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Prophylactic vaccinations in chronic kidney disease: Current status

Alicja E Grzegorzewska*

Department of Nephrology, Transplantology, and Internal Diseases; Poznań University of Medical Sciences; Poznań, Poland

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Abbreviations: ACIP, the Advisory Committee on Immunization Practices; anti-HBs, antibodies to surface antigen of hepatitis B virus; BAFF, B-cell activating factor; CDC, Centers for Disease Control and Prevention; CKD, chronic kidney disease; ESRD, end-stage renal disease; GFR, glomerular filtration rate; HBsAg, surface antigen of hepatitis B virus; HBV, hepatitis B virus; HD, hemodialysis; IL, interleukin; IFN, interferon; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine; PTH, parathyroid hormone; RRT, renal replacement therapy; Th, T helper; TLR, toll-like receptor; TNF-α, tumor necrosis factor α

In this review, recent data on results concerning prophylactic vaccinations against hepatitis B virus, influenza viruses, and pneumococci are presented. Effects of active immunization in chronic kidney disease depend on category of glomerular filtration rate (GFR). The lower GFR category the better results of response to vaccination. Abnormalities in toll-like receptors and down-regulation of B-cell activating factor receptor in transitional B cells were recently included into uremia-associated deficits in immunocompetence. Development of novel, more potent vaccines containing toll-like receptor agonists as adjuvants may help to achieve more effective immunization against hepatitis B virus in immunocompromised patients. Experimental studies announce further vaccine adjuvants. A vaccine against hepatitis C virus is not available yet, but promising results were already obtained in the experimental and preliminary clinical studies. Prophylactic vaccinations against influenza viruses and pneumococci become increasingly popular in dialysis facilities due to their proved benefits.

Introduction

Chronic kidney disease (CKD) patients are at increased risk of incidence and severity of infections because of their impaired immunocompetency and greater exposure to microbes due to frequent contacts with medical care facilities for CKD diagnosis or treatment, including repeated dialysis sessions. Infections are on the second place following cardiovascular diseases among causes of death in dialysis patients.[1,2] Successful renal transplantation does not solve the problem of infections due to the use of immunosuppressants.[3] Prophylaxis by vaccination is the best method to avoid acute and chronic consequences of infections. However, CKD patients show remarkable deterioration of immunologic functions, what decreases development of protective antibodies in response to vaccination compared to healthy subjects.[4] Novel vaccine adjuvants may help to achieve better results of vaccinations.[5] Moreover, development of targeted nanodelivery systems carrying vaccine components (antigens and adjuvants) to dendritic cells represents a promising strategy to increase vaccine response rates.[6] Effects of active immunizations of CKD patients attract attention of clinicians and pharmaceutical agencies, and are systematically summarized and evaluated.[7-9]

The objective of this review is to announce advances in recognition of immunocompromised state in CKD patients, novel issues concerning prophylactic vaccinations against hepatitis B virus, influenza, pneumococci and other microbes in this group as well as progress in development of hepatitis C vaccine which is crucial for patients with altered immunocompetence, especially those receiving maintenance extracorporeal dialysis therapy. In this review, I am focusing only on data published in the last 5 y.

*Correspondence to: Alicja E Grzegorzewska; Email: alicja_grzegorzewska@yahoo.com
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CKD as an Immunocompromised State

Immune abnormalities, accelerating with progression of renal disease visualized by deterioration of glomerular filtration rate (GFR) category (**Table 1**), are well-known feature of CKD.[10] Increasing serum levels of parathyroid hormone (PTH), being immunologic mediator, may contribute to altered host defenses.[11] Recently, a role of toll-like receptor (TLR) family in recognition of antigens and in facilitating antigen uptake by dendritic cells has been underlined.[12] TLRs belong to pattern recognition receptors. However, data concerning TLRs in dialysis patients are not consistent. In the study by Gollapudi et al., up-regulation of TLR2 and TLR4 (but not TLR7 or TLR 9) expressions on monocytes and TLR4 on polymorphonuclear leukocytes of hemodialysis (HD) patients was demonstrated.[13] In the other study on uremic patients, TLR4 expression in peripheral blood

Table 1. Glomerular filtration categories in accordance with "Kidney Disease: Improving Global Outcomes (KDIGO) Chronic Kidney Disease (CKD)" Work Group[34]

GFR category	Estimated GFR (ml/min/1.73 m^2 body surface area)
G1	≥90
G2	60–89
G3a	45–59
G3b	30–44
G4	15–29
G5	<15

GFR – glomerular filtration rate

mononuclear cells was shown to be down-regulated, especially in individuals using conventional instead of ultrapure dialysate.[14] In uremic patients due to diabetic nephropathy, pro-inflammatory CD14(+)CD16(+) monocytes and TLR4 expression were significantly up-regulated concomitantly with increased serum levels of inflammatory markers – interleukin (IL) −6 and C-reactive protein.[15] Immunological dysfunction in this group of patients was attributed to the activation of TLR4/NF-κB and STAT5 signaling pathways.[15] Lipopolysaccharide stimulation of TLR4 on neutrophils activates signal transduction pathway leading to pro-inflammatory cytokine secretion, like tumor necrosis factor α (TNF-α), IL-6 or IL-8, whereas anti-inflammatory IL-10 is decreased.[13,16] In dialysis patients, this production was heightened, while the response to TLR2 stimulation with peptidoglycan was unchanged in these subjects.[13] TLR9 is a key participating molecule in innate and mucosal immunity. TLR9 is expressed mainly by B cells and dendritic cells. It is involved in T helper (Th) 1-type immune response and decreases in the pro-inflammatory response. TLR9-mediated immune response may be activated by synthetic oligodeoxynucleotides containing unmethylated CpG motifs.[17] TLR agonists were already used as vaccine adjuvants and are being tried in elaboration of novel vaccines.[18]

Significantly altered B cell-associated immunity is a well-known phenomenon related to GFR category 5 (end-stage renal disease, ESRD).[19] Pahl et al. clearly showed that B-cell lymphopenia is associated with the downregulation of B-cell activating factor (BAFF) receptor in transitional B cells. This resulted in resistance to the biological actions of BAFF being a potent B-cell differentiation and survival factor.[20] Results of this study added new issues to uremia-associated impairment in immunocompetence. In experimental studies, BAFF was a target under conditions of abnormal B-cell activation and differentiation leading to generation of high titers of auto-antibodies.[21] However, agonists of BAFF receptors were not examined yet in vaccinology.

