

*Editorial Review*

## Vaccination and chronic kidney disease

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**Keywords:** chronic kidney disease; vaccination

### Introduction

Infectious diseases are the second most common cause of death in end-stage renal disease (ESRD) patients [1]. Patients with chronic kidney disease (CKD) are immunocompromised and haemodialysis (HD) patients are at high risk for several infections, due to exposure to blood products [2]. CKD patients present impaired cell-mediated and humoral immunity, reducing activities of the immune system cells (B-cell, T-cell, monocytes, macrophages, . . .) leading to a lower seroconversion rate, a lower peak of antibody titers and a quicker decline of antibody levels in these patients as compared with healthy subjects [2]. Usual schedules of vaccination may thus be ineffective. The aim of this paper is to review the studies on the use of vaccines in ESRD patients, in order to determine whether dosage adjustment is necessary in these patients.

### *Hepatitis B virus (HBV) vaccination*

Hepatitis B is one of the most serious infectious diseases in the world. It is estimated that 200–500 million of people are infected. The virus can be transmitted by blood, other corporal fluids, vertically or horizontally among high-risk groups including CKD patients. These patients are exposed to blood products, internally contaminated dialysis equipment and cross-contamination from environmental surfaces [2]. The use of HBV vaccine and preventive measures have helped reduce the annual incidence of HBV infection in patients on dialysis, from 3% to 0.05% between 1976 and 1997 in the USA [3]. It is thus important and useful to vaccinate these patients. The usual vaccination schedule in healthy adults ranged from 10 to 20 µg per dose in a three- or four-shot schedule (0, 1, 2, 12 or 0, 1, 6 months).

The effectiveness of HBV vaccination was found to be lower in ESRD patients than in subjects without CKD [2]. Those patients commonly presented lower seroconversion

rates, lower peak antibody titers and a rapid decline of antibody levels [4]. Furthermore, some ‘negative factors’ affected seroconversion rates among these patients (age, gender, obesity, nutritional status and smoking) [5]. In order to improve the response to the vaccine, various methods were tested.

Many studies (Table 1) have tested the effectiveness of higher doses of vaccine with 40 µg in a four-shot schedule. Seroconversion rates were found in 60–90.5% of ESRD patients [5–9].

All of these studies tried to improve the immune response by vaccinating with higher doses than the standard 10–20 µg. One study compared 40 µg versus 20 µg in 121 patients with moderate renal insufficiency (at Months 0, 1, 6 in a three-shot schedule). Seroconversion rate was superior in patients with a high dose of 40 µg than in patients with a standard dose of 20 µg. However, this was not statistically significant for the three- or four-shot vaccination schedule. The authors recommended the use of three doses of 20 µg in patients with renal impairment. A fourth dose could be administered in patients who failed to respond [10].

Another study compared intradermal (ID) and intramuscular (IM) vaccination in ESRD patients. The ID group of patients received 5 µg of vaccine on a bimonthly schedule, while the IM group of patients were administered 40 µg on a four-dose vaccination schedule. Most patients reached a high seroconversion rate, 97.6% for the ID group and 90.5% for the IM group. The authors recommended using 5 µg every 2 weeks up to a peak antibody titer > 1000 IU/l or for a total duration of administration of 18 months [8].

Another suggestion was to use standard 20 µg doses repeatedly. One study tried to raise the protective rate among ESRD patients by using 20 µg every month until they reached 100 UI/l of antibody titers, or up to 10 doses. After 5 months, seroconversion rate reached 42%; after 12 months it was 70% [11].

Early vaccination of patients before they start dialysis has been used in order to improve the response rate. One of the largest studies performed on this topic included 61 RI patients. The authors concluded that patients not yet on dialysis had a better immune response to HBV vaccine than dialysis patients [12].

