

In The Name of GOD



HBV Vaccination in Patients with Kidney Disease & Kidney Transplant Candidate

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Introduction

- ▶ **HBV** infection is a **widespread** but **preventable** disease. The **hepatitis B vaccine** usually provides good protection against infection.
- ▶ The prevalence of **HBV infection** in hemodialysis (**HD**) patients varies significantly between countries, ranging from very low in developed countries to very high in some developing countries.
- ▶ **HD patients** are susceptible to infection with **HBV** and **HCV** resulting from blood transfusion, frequent injections, partial immunosuppression, or history of transplantation.
- ▶ **Renal transplant recipients** are known to have severe and rapid progression of hepatitis B. There is also concern of reactivation of latent infection due to immunosuppression.



Timing of vaccination in patients with chronic kidney disease

- ▶ Hepatitis B vaccination is recommended for **all CKD patients**.
- ▶ Timing of vaccination appears to **be critical** to optimize response.
- ▶ Because **immune system abnormalities** correlate with the **degree of renal failure**, patients with **CKD who do not require dialysis** may have a **stronger** immune system and **higher** antibody response rate to HBV vaccination than patients who are on renal replacement therapy.
- ▶ **Patients with uremia** who were vaccinated **before** they required dialysis have **higher seroprotecting** rates and antibody titers.



General Principle in Kidney Transplant Recipients

- ▶ It is usually accepted that, in **solid-organ recipients** receiving immunosuppression, the immune system will **not** be able to mount a response as effective as in normal subjects.
- ▶ Most immunosuppressive regimens after solid-organ transplant include a combination of **steroids** and **calcineurin inhibitors**, such as cyclosporin and tacrolimus.
- ▶ Under these regimens, both **T- and B-cell responses** are impaired through blockage of cellular proliferation after antigen stimulation as well as inhibition of cytokine production necessary for such stimulation



General Principle in Kidney Transplant Recipients

- ▶ Based on guidelines from the **United States Advisory Committee on Immunization Practices, WHO, American Society of Transplantation Infectious Disease Community of Practice and the Infectious Diseases Society of America**: **Organ transplant recipients** need appropriate vaccinations **before and after transplantation**.
- ▶ The 2009 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines on the monitoring, management and treatment of kidney transplant recipients recommends that these patients are given approved, **inactivated vaccines** according to the recommended schedules for the **general population**, with the **exception of hepatitis B** vaccination (for which they recommend a **modified protocol**).
- ▶ **Live vaccines** could cause disseminated disease and are generally **contraindicated** in transplant recipients.

A decorative graphic on the left side of the slide. It features a dark grey arrow pointing to the right at the top. Below the arrow, several thin, curved lines in shades of blue and grey sweep downwards and to the right, creating a sense of movement and flow.

Timing of vaccination in Kidney Transplant Candidate

- In general, primary immunizations should be **given before transplantation**, as early as possible during the course of disease, since the immune response to vaccines is decreased in patients with end-stage organ disease.
- The **first 6 months after transplantation** are associated with the **poorest response** as patients are usually heavily immunosuppressed.
- This period has also been associated with a **higher chance of graft dysfunction and rejection**.
- Vaccinating **too close to transplantation** may also result in **ineffective** protection.



US Advisory Committee on Immunization Practices in CKD

- **Higher vaccine dosages** or an increased number of doses are recommended for subjects **with CKD (eGFR <30 ml/min)**.
- Patients should receive **four doses of hepatitis B vaccine** as early as possible in the course of disease.
- **Recombinant** hepatitis B vaccine is recommended.
- Use **special formulations** of vaccine (**40 mcg/ml**) or **two 1 ml 20 mcg** doses given at **one site**.
- **Double dose (40 mcg)** and **four doses intramuscular** vaccine at **0, 1, 2 and 6 month** intervals give better seroprotecting rate.
- **Deltoid** region is preferred to ensure intramuscular administration. Intradermal administration has no advantage over **intramuscular** administration.

summarized from Recommendations of the Advisory Committee on Immunization Practices (ACIP)



Group	Recombivax HB*			Engerix-B [‡]		
	Dose	Volume	Schedule	Dose	Volume	Schedule
Patients aged > 20 years						
Predialysis [§]	10 µg	1.0 ml	0, 1, 6 months	20 µg	1.0 ml	0, 1, 6 months
Dialysis-dependent	40 µg	1.0 ml [¶]	0, 1, 6 months	40 µg	2 × 1.0 ml	0, 1, 2, 6 months
Patients aged < 20 years [#]	5 µg	0.5 ml	0, 1, 6 months	10 µg	0.5 ml	0, 1, 6 months
Staff members aged > 20 years	10 µg	1.0 ml	0, 1, 6 months	20 µg	1.0 ml	0, 1, 6 months

*Merck & Company, Inc.

[‡]GlaxoSmithKline Biologicals, Inc.

[§]Immune response can depend on the degree of renal insufficiency.

[¶]Special formulation.

[#]Doses for all persons aged < 20 years approved by the US FDA; for haemodialysis patients higher doses may be more immunogenic.

Note: All doses should be administered intramuscularly in the deltoid.

CKD: Chronic kidney disease.

Serologic Testing:

- Assess antibody titer to hep B surface antigen (anti-HBs). An **HBS antibody titer above 10 IU/L** was considered as cut-off point for seroconversion.
- **First titer** should be done **1-2 months** after the **primary course** is completed and **annually thereafter**
- **Revaccination** with **full doses** is recommended for persons who do **not** develop protective antibody titer **after primary course**.
- Antibody titer **falls with time** in everybody including patients on dialysis and kidney transplant recipients, necessitating **annual monitoring**.
- **Booster dose** should be given if anti-HBs titer falls **below 10 mU/ml**.
- Hepatitis B **can develop** after kidney transplantation **when antibody levels** become **undetectable**.

Immunoadjuvants & immunostimulants

- ▶ Compared to a response rate of **over 90% in the normal population**, only **50 to 60% of those with ESRD** achieve protective antibody levels following immunization against HBV.
- ▶ **Anemia, hepatitis C infection, elderly age, obesity and iron overload** states are associated with decreased antibody response.
- ▶ Various strategies have been utilized to overcome **the low seroconversion rate in ESRD patients**, including co-administering **zinc, gamma-interferon, thymopentin, interleukin-2, and levamisole** as immunostimulants or adjuvants as well as **changing the injection mode** (intradermal versus intramuscular) or **doubling the vaccine dose**.
- ▶ the **safety** of immunoadjuvants in patients **post renal transplantation** has yet to be established and **the risk of rejection** directly caused by immunoadjuvants needs to be excluded.



Thank you