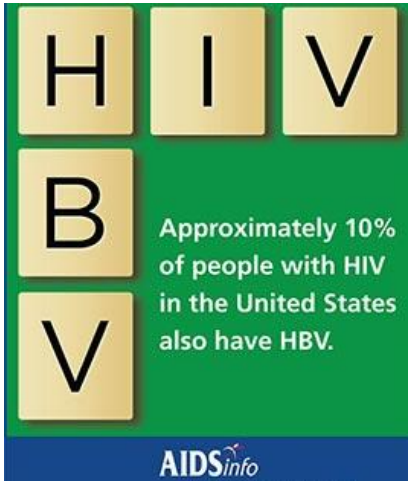
HBV:

HIV ile İnfekte Olgularda Tedavi

Dr. Süda TEKİN

Koç Üniversitesi Hastanesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Bölümü

Neler konuşulacak?



- HIV&HBV
  - Epidemiyoloji
  - İnfeksiyonların etkileri
- HIV&HBV Tedavi

  Özel gruplarda yönetim
- HIV&HBV Korunma yolları

HBV

WORLD HEPATITIS DAY 2017

ELIMINATE ~~HEPATITIS~~ NOhep

World Hepatitis Day, 28 July 2017

Pakistan tackles high rates of hepatitis from many angles

27 July 2017 -- On World Hepatitis Day, WHO is calling on countries to step up efforts to eliminate hepatitis by 2030. With one of the world's highest rates of hepatitis C, Pakistan is tackling this serious health issue from many angles to improve prevention, diagnosis and treatment.

Read the story from Pakistan

325 million

325 million people were living with chronic hepatitis infections worldwide in 2015.

1.34 million

1.34 million people died of hepatitis in 2015 globally.

