# Infectious Complications and Vaccination in Chronic Kidney Disease

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**Before You Start: Things You Need to Know**

- Infections are the second most common cause of morbidity and mortality in chronic kidney disease (CKD) patients.
- Infections increase the risk of adverse cardiovascular events in CKD.
- Uraemia-induced immune dysfunction, frequent visits to health-care facilities, frequent hospitalisation, need for vascular catheters and extracorporeal treatment increase infection risk.
- Preventing infections is of utmost importance both in pre-dialysis and dialysis-dependent CKD patients.

## 18.1 Infections and Chronic Kidney Disease

Chronic kidney disease (CKD) is recognised as an important global health-care concern. The National Chronic Kidney Disease Fact Sheet 2010 released by Centers for Disease Control and Prevention (CDC) estimates that >10 % of the US population aged 20 years or older have CKD. Besides being common, CKD affects the poor disproportionately and has major impact on the outcome of other major non-communicable diseases like diabetes and hypertension, 35 and 20 % of whom develop CKD [1].

Infection control remains a major public health goal worldwide. Over the last few decades, a complex interplay between infections and CKD has become evident. A number of infections can cause kidney disease, and CKD predisposes patients to various infections. Chronic infections with organisms like hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) are responsible for a substantial proportion of CKD in some parts of the world. In addition, infection-related acute kidney injury may not recover completely and lead to CKD.

The high incidence of infections in CKD patients, including those on dialysis and after kidney transplantation, has been known for decades. Infections are the second most common cause of morbidity and mortality in these patients after cardiovascular disease [2]. A number of risk factors increase the risk for infections in patients

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with kidney disease (Box 18.1). These include alterations in specific functions of various components of innate and adaptive immune system (Box 18.2). These changes are also responsible for poor response to vaccinations and failure to maintain protective antibody titres in CKD.

Though infections and cardiovascular disease may appear to be distinct clinical problems, modulation of underlying inflammatory state may be a common denominator linking the two in CKD. Data from United States Renal Data System (USRDS) Wave 2 study showed that the presence of bacteremia or septicaemia was associated with increased risk of death [hazard ratio (HR) 2.33, 95 % confidence interval (CI) 1.38–2.28], myocardial infarction (HR 1.78, 95 % CI 1.38–2.28), heart failure (HR 1.64, 95 % CI 1.39–1.95), peripheral vascular disease (HR 1.64, 95 % CI 1.34–2.0) and stroke (HR 2.04, 95 % CI 1.27–3.28) [3]. Analysis of USRDS data revealed that the risk of cardiovascular events was increased by 25 and 18 % at 1 and 3 months after an episode of infection-related hospitalisation compared to control periods [4]. These observational studies lend support to the intriguing hypothesis that the superimposition of macro-inflammatory events like bacterial infections over the persistent micro-inflammatory state of CKD might increase cardiovascular disease risk, despite apparent recovery from the infectious episode.

**Box 18.1. Risk Factors for Infections in Kidney Disease**

1. Old age
2. Female sex
3. African American race
4. Presence of diabetes mellitus
5. Malnutrition
6. Hypoalbuminaemia
7. Impaired cutaneous defence
   (a) Severe oedema
   (b) Use of vascular access and peritoneal dialysis catheters
   (c) Needlestick injury for native arteriovenous fistulae or grafts
8. Therapy related
   (a) Use of immunosuppressive drugs for treatment of basic disease
   (b) RBC or blood products transfusion
   (c) Contaminated caregiver's hands or gloves, equipment, supplies and environmental surfaces
   (d) Use of iron preparations*
   (e) Bioincompatible dialysis*
9. Increased hospitalisation for non-infectious complications
10. Immunological dysfunction
11. Poor vaccine response

*Increase oxidative stress

**Box 18.2. Immune System Alterations in CKD**

1. *Polymorphonuclear leucocyte dysfunction*
   (a) Increased reactive oxygen species production
   (b) Increased apoptosis
   (c) Spontaneous activation and degranulation
   (d) Decreased phagocytosis
2. *Depletion of antigen presenting cells*
3. *Monocyte dysfunction*
   (a) Increased circulating monocytes (especially $CD14^{+}CD16^{+}$ monocytes)
   (b) Increased reactive oxygen species production
   (c) Increased basal integrin, toll-like receptor (TLR)-2 and TLR-4 expression
   (d) Increased cytokine production
   (e) Decreased phagocytosis
4. *T-cell dysfunction*
   (a) Decreased regulatory T (Treg) cells
   (b) Reduced CD4/CD8 T-cell ratio
   (c) Decreased memory T cells (both central and naïve)
5. *B-cell dysfunction*
   (a) Decreased B-cell number
   (b) Decreased antibody production