Vaccination Against Hepatitis B Virus

Effective hepatitis B vaccination not only confers protection against hepatitis B, but also predicts better survival of dialysis patients.[8] Infection-cause mortality was shown to be lower in responders than in non-responders to hepatitis B vaccination.[22]

Despite decreased immunocompetence, multiple other reasons of hepatitis B vaccination failure were recognized in CKD patients (older age at the primary vaccination, male gender, type of renal disease leading to ESRD, co-morbid diseases, malnutrition, especially low serum albumin level,[23] but also obesity). In last years, further factors have been indicated as having impact on effects of hepatitis B vaccination, like protein catabolic rate.[24] Since the beginning of the current century, genetic factors involved in synthesis, regulation or stability of Th1/Th2 cytokines are explored as possible factors contributing to non-response to hepatitis B vaccination. Results of these studies indicate that in renal replacement therapy (RRT) subjects, there is a relatively weak association between polymorphisms of genes encoding Th cell cytokines and development of antibodies to surface antigen of hepatitis B virus (anti-HBs) in response to hepatitis B vaccination or hepatitis B virus (HBV) infection.[25-30]

Active immunization against HBV may be less effective in ESRD patients due to vitamin D deficiency.[31] Vitamin D related genetic background may contribute to lower response to hepatitis B vaccination. The *VDR* rs1544410 AA genotype may play a negative role (but not as an independent factor) in determining response to hepatitis B vaccination in RRT patients.[32]

Dialysis quality improves over years. Currently used dialyzers may contribute higher response rates to hepatitis B vaccine.[33]

The lower GFR category the less pronounced CKD-related deterioration in immunocompetence and lower expression of acquired factors contributing to worse response to active immunization. That is the reason that HBV vaccination was formerly recommended at lower GFR categories.[7-9] However, "Kidney Disease: Improving Global Outcomes (KDIGO) CKD" Work Group recommends that all adults at high risk of progression of CKD (GFR categories G4-G5) should be immunized against hepatitis B, and the response confirmed by appropriate serological testing (grade 1B).[34] The recent recommendations of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) also indicate a need for advanced vaccination strategy for adults with GFR categories G4-G5.[35] A question arises whether it is not too late to start vaccination at GFR category G4. More recent studies confirmed occurrence of higher seroconversion rates in response to HBV vaccination in GFR category 3–4 patients than in those already on HD, although vaccine doses were lower in the former group.[36] On the other hand, GFR category 3–4 patients required higher doses of vaccine to show seroconversion rates comparable to those of healthy medical staff.[36] Vaccination efficacy may be increased in dialysis patients with further doses of HBV vaccine.[37] It would be interesting to know whether hepatitis B vaccination, introduced in many countries in the childhood vaccination schedules, will influence on the prevalence of non-responders among dialysis patients.

In 2011, the ACIP CDC recommended that hepatitis B vaccination should be administered to all previously unvaccinated adults aged 19 through 59 y with diabetes mellitus (type 1 and type 2) as soon as possible after a diagnosis of diabetes is made.[38] This recommendation is very important for nephrology

community, as diabetes is the most frequent cause of ESRD among incident and prevalent ESRD patients.[39]

Novel hepatitis B vaccines (HB-AS04, HB-AS02, HBsAg-1018) contain agonists of TLR4 and TLR9. TLR agonists directly activate immune system through stimulation of TLRs.

A novel vaccine (Fendrix®, GlaxoSmithKline Biologicals) was licensed in Europe in February 2005. It is also referred as HB-AS04, because contains 20 μg of recombinant HBV surface antigen (HBsAg) adjuvanted with AS04 [50 μg 3–0-desacyl-4'-monophosphoryl lipid A adsorbed on aluminum salt (500 μg Al 3+)]. AS04 acts as a TLR4 agonist and induces higher levels of memory B cells as compared to aluminum alone formulations.[40] This vaccine was already reported to be more efficient than standard recombinant vaccine (Engerix-B®) in pre-dialysis and HD patients. More recent studies confirmed its beneficial effect in HD subjects.[41] Revaccinating non-responders with 3 doses of Engerix-B® (renal function of this group was not mentioned) using either a single dose of HBVaxPro-40 or Fendrix elicited significantly better responses than those obtained using 3 additional Engerix-B doses. Diabetic patients or those using immunosuppressive medication were excluded from this study.[42]

HB-AS02 is an investigational hepatitis B vaccine which contains 20 μg recombinant HBsAg formulated with an oil-in-water emulsion-based adjuvant system AS02 containing monophosphoryl lipid (MPL), a detoxified derivative of the lipopolysaccharide molecule of the bacterial wall of *Salmonella minnesota*, and an immunostimulant named QS21 extracted from *Quillaja saponaria*, the Chilean soapbark tree (50 μg MPL + 50 μg QS21). In healthy adult volunteers, HBV-AS02 has been shown to elicit high level anti-HBs responses with relatively good tolerance.[43] This vaccine was also reactogenic in approximately 77% of CKD patients who failed to respond to prior vaccination with a conventional hepatitis B vaccine and provided higher anti-HBs concentrations following a booster dose than a conventional vaccine.[44] Three doses of HBV-AS02 vaccine (at 0, 1, and 6 months) have been shown to induce more rapid seroprotection (at 12 months, seroprotection rates of 94 and 79%, respectively) and higher anti-HBs concentrations in patients with renal insufficiency than 4 doses (at 0, 1, 2, and 6 months) of HBV-AS04.[45,46]

Close to full registration is the novel vaccine known as HBsAg-1018 (Heplisav, Dynavax Technologies, Düsseldorf, Germany) adjuvanted with TLR9 - CpG oligodeoxynucleotide.[47] In healthy subjects 18–55 y of age, 2-dose regimen of HBsAg-1018 at a 0–4 weeks induced a superior antibody response than a 3-dose regimen of a standard hepatitis B vaccine.[48] In another study, 2-dose regimen of HBsAg-1018 at 0–4 weeks elicited an antibody response in healthy young adults that was similar to a 0–8 weeks schedule.[49] HBsAg-1018 improved immunogenicity in non-responders to standard hepatitis B vaccination.[50] In healthy adults ≥ 40 y of age, 3-dose regimen of HBsAg-1018 given at 0, 1, and 6 months demonstrated superior seroprotection with 2–3 doses when compared to the conventional hepatitis B vaccination.[51,52] In CKD subjects 18–75 y of age, 3 doses of HBsAg-1018 induced significantly higher, earlier, and more durable seroprotection than 4 double doses of the conventional hepatitis B vaccine.[53] However, HBsAg-1018 was associated with significantly more injection-site tenderness than the conventional vaccine (63.2% – 81.8% vs. 15.4% – 18.8%).[54]