HBV

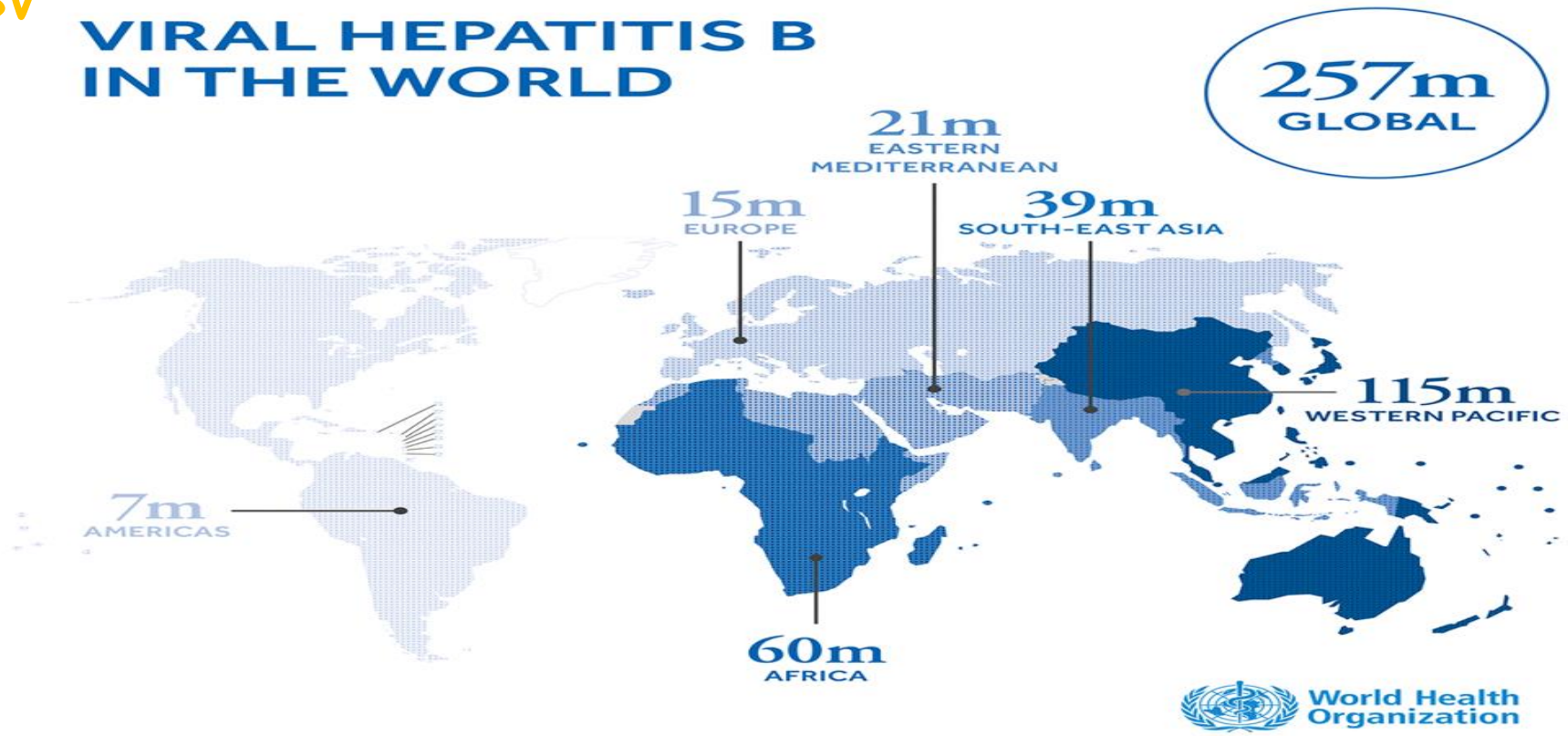