These studies suffer from relative disparities. Some authors reported that certain factors could influence the antibody levels, considered as being protective. Elderly ESRD

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**Table 1.** Studies on hepatitis B vaccination and ESRD patients

Authors	Patients	Dose, vaccine, mode	Vaccination schedule (months)	Results seroconversion rate <sup>a</sup>
Kara <i>et al.</i> [5]	15 HD	40 µg, Engerix B <sup>®</sup> or HB Vax IIB, IM	0, 1, 2, 6	12 (80%)
Liu <i>et al.</i> [6]	47 HD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 2, 6	37 (78.7%)
	22 PD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 2, 6	17 (77.3%)
Bel'eed <i>et al.</i> [7]	136 HD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 2, 3	90 (66%)
	55 PD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 2, 3	36 (66%)
	19 CKD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 2, 3	13 (68%)
Charest <i>et al.</i> [8]	41 HD	5 µg, recombinant HB vaccine, ID	Every 2 weeks	40 (97.6%)
	42 HD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 2, 6	38 (90.5%)
DaRoza <i>et al.</i> [9]	165 CKD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 6	136 (82%)
McNulty <i>et al.</i> [10]	51 CKD	20 µg, Engerix-B <sup>®</sup> , IM	0, 1, 6	29 (57%)
	55 CKD	40 µg, Engerix-B <sup>®</sup> , IM	0, 1, 6	37 (67%)
Jadoul <i>et al.</i> [11]	23 HD	20 µg, Engerix-B <sup>®</sup> , IM	Every month	16 (70%) after 12 months
Tong <i>et al.</i> [17]	82	20 µg, Engerix B <sup>®</sup> , IM	0, 1, 2, 6	84%
	83	20 µg, Fendrix <sup>®</sup> , IM	0, 1, 2, 6	91%

HD: haemodialysis patients, PD: peritoneal dialysis patients, CKD: chronic kidney disease patients, IM: intramuscular vaccination, ID: intradermal vaccination.

<sup>a</sup>Antibody level >10 UI/l.

patients seemed to have a lower rate of seroconversion than younger patients [10,11,13]. Unexpectedly, there was no apparent correlation between the seroconversion rate and severity of RI in one study that included patients with mild to moderate CKD [10]. However, another study found an association (not statistically significant) between the glomerular filtration rate (GFR) and the seroconversion rate in patients with severe renal impairment (GFR < 30 ml/min) [9]. These different results may be due to diverse inclusion criteria. Indeed, DaRoza's [9] patients had worse renal dysfunction than in the other study. [10].

HBV vaccination is a critical issue in ESRD patients because they are a high-risk group for developing infection. Thus, patients with CKD must be immunized as soon as possible and before starting dialysis, where possible. The trends in all studies are characterized by a huge disparity; this may be due to certain factors influencing the immunogenic response of patients to the vaccine. Advanced age, male gender, previous blood transfusions are associated with poor seroconversion rates [2]. Several ways of improving seroconversion have been tested with various results. The recommended vaccination schedule is four doses of 40 µg of Engerix B<sup>®</sup> (GlaxoSmithKline) vaccine at 0, 1, 2 and 6 months or three doses 20 µg of Recombivax HB<sup>®</sup> (Merck) vaccine at 0, 1 and 6 months [14–16]. Booster doses can be given to patients whose antibody titers fall under 10 UI/l [4]. However, ID administration of HBV vaccine may also represent an alternative and cost-effective method [8]. Nevertheless, Tong's study [17] tested Fendrix<sup>®</sup> (GlaxoSmithKline), a new hepatitis B vaccine containing HBsAg adjuvanted with 3-*O*-desacyl-4'-monophosphoryl lipid A (MPL) and aluminium phosphate in predialysis and dialysis patients. This study showed an increased geometric mean titer of HBs antibody, but not an increased number of patients with seroconversion with single 20 µg doses of Fendrix<sup>®</sup> administered at 0, 1, 2 and 6 months compared to Engerix<sup>®</sup> (40 µg with the same vaccine schedule). Furthermore, Fendrix<sup>®</sup> is recommended for pre-haemodialysis and haemodialysis patients in its SmPC.

In conclusion, HBV vaccination in patients with kidney disease remains highly recommendable. The sooner they

are vaccinated, the better the response. Dose recommendation is four 40 µg doses of Engerix B<sup>®</sup>, three doses of Recombivax HB<sup>®</sup> or four 20 µg doses of Fendrix<sup>®</sup> (see Table 1).

#### *Hepatitis A virus (HAV) vaccination*

HAV vaccination among the general population has been used for decades. It is a safe and effective vaccine. However, data in ESRD patients are limited. The recommended vaccination schedule in healthy adult subjects is one dose of 1440 ELU at 0 and between 6 and 12 months.