## 18.2 Epidemiology of Infections in CKD

For the purposes of discussion of infections, it is useful to divide the CKD population into two groups: pre-dialysis CKD and dialysis-dependent CKD. Besides becoming a defining moment for patient and treating physician as this change affects patient's daily lifestyle and management, initiation of dialysis also alters the risk and consequences of infection by repeatedly breaching the physical defences and altering immune functions.

Pre-dialysis CKD patients have 3 times more risk of developing infectious complications as compared to general population [5]. Based on the 2001 Medicare data, urinary tract infection (UTI), pneumonia and bacteraemia or sepsis were four times, three times and four times, respectively, more common in pre-dialysis CKD population in the USA compared to the general population [5]. Sepsis and pneumonia were encountered in end stage renal disease (ESRD) patients ten times and five times more commonly than general population [5]. Recent data from Cardiovascular Health Study (CHS) showed that after a median follow-up of 11.5 years, risk of all-cause hospitalisation secondary to infectious events increased 16, 37 and 64 % in participants over the age of 65 with estimated glomerular filtration rate (eGFR) of (calculated using serum cystatin C level) 60–89, 45–59 and 15–44 mL/min/1.73 $m^2$, respectively, as compared to those with eGFR ≥90 mL/min/1.73 $m^2$ [6]. The risks of UTI and pneumonia were 160 and 80 % more in patients with eGFR 15–44 mL/min/1.73 $m^2$ when compared to those with eGFR ≥90 mL/min/1.73 $m^2$ [6].

The USRDS 2012 Annual Data Report identified infections as an important consequence of declining GFR [2]. In this report, mortality rates due to infection in the US ESRD population on haemodialysis in 2010 were 40 and 21 per 1,000 patient-years at risk at 2 months and 12 months after initiation of dialysis, respectively, after adjustment for age, gender, race, Hispanic ethnicity and primary diagnosis [2]. Also, hospitalisation rates due to infection in CKD stages 4–5 were 50–72 % higher than the rates for lower stages of CKD. In 2010, hospitalisation rates in haemodialysis patients in the USA were 0.46 and 0.11 per patient per year for infections overall and vascular access-related infections, respectively [2]. Rehospitalisation rate during transition to dialysis was highest if the index hospitalisation was infection related. During the quarter before initiation of dialysis, 44 % of patients were readmitted within 30 days of discharge after an infection-associated hospitalisation [2]. In the quarter after dialysis initiation, 44 % of patients died or needed rehospitalisation within 30 days of discharge after infection-associated hospitalisation [2]. Therefore, it appears that infections not only lead to acute problems but may also identify patients at higher risk of repeated hospitalisations. Whether this risk is related to infections or is a marker of otherwise poor underlying state is not clear.

### 18.2.1 Urinary Tract Infections (UTI)

UTIs are more common in certain subpopulations with CKD. These include patients with vesicoureteric reflux; interference with the normal flow of urine, either due to structural lesions, stricture, renal stone disease or secondary to functional problems like neurogenic bladder and diabetic cystopathy; or specific abnormalities like polycystic kidney disease. In addition to the frequency, some conditions can lead to more severe and/or special forms of UTI such as acute pyelonephritis, renal abscesses, renal papillary necrosis, emphysematous and xanthogranulomatous pyelonephritis or renal mucormycosis.

Another important consideration is distinguishing colonisation from true UTI especially in patients with underlying risk factors. A diagnosis of UTI should be made only when a patient is symptomatic, urinalysis shows significant pyuria (>9 pus cells/hpf) and urine culture shows a significant growth. Asymptomatic bacteriuria is treated only in pregnant females and patients who have to undergo either surgery or instrumentation of the urinary tract which may involve mucosal breach.

Established UTI in patients with CKD is treated as in general population. However, certain important considerations apply in this situation.