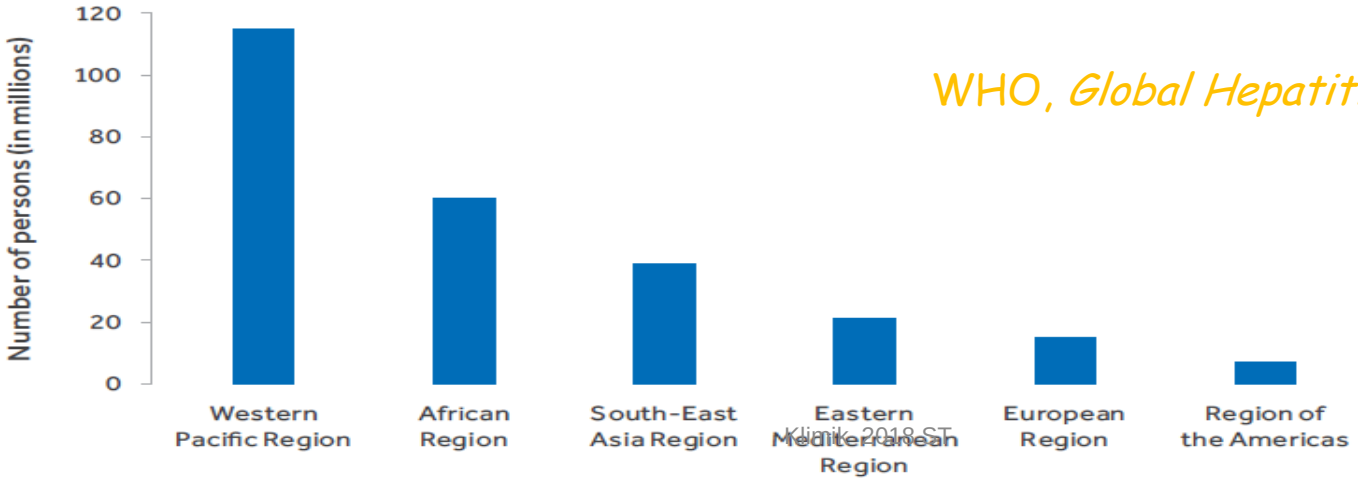
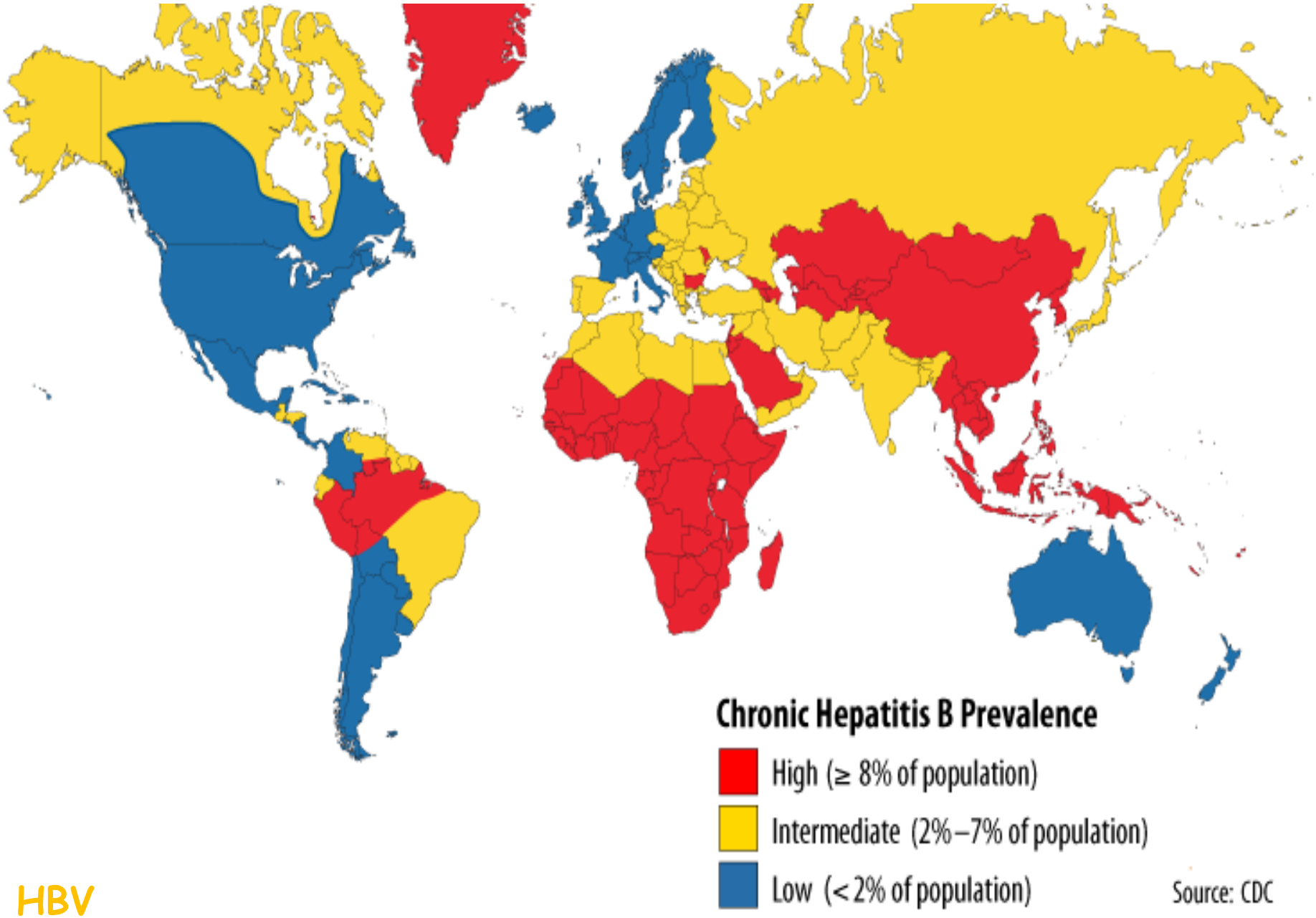