Novel hepatitis B vaccines may provide not only quicker, better and longer seroprotection against HBV, but also improve compliance and reduce costs due to the simplified vaccination schedules.[55] However, hepatitis B vaccines with novel adjuvants are still under investigation. When compared to standard vaccines, adjuvanted vaccines should not be considered as an one only group, due to their involvement in various immunological pathways, and therefore different mode of action.[56]

Experimental Adjuvants for Hepatitis B Vaccines

In experimental studies on mice and guinea pigs, a polysaccharide adjuvant derived from delta inulin (Advax™) was investigated. HBsAg with Advax™ enhanced both anti-HBs antibody titers, and anti-HBs CD4 and CD8 T-cells, with increases in Th1, Th2 and Th17 cytokine responses. Advax™ adjuvant similarly enhanced humoral and cellular immune responses in guinea pigs to a third generation preS-HBsAg vaccine.[57]

In female Balb/c mice, immunization with hepatitis B vaccine and nano-complex Hep-c increased the lymphocyte proliferation and specific IgM and IgG2a compared to the hepatitis B vaccine immunized group. Hep-c significantly increased the IFN-γ and IL-4 cytokine levels compared to the hepatitis B vaccine immunized group.[58]

In mice, cyclic diguanylate (c-di-GMP) was a more potent activator of both humoral and Th1-like immune responses comparing it with lipopolysaccharide, CpG oligonucleotides, and a conventional aluminum salt based adjuvant.[59]

Hemokinin-1 (HK-1) activates B cells for proliferation, survival, differentiation into plasma cells, and enhances humoral response toward increased antibody production. The HK-1 coding sequence was sub-cloned as single or triple copies in-frame downstream of S2 HBsAg in the proVAX/S2 construct. Compared to mice immunized with proVAX/S2 or proVAX/S2-HK-1, proVAX/S2–3HK-1 induced a higher level of IgG production.[60]

Immunostimulants for Better Response to Hepatitis B Vaccination

A recently meta-analysis of 5 studies that fulfilled the inclusion criteria showed that, for impaired immune response in HD patients, it might be reasonable to recommend the administration of levamisole, which increases the number of natural killer cells, enhances B lymphocyte function, stimulates depressed T-cell activity, stimulates antigen-presenting cells, and improves the chemotaxis of granulocytes.[61]

In subjects aged >40 years, 200 mg zinc sulfate orally daily for 30 d had no effect on level of immunity in response to hepatitis B vaccine.[62] Serum zinc level was not monitored in this study.

Selenium once a day orally in a dose of 200 μg was added at the beginning of accelerated (0–10–21 day) schedule of hepatitis

B vaccination and continued for 30 d in insulin-dependent diabetes mellitus patients. Subjects receiving selenium showed seroconversion to protective level of anti-HBs in 74.2% cases, what was significantly higher than in control patients (48.4%).[63]

Progress in Hepatitis C Virus Vaccines

In the absence of HCV vaccine, the prevalence of HCV infection among HD patients is several times greater than that of the general population.[64] However, there are already promising vaccine candidates in development. The newest research in this field was recently summarized in the review by Fauvelle et al.[65] In experimental, pre-clinical or preliminary clinical studies, the different technologies for vaccine production, novel immunogens or adjuvants were used in vaccine candidates: HCV core protein with adjuvant ISOMATRIX™, purified E1E2 glycoproteins (from HCV genotype 1a) adjuvanted with MF59C.1, adenoviral vectors, or virosome-formulated CD4 and CD8 synthetic peptides. However, the authors have underlined that HCV vaccine development, also very promising, needs further efforts and resources until an effective vaccine becomes available.[65]

Combined Vaccines Against Hepatotropic Viruses

In HD patients, combined hepatitis A and B vaccine improves the seroprotection against HBV compared with hepatitis B monovalent vaccine.[66]

Chimeric HBV-HCV envelope proteins were recently developed and such particles elicited a strong specific neutralizing antibody response against HCV and HBV envelope proteins in rabbits.[67] These data may be a chance for the development of a bivalent vaccine able to prevent infection from both HBV and HCV.

Vaccination Against Influenza

According to the KDIGO CKD Work Group recommendations (2012) all adults with CKD should be offered annual influenza vaccination, unless contraindicated (grade 1B).[34] Vaccination with trivalent inactivated influenza vaccine is recommended for patients with altered immunocompetence, whereas live attenuated influenza virus vaccine is usually contraindicated.[68]

Data collected from 1998 to 2009 in Taiwan have shown that influenza vaccination coverage increased in HD patients from 1.14% in 1998 to 38.0% in 2009.[69] United States Renal Data System files have indicated that over 115,000 adult HD patients was vaccinated each year from 1999 to 2005 against influenza. Vaccination coverage increased from 47% in 1999 to 60% in 2005.[70] In dialysis patients in a London district general hospital in years 2009–2010, uptake of influenza vaccination in both years was 50%, and 13% and 17% in years 2009 and 2010, respectively.[71]

In April 2009, a novel influenza A virus (H1N1) caused a pandemic. The World Health Organization strongly recommended a worldwide vaccination against influenza A(H1N1) pdm09 patients with ESRD and those who received renal graft.[72] In March 2011, AS03, an adjuvant system containing α-tocopherol and squalene in an oil-in-water (o/w) emulsion, was considered for the development of novel influenza vaccines. With this adjuvant, antibody response was higher than that obtained with aluminum hydroxide.[73] AS03 has been safely administered with the A(H1N1) pdm09 and the H5N1 strains to thousands of healthy adults.[74] The rate of seroconversion to AS03 adjuvanted A(H1N1) pdm09 vaccine was 57% – 64.2% in HD patients[75,76] and 35% – 44% in renal transplant patients[75,77], whereas it was 90% – 93.8% in a control population.[75,76] Vaccine dose was an independent factor for response to pandemic A(H1N1) vaccination in HD subjects.[78] Annual influenza vaccination is also recommended for HD or kidney transplanted adolescents or young adults.[79]

In the studies which were published after appearance of recommendations of KDIGO, higher response rates after a single dose of H1N1 influenza vaccine were shown in peritoneal dialysis than in HD subjects.[80] Quintana et al. have reported that the seroconversion rate at 42 d after 2 doses of A(H1N1) pdm09 vaccine was 80% in the HD group, 64.9% in the renal allograft recipients group with good allograft function, 100% in the advanced CKD group, and 71.4% in the peritoneal dialysis group. In pre-dialysis, HD and peritoneal dialysis patients, a response to vaccination was similar to that in the general population vaccinated with one dose, but it was weaker in graft recipients on triple immunosuppressive therapy including calcineurin inhibitors, mycophenolate and steroids.[81]

In HD patients, negative predictors of response to influenza A (H1N1) pdm09 vaccination included age $\geq$ 65 y and hemoglobin level $<$ 10 g/dL.[82]