First, if the basic disease leading to CKD is associated with any structural or functional alteration in the urinary tract, the initial treatment course is given for extended period (2–4 weeks depending on whether it is lower or upper UTI), and prophylaxis is given for 6–12 months if there are recurrent episodes of UTI. Second, the choice of antibiotics and their dosage may have to be changed in accordance with the degree of renal dysfunction. Nitrofurantoin which is commonly used for treatment and prophylaxis of UTI in general population is contraindicated in patients with eGFR <50 mL/min/1.73 $m^2$. Third, risk of other complications like hyperkalaemia in CKD patients especially those on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers may forbid long-term use of drugs like trimethoprim-sulphamethoxazole which are commonly used in general population for prophylaxis. Fourth, cyst infection is a unique form of kidney infection seen in polycystic kidney disease patients which requires prolonged course of antibiotics (up to 6 weeks) and at times may be refractory and thus require surgical intervention. Whereas trimethoprim-sulphamethoxazole remains the first choice in acute, uncomplicated, lower UTI in patients with CKD stage 3a, either ciprofloxacin or extended spectrum penicillin like pivmecillinam (especially in European countries where it is available) are recommended in CKD stages 3b to 5. It is important to note that the duration of treatment of acute, uncomplicated, lower UTI in females and males without any predisposing factors is different at 3 and 7 days, respectively. It is very important that attempts at modifying risk factors for recurrent UTI (e.g. surgical relief of obstruction, clean intermittent self-catheterisation in large volume neurogenic bladder) are made early as treatment becomes increasingly difficult because of urinary tract colonisation with drug-resistant organisms.

### 18.2.2 Pneumonia

Community-acquired pneumonia is a common cause of hospitalisation in general population. The risk of pneumonia increases progressively with fall in GFR. This risk further translates into increased severity of disease at admission and higher mortality rates during admission and at 1 month after discharge. *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia in CKD patients [7]. Vaccination against pneumococcus has been shown to be beneficial in improving outcomes. CKD patients are also at increased risk of developing severe forms of influenza.

### 18.2.3 HIV Infection

The prevalence of CKD is increased in incident patients of HIV infection starting antiretroviral therapy. About one-third of patients with HIV infection have CKD. The spectrum of renal involvement in HIV infection ranges from asymptomatic proteinuria to nephrotic syndrome, acute kidney injury or progressive decrease in GFR. The majority of patients have HIV-associated nephropathy (HIVAN) which most frequently presents as nephrotic syndrome and is characterised histologically by collapsing glomerulopathy and variable tubulo-interstitial involvement. African American race, decreased CD4 counts and family history of kidney disease are risk factors for development of HIVAN. All patients with HIVAN should be given antiretroviral therapy irrespective of their eGFR. In CKD patients, the presence of HIV infection is considered a risk factor for accelerated decline in GFR. Conversely, presence of CKD is also a risk factor for progression of HIV infection. Drug interactions and drug-induced kidney injury are very important treatment considerations in patients with HIV and CKD. Calcium channel blockers are contraindicated in patients using protease inhibitors. The risk of lactic acidosis does not forbid the use of nucleoside analogues in patients with CKD, but careful monitoring is advisable. Ensuring adequate hydration (daily water intake >1.5 L) is of paramount importance in patients who take indinavir to prevent indinavir nephrolithiasis. Though annual screening for renal involvement by urine protein and eGFR estimation is recommended, this frequency should be increased to biannually in patients who take drugs like tenofovir and indinavir and are at risk

of drug-induced kidney injury. Finally, as the life expectancy of HIV-infected population on therapy has progressively increased, unrelated risk factors for CKD, e.g. diabetes, hypertension, etc., have also become important now.

### 18.2.4 Vascular Access-Related Infections

Patients with CKD are at risk of potentially lethal vascular access-related infections later in the course of disease because attention is not paid to timely creation of appropriate access. As a result, large proportions of CKD patients start dialysis with central venous catheters. The risk is highest for non-tunnelled central venous catheters followed by tunnelled ones, arteriovenous grafts and native arteriovenous (AV) fistulae. Amongst 1846 participants in the HEMO study, of whom only 7.6 % were using catheters, first infection-related hospitalisation was due to non-access-related infection in 79 % patients [8]. However, in HD population using catheters for vascular access at a large centre in the USA, non-access-related infections accounted for just 12 % of all proven infectious episodes [9]. *Staphylococcus aureus*, coagulase-negative staphylococci and enterococci are the most common organisms responsible for access-related bloodstream infections and may become complicated by infective endocarditis or osteomyelitis. Of particular concern are infections with multidrug-resistant bacteria and nosocomial transmission to other patients. As a result of these problems, timely creation of AV fistulae, dubbed the 'Fistula First' initiative, is targeted at reducing catheter usage.