One study tested HAV vaccination with Havrix<sup>®</sup> (GlaxoSmithKline, 720 ELU at 0, 1 and 6 months) in ESRD patients. The 1440 ELU Havrix<sup>®</sup> was not available at the time of the study. The authors concluded that the vaccine was safe and effective, in accordance with the safety and efficiency profiles reported in healthy subjects [18].

In conclusion, HAV vaccination in ESRD patients is well tolerated and immunogenic [18,19]. The Advisory Committee on Immunisation Practices (ACIP) recommends using the standard dose and schedule in adult ESRD patients (1440 ELU, 1 ml) of Havrix<sup>®</sup> at 0 and between 6 and 12 months [15].

#### *Varicella vaccination*

Varicella is a common benign infectious disease in the paediatric population. However, it may be severe and even fatal in immunocompromised ESRD children. Furthermore, zoster disease, the reactivation form of varicella usually seen in the adult and elderly population, can occur. Again, effective vaccination is a critical issue for these patients. The usual vaccine schedule for healthy subjects older than 13 years is two doses of 1350 plaque-forming units (PFU) with an interval of 4 to 8 weeks or two doses of 10<sup>3.7</sup> PFU with an interval of 6 to 8 weeks.

Response to varicella vaccination was tested in children with CKD and dialysis patients waiting for kidney transplantation. It was generally well-tolerated and protective

**Table 2.** Studies on *influenza* vaccination and ESRD patients

Authors	Patients	Vaccine/dose	Results of the protection rates for the 3 vaccine virus antigen		
			H3N2	H1N1	B
Antonen <i>et al.</i> [25]	42 HD	Vaxigrip®/15 µg	36%	60%	78%
	15 PD		67%	79%	79%
	20 CKD		35%	70%	90%
Antonen <i>et al.</i> [26]	23 HD	Vaxigrip®/15 µg	78%	Not studied	Not studied
Vogtländer <i>et al.</i> [27]	44 HD	Influvac®/15 µg (0, 8 weeks)	77%	46%	87%

HD: haemodialysis patients, PD: peritoneal dialysis patients, CKD: chronic kidney disease patients.

antibody titers were obtained for almost all children. However, a second and a third booster dose (1350 to 2000 PFU for each dose [20,21]) were necessary, in order to obtain a high rate of seroconversion and a persistence of protective antibody titers. Some of these children underwent renal transplantation thereafter; zoster or varicella infections were minimal [20–22]. Furthermore, varicella infection was more frequent and more serious among non-immunized post-transplant patients than vaccinated post-transplant patients [22].

In conclusion, varicella vaccination is safe and effective in ESRD patients and is thus recommended in these patients. However, sometimes an additional booster dose of vaccine may be necessary, to reach appropriate antibody levels in children with ESRD. Webb *et al.* thus recommended using a  $2 \times 2000$  PFU-dose regimen and monitoring anti-VZV IgG titers in order to decide when to administer a third dose [20]. However, for ESRD patients older than 12 years, available guidelines recommend two doses of 0.5 ml with no booster doses [15,16].

### *Influenza vaccination*

*Influenza* is a common infection that is responsible for many deaths. From 1972 through 1992, *influenza* epidemics accounted for a total of 426 000 deaths in the United States [23]. Because of the virulence and the pathogenic power of this virus, *influenza* vaccination of the general population is very common, with a relative efficacy of a single dose injection of 15 µg. In the CKD population, the use of this vaccine is recommended. Indeed, the risk of hospitalization or death was decreased in vaccinated HD patients compared with non-vaccinated HD patients. Among patients on continuous ambulatory peritoneal dialysis (CAPD), those who were not vaccinated had a greater risk of hospitalization than immunized patients [24]. The usual dose for healthy adult subject is a single shot of 15 µg.

Several studies showed comparable response rates between CKD patients and healthy subjects. These studies demonstrated that *influenza* vaccination was safe and effective in patients with CKD despite an impaired antibody response [25–28] (Table 2). Some differences were observed according to the method of dialysis (peritoneal dialysis or haemodialysis), or the type of the viral antigen. Furthermore, correction of vitamin D deficiency among HD patients may improve immune response [25]. In order to obtain higher levels of antibodies, a booster immunization with a supplemental dose was tested, but with no success [27].