The main benefits of influenza vaccination of HD patients included lower probability of pneumonia/influenza, respiratory failure, intensive care unit stay, and lower mortality.[69,83] A serious complication of influenza vaccination is antineutrophil cytoplasmic antibody vasculitis, which has been reported in 8 cases, mainly in women.[84]

In the most recent recommendations by the ACIP CDC, 1 dose of inactivated influenza vaccine annually is recommended for adults with estimated GFR $<$30 ml/min/1.73 m^2(GFR categories G4-G5).[35]

Vaccination Against Streptococcus Pneumoniae

Thirteen-valent pneumococcal conjugate vaccine (PCV13) or 23-valent pneumococcal polysaccharide vaccine (PPSV23) is recommended for patients with altered immunocompetence.[68,85] The KDIGO CKD Work Group recommends that all adults with estimated GFR $<$30 mL/min/1.73 m2 (GFR categories G4-G5) and those at high risk of pneumococcal infection (e.g., nephrotic syndrome, diabetes, or those receiving immunosuppression) should receive the pneumococcal polyvalent (conjugate,

Table 2. The Advisory Committee on Immunization Practices of Centers for Disease Control and Prevention recommendations for selected vaccinations in chronic kidney disease adults with glomerular filtration categories G4-G5[35]

Vaccine	Vaccination schedule
Tetanus, diphtheria, acellular pertussis (Td/Tdap)	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years
Varicella	2 doses
Human papillomavirus (for those who did not get any or all doses when they were younger)	Female: 3 doses through age 26 y Male: 3 doses through age 21 yrs
Zoster	1 dose (severe immunodeficiency is a contraindication)
Measles, mumps, rubella	1 or 2 doses
Recommended vaccinations if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle)	
Meningococcal	1 or more doses of inactivated vaccine
Hepatitis A	2 doses
Haemophilus influenzae type b	1 or 3 doses of inactivated vaccine

polysaccharide) vaccine unless contraindicated (grade 1B), and that all adults with CKD who have received pneumococcal vaccination should be offered revaccination within 5 y (grade 1B).[34] In the recent recommendations by the ACIP CDC, 1 dose of PCV13 or 1 – 2 doses of PPSV23 are advised for CKD adults with GFR categories G4-G5 and for those with nephrotic syndrome.[35]

However, only 22% of HD patients a London district general hospital underwent pneumococcal vaccination in the 5 analyzed years.[71] Vaccination against pneumococcal disease was associated with improved survival in dialysis patients.[83,86]

Polyvalent pneumococcal vaccine is administered via intramuscular or subcutaneous route. Development of pneumococcal vaccine that could be given intranasally in spray may increase not only acceptance for vaccination, but also exhibit elevated *Streptococcus pneumoniae*-specific IgA, IgG2c, and IgG1 antibodies in serum and bronchoalveolar lavage fluid.[87]

Other Vaccinations

The ACIP CDC recommendations for other vaccinations in adults with GFR categories G4-G5 are presented in **Table 2**.

Closing Remarks

Numerous studies indicate positive effects of vaccination in CKD/RRT patients. Many infections influencing morbidity and mortality of these patients might be prevented by vaccination. Adverse effects of vaccinations are not frequent, also in these specific patients. The calendar of vaccinations for CKD/RRT patients[35] should become more popular in dialysis facilities worldwide for keeping a persistent immunity against influenza viruses and pneumococci as well as HCV in the future. Effects of hepatitis B vaccination are a good example of advantages resulting from a consequent strategy, as is the inclusion of the vaccine in the childhood vaccination schedules.

At present, it seems to be important to propagate among CKD patients a wider use of vaccines against influenza and pneumococci. From the clinical point of view, it would be worthy to know whether novel vaccines, like Fendrix, could elicit such a seroprotection rate in defined nonresponders to hepatitis B vaccination among HD patients that is enough high for recommendation of this vaccine to all immunocompromised patients.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

1. Neovius M, Jacobson SH, Eriksson JK, Elinder CG, Hylander B. Mortality in chronic kidney disease and renal replacement therapy: a population-based cohort study. BMJ Open 2014; 4: e004251; PMID:24549162; http://dx.doi.org/10.1136/bmjopen-2013-004251
2. Ortiz A, Covic A, Fliser D, Fouque D, Goldsmith D, Kanbay M, Mallamaci F, Massy ZA, Rossignol P, Vanholder R, et al. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. Lancet 2014; 383: 1831-43; PMID:24856028; http://dx.doi.org/10.1016/S0140-6736(14)60384-6
3. Kalia H, Fabrizi F, Martin P. Hepatitis B virus and renal transplantation. Transplant Rev (Orlando) 2011; 25: 102-9; PMID:21530218; http://dx.doi.org/10.1016/j.trre.2011.02.001
4. Vermeiren AP, Hoebe CJ, Dukers-Muijrers NHJ. High non-responsiveness of males and the elderly to standard hepatitis B vaccination among a large cohort of healthy employees. Clin Virol 2013; 58: 262-4; http://dx.doi.org/10.1016/j.jcv.2013.07.003
5. Coffman RL, Sher A, Seder RA. Vaccine adjuvants: putting innate immunity to work. Immunity 2010; 33: 492-503; PMID:21029960; http://dx.doi.org/10.1016/j.immuni.2010.10.002
6. Cruz LJ, Tacken PJ, Rueda F, Domingo JC, Albericio F, Figdor CG. Targeting nanoparticles to dendritic cells for immunotherapy. Methods Enzymol 2012; 509: 143-63; PMID:22568905; http://dx.doi.org/10.1016/B978-0-12-391858-1.00008-3
7. Grzegorzewska AE. Hepatitis B vaccination in chronic kidney disease: review of evidence in non-dialyzed patients. Hepat Mon 2012; 12: e7359; PMID:23326280; http://dx.doi.org/10.5812/hepatmon.7359
8. Grzegorzewska AE. Hepatitis B vaccination in chronic kidney disease patients: a call for novel vaccines. Expert Rev Vaccines 2014; 13: 1317-26; PMID:25148051; http://dx.doi.org/10.1586/14760584.2014.944508
9. Mathew R, Mason D, Kennedy JS. Vaccination issues in patients with chronic kidney disease. Expert Rev Vaccines 2014; 13: 285-98; PMID:24405403; http://dx.doi.org/10.1586/14760584.2014.874950
10. Vaziri ND, Pahl MV, Crum A, Norris K. Effect of uremia on structure and function of immune system. J Ren Nutr 2012; 22: 149-56; PMID:22200433; http://dx.doi.org/10.1053/j.jrn.2011.10.020
11. Geara AS, Castellanos MR, Bassil C, Schuller-Levis G, Park E, Smith M, Goldman M, Elsayegh S. Effects of parathyroid hormone on immune function. See comment in PubMed Commons belowClin Dev Immunol 2010; 2010: pii: 418695
12. Brigotti M, Carnicelli D, Arfilli V, Tamassia N, Borsetti F, Fabbri E, Tazzari PL, Ricci F, Pagliaro P, Spisni E, et al. Identification of TLR4 as the receptor that recognizes Shiga toxins in human neutrophils. See comment in PubMed Commons belowJ Immunol 2013; 191: 4748-58; PMID:24068665