Despite decreasing vascular access and PD catheter-related infections, hospitalisation rates due to infection in 2010 in the US ESRD population were 31 % higher compared to 1994 [2]. The increase was more striking (43 %) in the HD population [2].

### 18.2.5 Blood-Borne Infections

Patients with CKD are at risk of acquiring blood-borne infections like hepatitis B and C due to repeated skin punctures, need of blood or blood products and sharing of contaminated machines, surfaces or supplies in hospitals. Better staff training, improved infection control practices, regular screening and universal vaccination of patients and staff have reduced the HBV prevalence and seroconversion rates [10]. However, HCV infection still remains an important problem with prevalence ranging from 0.7 to 18.1 % in Asia-Pacific countries and 2.7 to 20 % in Europe [10, 11]. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend the use of nucleic acid-based testing to screen patients for these infections in areas with high prevalence so as to not miss occult infections (see Chap. 20). However, this recommendation is not universally followed. KDIGO also recommends strict infection control measures as the most important tool for preventing its spread.

### 18.2.6 Tuberculosis

Tuberculosis is an important infection in patients with CKD, with 10–15 times increased incidence in both endemic and non-endemic regions as compared to general population [12, 13]. The diagnosis is not straightforward as the disease is more commonly extra-pulmonary with variable nonspecific manifestations like fever, weight loss, malaise, etc., which frequently delay diagnosis. Therefore, a high index of suspicion is required. As definitive diagnosis by culture takes a long time and absence of acid-fast bacilli on staining does not rule out tuberculosis, treatment is often started empirically in a significant proportion of patients on the basis of strong clinical suspicion and suggestive investigations, e.g. granulomatous inflammation on histopathology [12]. There is controversy about the need and optimal method of screening for latent tuberculosis [12]. However, the utility of screening in endemic regions with high prevalence of this disease is not clear. Interferon gamma assays like QuantiFERON-TB Gold test have been shown to be better than tuberculin skin test for detecting latent tuberculosis [14]. Tuberculosis is treated as in non-CKD population, but drug dose modification for level of eGFR is recommended.

### 18.2.7 Other Infections

The incidences of dyspepsia and gastroduodenal disease are more in CKD patients as compared to general population. Though *Helicobacter pylori* infection has been found to be less prevalent in haemodialysis and peritoneal dialysis patients, whenever present, it is treated as in patients with normal renal function [15]. Similarly, infective endocarditis is also treated as in general population. Patients with CKD and risk factors for development of infective endocarditis (prosthetic heart valves, valvular heart disease, valvular calcification, etc.) should receive antibiotic prophylaxis (amoxicillin 2 g or clindamycin 600 mg) prior to invasive dental and periodontal procedures.

It has been shown that mortality after septic shock due to various reasons is significantly more in patients with reduced GFR. In fact, eGFR <60 mL/min/1.73 $m^2$ remains an independent predictor of early and late mortality in patients with septic shock even after correction for comorbidities like diabetes, hypertension and cardiovascular disease.

The treatment of essentially all infectious diseases is same as in general population. However, drug dose modification or choosing alternative drug may be required as per patient's eGFR.

## 18.3 Infection Control in CKD

Globally, infection control and prevention are one of the biggest goals of public health. According to the World Health Organization (WHO), the objective of infection prevention and control is to ensure protection of those who might be vulnerable to an infection either in general community or while utilising health-care facilities. WHO identifies hygiene as the basic principle of infection prevention and control.

Patients with CKD are treated in the same manner as in general non-CKD population for established infections. Important considerations in this population include the assessment of comorbidities and risk factors, antimicrobial dose adjustment for level of kidney function, consideration of drug interaction and preventing superimposed acute kidney injury due to infections and use of radiocontrast agents or drugs used to treat the infection.

