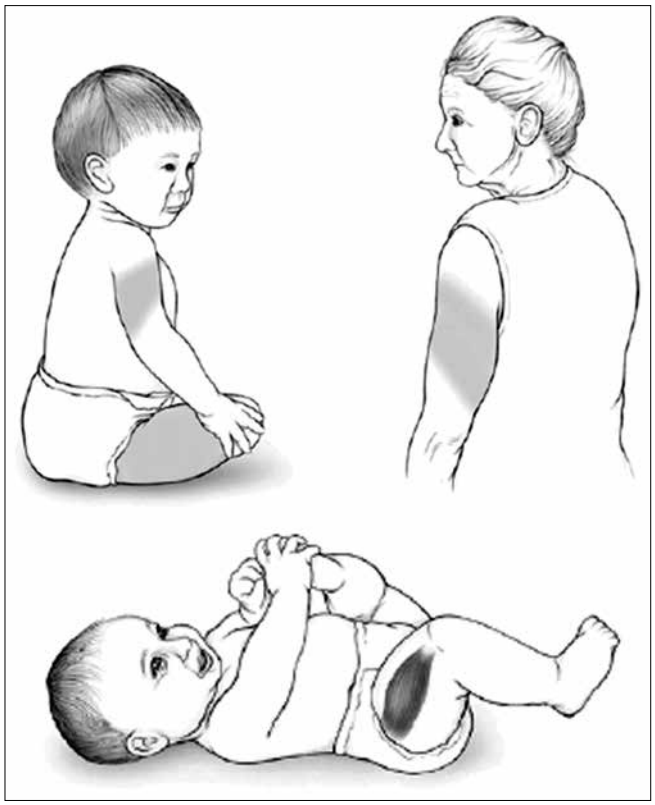

Figure 1: Preferred site for vaccine injections (diagrammatic)

- Subcutaneous injection – use appropriate needle, pierce at 45° [Figure 2]

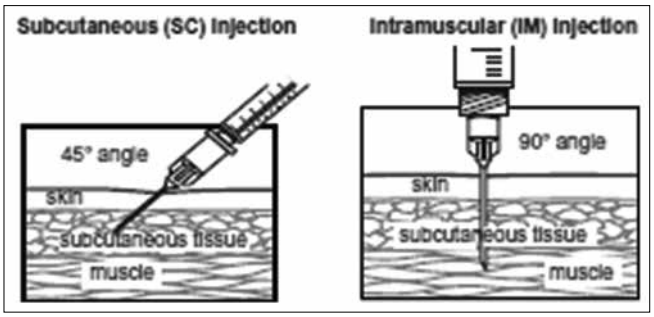

Figure 2: Technique of administering vaccines

- Intradermal injection – requires expertise and should be administered only be specialists.

f. Postvaccination - After vaccination, receiver should be observed for about 15 min. Vaccination-related events should be noted and informed to regulatory authorities.

Contraindications and precautions of each vaccine should be followed at each visit.

There should be a checklist for immunization at all facility centers. The checklist should include education, protocol of administration, vaccine handling, administering immunization, and recording of procedures. The checklist should be filled at every visit for individual receiver.