13. Gollapudi P, Yoon JW, Gollapudi S, Pahl MV, Vaziri ND. Leukocyte toll-like receptor expression in end-stage kidney disease. Am J Nephrol 2010; 31: 247-54; PMID:20090311; http://dx.doi.org/10.1159/000276764
14. Wang ZS, Xu DM, Guan GJ, Cui MY, Wei Y, Tang LJ, Jia XY, Li WB. [Clinical significance of toll-like receptor 4 expression on the surface of peripheral blood mononuclear cells in uremic patients]. [Article in Chinese] Zhonghua Yi Xue Za Zhi 2010; 90: 2389-91
15. Yang M, Gan H, Shen Q, Tang W, Du X, Chen D. Proinflammatory CD14+CD16+ monocytes are associated with microinflammation in patients with type 2 diabetes mellitus and diabetic nephropathy uremia. Inflammation 2012; 35: 388-96; PMID:21847775; http://dx.doi.org/10.1007/s10753-011-9374-9
16. Vallés PG, Melechuck S, González A, Manucha W, Bocanegra V, Vallés R. Toll-like receptor 4 expression on circulating leucocytes in hemolytic uremic syndrome. Pediatr Nephrol 2012; 27: 407-15; http://dx.doi.org/10.1007/s00467-011-2014-7
17. Zhou ZX, Zhang J, Sun L. C7: a CpG oligodeoxynucleotide that induces protective immune response against megalocytivirus in Japanese flounder (Paralichthys olivaceus) via Toll-like receptor 9-mediated signaling pathway. Dev Comp Immunol 2014; 44: 124-32; PMID:24333437; http://dx.doi.org/10.1016/j.dci.2013.12.002
18. Chua BY, Johnson D, Tan A, Earnest-Silveira L, Sekiya T, Chin R, Torresi J, Jackson DC. Hepatitis C VLPs delivered to dendritic cells by a TLR2 targeting lipopeptide results in enhanced antibody and cell-mediated responses. PLoS One 2012; 7: e47492; PMID:23091628; http://dx.doi.org/10.1371/journal.pone.0047492
19. Kim KW, Chung BH, Jeon EJ, Kim BM, Choi BS, Park CW, Kim YS, Cho SG, Cho ML, Yang CW. B cell-associated immune profiles in patients with end-stage renal disease (ESRD). Exp Mol Med 2012; 44: 465-72; PMID:22617684; http://dx.doi.org/10.3858/emm.2012.44.8.053
20. Pahl MV, Gollapudi S, Sepassi L, Gollapudi P, Elahimehr R, Vaziri ND. Effect of end-stage renal disease on B-lymphocyte subpopulations, IL-7, BAFF and BAFF receptor expression. Nephrol Dial Transplant 2010; 25: 205-12; PMID:19684120; http://dx.doi.org/10.1093/ndt/gfp397
21. Zhou L, Sun L, Wu H, Zhang L, Chen M, Liu J, Zhong R. Oridonin ameliorates lupus-like symptoms of MRL(lpr/lpr) mice by inhibition of B-cell activating factor (BAFF). Eur J Pharmacol 2013; 715: 230-7; PMID:23712004; http://dx.doi.org/10.1016/j.ejphar.2013.05.016
22. Lin SY, Liu JH, Wang SM, Wang IK, Tsai CA, Liu YL, Lin HH, Chang CC, Huang CC. Association of response to hepatitis B vaccination and survival in dialysis patients. BMC Nephrol 2012; 13: 97; PMID:22935561; http://dx.doi.org/10.1186/1471-2369-13-97
23. Brown CM, Donlon S, O'Kelly P, Casey AM, Collier C, Conlon PJ, Walshe JJ. A prospective study of hepatitis B vaccination - a comparison of responders versus nonresponders. Ren Fail 2011; 33: 276-9; PMID:21401350; http://dx.doi.org/10.3109/0886022X.2011.559300
24. Al Saran K, Sabry A, Al Halawany Z, Ismail M. Factors affecting response to hepatitis B vaccine among hemodialysis patients in a large Saudi Hemodialysis Center. Saudi J Kidney Dis Transpl 2014; 25: 185-91; PMID:24434410; http://dx.doi.org/10.4103/1319-2442.124572
25. Grzegorzewska AE, Wobszal P, Jagodziński PP. Interleukin-18 promoter polymorphism and development of antibodies to surface antigen of hepatitis B virus in hemodialysis patients. Kidney Blood Press Res. 2012; 35: 1-8; PMID:21832842; http://dx.doi.org/10.1159/000329932
26. Grzegorzewska AE, Wobszal PM, Mostowska A, Jagodziński PP. Antibodies to hepatitis B virus surface antigen and interleukin 12 and interleukin 18 gene polymorphisms in hemodialysis patients. BMC Nephrol 2012; 13: 75; PMID:22863216; http://dx.doi.org/10.1186/1471-2369-13-75
27. Grzegorzewska AE, Wobszal PM, Sowińska A, Mostowska A, Jagodziński PP. Association of the interleukin-12 polymorphic variants with the development of antibodies to surface antigen of hepatitis B virus in hemodialysis patients in response to vaccination or infection. Mol Biol Rep 2013; 40: 6899-911; PMID:24158609; http://dx.doi.org/10.1007/s11033-013-2809-7
28. Grzegorzewska AE, Pajzderski D, Sowińska A, Mostowska A, Jagodziński PP. IL4R and IL13 polymorphic variants and development of antibodies to surface antigen of hepatitis B virus in hemodialysis patients in response to HBV vaccination or infection. Vaccine 2013; 31: 1766-70; PMID:23462527; http://dx.doi.org/10.1016/j.vaccine.2013.02.023
29. Grzegorzewska AE, Pajzderski D, Sowińska A, Jagodziński PP. Polymporphism of monocyte chemoattractant protein 1 (MCP1 –2518 A/G) and responsiveness to hepatitis B vaccination in hemodialysis patients. Pol Arch Med Wewn 2014; 124: 10-8; PMID:24382482
30. Grzegorzewska AE, Pajzderski D, Sowińska A, Jagodziński PP. Monocyte chemoattractant protein-1 gene (MCP-1-2518 A/G) polymorphism and serological markers of hepatitis B virus infection in hemodialysis patients. Med Sci Monit 2014; 20: 1101-16; PMID:24975639; http://dx.doi.org/10.12659/MSM.891009
31. Zitt E, Sprenger-Mähr H, Knoll F, Neyer U, Lhotta K. Vitamin D deficiency is associated with poor response to active hepatitis B immunisation in patients with chronic kidney disease. Vaccine 2012; 30: 931-5; PMID:22142584; http://dx.doi.org/10.1016/j.vaccine.2011.11.086