### 18.3.1 Vaccination in CKD Patients

In addition to general measures, timely vaccination is important in infection control (Box 18.3). The impact of vaccination in preventing, eliminating and eventually eradicating the disease has been convincingly demonstrated throughout the world through the universal immunisation programmes. The Advisory Committee on Immunization Practices (ACIP) in the USA annually updates and recommends immunisation schedules for children and adults. Kidney disease patients are classified at having high infection risk. Although vaccination is effective in CKD, these patients mount an inferior response to vaccination and suffer relatively rapid decline in protective antibody titres as compared to general population.

It is important to assess and record immunisation history of every CKD patient at initial presentation. *Physician should be aware of differences between contraindications and precautions with respect to vaccination*. While a contraindication precludes vaccination because of significant risk of adverse events, a precaution either means slightly increased risk of adverse events or decreased immune response to vaccine.

**Box 18.3. Measures Aimed at Reducing Infections in CKD Patients**

1. Vaccination against vaccine-preventable diseases
2. Timely creation of dialysis access
3. Maximising use of native arteriovenous fistulae in prevalent and incident haemodialysis patients
4. Universal precautions to be followed at health-care facilities
5. Rationalising antibiotic use according to local antimicrobial resistance data
6. Practising hand hygiene by patient and care giver

Severe allergic reaction or anaphylactic response to a vaccine or its constituents (e.g. egg, gelatin, latex, adjuvants) is a contraindication. Usually, vaccines are not administered even in situations where precaution is advised. It is important to note that not all contraindications or precautions are permanent. Mild acute febrile illnesses, previous mild local reactions and breast-feeding are not contraindications to vaccination. Vaccination should be deferred for 4 weeks after recovery from acute febrile illnesses. Live virus vaccines (varicella, zoster and MMR) are contraindicated in pregnancy and states of severe immunosuppression, e.g. primary or acquired immunodeficiency, steroid dose equivalent of prednisolone dose ≥20 mg/day for ≥2 weeks, malignancies involving the bone marrow or lymphatic system, etc. Particular attention should be paid to storage conditions, vaccine diluents, dose, site and type of administration. Adult vaccines are usually administered by intramuscular route except varicella, zoster, MMR and inactivated meningococcal polysaccharide vaccine which are given by subcutaneous route. Multiple vaccines can be administered simultaneously, but sites should be separated by at least 1–2 in. However, if immune globulin is also administered, a different anatomic site should be used.

All HbsAg-negative and anti-HBs negative patients must be vaccinated against HBV at the time of initial diagnosis irrespective of the stage of CKD. Higher dose of 40 μg in a four-dose schedule (0–2 and 6 months) has been shown to achieve higher seroconversion rates [17]. Though seroconversion rates in pre-dialysis stages of CKD are better, they are still suboptimal as compared to general population. An anti-HBs titre of >10 IU/L is considered protective and titre below this level warrants booster dose. A number of strategies have been used to increase the immunogenicity: these include increasing dose and frequency of vaccination, intradermal route of administration, using pre-S2/S antigens, use of adjuvants like 3-0-desacyl-4′-monophosphoryl lipid A adsorbed on aluminium phosphate and immunostimulants like levamisole and granulocyte macrophage colony stimulating factor [18]. The data, however, is inconclusive because of small sample sizes, variable doses and schedules and conflicting results. The antibody titres should be monitored annually in all previously vaccinated patients to ensure maintenance of protective levels.

Annual vaccination against influenza decreases the risk of hospitalisation and death in CKD patients [17]. Only inactivated influenza vaccine is recommended. Pneumococcal vaccination is also recommended for all patients with renal failure. A recent, large retrospective analysis of about 37,000 patients on dialysis in the USA has shown that vaccination against influenza and pneumococcus was independently associated with survival [19]. As compared to no vaccination, adjusted odds ratio of all-cause mortality amongst patients vaccinated for influenza alone and both influenza and pneumococcal vaccination were 0.79 (95 % CI, 0.72–0.86) and 0.70 (95 % CI, 0.62–0.78), respectively [19]. The recent KDIGO clinical practice guidelines for management of CKD also recommend vaccination against influenza, pneumococcus and HBV. ACIP recommends that except for meningococcal and hepatitis A vaccines, all other recommended vaccines should be considered in adult patients with CKD if they have not received them (Table 18.1). Though not routinely recommended in CKD, *Haemophilus influenzae* type b vaccination elicits adequate immunological response in dialysis patients and should be given to eligible patients [20]. Vaccination against *Staphylococcus aureus* has not been found to be effective in preventing septicaemia in dialysis patients and is not recommended. Routine paediatric immunisation schedule should be followed in children with CKD. Only inactivated polio vaccine should be used in patients with renal failure. As previously stated, live influenza vaccine is contraindicated, and caution is required before use of other live vaccines in children with CKD.