Because of the virulence and risks associated with *influenza* virus infection, vaccination is a universal health issue and is recommended all over the world. Injection of a single dose of 15 µg shows good efficacy in the CKD population. Vaccination against *influenza* decreases mortality and results in decreased hospitalization.

In conclusion, *influenza* vaccination is highly recommended among ESRD patients. Antibody titers can be lower than those in healthy subjects. However, satisfactory protective rates can be reached by annual vaccination. It is thus recommended to vaccinate adult ESRD patients against *influenza* each year, using a standard dose (15 µg annually) [15,16].

### *Haemophilus influenzae type B conjugate vaccine*

Data on the use of *Haemophilus influenzae* type B vaccine among ESRD patients are limited. In a multicentre study, the safety and efficacy of the vaccine were determined in 10 CAPD children, where 90% of the patients reached a protective rate of antibodies [29]. ESRD patients should thus receive the same doses as for healthy subjects [15].

### *Measles, mumps and rubella vaccine*

All children should be treated with measles, mumps and rubella vaccines (MMR), including dialysis patients. Seroconversion rates among this population were evaluated in 10 dialysis patients, 8 responded to measles vaccine, 5 to mumps vaccine and 8 to rubella vaccine alone. However, only three children responded to all three vaccines [30]. It is thus recommended to assess the seroconversion after vaccination (standard doses) among these patients [15]. The usual vaccination schedule begins with one shot at 1 year old and another between 3 and 6 years old. For adult patients, one single dose should be used [15].

### *Poliovirus vaccine*

Inactivated poliovirus vaccine is not very common because it is only recommended for specific groups of persons, and because the general population is not extensively exposed to the virus. However, for these specific exposed groups vaccination is recommended, including ESRD patients with inactivated poliovirus vaccine. The efficiency and safety of inactivated poliovirus vaccine was assessed in 49 chronic dialysis patients, resulting in 86% of patients having sufficient antibody levels [31]. It is thus recommended to

vaccinate ESRD patients with a primary series of standard dose schedule (three doses with an interval of 1–2 months). [15].

#### *Staphylococcus aureus vaccination*

*Staphylococcus aureus* is a major cause of nosocomial and community-acquired infections. Patients undergoing dialysis represent a high-risk group of developing infection to *S. aureus* due to the violation of the skin barrier. It is an important cause of complications and death in patients on chronic HD [32]; however, there is no vaccine currently available for clinical use.

Some studies have demonstrated that ESRD patients present an impaired immunological response, in comparison with healthy subjects, with a 50% reduction of IgG levels 6 months after a 25- $\mu$ g vaccination with a monovalent conjugated *S. aureus* type 5 capsular polysaccharide [33]. However, ESRD patients reached protective antibody levels (80  $\mu$ g/ml) only for  $\sim$ 6 months. In another study, the effectiveness and the good tolerance of a single injection of a bivalent conjugate vaccine containing *S. aureus* type 5 and 8 capsular polysaccharide (StaphVax<sup>®</sup>, Nabi, 25  $\mu$ g of each capsular polysaccharide) have been demonstrated. As previously shown, it only provided a partial and time-limited protection in ESRD patients. The decrease in vaccine efficacy occurred after  $\sim$ 40 weeks, and the authors considered the study to be a failure because of those results [34].

In order to prolong the efficacy of the vaccine, a higher dose of the same vaccine (StaphVax<sup>®</sup>, Nabi, 100  $\mu$ g of each capsular polysaccharide) was tested in ESRD patients. The vaccine was efficient in these patients in comparison with patients receiving placebo during 40 weeks, and it was well tolerated during the study period. However, after 50 weeks, the reduction of *S. aureus* bacteremias (26%) in the group that received the vaccine as compared to the placebo group was not statistically significant [35].

Data are thus limited, and there is no current recommendation for the use of *S. aureus* vaccine in CKD patients. However, according to existing studies, the response is partial and the protection levels of antibodies decrease after several months.