32. Grzegorzewska AE, Jodłowska E, Mostowska A, Sowińska A, Jagodziński PP. Single nucleotide polymorphisms of vitamin D binding protein, vitamin D receptor and retinoid X receptor α genes and response to hepatitis B vaccination in renal replacement therapy patients. Expert Rev Vaccines 2014; 13: 1395-403; PMID:25245883; http://dx.doi.org/10.1586/14760584.2014.962521
33. Duranti E, Duranti D. Polymethylmethacrylate strengthens antibody response in hemodialysis patients not responding to hepatitis B vaccine: preliminary data. Minerva Med 2011; 102: 469-74; PMID:22193378
34. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl 2013; 3: 1-150; http://dx.doi.org/10.1038/kisup.2012.73
35. Recommended Adult Immunization Schedule — United States – 2015. http://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html. Accessed February 22, 2015)
36. Ghadiani MH, Besharati S, Mousavinasab N, Jalalzadeh M. Response rates to HB vaccine in CKD stages 3–4 and hemodialysis patients. J Res Med Sci 2012; 17: 527-33; PMID:23626628
37. Roznovský L, Tvrdík J, Kabieszová L, Petrousová L, Országová I, Hozáková L, Lochman I, Kloudová A, Valkovský I, Letocha P, et al. [Vaccination against hepatitis B in patients with chronic renal failure–twenty years follow-up]. [Article in Czech] Vnitr Lek 2011; 57: 808-14
38. Sawyer MH, Hoerger TJ, Murphy TV, Schillie SF, Hu D, Spradling PR, Byrd KK, Xing J, Reilly ML, Tohme RA, Moorman A, Smith EA, Baack BN, Jiles RB, Klevens M, Ward JW, Kahn HS, Zhou F. Use of hepatitis B vaccination for adults with diabetes mellitus: recommendations of the Advisory Committee on Immunization Practices (ACIP). Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep 2011; 60: 1709-25; PMID:22189894
39. US. Renal Data System, USRDS 2013 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2013; http://www.usrds.org/atlas.aspx
40. Garçon N. Preclinical development of AS04. Methods Mol Biol 2010; 626: 15-27; http://dx.doi.org/10.1007/978-1-60761-585-9_2
41. Polito P, Di Lullo L, Iannacci GR, Cecilia A, Galderisi C, Gorini A. [Seroconversion and immune response after anti-HBV vaccination in patients on chronic hemodialysis: comparison of two vaccines].[Article in Italian] G Ital Nefrol 2011; 28: 525-30
42. Hoebe CJ, Vermeiren AP, Dukers-Muijrers NH. Revaccination with Fendrix® or HBVaxPro® results in better response rates than does revaccination with three doses of Engerix-B® in previous non-responders. Vaccine 2012; 30: 6734-7; PMID:22981848; http://dx.doi.org/10.1016/j.vaccine.2012.08.074
43. Beran J, Hobzova L, Wertzova V, Kuriyakose S, Leyssen M, Surquin M, Houard S. Safety and immunogenicity of an investigational adjuvanted hepatitis B vaccine (HB-AS02V) in healthy adults. Hum Vaccin 2010; 6: 578-84; PMID:20523113; http://dx.doi.org/10.4161/hv.6.7.11883
44. Tielemans CL, Vlasak J, Kosa D, Billiouw JM, Verpooten GA, Mezei I, Ryba M, Peeters PC, Mat O, Jadoul MY, et al. Immunogenicity and safety of an investigational AS02(v)-adjuvanted hepatitis B vaccine in patients with renal insufficiency who failed to respond or to maintain antibody levels after prior vaccination: results of two open, randomized, comparative trials. Vaccine 2011; 29: 1159-66; PMID:21167859; http://dx.doi.org/10.1016/j.vaccine.2010.12.009
45. Surquin M, Tielemans CL, Kulcsár I, Ryba M, Vörös P, Mat O, Treille S, Dhaene M, Stolear JC, Kuriyakose SO, et al. Rapid, enhanced, and persistent protection of patients with renal insufficiency by AS02(V)-adjuvanted hepatitis B vaccine. Kidney Int 2010; 77: 247-55; PMID:19940840; http://dx.doi.org/10.1038/ki.2009.454
46. Surquin M, Tielemans C, Nortier J, Jadoul M, Peeters P, Ryba M, Roznovsky L, Domán J, Barthelemy X, Crasta PD, et al. Anti-HBs antibody persistence following primary vaccination with an investigational AS02 (v)-adjuvanted hepatitis B vaccine in patients with renal insufficiency. Hum Vaccin 2011; 7: 913-8; PMID:21892006; http://dx.doi.org/10.4161/hv.7.9.16225
47. Heplisav approval status. http://www.drugs.com/history/heplisav.html. Accessed February 23, 2015
48. Halperin SA, Ward B, Cooper C, Predy G, Diaz-Mitoma F, Dionne M, Embree J, McGeer A, Zickler P, Moltz KH, et al. Comparison of safety and immunogenicity of two doses of investigational hepatitis B virus surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide and three doses of a licensed hepatitis B vaccine in healthy adults 18–55 years of age. Vaccine 2012; 30: 2556-63; PMID:22326642; http://dx.doi.org/10.1016/j.vaccine.2012.01.087
49. Halperin SA, McNeil S, Langley JM, Smith B, MacKinnon-Cameron D, McCall-Sani R, Heyward WL, Martin JT. Safety and immunogenicity of different two-dose regimens of an investigational hepatitis B vaccine (hepatitis B surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide) in healthy young adults. Vaccine 2012; 30: 5445-8; PMID:22704926; http://dx.doi.org/10.1016/j.vaccine.2012.05.074
50. Halperin SA, Ward BJ, Dionne M, Langley JM, McNeil SA, Smith B, Mackinnon-Cameron D, Heyward WL, Martin JT. Immunogenicity of an investigational hepatitis B vaccine (hepatitis B surface antigen co-administered with an immunostimulatory