Table 2 (with graph). Prevalence of HBV infection (HBsAg) in the general population by WHO region, 2015: the WHO African and Western Pacific regions have the highest prevalence and the largest number of persons living with HBV



WHO, *Global Hepatitis Report*, 2017


Chronic Hepatitis B Prevalence
High (≥ 8% of population)
Intermediate (2%–7% of population)
Low (< 2% of population)
Source: CDC

HBV

Global HIV Epidemisi, 2016

WORLD AIDS DAY

36.7 million

people now estimated to be living with HIV

[30.8–42.9 million]

During 2016...

1.8 million

people newly infected

[1.6–2.1 million]

1.0 million

HIV-related deaths

[830 000–1.2 million]

World Health Organization

WORLD AIDS DAY
1 DECEMBER 2017

20.9 MILLION

PEOPLE ON HIV TREATMENT BY MID-2017

UNIVERSAL HEALTH COVERAGE IN HIV
#EVERYBODYCOUNTS #MYRIGHTTOHEALTH

HIV ile infekte Kişiler, DSÖ, 2016

36.7 million people living with HIV globally

- Africa: 25.6 million
- Americas: 3.3 million
- South-East Asia: 3.5 million
- Europe: 2.4 million
- Eastern Mediterranean: 360 000
- Western Pacific: 1.5 million

