



# HIV POZİTİF HASTALARDA BAĞIŞIKLAMA

DR. HÜSNÜ PULLUKÇU

Ege ÜTF Enfeksiyon Hastalıkları ve  
Klinik Mikrobiyoloji AD



18.03.2017 Adana.EKMUD

# HIV POZİTİF HASTALARDA AŞI İLE KORUNULABİLEN HASTALIKLAR İÇİN ARTMIŞ RİSK VAR MI?

---



---

HIV POZİTİF HASTALARDA AŞI İLE  
KORUNULABİLEN HASTALIKLAR  
İÇİN ARTMIŞ RİSK VAR MI?

# ARTMIŞ RİSK

- İnvaziv pnömokok enfeksiyonları
- HBV'de siroza gidiş ve HCC
- Ağır İnfluenza olguları
- HPV bulaşı
- Ölümcül kızamık olguları

# Çeşitli Rehberlerde ve Kitaplarda Yerini Almış



## Recommended Immunizations for HIV Positive Adults

Immunization Name	Associated Disease	Dosage	Comments and Warnings
<b>Recommended for All HIV Positive Adults</b>			
Hepatitis B virus (HBV)	Hepatitis B	3 shots over a 6-month period	Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
Influenza	Flu	1 shot	Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. The nasal spray vaccine (FluMist/LAIV) should not be used in this population.
Polysaccharide pneumococcal	Pneumonia	1 or 2 shots	Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is $< 200$ cells/mm <sup>3</sup> when the vaccine is given, immunization should be repeated when CD4 count is $\geq 200$ cells/mm <sup>3</sup> . Repeat one time after 5 years.
Tetanus and Diphtheria Toxoid (Td)	1. Lockjaw 2. Diphtheria	1 shot	Repeat every 10 years.
Tetanus, Diphtheria, and Pertussis (Tdap)	1. Lockjaw 2. Diphtheria 3. Pertussis	1 shot	Recommended for adults 64 years of age or younger and should be given in place of next Td booster. Can be given as soon as 2 years after last Td for persons in close contact with babies under 12 months and health care workers.

# 2015 Recommended Immunizations for Adults: By Health Condition

If you have this health condition, talk to your healthcare professional about these vaccines

If you have this health condition, talk to your healthcare professional about these vaccines	Flu Influenza	Td/Tdap Tetanus, diphtheria, pertussis	Shingles Zoster	Pneumococcal		Meningococcal	MMR Measles, mumps, rubella	HPV Human papillomavirus		Chickenpox Varicella	Hepatitis A	Hepatitis B	Hib <i>Haemophilus influenzae</i> type b
				PCV13	PPSV23			for women	for men				
Pregnancy		*see below			1 - 2 doses								
Weakened Immune System			SHOULD NOT GET VACCINE				SHOULD NOT GET VACCINE		3 doses through age 26 years	SHOULD NOT GET VACCINE		3 doses	post-EBCT* recipients only
HIV: CD4 count less than 200						1 or more doses							
HIV: CD4 count 200 or greater		1 dose of Tdap		1 dose							2 doses	3 doses	1 or 3 doses
Kidney disease or poor kidney function	Flu vaccine every year	followed by Td booster every 10 years			1 - 2 doses				1 doses through age 26 years	2 doses			
Asplenia (if you do not have a spleen or if it does not work well)			1 dose for those 50 years or older			1 or more doses	1 or 2 doses					3 doses	1 or 3 doses
Heart disease Chronic lung disease Chronic alcoholism													1 or 3 doses
Diabetes (Type 1 or Type 2)				1 dose		1 or more doses						3 doses	
Chronic Liver Disease											2 doses		

## More Information:

There are several flu vaccines available. Talk to your healthcare professional about which flu vaccine is right for you.

\* If you are pregnant, you should get a Tdap vaccine during the 3<sup>rd</sup> trimester of every pregnancy to help protect your babies from pertussis (whooping cough).

You should get zoster vaccine even if you've had shingles before.

There are two different types of pneumococcal vaccine: PCV13 (conjugate) and PPSV23 (polysaccharide). Talk with your healthcare professional to find out if one or both pneumococcal vaccines are recommended for you.

Your healthcare professional will let you know how many doses you need.

If you were born in 1957 or after, and don't have a record of being vaccinated or having had measles, mumps and rubella, talk to your healthcare professional about how many doses you may need.

Recommended for you if you did not get it when you were a child.

There are two HPV vaccines but only one HPV vaccine (Gardasil®) should be given to men.

If you are a male 22 through 26 years old and have sex with men you should complete the HPV vaccine series if you have not already done so.

Your healthcare professional will let you know how many doses you need.

\* Hematopoietic stem cell transplant



**Recommended For You:** This vaccine is recommended for you unless your healthcare professional tells you that you cannot safely receive it or that you do not need it.



**May Be Recommended For You:** This vaccine is recommended for you if you have certain other risk factors due to your age, health, job, or lifestyle that are not listed here. Talk to your healthcare professional to see if you need this vaccine.



**YOU SHOULD NOT GET THIS VACCINE**

If you are traveling outside the United States, you may need additional vaccines. Ask your healthcare professional about which vaccines you may need at least 6 weeks prior to your travel.

For more information, call 1-800-CDC-INFO (1-800-232-4636) or visit [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines)



U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention





## Vaccine Information for Adults



### Adult Vaccination Home

[Reasons to Vaccinate](#)

### ▶ Recommended Vaccines for Adults

[Adult Vaccination Records](#)[Finding and Paying for Vaccines](#)[Vaccine-Preventable Adult Diseases](#)[Resources](#)

### Related Links

[Recommended Immunizations for Adults !\[\]\(1f56542a42e2413e44a2b2023033aa2e\_img.jpg\) \[2 pages\]](#)[Vaccines: The Basics](#)[Vaccine Information Statements](#)[ACIP Vaccination Recommendations](#)[Adult Vaccination Resources for Healthcare Professionals](#)[Vaccines Home](#) > [Adult Vaccination Home](#) > [Recommended Vaccines for Adults](#)

## HIV Infection and Adult Vaccination

Vaccines are especially critical for people with chronic health conditions such as HIV infection.

**If you have HIV infection and your CD4 count is 200 or greater[1], talk with your doctor about:**

- Influenza vaccine each year to protect against seasonal flu
- Tdap vaccine to protect against whooping cough and tetanus
- Pneumococcal vaccine to protect against pneumonia and other pneumococcal diseases
- Hepatitis B vaccine series to protect against hepatitis B
- HPV vaccine series to protect against human papillomavirus if you are a man or woman up to age 26 years
- MMR vaccine to protect against measles, mumps, and rubella if you were born in 1957 or after and have not gotten this vaccine or have immunity to these diseases
- Varicella vaccine to protect against chickenpox if you were born in 1980 or after and have not gotten two doses of this vaccine or have immunity to this disease

**If you have HIV infection and your CD4 count is less than 200[2], talk with your doctor about:**


- Influenza vaccine each year to protect against seasonal flu
- Tdap vaccine to protect against whooping cough and tetanus
- Pneumococcal vaccine to protect against pneumonia and other pneumococcal diseases
- Hepatitis B vaccine series to protect against hepatitis B
- HPV vaccine series to protect against human papillomavirus if you are a man or woman up to age 26 years


### Footnotes

1. If CD4 percentages are available, CD4 percentage should be 15% or greater.
2. If CD4 percentages are available, CD4 percentage is less than 15%.

 [Print page](#)

### Contact Us:

 Centers for Disease Control and Prevention  
1600 Clifton Rd  
Atlanta, GA 30333

 800-CDC-INFO  
(800-232-4636)  
TTY: (888) 232-6348  
[Contact CDC-INFO](#)

**Figure 2. Vaccines that might be indicated for adults based on medical and other indications<sup>1</sup>**

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) <sup>4,6,7A,11</sup>	HIV infection CD4+ T lymphocyte count <sup>4A,7A,11</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) <sup>4,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel
				< 200 cells/µL	≥ 200 cells/µL							
Influenza <sup>2,3</sup>			1 dose IIV annually			1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>2,3</sup>		1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella <sup>4</sup>		Contraindicated		2 doses								
Human papillomavirus (HPV) Female <sup>2,3</sup>		3 doses through age 26 yrs		3 doses through age 26 yrs								
Human papillomavirus (HPV) Male <sup>2,3</sup>		3 doses through age 26 yrs		3 doses through age 21 yrs								
Zoster <sup>6</sup>		Contraindicated		1 dose								
Measles, mumps, rubella (MMR) <sup>2,7</sup>		Contraindicated		1 or 2 doses								
Pneumococcal 13-valent conjugate (PCV13) <sup>2,8</sup>				1 dose								
Pneumococcal polysaccharide (PPSV23) <sup>8</sup>				1 or 2 doses								
Meningococcal <sup>2,9</sup>				1 or more doses								
Hepatitis A <sup>7,10</sup>				2 doses								
Hepatitis B <sup>7,11</sup>				3 doses								
<i>Haemophilus influenzae</i> type b (Hib) <sup>7,12</sup>		post-HSCT recipients only		1 or 3 doses								

<sup>1</sup>Covered by the Vaccine Injury Compensation Program



For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster



Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)



No recommendation



## TÜRKİYE ENFEKSİYON HASTALIKLARI VE KLİNİK MİKROBİYOLOJİ UZMANLIK DERNEĞİ

Erişkin Bağışıklama Rehberi Çalışma Grubu



TC Sağlık Bakanlığı

SAĞLIK BAKANLIĞI



HALK SAĞLIĞI  
UZMANLARI DERNEĞİ



TÜRK GERİATRİ  
DERNEĞİ



TÜRK HEMATOLOJİ  
DERNEĞİ



TÜRK İÇ HASTALIKLARI  
UZMANLIK DERNEĞİ



TÜRK TORAKS DERNEĞİ



TÜRKİYE AİLE  
HEKİMLERİ UZMANLIK  
DERNEĞİ



VİRAL HEPATİTLE  
SAVAŞIM DERNEĞİ





SAYFA: 64

## 4.5. HIV ile Enfekte Hastalarda Aşılama

### 4.5.1. Giriş

HIV ile enfekte hastalarda hücresel immün yetmezlik, B hücre fonksiyonunda bozukluk ve yetersiz humoral immün cevap hastanın immünsupresyon durumunu belirler. İmmünsupresyon ilerledikçe enfeksiyonlara yatkınlık artar ki, bunların bir kısmı aşı ile önlenbilir hastalıklardır. Bu yüzden, bu hastalarda aşılama önemlidir. Ancak, enfeksiyonlara yatkınlığı arttıran immünsupresyon, ne yazık ki, aşıya cevabı da olumsuz yönde etkiler. HIV ile enfekte hastalarda aşı önerisinde bulunurken hem hastanın immünsupresyon durumu hem de uygulanacak aşının tipini dikkate almak gerekir.

# AMA PRATİK HAYAT BİR AZ FARKLI

- Hangi aşı?
- Ne zaman?
- Hangi dozlarda?
- Ödeniyor mu?
- Biz yapalım

# Başıřıklığı Baskılanan Hastalar içerisinde Ayrı bir Grup

- Bazı aşılar hem yapılabilir hem kontredikedir
- Bazı aşılar gerektiğinde yapılabilir
- Ne zaman ?
- Hangi dozda?
- Takip?



Human Vaccines & Immunotherapeutics

# BAZI SAPTAMALAR VAR

ISSN: 2164-5515 (Print) 2164-554X (Online) Journal homepage: <http://www.tandfonline.com/loi/khvi20>

## Vaccination in HIV positive adults: Need to address

Bhumika Bhatt, Harashish Jindal, Shashikantha Sk, Jagbir Singh Malik,  
Kalpana Sangwan & Junior resident

- Ölü ve inaktive aşılar da risk yok, kullanabilirsin
- Düşük CD 4 düzeyi varsa canlı aşı kullanma!



# Immunization for HIV-positive individuals

Anna Maria Geretti<sup>a,b</sup> and Tomas Doyle<sup>a</sup>

<sup>a</sup>Department of Virology, Royal Free Hampstead NHS Trust and <sup>b</sup>Department of Virology, University College Medical School, London, UK

Correspondence to Dr Anna Maria Geretti, MD, MSc, PhD, FRCPath, Department of Virology, Royal Free Hampstead NHS Trust & University College London Medical School, Pond Street, London NW3 2QG, UK  
Tel: +44 2077940500;  
e-mail: a.geretti@medsch.ucl.ac.uk

**Current Opinion in Infectious Diseases** 2010, 23:32–38

## **Purpose of review**

This review summarizes recent literature addressing infection, with a specific focus on emerging evidence positive adults.