phosphorothioate oligodeoxyribonucleotide) in nonresponders to licensed hepatitis B vaccine. Hum Vaccin Immunother 2013; 9: 1438-44; PMID:23571179; http://dx.doi.org/10.4161/hv.24256
51. Sablan BP, Kim DJ, Barzaga NG, Chow WC, Cho M, Ahn SH, Hwang SG, Lee JH, Namini H, Heyward WL. Demonstration of safety and enhanced seroprotection against hepatitis B with investigational HBsAg-1018 ISS vaccine compared to a licensed hepatitis B vaccine. Vaccine 2012; 30: 2689-96; PMID:22342916; http://dx.doi.org/10.1016/j.vaccine.2012.02.001
52. Heyward WL, Kyle M, Blumenau J, Davis M, Reisinger K, Kabongo ML, Bennett S, Janssen RS, Namini H, Martin JT. Immunogenicity and safety of an investigational hepatitis B vaccine with a Toll-like receptor 9 agonist adjuvant (HBsAg-1018) compared to a licensed hepatitis B vaccine in healthy adults 40–70 years of age. Vaccine 2013; 31: 5300-5; PMID:23727002; http://dx.doi.org/10.1016/j.vaccine.2013.05.068
53. Janssen RS, Mangoo-Karim R, Pergola PE, Girndt M, Namini H, Rahman S, Bennett SR, Heyward WL, Martin JT. Immunogenicity and safety of an investigational hepatitis B vaccine with a toll-like receptor 9 agonist adjuvant (HBsAg-1018) compared with a licensed hepatitis B vaccine in patients with chronic kidney disease. Vaccine 2013; 31: 5306-13; PMID:23727422; http://dx.doi.org/10.1016/j.vaccine.2013.05.067
54. Halperin SA, Ward BJ, Dionne M, Langley JM, McNeil SA, Smith B, Mackinnon-Cameron D, Heyward WL, Martin JT. Immunogenicity of an investigational hepatitis B vaccine (hepatitis B surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide) in nonresponders to licensed hepatitis B vaccine. Hum Vaccin Immunother 2013; 9: 1438-44; PMID:23571179; http://dx.doi.org/10.4161/hv.24256
55. Kuan RK, Janssen R, Heyward W, Bennett S, Nordyke R. Cost-effectiveness of hepatitis B vaccination using HEPLISAV™ in selected adult populations compared to Engerix-B® vaccine. Vaccine 2013; 31: 4024-32; PMID:23707166; http://dx.doi.org/10.1016/j.vaccine.2013.05.014
56. Di Pasquale A, De Ridder M, Van Der Meeren O. Hepatitis B virus vaccine in chronic kidney diseases: improved immunogenicity by adjuvants? Limits of a meta-analysis. Vaccine 2012; 30: 5586; PMID:22749597; http://dx.doi.org/10.1016/j.vaccine.2012.06.023
57. Saade F, Honda-Okubo Y, Trec S, Petrovsky N. A novel hepatitis B vaccine containing Advax™, a polysaccharide adjuvant derived from delta inulin, induces robust humoral and cellular immunity with minimal reactogenicity in preclinical testing. Vaccine 2013; 31: 1999-2007; PMID:23306367; http://dx.doi.org/10.1016/j.vaccine.2012.12.077
58. Fakharzadeh S, Kalanaky S, Hafizi M, Goya MM, Masoumi Z, Namaki S, Shakeri N, Abbasi M, Mahdavi M, Nazaran MH. The new nano-complex, Hep-c, improves the immunogenicity of the hepatitis B vaccine. Vaccine 2013; 31: 2591-7; PMID:23583463; http://dx.doi.org/10.1016/j.vaccine.2013.03.030
59. Gray PM, Forrest G, Wisniewski T, Porter G, Freed DC, DeMartino JA, Zaller DM, Guo Z, Leone J, Fu TM, et al. Evidence for cyclic diguanylate as a vaccine adjuvant with novel immunostimulatory activities. Cell Immunol 2012; 278: 113-9; PMID:23121983; http://dx.doi.org/10.1016/j.cellimm.2012.07.006
60. Chen X, Zhang W, Gao W, Zou Q, Feng C, Liu H, Zhou C, Zhang Y, Wang B. Hemokinin-1 as an adjuvant molecule enhancing humoral and memory responses to HBsAg DNA vaccination. Viral Immunol 2012; 25: 289-96; PMID:22876773; http://dx.doi.org/10.1089/vim.2012.0015
61. Sanadgol H. Levamisole usage as an adjuvant to hepatitis B vaccine in hemodialysis patients, yes or no? Nephrourol Mon 2013; 5: 673-8; PMID:23577329; http://dx.doi.org/10.5812/numonthly.3985
62. Afsharian M, Vaziri S, Janbakhsh AR, Sayad B, Mansouri F, Nourbakhsh J, Qadiri K, Najafi F, Shirvanii M. The effect of zinc sulfate on immunologic response to recombinant hepatitis B vaccine in elderly: Zinc sulfate and immunologic response to recombinant hepatitis B vaccine. Hepat Mon 2011; 11: 32-5; PMID:22087114
63. Janbakhsh A, Mansouri F, Vaziri S, Sayad B, Afsharian M, Rahimi M, Shahebrahimi K, Salari F. Effect of selenium on immune response against hepatitis B vaccine with accelerated method in insulin-dependent diabetes mellitus patients. Caspian J Intern Med 2013; 4: 603-6; PMID:24009944
64. Mbaeyi C, Thompson ND. Hepatitis C Virus Screening and Management of Seroconversions in Hemodialysis Facilities. Seminar Dial 2013; 26: 439-46; http://dx.doi.org/10.1111/sdi.12097
65. Fauvelle C, Lepiller Q, Felmlee DJ, Fofana I, Habersetzer F, Stoll-Keller F, Baumert TF, Fafi-Kremer S. Hepatitis C virus vaccines - progress and perspectives. Microb Pathog 2013; 58: 66-72; PMID:23499591; http://dx.doi.org/10.1016/j.micpath.2013.02.005
66. Tung J, Carlisle E, Smieja M, Kim PT, Lee CH. A randomized clinical trial of immunization with combined hepatitis A and B versus hepatitis B alone for hepatitis B seroprotection in hemodialysis patients. Am J Kidney Dis 2010; 56: 713-9; PMID:20630640; http://dx.doi.org/10.1053/j.ajkd.2010.04.015
67. Beaumont E, Patient R, Hourioux C, Dimier-Poisson I, Roingeard P. Chimeric HBV-HCV envelope proteins elicit broadly neutralizing antibodies and constitute a potential bivalent prophylactic vaccine. Hepatology 2012; ; http://dx.doi.org/10.1002/hep.26132