#### *Diphtheria and tetanus vaccination (tetanus and diphtheria toxoids)*

Seroconversion rate has been shown to be lower in dialysis patients than in healthy subjects after *diphtheria* and *tetanus* vaccination [36]. A short-term study showed that *tetanus* vaccination (with booster injection) in HD patients led to 96.5% of seroconversion rate ( $> 0.06$  HU/ml), but rapidly declined after 6 months [37]. In one study, the immunological status after *tetanus* (40 UI) and *diphtheria* (4 UI) toxoids vaccination was tested among 21 HD patients without protection before vaccination. Five years after the vaccination, 15 patients (71%) had a protective antibody level for *tetanus* and 7 (33%) for *diphtheria*. The authors thus recommended monitoring antibody levels and sufficient booster doses of *diphtheria* vaccine [38].

In conclusion, *diphtheria* and *tetanus* infections can be prevented by using vaccines in ESRD patients. However,

because of impaired seroconversion rates, monitoring of antibody levels is recommended and a booster may be used in non-responding patients.

#### *Pneumococcal vaccination*

Pneumococcal vaccination is commonly used with success in healthy subjects and an appropriate level of antibodies may remain for several years. It is also well tolerated. However, the immune response in patients with CKD decreases with time. More than 75% of dialysis patients have an adequate response to the vaccine, but their antibody levels are considerably lower than those of healthy vaccinated adults and they decline rapidly (within 6 months to 5 years), while they remain sufficient in healthy subjects after 5 years [39–41]. Vaccination is thus recommended in these patients with standard doses of 23-valent pneumococcal polysaccharide vaccine, but revaccination should be performed within 3–5 years [15].

#### *Vaccination in ESRD patients infected with HIV*

Immunological response to most vaccines in ESRD patients is impaired. Consequently, higher dosages of vaccine or supplemental shots are needed for these patients compared with patients with normal renal function. The impact of HIV infection on the efficacy and safety of vaccination in CKD patients remains unclear.

Only HBV vaccine has been studied in ESRD HIV-infected patients. Theoretically, the immunological response is likely to be more altered in those patients than in non-HIV CKD patients or in HIV patients with normal renal function. In fact, some studies conducted on normal renal function patients showed that antibody titers are reduced and protective antibody titers decline rapidly after vaccination against HBV (20  $\mu$ g of GenHevac<sup>®</sup>, Pasteur Vaccin) in HIV patients compared to non-HIV patients [42,43]. A low response to *tetanus* and pneumococcal vaccination in HIV-infected patients was also reported in patients without renal impairment [44]. Finally, one study evaluated the development of protective antibodies to HBV vaccine in HIV-infected patients on HD [45]. Of these, 53.4% patients developed protective antibodies after using the same doses and schedule as non-HIV ESRD patients. The authors conclude that HBV vaccination should be offered to all HIV ESRD patients.

Consequently, vaccination should be performed at the earliest stage of HIV-infection in the ESRD population with the adapted treatment (40  $\mu$ g in a three- to four-shot schedule) and to use booster doses if the antibody (anti-HBs) titers fall under 10 UI/l [46]. Recommendation for others vaccines are available in the literature [46,47]; however, clinical experience on this topic is limited and the use of vaccines in ESRD HIV-infected patients is likely to be inadequate or transient at the standard doses and schedule.

#### *Vaccination of asplenic ESRD patients*

Asplenic patients are more likely to develop overwhelming sepsis with certain organisms than are healthy subjects. In addition, their responses to vaccination are impaired. Thus,

although these patients should be vaccinated against some pathogenic agents [48], there is no available recommendation on the use of vaccine in asplenic ESRD patients.

*In conclusion, it is impossible to make specific recommendation for asplenic ESRD patients. These patients should therefore be vaccinated as soon as possible prior to the splenectomy. Adjuvant therapy to vaccination*

Another way to improve the immunological response of vaccines in ESRD patients is to use an adjuvant therapy to vaccination, in order to stimulate the immune system of these patients. Several compounds have been tested, thymopentin, levamisole, zinc, interleukin, interferon, erythropoietin, immunomodulator. One of the most studied adjuvant drugs was GM-CSF (granulocyte macrophage colony-stimulating factor).