All patients with advanced CKD should preferably be vaccinated before renal transplantation. The seroconversion rates come down drastically if vaccines are administered after transplantation. Live vaccines are contraindicated in renal transplant recipients, and it is preferable to postpone other vaccinations till 6 months after transplant.

Despite recommendations, vaccination rates remain low, varying from 26 to 65 % and 15 to

**Table 18.1** Vaccine recommendations for adult patients (age ≥19 years) with chronic kidney disease

| Vaccine | Dose | Frequency | Considerations |
|---|---|---|---|
| Hepatitis B[a] | 3–4 | Once. Revaccinate with booster dose if anti-HBs titres fall <10 mIU/L | Check anti-HBs titres |
| Inactivated influenza | Single | Annual | Intranasally administered live, attenuated influenza vaccine not recommended in renal failure patients |
| Tetanus, diphtheria, pertussis (Td/Tdap)[b] | Single | Every 10 years | None |
| Varicella | Two (4 weeks apart) | Once | None |
| Human papillomavirus female (HPV2/HPV4)[c] | Three doses | Once | Not recommended beyond 26 years of age |
| Human papillomavirus male (HPV4) | Three doses | Once | Not recommended beyond 21 years of age |
| Zoster | Single | Once | Recommended for all adults aged ≥60 years irrespective of past history of herpes zoster |
| Measles, mumps, rubella (MMR) | 1–2[d] | Once | None |
| Pneumococcal polysaccharide (PPSV23) | 1–2 | Revaccinate once after 5 years till 64 years of age<br>Revaccinate again at ≥65 years if ≥5 years have elapsed since last dose<br>No revaccination if vaccinated ≥65 years of age | None |
| Pneumococcal 13-valent conjugate (PCV13) | 1–2 | Not previously received PCV13 or PPSV23: Give single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later<br>Previously received one dose of PPSV23: PCV13 1 or more years after the PPSV23, repeat PPSV23 dose no sooner than 8 weeks after PCV13 and at least 5 years after the most recent dose of PPSV23<br>Previously received two doses of PPSV23: PCV13 1 or more years after the PPSV23 | None |
| Meningococcal[e] | Two | Revaccinate every 5 years till risk factors present | Recommended only in adults with anatomic or functional asplenia or persistent complement component deficiencies, HIV infection or high risk, e.g. occupational exposure, dormitory residence |
| Hepatitis A | Two | Once | Recommended only in adults with risk factors, e.g. occupational exposure, gay men, chronic liver disease, travel to endemic areas |

Source: Data from Advisory Committee on Immunization Practices (ACIP) [16]
All are recommended in CKD patients without documented previous vaccination or disease except meningococcal and hepatitis A vaccines which are recommended only in certain high-risk groups. Note that zoster vaccination is recommended irrespective of previous zoster infection
[a]40 μg/mL (Recombivax HB®) administered on a three-dose schedule at 0, 1 and 6 months or two doses of 20 μg/mL (Engerix-B®) administered simultaneously on a four-dose schedule at 0, 1, 2 and 6 months

**Table 18.1** (continued)

[b]Substitute first dose of Tdap for Td booster, then boost with Td every 10 years; give primary vaccination if it is not received and no evidence of previous infection.
[c]HPV2: bivalent human papillomavirus vaccine, HPV4: quadrivalent human papillomavirus vaccine
[d]Two doses recommended for adults who are students in postsecondary educational institutions, work in a health-care facility or plan to travel internationally
[e]Meningococcal conjugate vaccine quadrivalent (MCV4) preferred in patients aged ≤55 years, meningococcal polysaccharide vaccine (MPSV4) preferred in patients aged ≥56 years. Administer in a two-dose schedule at either 0 and 6–12 months (Havrix) or 0 and 6–18 months (Vaqta)

46 % in dialysis and pre-dialysis CKD patients, respectively. Targeted interventions at educating health-care staff coupled with regular monitoring and review have been shown to improve vaccination rates.