## **Recent findings**

There are few controlled studies on the clinical efficacy in HIV-infected adults receiving highly active antiretroviral data indicate that HAART restores vaccine immunogenicity and persistence of immune responses, while reducing the

- CD4 >200 olanlarda etkinlik daha iyi
- Çok düşük CD4 düzeylerinde aşı işe yaramayabilir

## Vaccination in HIV-Infected Adults

Nancy F. Crum-Cianflone, MD, MPH<sup>1,2</sup> and Mark R. Wallace, MD<sup>3</sup>

- Olabilirse önce HART başlansın
- ART altında RNA (-), CD4 > 200 hücre/mm<sup>3</sup> (%15 < ise) herhangi bir aşı yapılabilir
- CD4 düşükse asla canlı aşı kullanma

# Immunization in Patients with HIV Infection

## Are Practical Recommendations Possible?

*Brian Eley*

Paediatric Infectious Diseases Unit, Red Cross Children's Hospital, School of Child and Adolescent Health, University of Cape Town, Cape Town, South Africa

- Aşılama HIV viral yükü kısa bir süre arttırabilir  
Bu önemsizdir
- Herhangi bir aşılama sonrası viral yük yaklaşık dört hafta ölçülmemelidir

# HADI AŐILARA BAŐLAYALIM

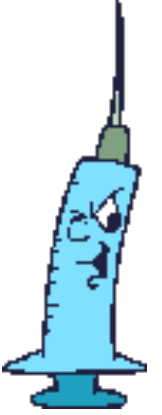




# TÜM HIV (+) HASTALARA ÖNERİLEN AŞILAR

Recommended for All HIV Positive Adults			
Hepatitis B virus (HBV)	Hepatitis B	3 shots over a 6-month period	Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
Influenza	Flu	1 shot	Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. The nasal spray vaccine (FluMist/LAIV) should not be used in this population.
Polysaccharide pneumococcal	Pneumonia	1 or 2 shots	Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is $< 200$ cells/mm <sup>3</sup> when the vaccine is given, immunization should be repeated when CD4 count is $\geq 200$ cells/mm <sup>3</sup> . Repeat one time after 5 years.
Tetanus and Diphtheria Toxoid (Td)	1. Lockjaw 2. Diphtheria	1 shot	Repeat every 10 years.
Tetanus, Diphtheria, and Pertussis (Tdap)	1. Lockjaw 2. Diphtheria 3. Pertussis	1 shot	Recommended for adults 64 years of age or younger and should be given in place of next Td booster. Can be given as soon as 2 years after last Td for persons in close contact with babies under 12 months and health care workers.

# MEŞHUR İNFLUENZA (İNAKTİF SUBÜNİT AŞI)



- Aşı ile ilgili polemikler
  - Etkisiz ! Ben olmuyorum !
  - Aşı olsam da yine grip oluyorum
  - Adjuvan sorunu!
  - Squalen !
  - Yönetim ile sağlık otoritesi arasında görüş farklılığı

# MEŞHUR İNFLUENZA (İNAKTİF SUBUNIT AŞI)

- AŞILAMA ORANI ABD'DE % 42

# İNFLUENZA

- Artmış risk var mı?



Contents lists available at [ScienceDirect](#)

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)

Influenza vaccination in HIV-infected individuals: Systematic review and assessment of quality of evidence related to vaccine efficacy, effectiveness and safety

Cornelius Remschmidt\*, Ole Wichmann, Thomas Harder

*Immunization Unit, Robert Koch Institute, Berlin, Germany*

Since influenza infection in patients with human immunodeficiency virus (HIV) is associated with prolonged duration and increased severity of illness compared to the general population [1–6], annual vaccination against seasonal influenza is recommended by many national immunization guidelines. Trivalent



# İNFLUENZA AŞISI

- Trivalan inaktive subunit aşısı her yıl influenza sezonu öncesinde önerilmektedir
- Canlı atenüe aşı (LAIV) kullanımı önerilmez
- Yeterli veri yok
- Potansiyel enfeksiyon riski

# ancak 57 hastanın içinde olduğu bir çalışmada yan etki görülmemiş

## CONCISE COMMUNICATION

### Comparison of the Safety, Vaccine Virus Shedding, and Immunogenicity of Influenza Virus Vaccine, Trivalent, Types A and B, Live Cold-Adapted, Administered to Human Immunodeficiency Virus (HIV)-Infected and Non-HIV-Infected Adults

James C. King, Jr.,<sup>1</sup> John Treanor,<sup>4</sup> Patricia E. Fast,<sup>5</sup> Mark Wolff,<sup>2</sup> Lihan Yan,<sup>2</sup> Dominic Iacuzio,<sup>3,a</sup> Bernard Readmond,<sup>1</sup> Diane O'Brien,<sup>4</sup> Kenneth Mallon,<sup>5</sup> William E. Highsmith,<sup>1</sup> John S. Lambert,<sup>1</sup> and Robert B. Belshe<sup>6</sup>

<sup>1</sup>University of Maryland Medical Center, Baltimore, <sup>2</sup>EMMES Corp., Potomac, and <sup>3</sup>National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland; <sup>4</sup>University of Rochester Medical Center, Rochester, New York; <sup>5</sup>Aviron, Mountain View, California; <sup>6</sup>Saint Louis University School of Medicine, St. Louis, Missouri

Fifty-seven human immunodeficiency virus (HIV)-infected (CDC class A1-2) and 54 non-

cantly more common in LAIV recipients regardless of HIV status. No prolonged shedding of LAIV was observed in HIV-infected participants. HIV RNA levels were not increased and CD4 counts were not decreased in HIV-infected LAIV recipients compared with placebo recipients after immunization. Shedding of LAIV and increases in antibody titers were infre-

# Subunit Aşının yan etkileri HIV(-) kişilerle aynı

- 30000 den fazla hastada influenza aşısı sonrasında HIV-RNA düzeyleri ve CD+ sayılarının etkilenmediği gözlenmiş

# Aşıya yanıt HIV(-) kişilerle aynı



## Randomized Controlled Trial to Compare Immunogenicity of Standard-Dose Intramuscular Versus Intradermal Trivalent Inactivated Influenza Vaccine in HIV-Infected Men Who Have Sex With Men in Bangkok, Thailand

Shikha Garg,<sup>1,2</sup> Prasert Thongcharoen,<sup>6</sup> Prabda Praphasiri,<sup>2</sup> Anupong Chitwarakorn,<sup>4</sup> Pornchai Sathirapanya,<sup>8</sup> Stefan Fernandez,<sup>3</sup> Kamonthip Rungrojcharoenkit,<sup>3</sup> Wanee Chonwattana,<sup>2</sup> Philip A. Mock,<sup>2</sup> Wichuda Sakwicha,<sup>2</sup> Jacqueline M. Katz,<sup>2</sup> Marc-Alain Widdowson,<sup>2</sup> Marcel E. Curfio,<sup>1,3</sup> Robert V. Gibbons,<sup>5</sup> Timothy H. Holtz,<sup>1,3</sup> Fatimah S. Dawood,<sup>2</sup> and Sonja J. Olsen<sup>2,3</sup>

- Ancak 2009 epidemisinde düşük antikor yanıtları gözlenmiş



# ANTİKOR YANITINI NASIL ARTTIRALIM?

- 2. doz aşı?

AIDS, 1994 Apr;8(4):469-76.

**Antibody response to influenza, tetanus and pneumococcal vaccines in HIV-seropositive individuals in relation to the number of CD4+ lymphocytes.**

Kroon FP<sup>1</sup>, van Dissel JT, de Jong JC, van Furth R.

## Author information

<sup>1</sup>Department of Infectious Diseases, University Hospital Leiden, The Netherlands.

## Abstract

**OBJECTIVE:** To establish when the formation of antibodies against T-lymphocyte-dependent and -independent antigens is impaired during HIV infection.

**DESIGN:** Prospective study on antibody formation before and 30 days and 60 days after vaccination with tetravalent influenza vaccine, tetanus toxoid and pneumococcal vaccine; booster with influenza vaccine was administered 30 days after initial vaccination.

**RESULTS:** In HIV-infected individuals with  $< 100 \times 10^6/l$  CD4+ lymphocytes almost no influenza antibodies were formed; CD4+ counts between 100 and  $300 \times 10^6/l$  correlated with suboptimal antibody formation; CD4+ counts  $> \text{ or } = 300 \times 10^6/l$  yielded more individuals with protective antibody titres. Thirty days after vaccination, protective antibody titres against the four influenza strains had been achieved in 24% of all HIV-infected individuals for A/Beijing (H3N2) (controls, 90%), 59% for A/Taiwan (H1N1) (controls, 80%), 18% for B/Beijing (controls, 30%) and 37% for B/Panama (controls 90%). Booster vaccination after 1 month did not increase antibody levels. Anti-tetanus toxin antibody formation, which is also T-lymphocyte-dependent, was correlated with the number of CD4+ lymphocytes. After pneumococcal vaccination (T-lymphocyte-independent), normal antibody formation was observed in HIV-infected individuals, including those with low CD4+ counts.

**CONCLUSIONS:** Influenza vaccination should not be administered to HIV-infected individuals with CD4+ counts  $< 100 \times 10^6/l$ .

*Clin Infect Dis.* 2011 Jan 1;52(1):122-7. doi: 10.1093/cid/ciq003.

## Immune response after two doses of the novel split virion, adjuvanted pandemic H1N1 influenza A vaccine in HIV-1-infected patients.

Bickel M<sup>1</sup>, von Hentig N, Wieters I, Khaykin P, Nisius G, Haberl A, Stephan C, Herrmann E, Doerr HW, Brodt HR, Allwinn R.

[ClinicalTrials.gov \(NCT01011114\)](http://clinicaltrials.gov/ct2/show/study/NCT01011114).

**METHODS:** Diagnostic study of adult HIV-1-infected patients scheduled for H1N1 influenza A vaccination. Blood samples were taken before and 21 days after the first dose and 21 days after the second dose of the vaccine. Antibody (AB) titers were determined by hemagglutination inhibition assay. Seroconversion was defined by either an AB titer  $\leq 1:10$  before and  $\geq 1:40$  after or  $\geq 1:10$  before and a  $\geq 4$ -fold increase in AB titer 21 days after vaccination.

**RESULTS:** One hundred thirty-five patients received 2 doses of the H1N1 vaccine and were analyzed. The rate of seroconversion was 68.2% (95% confidence interval, 59.6-75.9) after the first dose and 91.9% (95% confidence interval, 85.9-95.9) after the second dose. Patients who did not seroconvert had a lower mean nadir CD4 cell count ( $\pm$  standard deviation;  $81 \pm 99$  vs  $190 \pm 148$  cells/ $\mu$ L;  $P = .006$ ), had a longer duration of HIV infection ( $\pm$  standard deviation;  $13.1 \pm 5.9$  vs  $8.8 \pm 6.8$  years;  $P = .04$ ), and were more likely to have an AB titer  $\geq 1:40$  before vaccination (4% vs 55%;  $P < .001$ ) when compared with patients with seroconversion. No other differences were found between the 2 groups, including AIDS status, highly active antiretroviral therapy status, HIV RNA - polymerase chain reaction load  $<50$  copies/mL, CD4 cell count, sex, body mass index, and chronic hepatitis.

**CONCLUSION:** Among HIV-infected patients, the rate of seroconversion after the first dose of an adjuvanted H1N1 influenza A vaccine was 68% and increased to 92% after a second doses.



# ANTİKOR YANITINI NASIL ARTTIRALIM?

- Antijen miktarını arttıralım

Annals of Internal Medicine

ORIGINAL RESEARCH

## Improved Immunogenicity With High-Dose Seasonal Influenza Vaccine in HIV-Infected Persons

A Single-Center, Parallel, Randomized Trial

Noah McKittrick, MD; Ian Frank, MD; Jeffrey M. Jacobson, MD; C. Jo White, MD; Deborah Kim, RPh; Rosemarie Kappes, RN, MPH; Carol DiGiorgio, RN; Thomas Kenney, BS; Jean Boyer, PhD; and Pablo Tebas, MD, for the Center for AIDS Research

**RESULTS:** 195 participants enrolled, and 190 completed the study (93 in the standard-dose group and 97 in the high-dose group). The seroprotection rates after vaccination were higher in the high-dose group for the H1N1 (96% vs. 87%; treatment difference, 9 percentage points [95% CI, 1 to 17 percentage points];  $P = 0.029$ ), H3N2 (96% vs. 92%; treatment difference, 3 percentage points [CI, -3 to 10 percentage points];  $P = 0.32$ ), and influenza B (91% vs. 80%; treatment difference, 11 percentage points [CI, 1 to 21 percentage points];  $P = 0.030$ ) strains. Both vaccines were well-tolerated, with myalgia (19%), malaise (14%), and local pain (10%) the most frequent adverse events.