36.7 m ~ 2.7 m HBV ile infekte

Mother-to-child transmission

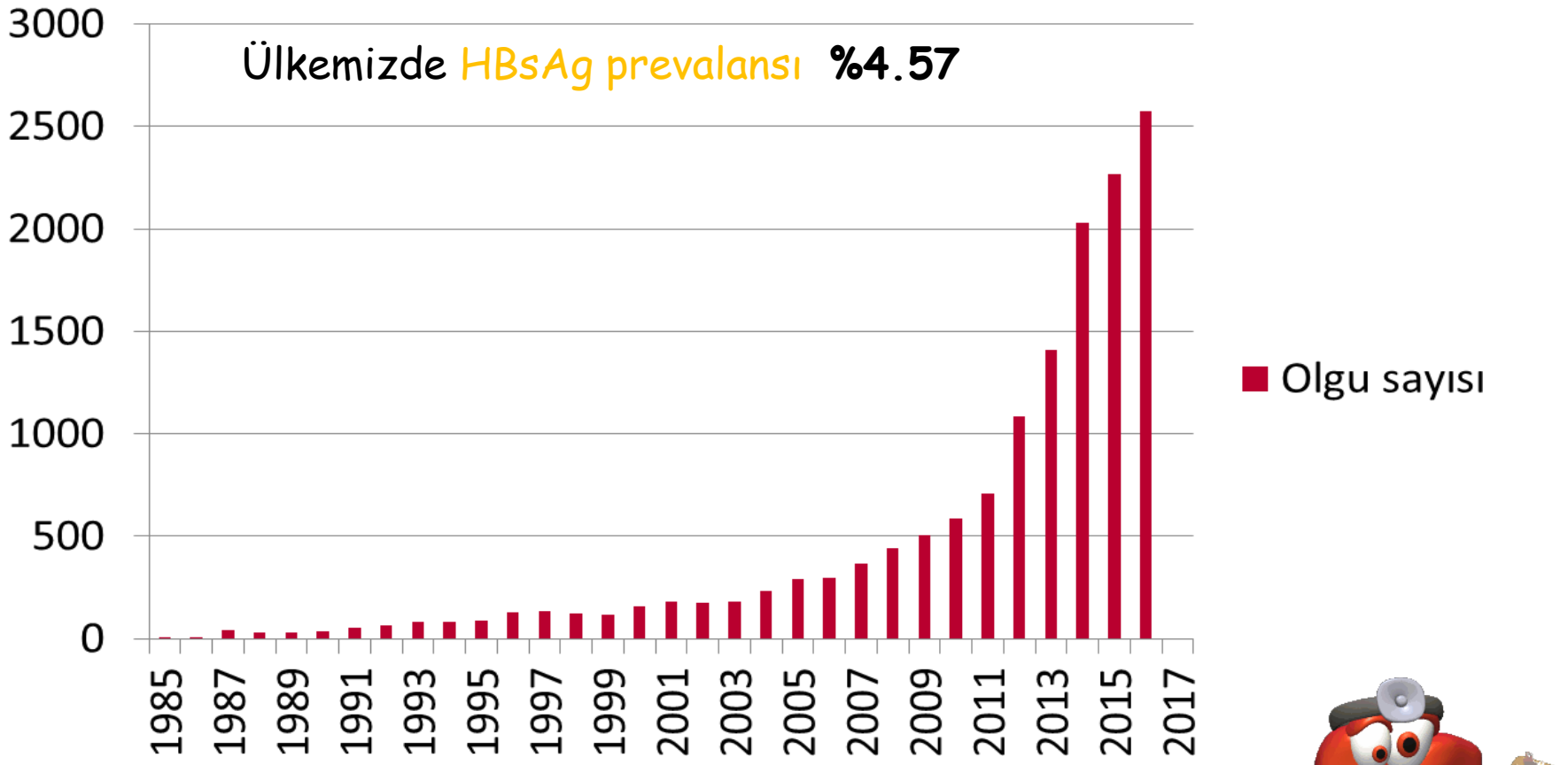
7 out of 10

Temmuz 2017

World Health Organization

Türkiye'de HIV/AIDS Olgularının Yıllara Göre Dağılımı