## Conclusion

Infections are common cause of morbidity and mortality in CKD patients. Increasing patient age, presence of multiple comorbidities, the underlying immunosuppressive uraemic milieu and the use of dialysis catheters contribute to the infection risk, complicate clinical presentation and make management complex. Prevention of infections requires institution and implementation of appropriate guidelines including vaccination (Boxes 18.4 and 18.5). Tuberculosis is an important infection in certain geographic areas and requires high degree of clinical suspicion for timely diagnosis.

**Box 18.4. What the Guidelines Say You Should Do?**

1. All general principles of infection control and management apply in CKD population.
2. Always consider drug dose modifications and try to prevent drug-induced nephrotoxicity in patients with CKD.
3. Trimethoprim-sulphamethoxazole is the drug of choice for acute, uncomplicated, lower UTI in patients with CKD stage 3a.
4. Ciprofloxacin or extended spectrum penicillin like pivmecillinam is the drug of choice for acute, uncomplicated, lower UTI in patients with CKD stage 3b to 5.
5. *Tuberculosis in CKD*
   (a) Tuberculin skin testing may be negative in CKD patients despite infection.
   (b) Patients with active tuberculosis should receive standard chemotherapeutic agents for standard duration with drug dose modifications for level of eGFR.
6. *HIV in CKD*
   (a) All patients with HIVAN should be given antiretroviral therapy irrespective of their eGFR.
   (b) Calcium channel blockers are contraindicated in patients using protease inhibitors.
   (c) Annual screening for renal involvement by urine protein and eGFR estimation is recommended. However, this frequency should be increased to biannually in patients who take drugs like tenofovir and indinavir.
   (d) Drug dose modification and interactions should be considered before prescribing drugs in CKD patients with HIV infection.
7. *Vaccination in CKD*
   (a) Consider individual's immune status and specific vaccine recommendations before using live vaccines in CKD patients.
   (b) All CKD patients should be vaccinated against hepatitis B virus, pneumococcus and influenza virus at diagnosis.
   (c) Revaccinate annually against influenza virus and every 5 years against pneumococcus.
   (d) Monitor anti-HB titres annually and revaccinate with booster dose if titres are below <10 IU/L.

**Box 18.5. Relevant Guidelines**

1. *KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease*

   Chapter 4: Other complications of CKD: CVD, medication dosage, patient safety, infections, hospitalizations, and caveats for investigating complications of CKD. Kidney Int Suppl. 2013;3(1):91–111. http://www.nature.com/kisup/journal/v3/n1/full/kisup201267a.html
2. *Scottish Intercollegiate Guidelines Network*

   Management of suspected bacterial urinary tract infection in adults. Scottish Intercollegiate Guideline Network Guideline No.88 July 2012 (http://www.sign.ac.uk/pdf/sign88.pdf).
3. *Advisory Committee on Immunization Practices (ACIP) Guideline*

   Advisory Committee on Immunization Practices (ACIP) recommended immunization schedules for persons aged 0 through 18 years and adults aged 19 years and olde--nited States, 2013. MMWR. 2013;62(Suppl 1):1. (http://www.cdc.gov/mmwr/pdf/other/su6201.pdf)
4. *Infectious Diseases Society of America Guideline*

   Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, Rodriguez RA, et al. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2005;40(11):1559–85. (http://cid.oxfordjournals.org/content/40/11/1559.long)
5. *British Thoracic Society Guideline*

   Milburn H, Ashman N, Davies P, Doffman S, Drobniewski F, Khoo S, et al. Guidelines for the prevention and management of Mycobacterium tuberculosis infection and disease in adult patients with chronic kidney disease. Thorax. 2010;65(6):557–70. (http://thorax.bmj.com/content/65/6/559.long)

**Before You Finish: Practice Pearls for the Clinician**

- Despite decrease in the rate of access-related and blood-borne infections, the overall rate of infections in dialysis patients remains high.
- Improving native arteriovenous fistula utilisation, reducing catheter use, timely vaccination and implementation of infection control guidelines are important for preventing access-related infections.
- CKD patients need to be vaccinated against hepatitis B virus, pneumococcus and influenza as early as possible.
- Vaccination response may be suboptimal and needs monitoring in subjects with CKD.
- Management considerations include measures to prevent acute kidney injury and drug toxicity.
- Tuberculosis is important in certain geographic areas and requires high degree of clinical suspicion for timely diagnosis.

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