**LIMITATIONS:** The effectiveness of the vaccine in preventing clinical influenza was not evaluated. The number of participants with CD4 counts less than  $0.200 \times 10^9$  cells/L was limited.

**CONCLUSION:** HIV-infected persons reach higher levels of influenza seroprotection if vaccinated with the high-dose trivalent vaccine than with the standard-dose.

**PRIMARY FUNDING SOURCE:** National Institute of Allergy and Infectious Diseases and Center for AIDS Research of the University of Pennsylvania.

# BU ARADA

- Aşıyı ne zaman yapalım?
  - Yeni aşı piyasaya çıkar çıkmaz
  - Soğuklar başlayınca
  - İnfluenza olguları görülmeye başlayınca
  - Olabildiğince geç



### Recommended for All HIV Positive Adults

Hepatitis B virus (HBV)	Hepatitis B	3 shots over a 6-month period	Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
Influenza	Flu	1 shot	Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. The nasal spray vaccine (FluMist/LAIV) should not be used in this population.
Polysaccharide pneumococcal	Pneumonia	1 or 2 shots	Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is $< 200$ cells/mm <sup>3</sup> when the vaccine is given, immunization should be repeated when CD4 count is $\geq 200$ cells/mm <sup>3</sup> . Repeat one time after 5 years.
Tetanus and Diphtheria Toxoid (Td)	1. Lockjaw 2. Diphtheria	1 shot	Repeat every 10 years.
Tetanus, Diphtheria, and Pertussis (Tdap)	1. Lockjaw 2. Diphtheria 3. Pertussis	1 shot	Recommended for adults 64 years of age or younger and should be given in place of next Td booster. Can be given as soon as 2 years after last Td for persons in close contact with babies under 12 months and health care workers.

# PPV ve PCV

- PPV23 .....1983' ten beri
- PCV 13.....2010'dan beri
  
- Pnömonokok enfeksiyonları için artmış risk var mı?



Contents lists available at [ScienceDirect](#)

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)



Review

Humoral immune responses to *Streptococcus pneumoniae* in the setting of HIV-1 infection


Lumin Zhang<sup>a</sup>, Zihai Li<sup>a</sup>, Zhuang Wan<sup>b</sup>, Andrew Kilby<sup>c</sup>, J. Michael Kilby<sup>a,c</sup>, Wei Jiang<sup>a,c,\*</sup>



## A B S T R A C T

---

*Streptococcus pneumoniae* (pneumococcus) remains one of the most commonly identified causes of bacterial infection in the general population, and the risk is 30–100 fold higher in HIV-infected individuals. Both innate and adaptive host immune responses to pneumococcal infection are important against pathogen invasion. Pneumococcal-specific IgA antibody (Ab) is key to control infection at the mucosal sites. Ab



GENEL POPÜLASYONA  
GÖRE 30-100 KAT  
YÜKSEK!!!



# Polisakkarit aşı olduđu için sorun yok

- CD4 düzeyinden bağımsız olarak yapılabilir
- Ancak CD4 düşük olanlarda yanıt oranı da düşecektir
- Ama CD4'ün düşüklüğü nedeniyle aşığı ertelememek gereklidir

ORIGINAL ARTICLE

## A Trial of a 7-Valent Pneumococcal Conjugate Vaccine in HIV-Infected Adults

Neil French, Ph.D., F.R.C.P., Stephen B. Gordon, M.D., F.R.C.P.,  
Thandie Mwalukomo, M.B., B.S., Sarah A. White, Ph.D.,  
Gershom Mwafulirwa, Dip.Med.Sci., Herbert Longwe, M.Phil.,  
Martin Mwaiponya, M.B., B.S., Eduard E. Zijlstra, M.D., Ph.D.,  
Malcolm E. Molyneux, M.D., F.R.C.P., and Charles F. Gilks, D.Phil., F.R.C.P.

### RESULTS

From February 2003 through October 2007, we followed 496 patients (of whom 44% were male and 88% were HIV-seropositive) for 798 person-years of observation. There were 67 episodes of pneumococcal disease in 52 patients, all in the HIV-infected subgroup. In 24 patients, there were 19 episodes that were caused by vaccine serotypes and 5 episodes that were caused by the 6A serotype. Of these episodes, 5 occurred in the vaccine group and 19 in the placebo group, for a vaccine efficacy of 74% (95% confidence interval [CI], 30 to 90). There were 73 deaths from any cause in the vaccine group and 63 in the placebo group (hazard ratio in the vaccine group,

*J Infect Dis.* 2015 Jun 1;211(11):1703-11. doi: 10.1093/infdis/jiu819. Epub 2014 Dec 23.

## Quantitative and Qualitative Antibody Responses to Immunization With the Pneumococcal Polysaccharide Vaccine in HIV-Infected Patients After Initiation of Antiretroviral Treatment: Results From a Randomized Clinical Trial.

Rodriguez-Barradas MC<sup>1</sup>, Serpa JA<sup>2</sup>, Munjal I<sup>3</sup>, Mendoza D<sup>1</sup>, Rueda AM<sup>4</sup>, Mushtaq M<sup>4</sup>, Pirofski LA<sup>5</sup>.

### ⊕ Author information

#### Abstract

**BACKGROUND:** Pneumococcal vaccination is recommended for human immunodeficiency virus-infected (HIV+) persons; the best timing for immunization with respect to initiation of antiretroviral therapy (ART) is unknown.

**METHODS:** Double-blind, placebo-controlled trial in HIV+ with CD4(+) T cells/μL (CD4) ≥ 200 randomized to receive the 23-valent pneumococcal polysaccharide vaccine (PPV23) or placebo at enrollment, followed by placebo or PPV23, respectively, 9-12 months later (after ≥6 months of ART). Capsular polysaccharide-specific immunoglobulin (Ig) G and IgM levels to serotypes 1, 3, 4, 6B, and 23F, and opsonophagocytic killing activity (OPA) to serotypes 6B and 23F were evaluated 1 month postvaccination.

**RESULTS:** One hundred seven subjects were enrolled, 72 (67.3%) were evaluable (36/group). Both groups had significant increases in pre- to 1-month postvaccination IgG levels, but negligible to IgM, and significant increases in OPA titers to serotype 6B but not to 23F. There were no significant differences between groups in serotype-specific IgM or IgG levels or OPA titers. For the combined groups, there was a significant correlation between serotype-specific IgG and OPA titers to 23F but not to 6B. There was no correlation between CD4, viral load and IgG responses.

**CONCLUSIONS:** In HIV+ with CD4 ≥ 200, delaying PPV23 until ≥6 months of ART does not improve responses and may lead to missed opportunities for immunization.

Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2014. This work is written by (a) US Government employee(s) and is in the public domain in the US.

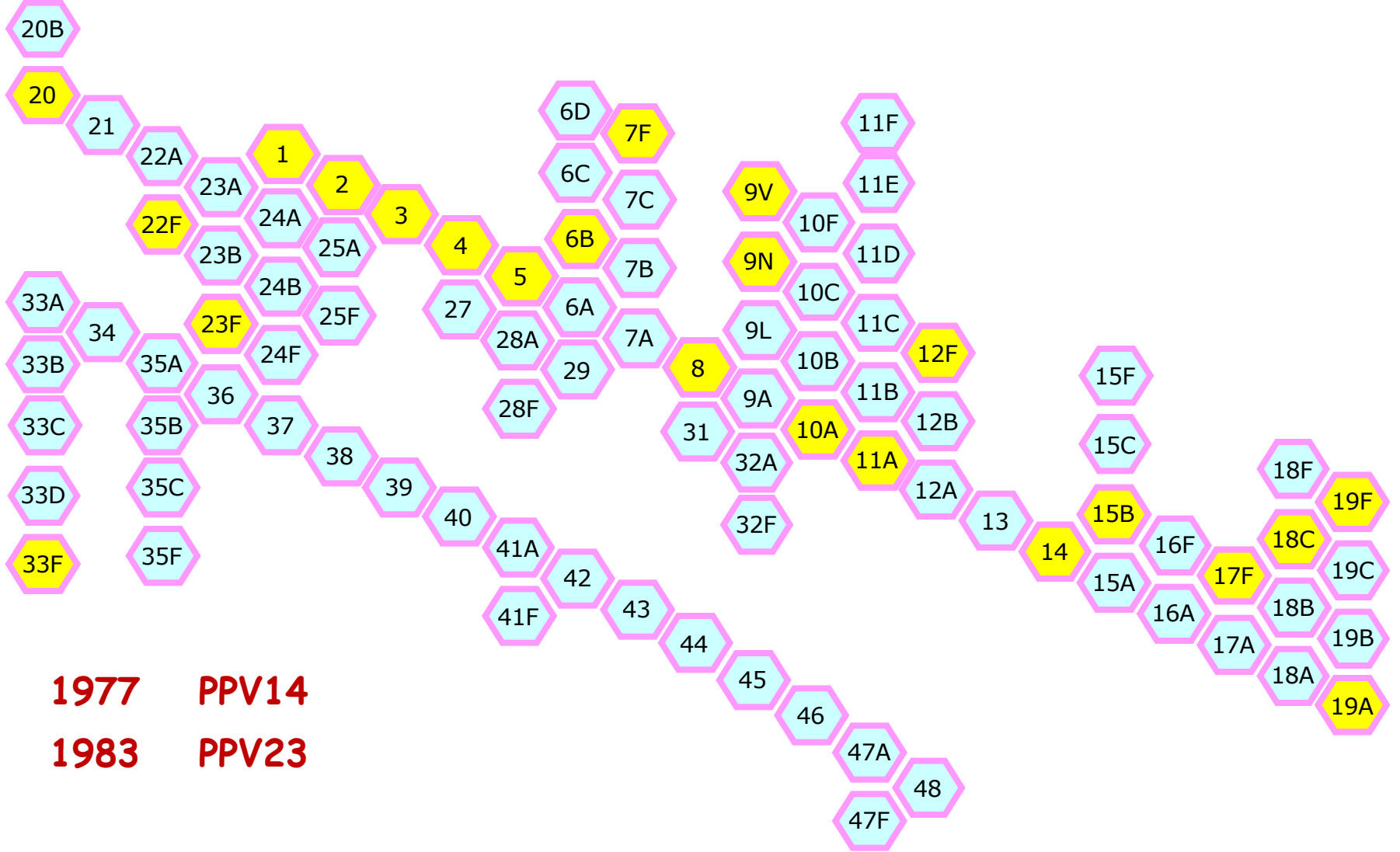
**KEYWORDS:** HIV; antibody; antiretroviral treatment; pneumococcal capsular polysaccharides; pneumococcal vaccine

PMID: 25538270 [PubMed - indexed for MEDLINE] PMCID: PMC4471434 [Available on 2016-06-01]