68. Baker C, Pickering L, Chilton L, Cieslak P, Ehresmann K, Englund J, Judson F, Keitel W, Lett S, Marcy M, et al. General recommendations on immunization - recommendations of the Advisory Committee on Immunization Practices (ACIP). National Center for Immunization and Respiratory Diseases. MMWR Recomm Rep 2011; 60: 1-64
69. Wang IK, Lin CL, Lin PC, Liang CC, Liu YL, Chang CT, Yen TH, Morisky DE, Huang CC, Sung FC. Effectiveness of influenza vaccination in patients with end-stage renal disease receiving hemodialysis: a population-based study. PLoS One 2013; 8: e58317
70. McGrath LJ, Cole SR, Kshirsagar AV, Weber DJ, Stürmer T, Brookhart MA. Hospitalization and skilled nursing care are predictors of influenza vaccination among patients on hemodialysis: evidence of confounding by frailty. Med Care 2013; 51: 1106-13; PMID:23969584; http://dx.doi.org/10.1097/MLR.0b013e3182a50297
71. Wilmore SM, Philip KE, Cambiano V, Bretherton CP, Harborne JE, Sharma A, Jayasena SD. Influenza and pneumococcal vaccinations in dialysis patients in a London district general hospital. Clin Kidney J 2014; 7: 27-32; PMID:24466425; http://dx.doi.org/10.1093/ckj/sft138
72. Kumar D, Morris MI, Kotton CN, Fischer SA, Michaels MG, Allen U, Blumberg EA, Green M, Humar A, Ison MG. Guidance on novel influenza A/H1N1 in solid organ transplant recipients. Am J Transplant 2010; 10: 18-25; PMID:19958321; http://dx.doi.org/10.1111/j.1600-6143.2009.02960.x
73. Morel S, Didierlaurent A, Bourguignon P, Delhaye S, Baras B, Jacob V, Planty C, Elouahabi A, Harvengt P, Carlsen H, et al. Adjuvant System AS03 containing α-tocopherol modulates innate immune response and leads to improved adaptive immunity. Vaccine 2011; 29: 2461-73; PMID:21256188; http://dx.doi.org/10.1016/j.vaccine.2011.01.011
74. Langley JM, Risi G, Caldwell M, Gilderman L, Berwald B, Fogarty C, Poling T, Riff D, Baron M, Frenette L, et al. Dose-Sparing H5N1 A/Indonesia/05/2005 Pre-pandemic Influenza Vaccine in Adults and Elderly Adults: A phase III, placebo-controlled, randomized study. J Infect Dis 2011; 203: 1729-38; PMID:21606531; http://dx.doi.org/10.1093/infdis/jir172
75. Broeders NE, Hombrouck A, Lemy A, Wissing KM, Racapé J, Gastaldello K, Massart A, Van Gucht S, Weichselbaum L, De Mul A, et al. Influenza A/H1N1 vaccine in patients treated by kidney transplant or dialysis: a cohort study. Clin J Am Soc Nephrol 2011; 6: 2573-8; PMID:21921153; http://dx.doi.org/10.2215/CJN.04670511
76. Labriola L, Hombrouck A, Marechal C, Van GS, Brochier B, Thomas I, Jadoul M, Goubau P. Immunogenicity of an adjuvanted 2009 pandemic influenza A (H1N1) vaccine in haemodialysed patients. Nephrol Dial Transplant 2011; 26: 1424-28; PMID:21273236; http://dx.doi.org/10.1093/ndt/gfq782
77. Brakemeier S, Schweiger B, Lachmann N, Glander P, Schonemann C, Diekmann F, Neumayer HH, Budde K. Immune response to an adjuvanted influenza A H1N1 vaccine (Pandemrix®) in renal transplant recipients. *Nephrol Dial Transplant* 2012; 27: 423-8; PMID:21613386; http://dx.doi.org/10.1093/ndt/gfr278
78. Dikow R, Eckerle I, Ksoll-Rudek D, Hampel H, Schwenger V, Zeier M, Schnitzler P, Sommerer C. Immunogenicity and Efficacy in Hemodialysis Patients of an $AS03_A$-Adjuvanted Vaccine for 2009 Pandemic Influenza A(H1N1): A Nonrandomized Trial. Am J Kidney Dis 2011; 57: 716-23; PMID:21349617
79. Esposito S, Mastrolia MV, Ghio L, Paglialonga F, Terranova L, Scala A, Edefonti A, Principi N. Influenza immunization in hemodialyzed or kidney transplanted adolescents and young adults. Expert Rev Vaccines 2014; 13: 1059-66; PMID:24972949
80. Azak A, Huddam B, Kocak G, Altas AB, Duranay M, Korukluoglu G. Antibody response after single H1N1 influenza vaccine in chronic dialysis patients. Ther Apher Dial 2013; 17: 55-9; PMID:23379494
81. Quintana LF, Serra N, De Molina-Llauradó P, Blasco M, Martinez M, Campos B, Bayas JM, Pumarola T, Campistol JM. Influence of renal replacement therapy on immune response after one and two doses of the A (H1N1) pdm09 vaccine. Influenza Other Respir Viruses 2013; 7: 809-14; PMID:23078139
82. Moon SJ, Lee SH, Byun YH, Yun GY, Kim SK, Seong BL, Kim AR, Sun Park E, Kim HJ, Lee JE, et al. Risk factors affecting seroconversion after influenza A/H1N1 vaccination in hemodialysis patients. BMC Nephrol 2012; 13: 165; PMID:23206898
83. Bond TC, Spaulding AC, Krisher J, McClellan W. Mortality of dialysis patients according to influenza and pneumococcal vaccination status. Am J Kidney Dis 2012; 60: 959-65; PMID:22694948
84. Duggal T, Segal P, Shah M, Carter-Monroe N, Manoharan P, Geetha D. Antineutrophil cytoplasmic antibody vasculitis associated with influenza vaccination. Am J Nephrol 2013; 38: 174-8; PMID:23941822
85. 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; PMID:23051612; http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm
86. Gilbertson DT, Guo H, Arneson TJ, Collins AJ. The association of pneumococcal vaccination with hospitalization and mortality in hemodialysis patients. Nephrol Dial Transplant 2011; 26: 2934-9; PMID:21317410
87. Bitsaktsis C, Iglesias BV, Li Y, Colino J, Snapper CM, Hollingshead SK, Pham G, Gosselin DR, Gosselin EJ. Mucosal immunization with an unadjuvanted vaccine that targets Streptococcus pneumoniae PspA to human Fcγ receptor type I protects against pneumococcal infection through complement- and lactoferrin-mediated bactericidal activity. Infect Immun 2012; 80: 1166-80; PMID:22158740