Ekim 1985 – Aralık 2016 Toplam: 14 695

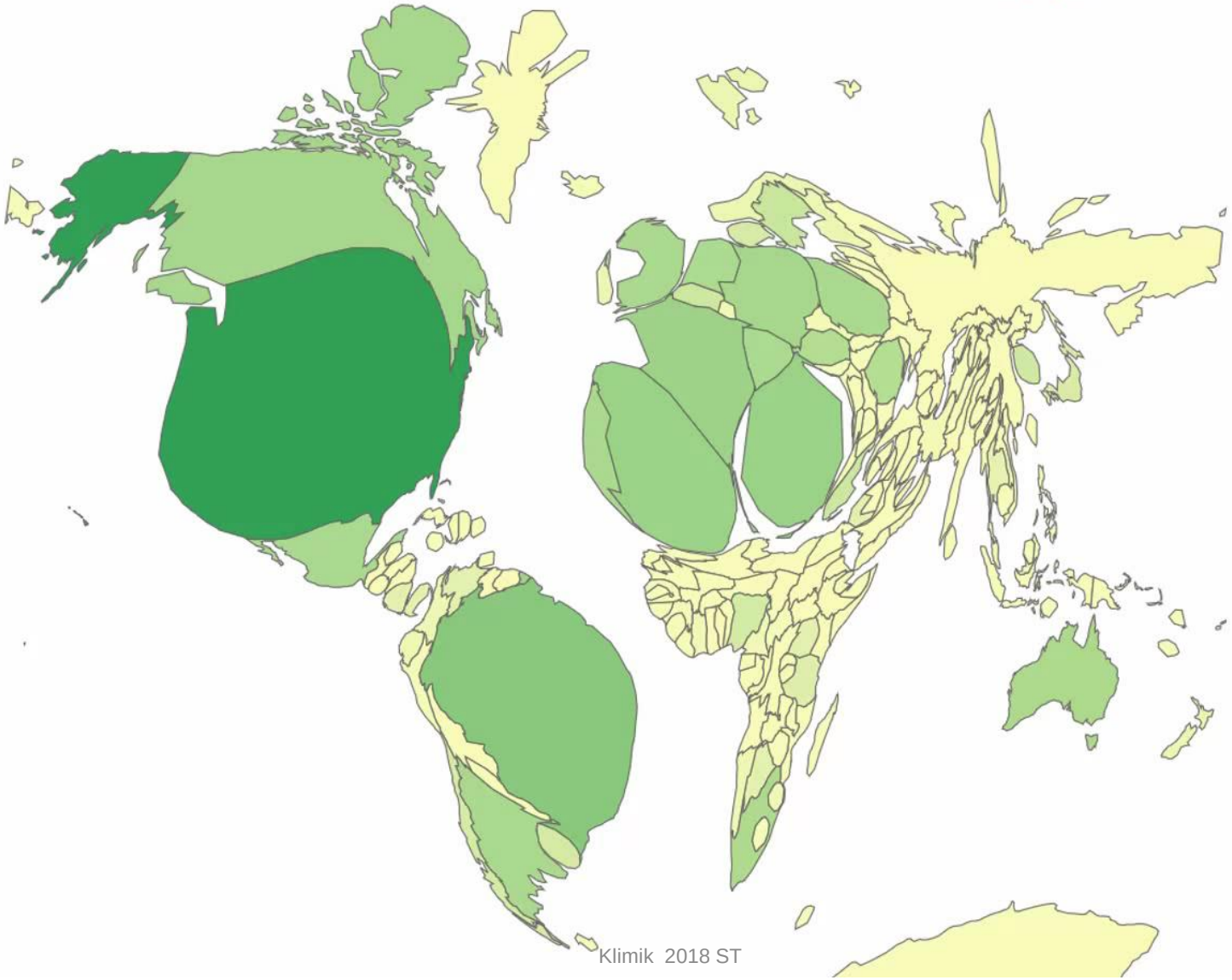


THSK Bulaşıcı Hastalıklar Daire Başkanlığı, 2016

HIV

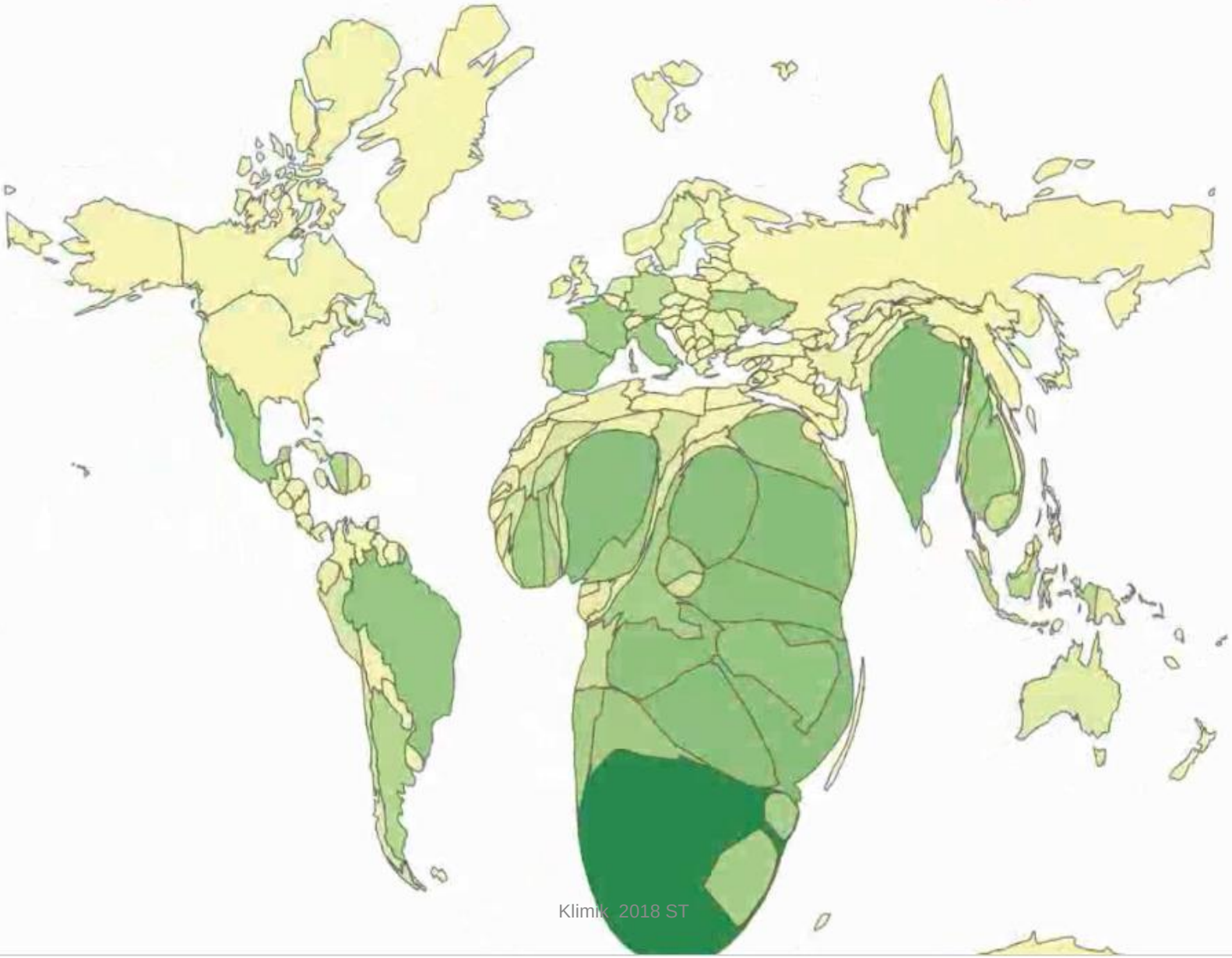
Countries with size proportional to people on ART, 2000-2016