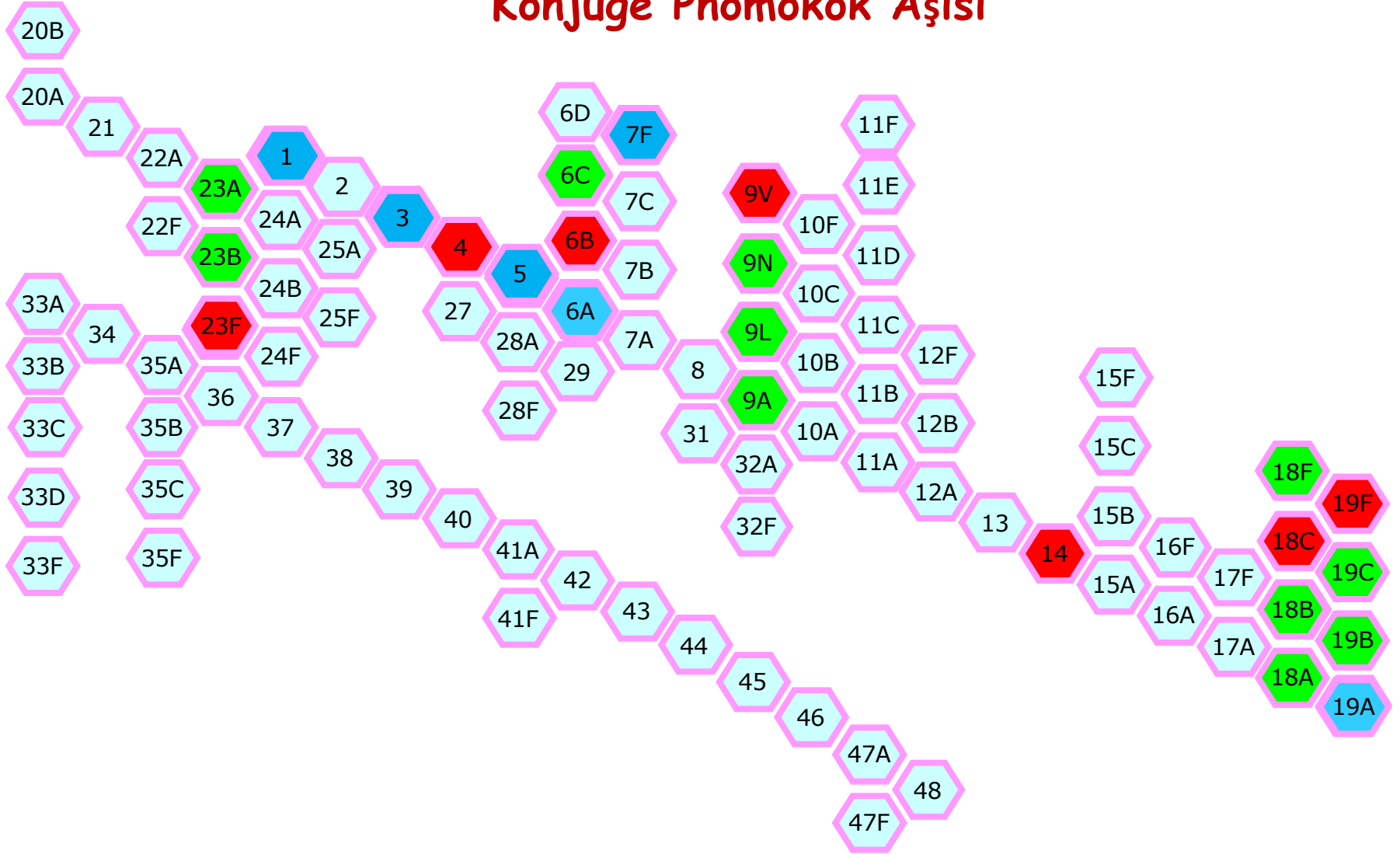
# Pnömonok Serotipleri

## Polisakkarit Aşılar



# Pnömonok Serotipleri

## Konjuge Pnömonok Aşısı

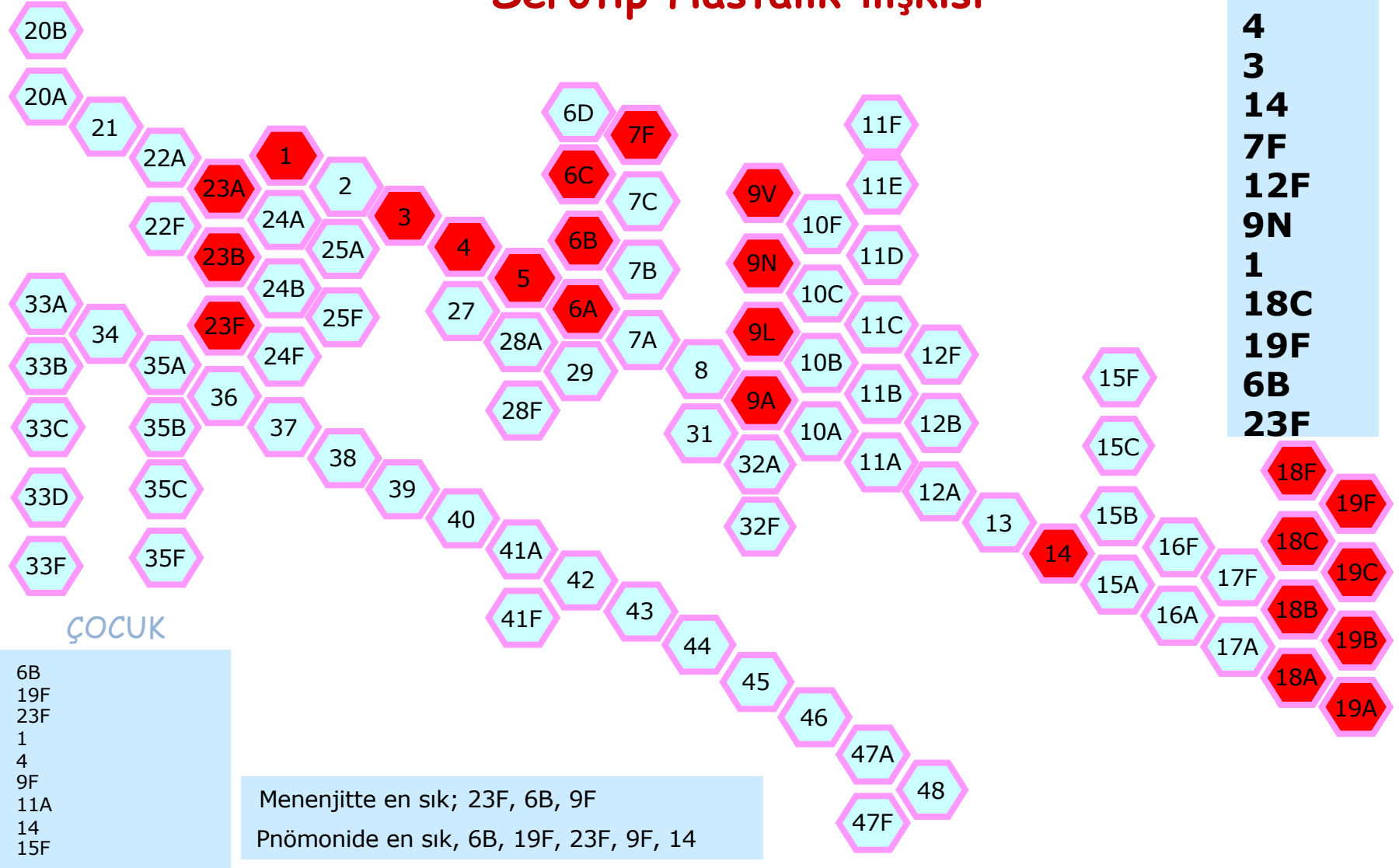




# Pnömonok Serotipleri

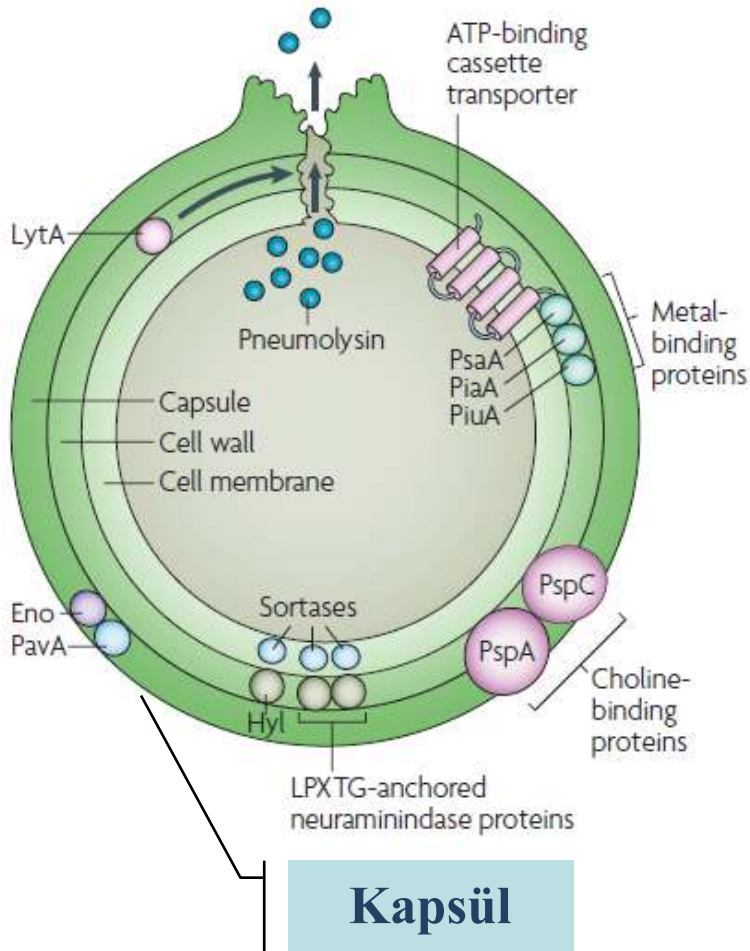
## Serotip Hastalık İlişkisi

ERİŞKİN





# 23-Valanlı Pnömonokokal Polisakkarid Aşı



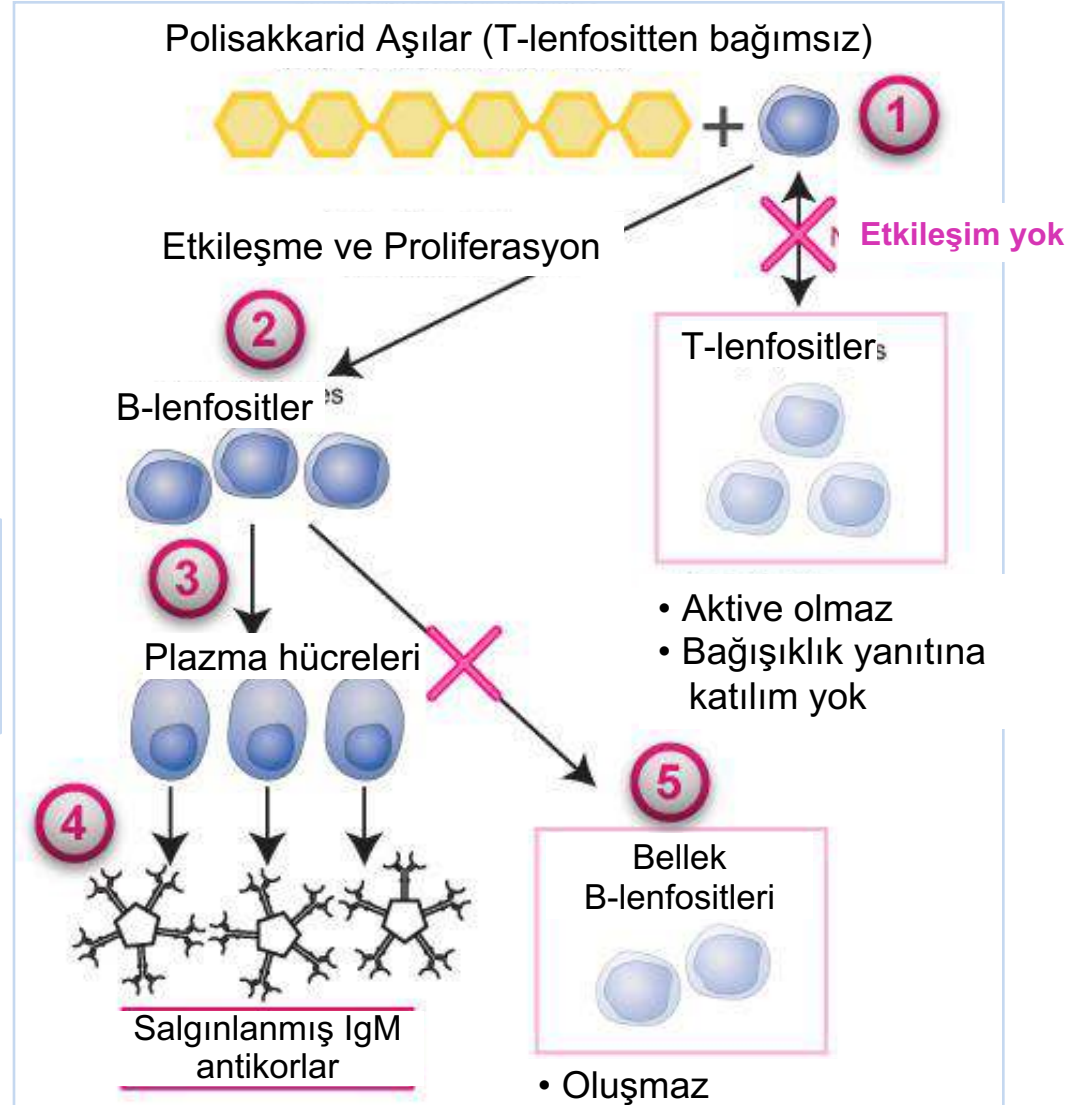
- PPA-23, pnömokokal kapsül polisakkaridlerinin **23 farklı serotipini** içeren bir aşıdır.
- **65 yaş ve üzeri grupta,** ayrıca **2-65 yaş arası risk gruplarında** endikedir.
- 2 yaştan küçük çocuklarda koruma sağlamaz.