GM-CSF can promote the proliferation and maturation of precursor cells into granulocytes and macrophage colonies. Many studies have tested the association of GM-CSF with HBV vaccination in order to enhance the immunological response to vaccination. Two meta-analyses regrouping 17 studies on this topic concluded that the use of GM-CSF was efficient and safe in ESRD patients (~180 patients included) [49,50]. However, there was a large heterogeneity in drug and vaccine dosages (from 50 µg to 300 µg and from 20 µg × 1 to 40 µg × 4, respectively). More studies are needed to determine the adequate doses of GM-CSF and HBV vaccine in ESRD patients.

Other compounds have been tested, to evaluate their influence on HBV vaccination. Some drugs show promising results, such as levamisole, as they enhance protective antibody response to hepatitis B vaccination in HD patients [51–53]. However, no study was able to demonstrate the benefit of other drugs, like thymopentin, as an adjuvant therapy for HBV vaccination in ESRD patients [54,55].

Several compounds have succeeded in demonstrating their efficiency in enhancing immune response to vaccines, like GM-CSF and levamisole. Consequently, until more precise information is available, vaccination against HBV should be performed alone according to the available recommendations. No data are available on the effects of adjuvant therapy on other vaccines, and further investigations are needed to assess the efficacy of such drugs in other vaccines.

#### *Vaccination and dialysis technique*

Most studies on the impaired efficacy of vaccines in ESRD patients were performed in HD patients and only a few included PD patients. However, some studies investigated the possible association between dialysis technique and the serological response to HBV or *influenza* vaccines.

PD patients presented a response rate similar to HD patients (66–77.3% versus 66–78.7% in PD and HD patients, respectively) in two studies described earlier in this review [6,7]. Furthermore, Fabrizi *et al.* [56] analysed the differences in immunological response to HBV vaccine between HD and PD patients after 5 to 40 µg of various HBV vaccines on 3 to 5 dose vaccination schedules. They concluded that dialysis technique does not have an impact on the

seroconversion rate after HBV vaccine in ESRD patients. In other studies, where the impact of *influenza* vaccine was assessed in PD and HD patients, the authors reported some small differences between the two groups of patients. When using the standard dose and schedule of vaccine, PD patients reached better protective antibody titers than those of HD patients, but lower than those of patients without renal impairment [25,28]. Because it is recommended to vaccinate HD patients with the standard dose of *influenza* vaccine each year [15] and because PD patients seem to have a better immunological response than HD patients, PD patients should receive the same dose regimen as HD patients.

Consequently, patients on peritoneal dialysis should be vaccinated with the same dose and schedule as patients on HD. This recommendation is only valid for HBV vaccine. However, it seems theoretically possible to extend this recommendation to other vaccines and especially for those that do not need dosage adjustment in ESRD patients, such as *influenza* vaccine.

#### *Non-dialysis patients*

Very few data are available on the use of vaccines in non-dialysis (ND) patients; most of these studies included ESRD patients not yet on dialysis. Two studies assessed the possible relationship between GFR and seroconversion rates in ND patients after HBV vaccine [9,10]. However from the results it was not possible to reach a conclusion as to the link (or absence of link) between these two parameters, because the data were not consistent. Since no clear data are available on the vaccination of non-terminal ND patients according to the level of renal function, it is difficult to make specific recommendations.

#### *Renal transplant patients*

The situation with renal transplant (RT) is not as encouraging as that of pretransplantation [28]. Several studies have assessed the efficacy and safety of HBV and *influenza* vaccines in RT patients in comparison to healthy subjects and ESRD patients.

RT patients had lower antibody response to vaccines (HBV and *influenza*) than healthy patients [7,28,57,58]. Only one study found a statistically significant antibody response to all the three strains (B, H1N1 and H3N2 types) of *influenza* virus after annual vaccination in renal transplant patients [57]. Furthermore, *influenza* vaccine was well tolerated and no acute allograft rejection occurred in any RT patients [28]. These findings are the same for HBV vaccination in RT patients. These patients had lower seroconversion rates than healthy subjects [58], even with a high dose of vaccine [7]. Although there are no clear recommendations on the vaccination on RT patients, available data suggest that HBV and *influenza* vaccination can be performed in these patients.