World Health Organization



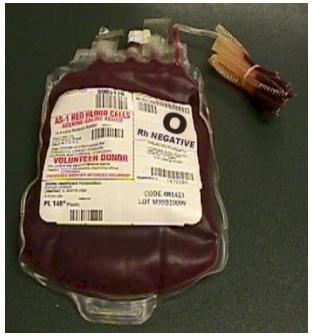
Countries with size proportional to people on ART, 2000-2016

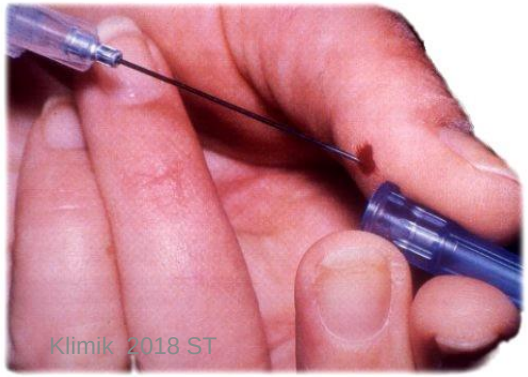
World Health Organization



HIV

HIV&HBV
Bulaşma Yolları





HIV olgularında hepatit B virusu koinfeksiyonu %6-13

MSM erkek HIV→**%9-17**

IV ilaç bağımlılarında **%7-10**

Heteroseksüel HIV →%4-6

Table 1. Prevalence and characteristics of HBV infection in 1,022 adult women from Botswana and South Africa.

Cohort Name / Location	Masibambisane / Durban	Sinikithemba and Cato Manor / Durban	Kimberley	Mma Bana / Gaborone	Total
Country of origin	South Africa	South Africa	South Africa	Botswana	South Africa + Botswana
Recruitment source	Antenatal clinics	Antenatal clinics	Paediatric clinics (mothers of HIV-infected children)	Antenatal clinics	All cohorts combined
HIV-status	Negative	Positive	Positive	Positive	Mixed
Number of individuals	72	426	81	443	1,022
Number with HBsAg (% of all individuals)[a]	6 (8.3)	40 (9.4)	9 (10.8)	17 (3.8)	72 (7.0)
Number with HBeAg (% of HBsAg+ individuals tested)[a]	1/6 (16.7)	12/40 (30.0)	1/4 (25.0)	2/10 (20.0)	16/60 (26.7)

Sun HY. *World J Gastroenterol*. 2014: 28;20:14598-614

Matthews PC, et al. Prevalence HBV Coinfection HIV-Positive Women. *PLoS ONE*.2017; 10: e0134037.