# Polisakkarid aşılar bağışıklığı nasıl uyarır? 1-8

## T-lenfositlerle etkileşim yok

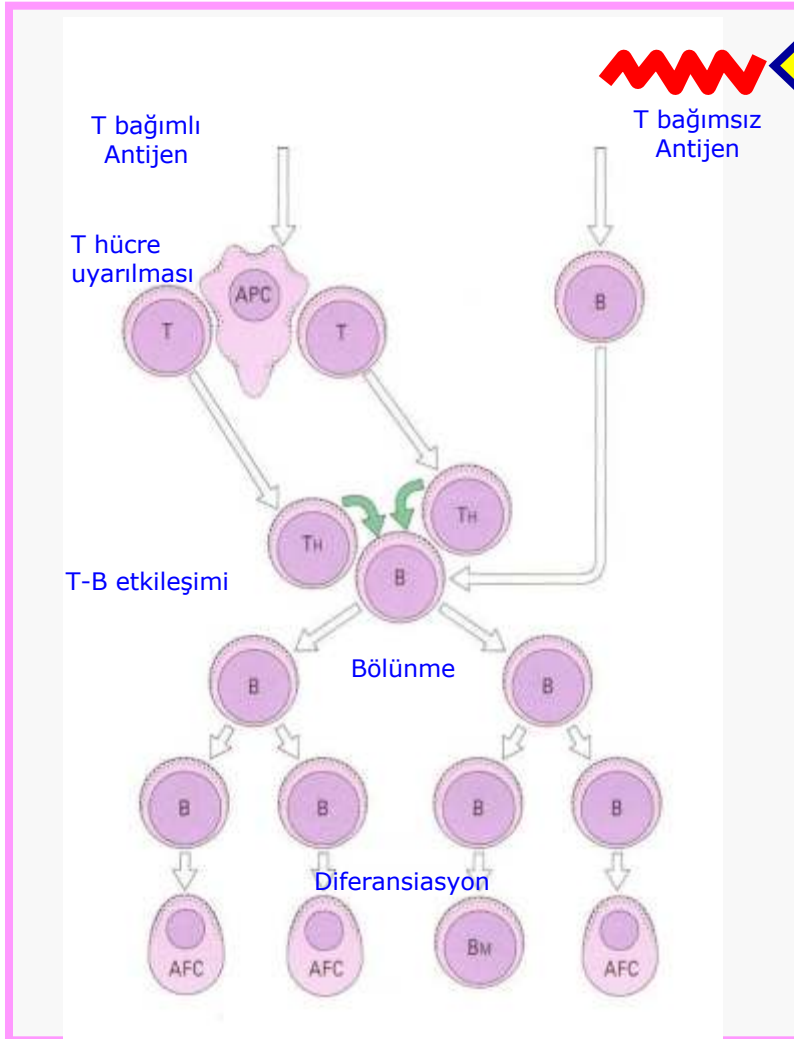
- IgM antikorlar
- Düşük afiniteli antikorlar
- Bağışıklık belleği oluşmaz

< 2 yaş çocuklarda ve yaşlılarda antikor yanıtları genellikle tutarsızdır



# Konjuge Pnömonokok Aşısı

PCV13



T bağımsız yanıtı T bağımlı hale getirir

T-helper hücreleri uyararak 2 yaşından küçüklerde bağışıklık sağlar

Antijenle yeniden karşılaşma güçlü booster yanıtını sağlar

Primer immünizasyonla ömür boyu bağışıklık sağlanabilir

# DİKKAT

- T hücreli bağışıklığı, yani anamnestik yanıtı sağlamak için 13 valanlı konjuge aşı,
- Serogrup kapsayıcılığını arttırmak için ve konjuge aşı sonrası antikor düzeyini arttırmak için de 23 valanlı polisakkarit aşı önerilmekte

# TANI KONDUKTAN SONRA



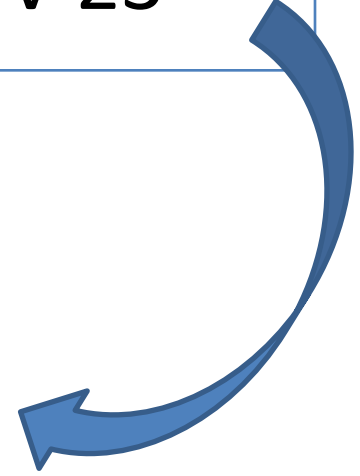
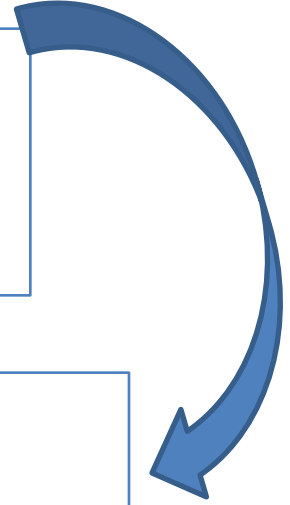
BİR DOZ PCV



SEKİZ HAFTA  
SONRA PPV 23



BEŞ YIL SONRA  
PPSV 23 LE RAPEL

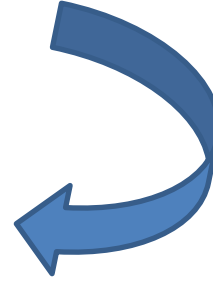




# KİŞİ DAHA ÖNCE PPV23 OLDUYSA



- EN AZ BİR YIL SONRA PCV 13
- BEŞ YIL SONRA RAPEL PPV23





### Recommended for All HIV Positive Adults

Hepatitis B virus (HBV)	Hepatitis B	3 shots over a 6-month period	Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
Influenza	Flu	1 shot	Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. The nasal spray vaccine (FluMist/LAIV) should not be used in this population.
Polysaccharide pneumococcal	Pneumonia	1 or 2 shots	Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is $< 200$ cells/mm <sup>3</sup> when the vaccine is given, immunization should be repeated when CD4 count is $\geq 200$ cells/mm <sup>3</sup> . Repeat one time after 5 years.
Tetanus and Diphtheria Toxoid (Td)	1. Lockjaw 2. Diphtheria	1 shot	Repeat every 10 years.
Tetanus, Diphtheria, and Pertussis (Tdap)	1. Lockjaw 2. Diphtheria 3. Pertussis	1 shot	Recommended for adults 64 years of age or younger and should be given in place of next Td booster. Can be given as soon as 2 years after last Td for persons in close contact with babies under 12 months and health care workers.

# HBV açısından

- Orta düzeyde endemik
- Ortak bulaş yolları
- Mutlaka tanı anında tarama testleri istenmeli
- Kişinin HBV açısından durumu belirlenmelidir

# 20 mcgr rekombinan aşı

- Yanıt oranı kişinin immünitesi ile yakından ilgilidir
- CD4 düzeyi 350'nin üzerinde olanlarda yüksek antikor düzeyleri görülmektedir
- Maalesef yanıt oranları normal popülasyona göre daha düşüktür

# HIV ile Infekte Hastalarda Standard Doz Hepatit B Aşısına Karşı Antikor Yanıtı

*Antibody Response to a Standard Dose of Hepatitis B Vaccine in HIV-Infected Patients*

Ayşe İnci<sup>1</sup>, Muzaffer Fincancı<sup>2</sup>

<sup>1</sup>Artvin Devlet Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, Artvin, Türkiye

<sup>2</sup>İstanbul Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, İstanbul, Türkiye

**Tablo 1. HIV ile Infekte Olgularda Standard Doz Hepatit B Aşısına Yanıt Oranları**

Araştırmacılar	Yıl	Yanıt (%)
Bruguera ve arkadaşları (9)	1992	23.8
Collier ve arkadaşları (10)	2001	37.1
Loke ve arkadaşları (11)	1990	33.3
Rodrigo ve arkadaşları (12)	1992	43.6
Landrum ve arkadaşları (13)	2009	35
Overton ve arkadaşları (14)	2005	17.5
Paitoonpong ve Suankratay (15)	2008	71.4
Tedaldi ve arkadaşları (16)	2004	37.2
Wong ve arkadaşları (17)	1996	42.9
Rey ve arkadaşları (18)	2000	55
Bu çalışma	2010	26.8



# HIV ile Infekte Hastalarda Standard Doz Hepatit B Aşısına Karşı Antikor Yanıtı

*Antibody Response to a Standard Dose of Hepatitis B Vaccine in HIV-Infected Patients*

Ayşe İnci<sup>1</sup>, Muzaffer Fincancı<sup>2</sup>

<sup>1</sup>Artvin Devlet Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, Artvin, Türkiye

<sup>2</sup>İstanbul Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, İstanbul, Türkiye

Çalışmamızda CD4 düzeyinin aşı yanıtını etkilemediği görülmüşken, antikor oluşmayan olguların HIV RNA değerlerinin, antikor oluşturan olgulardan istatistiksel olarak anlamlı derecede daha yüksek olduğu görülmüştür. Konuyla ilgili yapılmış çalışmalara bakıldığında yanıtı ve yanıtı olmayan olgularda CD4 sayısı ve HIV RNA düzeyinin etkili olduğunu bildiren çalışmalar olduğu gibi etkili olmadığını bildiren çalışmalar da vardır.

# Antikor yanıtını arttırmak için

- ÇİFT DOZ AŞI

Vaccine. 2005 Apr 22;23(22):2902-8.

**Randomized trial of recombinant hepatitis B vaccine in HIV-infected adult patients comparing a standard dose to a double dose.**

Fonseca MO<sup>1</sup>, Panq LW, de Paula Cavaleiro N, Barone AA, Heloisa Lopes M.

## Author information

<sup>1</sup>Infectious Diseases Department, University Medical School of São Paulo, Av Dr Eneas de Carvalho Aguiar 500, 100 andar, sala 12, CEP 05403-000 São Paulo, SP, Brazil. marisefonseca@medicina.ufmg.br

## Abstract

Because HIV and hepatitis B virus share many common risk factors, it is important to try to vaccinate HIV patients against hepatitis B. There are numerous reports describing a variety of dose schedules, limited success and markers associated with impaired response to HBV vaccine in these individuals. All studies have been small in size making it difficult to draw conclusions within and between studies. The purpose of this study was to evaluate a double dose of hepatitis B vaccine under more definitive guidelines: double blinded, randomized, controlled, with numbers for statistical validity. Two hundred and ten HIV infected subjects received a standard dose (20 microg) or a double dose (40 microg) of recombinant hepatitis B vaccine IM 0, 1 and 6 months. Ninety-four receiving standard dose and 98 receiving double dose completed the study. The seroconversion rate (anti-HBs > or = 10 mIU/mL) was 47 and 34% for double dose and standard dose, respectively (p = 0.07). A statistically significant higher seroconversion rate was associated with double dose comparing with standard dose for patients with CD4 cell counts > or = 350 cells/mm<sup>3</sup> (64.3% x 39.3%; p = 0.008) but made no difference to seroconversion in those with CD4 <350 (23.8% x 26.3%; p = 0.80). Double dose also improved seroconversion comparing with standard dose for patients with HIV viral load <10,000 copies/mL (58.3% x 37.3%; p = 0.01) but made no difference to seroconversion in those with HIV viral load > or = 10,000 copies/mL (16% x 17%; p = 0.7). Based on the results of this study, the best current strategy for hepatitis B vaccination in HIV patients would be to use a double dose as a primary series when the viral load is likely to be low and CD4 > or = 350, when there is likely to be an adequate immune response.

- ÜÇ KEZ ÇİFT DOZ AŞI
- %34 TEN %47 YE



## Abstract

Because HIV and hepatitis B virus share many common risk factors, it is important to try to vaccinate HIV patients against hepatitis B. There are numerous reports describing a variety of dose schedules, limited success and markers associated with impaired response to HBV vaccine in these individuals. All studies have been small in size making it difficult to draw conclusions within and between studies. The purpose of this study was to evaluate a double dose of hepatitis B vaccine under more definitive guidelines: double blinded, randomized, controlled, with numbers for statistical validity. Two hundred and ten HIV infected subjects received a standard dose (20 microg) or a double dose (40 microg) of recombinant hepatitis B vaccine IM 0, 1 and 6 months. Ninety-four receiving standard dose and 98 receiving double dose completed the study. The seroconversion rate (anti-HBs  $\geq$  10 mIU/mL) was 47 and 34% for double dose and standard dose, respectively ( $p = 0.07$ ). A statistically significant higher seroconversion rate was associated with double dose comparing with standard dose for patients with CD4 cell counts  $\geq$  350 cells/mm<sup>3</sup> (64.3% x 39.3%;  $p = 0.008$ ) but made no difference to seroconversion in those with CD4 <350 (23.8% x 26.3%;  $p = 0.80$ ). Double dose also improved seroconversion comparing with standard dose for patients with HIV viral load <10,000 copies/mL (58.3% x 37.3%;  $p = 0.01$ ) but made no difference to seroconversion in those with HIV viral load  $\geq$  10,000 copies/mL (16% x 17%;  $p = 0.7$ ). Based on the results of this study, the best current strategy for hepatitis B vaccination in HIV patients would be to use a double dose as a primary series when the viral load is likely to be low and CD4  $\geq$  350, when there is likely to be an adequate immune response.