In conclusion, for *influenza* vaccine, annual vaccination with the standard dose should be performed in RT patients [16]. For HBV vaccine, the preferred approach should be to vaccinate early before dialysis and to reach a protective antibody level in all patients before transplantation [16,58].

**Table 3.** Summary of recommendations for all vaccines in chronic dialysis patients

Vaccine	Age	Dose	Vaccination schedule/route of administration	Booster doses
Hepatitis B, Engerix B <sup>®</sup>	≥20 years	40 µg	0, 1, 2, 6 months/IM	Yes, when antiHBs <10 UI/l
	<20 years	10 µg	0, 1, 6 months/IM	Yes, when antiHBs <10 UI/l
Hepatitis B, HBVAXpro <sup>®</sup>	≥20 years	40 µg	0, 1, 6 months/IM	Yes, when antiHBs <10 UI/l
Hepatitis B, GenHevac B <sup>®</sup>	NA	20 µg	0, 1, 2, 4, 12 months/IM	Yes, when antiHBs <10 UI/l
Hepatitis B, Recombivax <sup>®</sup>	≥20 years	40 µg	0, 1, 6 months/IM	Yes, when antiHBs <10 UI/l
	<20 years	5 µg	0, 1, 6 months/IM	Yes, when antiHBs <10 UI/l
Hepatitis B, Fendrix <sup>®</sup>	≥15 years	20 µg	0, 1, 2, 6 months/IM	Yes
Hepatitis A, Havrix <sup>®</sup>	>17 years	1440 U	0, 6–12 months/IM	No
23 valent pneumococcal polysaccharide vaccine	>2 years	0.5 ml (25µg)	One single dose/IM or SC	No (revaccination in 3–5 years)
<i>Influenza</i>	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
Measles, mumps, 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 to 2 months	No (revaccination 1 year after the third dose)
<i>Diphtheria and tetanus toxoids</i>	7 years	0.5 ml	Three doses/IM	No
Varicella	1–12 years	0.5 mf	One single dose/SC	No
	>12 years	0.5 ml (minimum 1350 PFU)	0, 4–8 weeks/SC	No

NA: not available.

Furthermore, live vaccines should not be given to transplant patients, including MMR, varicella and oral poliovirus vaccines [59].

#### Contraindicated vaccines

Many vaccines have been used for years in ESRD populations. However, some vaccines are still contraindicated in these patients.

Live vaccines (yellow fever, polio, varicella and MMR vaccines) are generally avoided because they present a theoretical risk of vaccine-induced infection [15]. However, several studies investigated the efficacy and safety profiles for some of these vaccines (varicella and MMR vaccines) in ESRD patients, with success (only varicella and MMR vaccines). In contrast, oral poliovirus should not be used in ESRD and RT patients [15]. ESRD patients who need polio vaccination should receive the inactivated poliovirus vaccine.

#### Conclusion

Vaccination against the most common pathogenic agents is widely used among the healthy immuno-competent population. However it is less common in patients with renal disease because of the risk of side effects and doubts as to their efficacy in this population. These patients present impaired cell-mediated and humoral immunity and reduced activities of the immune system cells (B-cell, T-cell, monocytes, macrophages). In practice, this deficiency leads to lower seroconversion rates and a shorter protection period.

Because ESRD patients are immunocompromised, they represent a high-risk group for developing infectious diseases. Furthermore, HD patients are extensively exposed to pathogenic agents (exposure to blood products, internally

contaminated dialysis equipment and cross-contamination from environmental surfaces).

This review shows that vaccination of ESRD patients is, in general, well tolerated at standard doses or higher doses. Some vaccines may induce a high-enough seroconversion rate to confer protection against the disease (like *influenza*). However, other vaccines sometimes do not provide protection against the pathogenic agents (like HBV). In these cases, higher and/or supplemental booster doses are the more common solutions to reinforce immunity of the ESRD patients. Antibody levels must thus be monitored in order to assess the protective effects of the vaccines. Appropriate immunization of ESRD patients is essential and vaccination should not be avoided but adapted. Table 3 summarizes the recommendations for vaccinations in adult dialysis patients.

*Conflicts of interest statements.* None declared.

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*Received for publication: 26.7.06*

*Accepted in revised form: 6.11.07*