# Antikor yanıtını arttırmak için ÇİFT DOZ , DÖRT VE ÜZERİ SERİ

Original Contribution | April 13, 2011

## **Safety and Immunogenicity of 4 Intramuscular Double Doses and 4 Intradermal Low Doses vs Standard Hepatitis B Vaccine Regimen in Adults With HIV-1**

**A Randomized Controlled Trial** FREE

Odile Launay, MD, PhD; Diane van der Vliet, MD; Arielle R. Rosenberg, MD, PhD; Marie-Louise Michel, PhD; Lionel Piroth, MD, PhD; David Rey, MD; Nathalie Colin de Verdière, MD; Laurence Slama, MD; Karine Martin, PhD; Olivier Lortholary, MD, PhD; Fabrice Carrat, MD, PhD; for the ANRS HB03 VIH-VAC-B Trial

[\[+\] Author Affiliations](#)

JAMA. 2011;305(14):1432-1440. doi:10.1001/jama.2011.351.

Text Size: [A](#) [A](#) [A](#)



(anti-HBs) of at least 10 mIU/mL in patients who received at least 1 dose of vaccine. Patients with missing anti-HBs titer measurement at the final follow-up visit at week 28 were considered as nonresponders in the primary (efficacy) analysis.

**RESULTS:** A total of 437 patients were randomized to the 3 study groups, of whom 11 did not receive any vaccine. Of these, 396 had available anti-HBs titers at week 28. The percentage of responders at week 28 was 65% (95% confidence interval [CI], 56%-72%) in the IM20 × 3 group (n = 91), 82% (95% CI, 77%-88%) in the IM40 × 4 group (n = 119) (P < .001 vs IM20 × 3 group), and 77% (95% CI, 69%-84%) in the ID4 × 4 group (n = 108) (P = .02 vs IM20 × 3 group). No safety signal and no effect on CD4 cell count or viral load were observed.

**CONCLUSION:** In adults with HIV-1, both the 4 intramuscular double-dose regimen and the 4 intradermal low-dose regimen improved serological response compared with the standard HBV vaccine regimen.

**TRIAL REGISTRATION:** [clinicaltrials.gov/ct2/show/study/NCT00480702](https://clinicaltrials.gov/ct2/show/study/NCT00480702)

**3 KEZ TEK DOZ IM AŞI İLE %65**

**4 KEZ ÇİFT DOZ IM AŞI İLE %82**

**4 KEZ TEK DOZ ID AŞI İLE %77**



Full Text (PDF)

**Does increased hepatitis B vaccination dose lead to a better immune response in HIV-infected patients than standard dose vaccination: a meta-analysis?**

*Int J STD AIDS* February 2013 24: 117-122,  
first published on April 30, 2013

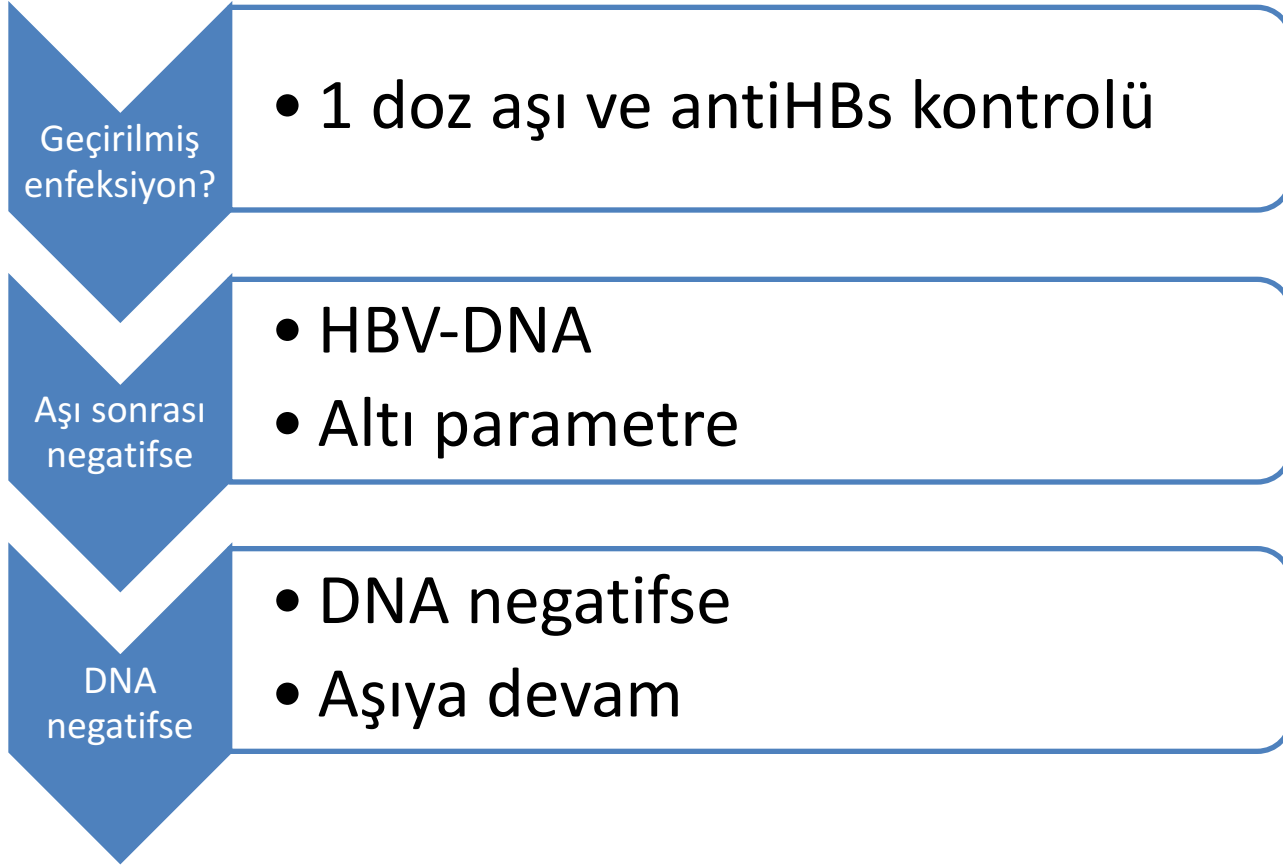
- 883 HIV(+) hasta
- Meta analiz
- Yüksek doz ile yanıt oranlarının daha yükseldiğini belirtiyor



# Yanıt oranları böyle olduğuna göre

- Aşılama sonrası antiHBs kontrolü yapalım mı?
- Ne zaman?
- Negatif çıkarsa ne yapalım?
- Adjuvan kullanımını ile ilgili yeterli veri yok

# Salt antiHBc olumluluđu



**ANAMNESTİK YANITIN MAALESEF % 16-48  
OLDUĐUNU AKILDA TUTALIM**

# AŐIYI YAPTIK, KORUYUCU TİTRE VAR

- Bu titre dűőer mi?
- Ne zaman ne kadar dűőer?
- Kontrol edelim mi?
- Rapel yapalım mı?

# ÇALIŞMALARA İHTİYAÇ VAR

- Genel popülasyonda 20 yıl sonra yapılan testlerde koruyuculuk %44
- Anamnestic yanıt %97
- HIV (+) hastalarda ?



# HEPATİTE GİRMİŞKEN

- HEPATİT A AŞISI, İNAKTİVE VİRÜS
- 1440 iu/MI
- MSM
- IV uyuşturucu
- Karaciğer hastalıkları
- Endemik bölgeye gidiş



**DUYARLI  
OLAN  
HERKESE  
YAPALIM**



- Tarama yapalım mı?
- 1440 iu/mL, 0,6 veya 12. aylar
- Serokonversiyon oranı %68-100

# Safety and Immunogenicity of an Inactivated Hepatitis A Vaccine among HIV-Infected Subjects

Mark R. Wallace,<sup>1</sup> Carolyn J. Brandt,<sup>1</sup> Kenneth C. Earhart,<sup>1</sup> Barbara J. Kuter,<sup>2</sup> Anthony D. Grosso,<sup>2</sup> Hassan Lakkis,<sup>2</sup> and Sybil A. Tasker<sup>1</sup>

<sup>1</sup>Naval Medical Center San Diego, San Diego, California, and <sup>2</sup>Merck, West Point, Pennsylvania

**Methods.** Ninety HIV-uninfected **99 HIV(-), 90 HIV (+) HASTA** vaccine (VAQTA; Merck), and 90 HIV-infected subjects were randomized, in double-blind fashion, to receive either the vaccine or placebo. The HIV-infected subjects were stratified by CD4 cell count, with 45 subjects having CD4 cell counts of  $\geq 300$  cells/mm<sup>3</sup> and 45 subjects having CD4 cell counts of  $< 300$  cells/mm<sup>3</sup>. Vaccine was given at weeks 0 and 24 of the study.

**Results.** Seroconversion rates at week 28 of the study were 94% among the HIV-infected subjects and 100% **90 HIV (+) HASTA SEROKONVERSIYON %94** infected subjects with CD4 cell counts of  $< 300$  cells/mm<sup>3</sup> had a **CD4  $\leq 300$  İSE %87** and HIV-infected subjects with CD4 cell counts of  $\geq 300$  cells/mm<sup>3</sup> had a seroconversion rate of 100%. The vaccine was well tolerated, and no adverse effect on either HIV load or CD4 cell count was found. **CD4  $\geq 300$  İSE %100**

**Conclusion.** Hepatitis A vaccine was both immunogenic and safe among HIV-infected subjects.

# Aşı kontrolü?

- Son aşıdan bir ay sonra kontrol edelim
- Negatifse yeniden aşılayalım
- Kaç doz?

# HEPATİT A İÇİN



Tablo 14. Erişkinlerde risk gruplarına göre 2016 aşı önerileri (ÖZET TABLO)

Aşı	KHN <sup>1</sup>	İmm. Komp. Hasta.	Aspleni <sup>2</sup>	SOT <sup>3</sup>	Romato. hast. <sup>4</sup>	HIV enf. <sup>5</sup> (CD4<200 /mm <sup>3</sup> )	HIV enf. <sup>5</sup> (CD4≥200 /mm <sup>3</sup> )	Sağlık çalışanı <sup>6</sup>	Gebe <sup>7</sup>
Td/Tdap	Green	Green	Green	Green	Green	Green	Green	Green	Green
İnfluenza	Green	Green	Green	Green	Green	Green	Green	Green	Green
PCV13	Green	Green	Green	Green	Green	Green	Green	Yellow	Yellow
PPSV23	Green	Green	Green	Green	Green	Green	Green	Green	Green
Hepatit B	Green	Green	Yellow	Green	Green	Green	Green	Green	Green
Hepatit A	Green	Green	Green	Green	Green	Green	Green	Green	Yellow
Zoster	Green	Red	Yellow	Green	Red	Red	Yellow	Yellow	Red
Suçiçeği	Green	Red	Yellow	Green	Red	Red	Yellow	Green	Red
KKK	Red	Red	Yellow	Green	Red	Red	Yellow	Green	Red
Meningokok	Yellow	Yellow	Green	Green	Yellow	Yellow	Yellow	Green	Yellow
Hib	Green	Green	Green	Green	Yellow	Yellow	Yellow	Green	Green
HPV	Green	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Green	Green

# Rutin aşılardan sonuncusu

Recommended for All HIV Positive Adults			
Hepatitis B virus (HBV)	Hepatitis B	3 shots over a 6-month period	Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
Influenza	Flu	1 shot	Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. The nasal spray vaccine (FluMist/LAIV) should not be used in this population.
Polysaccharide pneumococcal	Pneumonia	1 or 2 shots	Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is $< 200$ cells/mm <sup>3</sup> when the vaccine is given, immunization should be repeated when CD4 count is $> 200$ cells/mm <sup>3</sup> . Repeat one time after 5 years.
Tetanus and Diphtheria Toxoid (Td)	1. Lockjaw 2. Diphtheria	1 shot	Repeat every 10 years.
Tetanus, Diphtheria, and Pertussis (Tdap)	1. Lockjaw 2. Diphtheria 3. Pertussis	1 shot	Recommended for adults 64 years of age or younger and should be given in place of next Td booster. Can be given as soon as 2 years after last Td for persons in close contact with babies under 12 months and health care workers.

# Td/TdaP

- Tetanoz
- Difteri
- Asellüler boğmaca
  
- Aslında genel popülasyonla aynı
- Aşılama öyküsü yoksa 0,1,6-12
- 10 yılda bir rapel
- Rapellerden birisinin TdaP olması gerekli



## Antibody response to diphtheria, tetanus, and poliomyelitis vaccines in relation to the number of CD4+ T lymphocytes in adults infected with human immunodeficiency virus.

Kroon FP<sup>1</sup>, van Dissel JT, Labadie J, van Loon AM, van Furth R.

### Author information

<sup>1</sup>Department of Infectious Diseases, University Hospital Leiden, The Netherlands.

### Abstract

A prospective study of antibody production by adults infected with human immunodeficiency virus (HIV) after vaccination with T lymphocyte-dependent diphtheria toxoid, tetanus toxoid, and inactivated trivalent poliovirus vaccine was conducted. Individuals were divided into three groups according to CD4+ T-lymphocyte count: group 1 had a count of  $\leq 100-300 \times 10^6/L$ ; and group 3,  $> 300 \times 10^6/L$ . After vaccination, 61%, 70%, and 73% of the individuals in groups 1, 2, and 3, respectively, developed protective titers of antibody to diphtheria toxin; the mean postvaccination antibody titer of HIV-infected individuals was significantly lower than that of healthy controls not infected with HIV. Furthermore, the mean titers of antibodies to tetanus toxin and poliovirus were significantly lower in HIV-infected individuals with CD4+ lymphocyte counts of  $< 300 \times 10^6/L$  against tetanus and 78%-100% against polio. V

**Tdap İLE İLGİLİ VERİ YOK**

(secondary) antibody response after receipt of T lymphocyte-dependent vaccines.



# RİSK DURUMUNDA YAPILMASI GEREKLİ AŞILAR

- Human papilloma virüsü aşısı
- Meningokok aşısı
- MMR
- Varisella
- Seyahat ile ilgili aşılar


# Human Papilloma Virüs aşısı

AIDS PATIENT CARE and STDs  
Volume 28, Number 8, 2014  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/apc.2014.0121

CLINICAL AND EPIDEMIOLOGIC RESEARCH

## Vaccination in HIV-Infected Adults

Nancy F. Crum-Cianflone, MD, MPH<sup>1,2</sup> and Mark R. Wallace, MD<sup>3</sup>

- HIV(+) hastalarda HPV enfeksiyonu için risk 
- Aşı konjuge 2 ve 4 valanlı
- Dokuz valanlı yakında



## Distribution of human papillomavirus genotypes, assessment of HPV 16 and 18 viral load and anal related lesions in HIV positive patients: a cross-sectional analysis.

Tamalet C<sup>1</sup>, Obry-Roquet V, Ressiot E, Bregigeeon S, Del Grande J, Poizot-Martin I.

### ⊕ Author information

#### Abstract

Natural history of anal intraepithelial neoplasia and anal cancer is not fully understood. Factors associated with cytological abnormalities and predictors of progression to high-grade anal intraepithelial neoplasia still deserve investigation. The aim of this cross-sectional study was to assess the prevalence of HPV types, the relationship between HPV genotypes, HPV 16/18 viral load and cytological abnormalities in male and female HIV-infected patients. One hundred and twenty-two (72.6%) patients were infected with HPV, 75 (61%) had multiple HPV infection, and 94 (77%) had high-risk HPV infection. The most frequently identified HPV types were HPV 16 (64%), HPV 6 (39%), HPV 18 (31%), HPV 53 (14.7%), HPV 33 (10.6%), HPV 11 (8.2%), HPV 70 (5.7%), and HPV 64 (4.9%). The HPV types which were most frequently found in combination were HPV 6 + 16 (9.8%), 6 + 16 + 18 (8.2%), 16 + 18 (6.6%), 6 + 18 (4.9%), 16 + 33 (3.3%), 16 + 53 (3.2%). Median HPV16 and 18 viral loads were 6.1 log<sub>10</sub> copies/10(6) cells [IQR 5.0-7.3] and 6.1 log<sub>10</sub> copies/10(6) cells [IQR 5.7-6.0], respectively. Male gender (P = 0.03, OR: 1.2 [1.0-1.4]) and homo/bisexual transmission routes (P = 0.044, OR: 1.4 [1.0-1.9]) were associated with HPV 16 infection. An HPV 16 viral load cut-off  $\geq 5.3$  log<sub>10</sub> copies/10(6) cells and a CD4+ cell count  $\leq 200/\mu\text{l}$  were independent factors associated with abnormal cytology. In the absence of national consensus guidelines, a strict regular follow-up at shorter intervals is recommended for HIV-infected patients with abnormal cytology, especially low grade squamous intraepithelial lesions, an HPV 16 viral load  $\geq 5.3$  log/10(6) cells and a CD4+ cell count  $\leq 200/\mu\text{l}$ .

© 2013 Wiley Periodicals, Inc.

- Hastaların %77'sinin HPV enfeksiyonu için yüksek risk faktörü var
- En sık saptanan serotipler 16, 6, 18, 53, 33

# Öneriler

- Aşı öncesi test önerilmiyor
- Zaten hastalık bulgusu (genital siğil, anormal sitoloji, HPV-DNA pozitifliği gibi) olması aşı olmaya kontrendikasyon yaratmıyor
- 0,1-2, 6.aylar öneriliyor
- Cinsel aktif çağ öncesi olması en iyi



# Koruyuculuk

- HIV(-) >%95
- HIV(+)
  - Adölesan >%96
  - Adult kadın %92-100
  - Adult erkek > %95

Levin MJ, Moscicki AB, Song LY, et al. Safety and immunogenicity of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine in HIV-infected children 7 to 12 years old. *J Acquir Immune Defic Syndr* 2010; 55:197-204.

Kahn JA, Xu J, Kapogiannis BG, Rudy B, Gonin R, Liu N, Wilson CM, Worrell C, Squires KE. Immunogenicity and safety of the human papillomavirus 6, 11, 16, 18 vaccine in HIV-infected young women. *Clin Infect Dis* 2013;57:735-744.

# YAN ETKİ

Vaccine 32 (2014) 5657–5661

Contents lists available at [ScienceDirect](#)

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)



## Safety and immunogenicity of a quadrivalent human papillomavirus vaccine in HIV-infected and HIV-negative subjects and young adults

Vania Giacomet<sup>a</sup>, Francesca Penagini<sup>a</sup>, Daria Trabattini<sup>a</sup>, Veronica Rainone<sup>b</sup>, Giada Bernazzani<sup>a</sup>, Claudia Marziano<sup>c</sup>, Giorgio Bedogni<sup>d</sup>, Gian Vincenzo Zucotti<sup>a</sup>

**Table 2**

Cumulative incidence of side effects as detected immediately after the administration of the first, second and third vaccine dose in HIV-infected (HIV+) and HIV-negative (HIV–) subjects.

	HIV– N (%)	HIV+ N (%)
<b>Local</b>		
Pain	26 (18.8)	46 (32.6)
Erythema	8 (5.8)	16 (11.3)
Edema	10 (7.2)	11 (7.8)
Induration	14 (10.1)	18 (12.8)
<b>Systemic</b>		
Fever	0 (0)	4 (2.8)
Malaise	2 (1.4)	10 (7.1)
Headache	3 (2.2)	19 (13.5)

# HPV İÇİN

CSIRO PUBLISHING

*Sexual Health*, 2014, 11, 511–523

<http://dx.doi.org/10.1071/SH14015>

Re

## Vaccination against oncogenic human papillomavirus infection in HIV-infected populations: review of current status and future perspectives

*Lars Toft<sup>A,B</sup>, Martin Tolstrup<sup>A</sup>, Merete Storgaard<sup>A</sup>, Lars Østergaard<sup>A</sup> and Ole S. Søgaard<sup>A</sup>*

<sup>A</sup>Department of Infectious Diseases, Aarhus University Hospital, Skejby, 8200 Aarhus, Denmark.

<sup>B</sup>Corresponding author. Email: [larsnise@rm.dk](mailto:larsnise@rm.dk)

- 463 MAKALENİN İRDELENDİĞİ META-ANALİZ
- 3263 HIV(+) HASTA

## Conclusions

Based on the current available knowledge reviewed in this paper, both HPV vaccines appear to be safe and highly immunogenic in people infected with HIV. In the light of their high risk of HPV-associated cancers, recommending HPV vaccination in HIV-positive individuals of both sexes up to the age of 26 years seems to be very reasonable. Furthermore, it may also be justified to recommend HPV vaccination in HIV-infected women aged 26–45 but the expected vaccine efficacy would be less than among younger women. Finally, HPV vaccination of HIV-infected women before surgical treatment of precancerous cervical lesions may be justified. The current data strongly suggest that HPV vaccination induces protective immunity against vaccine-specific HPV infection in persons with HIV.



# MENİNGOKOK AŞISI

- 4 valanlı Konjuge aşı
- Polisakkarit aşı
- Çocukluk aşıları içinde
- Yurttan kalma
- Aspleni
- Kompleman eksiklikleri
- Endemik bölgeye seyahat
- Meningokoklarla çalışma



Centers for Disease Control and Prevention (CDC). Notes from the field: Serogroup C invasive meningococcal disease among men who have sex with men — New York City, 2010–2012. *MMWR Morb Mortal Wkly Rep* 2013 Jan 4; 61:1048. (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6151a4.htm>)

[PubMed abstract \(Free\)](#)

- New-York
- Ağustos 2010- Aralık 2012
- 18 olgu (12'si 2012'de, 10'u HIV(+), 5'i ex)
- Normalde yüzde 0.16
- MSM yüzde 12.6 !!!



# MMR

- Canlı, atenüe aşı
- CD4 200'ün altındaysa kontrendike!
- İhtiyaç var mı?
- HIV(+) hastalarda kızamık mortalitesi yüksek



## High need for MMR vaccination in HIV infected adults in Austria

K. Grabmeier-Pfistershammer<sup>a,\*,4</sup>, W. Poeppl<sup>b</sup>, H. Herkner<sup>c</sup>, V. Touzeau-Roemer<sup>a</sup>,  
Emilia Huschka<sup>a</sup>, A. Rieger<sup>a</sup>, H. Burgmann<sup>b</sup>

<sup>a</sup> Division of Immunology, Allergy and Infectious Diseases, Department of Dermatology, Medical University Vienna, Austria

<sup>b</sup> Division of Infectious Diseases and Tropical Medicine, Department of Medicine I, Medical University of Vienna, Austria

<sup>c</sup> Department of Emergency Medicine, Medical University of Vienna, Austria

Current guidelines recommend screening for HIV infected patients susceptible for vaccine preventable diseases and offering of immunization. However, data regarding the vaccination coverage among this group are largely missing. This study analyzed the serostatus for Measles, Mumps and Rubella of more than 700 HIV infected patients residing in Austria. These patients were representative for the Austrian HIV cohort regarding sex, age, transmission risk and HIV progression markers. 73.6% were on suppressive HAART, mean CD4 cell count was 603 c/μl. Seronegativity was 8.4% for Measles, 33.4% for Mumps and 18.8% for Rubella. In total, out of the 713 HIV infected adults analyzed, almost half (47.8%) would require MMR vaccination. In a multivariate analysis migration was significantly associated with seronegativity for Measles (OR 0.5, CI 0.27–0.9) and Mumps (OR 0.57, CI 0.39–0.81). Importantly due to the well preserved immune status of nearly all participants vaccination would be feasible in the majority of the seronegative patients. Thus, a proactive approach would largely reduce the number of patients at risk for vaccine-preventable diseases.

Figure 2. Vaccines that might be indicated for adults based on medical and other indications<sup>1</sup>

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) <sup>4,6,7,8,11</sup>	HIV infection CD4+ T lymphocyte count <sup>4,6,7,8,11</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) <sup>4,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel
				< 200 cells/µL	≥ 200 cells/µL							
Influenza <sup>2,3</sup>		1 dose IIV annually				1 dose IIV or LRV annually	1 dose IIV annually					
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>2,3</sup>	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs										
Varicella <sup>2,4</sup>		Contraindicated					2 doses					
Human papillomavirus (HPV) Female <sup>2,5</sup>		3 doses through age 26 yrs					3 doses through age 26 yrs					
Human papillomavirus (HPV) Male <sup>2,5</sup>		3 doses through age 26 yrs					3 doses through age 21 yrs					
Zoster <sup>6</sup>		Contraindicated					1 dose					
Measles, mumps, rubella (MMR) <sup>2,7</sup>		Contraindicated					1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13) <sup>2,8</sup>							1 dose					
Pneumococcal polysaccharide (PPSV23) <sup>8</sup>							1 or 2 doses					
Meningococcal <sup>2,9</sup>		1 or more doses										

Aşıya yanıt %81

# VARİSELLA AŞISI

- Canlı atenüe aşı
- CD4 ü <200 olanlarda kontrendike
- HIV (+) hastalarda artmış risk sözkonusu
- Kontrol edildiğinde bizde çoğu hasta geçirmiş
- Ancak seroloji negatifse



# SU ÇIÇEĞİ

National Institutes of Health

Advanced

Abstract ▾

Send to: ▾

[AIDS Res Hum Retroviruses](#). 2007 Jun;23(6):782-93.

## Evaluation of modified vaccinia virus Ankara as an alternative vaccine against smallpox in chronically HIV type 1-infected individuals undergoing HAART.

[Cosma A<sup>1</sup>](#), [Naqaraj R](#), [Staib C](#), [Diemer C](#), [Wopfner F](#), [Schätzl H](#), [Busch DH](#), [Sutter G](#), [Goebel FD](#), [Erflie V](#).

### ⊕ Author information

#### Abstract

The fear of malevolent use of variola virus by terrorists has led to the implementation of a health care worker vaccination program and to the consideration of vaccination for the general public. However, due to concerns about side effects of the classical smallpox vaccine, especially for immunocompromised individuals, a safer vaccine is urgently needed. We characterized the immunogenicity of modified vaccinia virus Ankara (MVA), one of the more promising alternative smallpox vaccines, in a cohort of 10 chronically HIV-1-infected individuals undergoing highly active antiretroviral therapy (HAART). Nine subjects received smallpox vaccination as children while one subject was never vaccinated against smallpox. All the subjects had CD4 counts >400 cells/mm<sup>3</sup> and 8 out of 10 had undetectable viral loads. MVA was able to elicit humoral and cellular immune responses in the majority of individuals. Vaccinia-specific antibodies were maintained over 1 year. Similar vaccine responses were maintained over 1 year. Similar vaccine responses in HIV-1-infected individuals was compared to smallpox-vaccinated healthy individuals. MVA could be used as a substitute vaccine against smallpox in chronically HIV-1-infected individuals with CD4 counts >400 cells/mm<sup>3</sup>.

PMID: 17604541 [PubMed - indexed for MEDLINE]



**Serolojisi negatif olan 10 hastaya  
2 doz aşı yapılmış (8 hasta  
çocukluğunda aşılanmış)  
CD4 düzeyleri>400**

Figure 2. Vaccines that might be indicated for adults based on medical and other indications<sup>1</sup>

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) <sup>4,6,7,8,11</sup>	HIV infection CD4+ T lymphocyte count <sup>4,6,7,8,11</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) <sup>4,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel
				< 200 cells/μL	≥ 200 cells/μL							
Influenza <sup>7,8</sup>			1 dose IIV annually			1 dose IIV or LAIV annually		1 dose IIV annually				1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>7,8</sup>	1 dose Tdap each pregnancy		Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella <sup>7,8</sup>		Contraindicated										2 doses
Human papillomavirus (HPV) Female <sup>7,8</sup>			3 doses through age 26 yrs					3 doses through age 26 yrs				
Human papillomavirus (HPV) Male <sup>7,8</sup>			3 doses through age 26 yrs					3 doses through age 21 yrs				
Zoster <sup>6</sup>		Contraindicated						1 dose				
Measles, mumps, rubella (MMR) <sup>7,8</sup>		Contraindicated						1 or 2 doses				
Pneumococcal 13-valent conjugate (PCV13) <sup>7,8</sup>							1 dose					

- 8 hafta arayla 2 doz (3 ay ?)
- Anti-herpetik ilaçlar -1 ila 14 gün sonlandırılmalı
- Klinik veri yok, ancak koruyuculuğu iyi

# ZOSTER AŞISI

Figure 2. Vaccines that might be indicated for adults based on medical and other indications<sup>1</sup>

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) <sup>6,7,8,11</sup>	HIV infection CD4+ T lymphocyte count <sup>6,7,8,11</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) <sup>8,12</sup>	Chronic liver disease	Diabetes	Healthcare personnel
				< 200 cells/µL	≥ 200 cells/µL							
Influenza <sup>2</sup>			1 dose IIV annually				1 dose IIV or LAVV annually	1 dose IIV annually				1 dose IIV or LAVV annually
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>7,8</sup>		1 dose Tdap each pregnancy	Substitute 1 time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella <sup>4</sup>		Contraindicated					2 doses					
Human papillomavirus (HPV) Female <sup>5</sup>			3 doses through age 26 yrs					3 doses through age 26 yrs				
Human papillomavirus (HPV) Male <sup>5</sup>			3 doses through age 26 yrs					3 doses through age 21 yrs				
Zoster <sup>6</sup>		Contraindicated					1 dose					
Measles, mumps, rubella (MMR) <sup>7,8</sup>		Contraindicated					1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13) <sup>7,8</sup>								1 dose				
Pneumococcal polysaccharide (PPSV23) <sup>8</sup>								1 or 2 doses				
Meningococcal <sup>9</sup>								1 or more doses				
Hepatitis A <sup>10</sup>								2 doses				
Hepatitis B <sup>11</sup>								3 doses				
<i>Haemophilus influenzae</i> type b (Hib) <sup>12</sup>			post-HSCT recipients only					1 or 3 doses				

<sup>1</sup>Covered by the Vaccine Injury Compensation Program



For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster



Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)



No recommendation





Online Expert Poster Review and Discussion

ARV Therapies and Therapeutic Strategies

*Reporting From*

The 19th Conference on Retroviruses  
and Opportunistic Infections (CROI)

JOINTLY SPONSORED BY THE POSTGRADUATE INSTITUTE FOR MEDICINE AND VIRALeD, LLC

**Zostavax<sup>®</sup> is Generally Safe and Immunogenic in HIV-  
Infected Adults with CD4 Counts  $\geq 200$  Cells/ $\mu$ L  
Virologically Suppressed on ART: Results of a Phase 2,  
Randomized, Placebo-Controlled Trial**

CA Benson, L Hua, JW Anderson, JH Jiang, DR Bozzolo, K Bergstrom, PW Annunziato, SW  
Read, R Pollard, D Rusin, J Lennox

for the ACTG A5247 Team

Abstract #96



## A5247 Study Design



- Multicenter (43 sites), double-blind, randomized (3:1), placebo-controlled safety, tolerability and immunogenicity study (N=395) of 2 doses of ZV administered on day 0 and at week 6
- **Inclusion Criteria:**
  - HIV-infected person age  $\geq 18$  years on stable ART; undetectable plasma HIV RNA; CD4  $\geq 200$  cells/ $\mu$ L
  - Hemoglobin  $\geq 7.0$  gm/dL; platelet count  $\geq 50,000$ / $\mu$ L; creatinine  $\leq 3$  x ULN; AST, ALT and alkaline phosphatase  $\leq 5$  x ULN
  - History of varicella or HZ  $>1$  year prior to entry or VZV seropositive at any time prior to entry

# A5247 Primary Safety Results

	ZV (N=295) N (Estimate % [95% CI])	Placebo (N=97) N (Estimate % [95% CI])	p-Value**
Primary Safety Endpoints	15 5.1% [2.9, 8.2]*	2 2.1% [0.3, 7.3]	0.261
Injection Site Reactions	124 42.0% [36.3, 47.9]	12 12.4% [6.6, 20.6]	<0.001
Rash	15 5.1% [2.9, 8.2]	4 4.1% [1.1, 10.2]	1.00
Fever	12 4.1% [2.1, 7.0]	6 6.2% [2.3, 13.0]	0.405

\*Based on exact permutation, adj. for 2-stage design;

\*\* Fisher's exact test

Benson CA, et al. 19<sup>th</sup> CROI; Seattle, WA; March 5-8, 2012; Abst. 96.

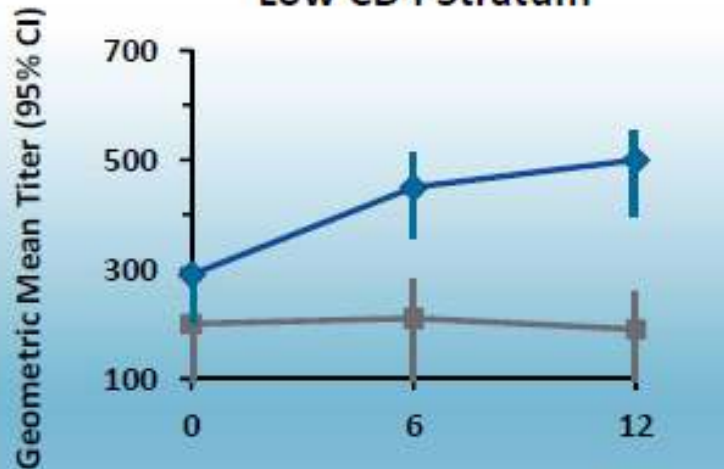




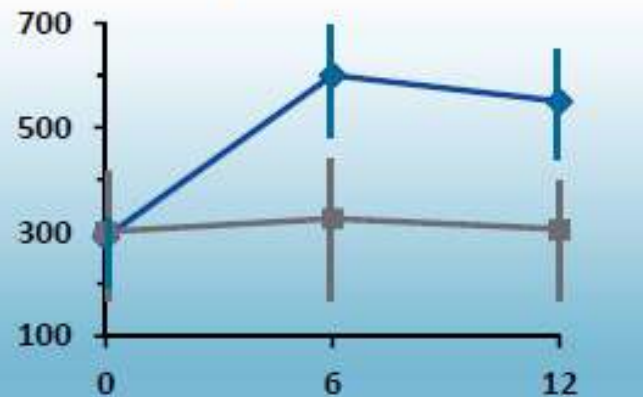
# VZV gpELISA Titers by CD4 Stratum



### Low CD4 Stratum



### High CD4 Stratum



n	140	134	130	149	150	143
GMT	288.4	473.9	506.8	296.8	594.9	552.6
95% CI	(245.7, 338.6)	(407.1, 551.6)	(437.6, 586.9)	(248.6, 354.5)	(511.7, 691.7)	(476.1, 641.4)
n	47	46	43	50	50	47
GMT	203.1	213.9	198.5	304.2	319.6	309.5
95% CI	(142.5, 289.6)	(147.6, 310.0)	(135.8, 290.0)	(210.9, 438.9)	(223.1, 457.8)	(212.1, 451.5)

# SEYAHAT İLE İLGİLİ AŞILAR

- Hepatit A
- Polio
- Sarı Humma
- Japon ensefaliti
- Tifo

# POLİO AŞISI

- Rehberlerde öneri yok
- Ancak endemik bölgeye gidilecekse inaktive polio aşısı önerilmekte
- CD4>300 , aşı yanıtı %78-100
- Oral canlı polio aşısı kontrendikedir!!!

# Sarı Humma Aşısı

- Canlı atenüe aşı
- Yellow fever Güney Amerika ve Afrikada endemik
- Mümkünse hastalarımız buralara gitmesin
- $CD4 < 200$ , aşı sonrası ensefalomyelit!!!
- Sinek ısırığından korun 😊
- İlla bu bölgelere gidecek ise  $CD4 > 200$  ise yapılabilir
- Yanıt oranı%83

Franco-Paredes C, Hidron A, Tellez I, Lesesne J, Del Rio C. HIV infection and travel: Pretravel recommendations and health-related risks. *Top HIV Med* 2009;17:2–11.

# TİFO AŞISI

- Endemik bölgeye gidilecekse
- İnaktive kapsüler polisakkarit aşı kullanılmalı
- Yanıt oranı düşük
- CD4<200 ise daha da düşük ☹
- Gıda-su hijyenine dikkat daha ön planda

Kroon FP, van Dissel JT, Ravensbergen E, Nibbering PH, van Furth R. Impaired antibody response after immunization of HIV-infected individuals with the polysaccharide vaccine against *Salmonella typhi* (Typhim-Vi). *Vaccine* 1999;17:2941–2945.

# JAPON ENSEFALITI





- Japon ensefaliti sezonunda, kırsal alanları içine alan bir aydan kısa dönem için gidenlere
- Japon ensefaliti salgını olan bölgelere gidenlere
- Ne yapacaklarını bilmeyenlere öneriliyor
- İnaktive aşı HIV(+) hastalarda kullanılabilir (28 gün arayla 2 doz, bir yıl sonra rapel)

# SONUÇ

- Rutin aşıları atlamamak gerekiyor
- CD4 sayısının yüksekliği aşıya yanıt için önemli
- CD4<200 olanlarda canlı aşılar kontrendike
- Risk durumunda aşı önemli

BITTiiii



# TEŐEKKÜRLER