Characterization of HIV-HBV co-infection in a multi-national HIV-infected cohort

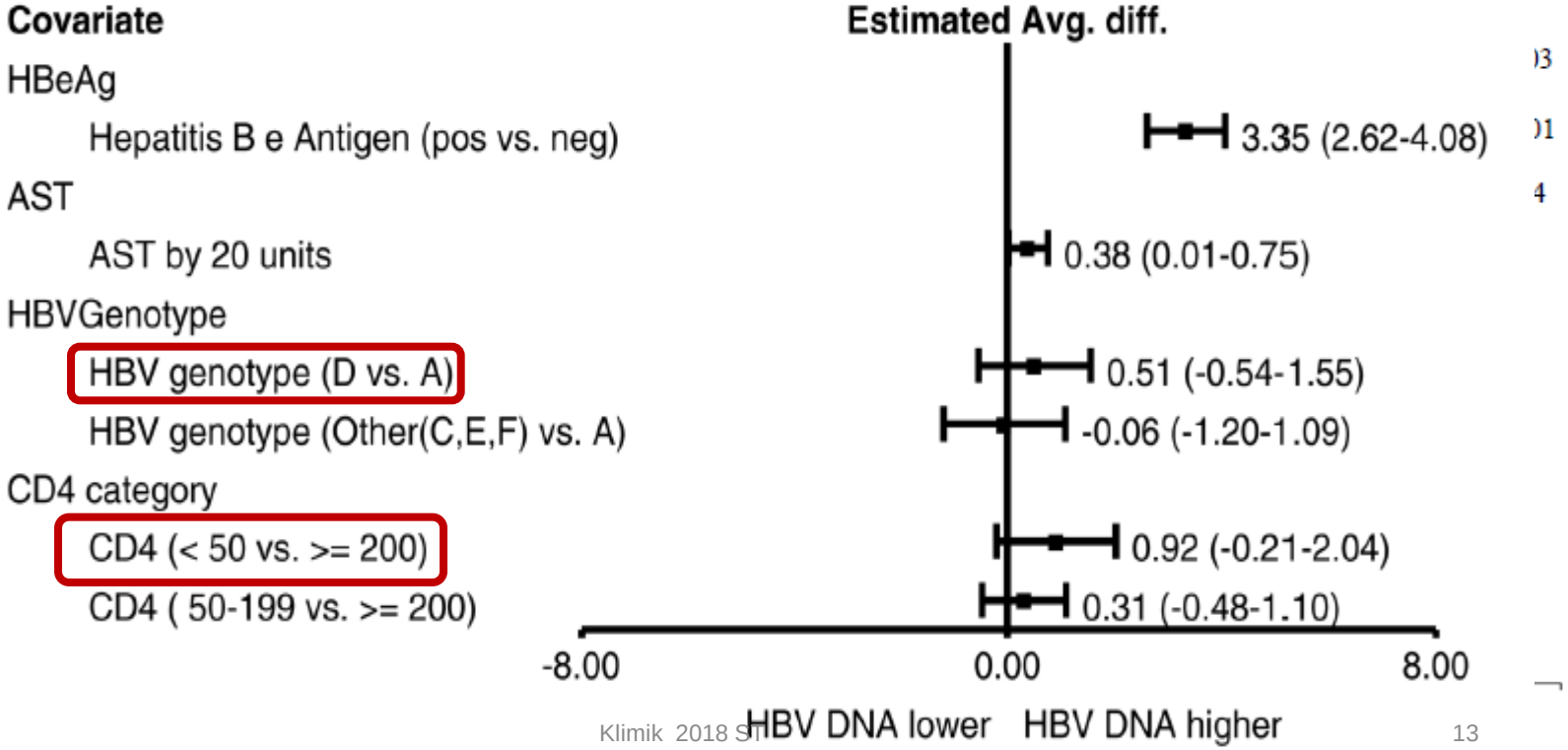
AIDS. 2013; 27(2):191-201.

Chloe L. THIO[1], Laura SMEATON[2], Melissa SAULYNAS[1], Hyon HWANG[1], Shanmugam

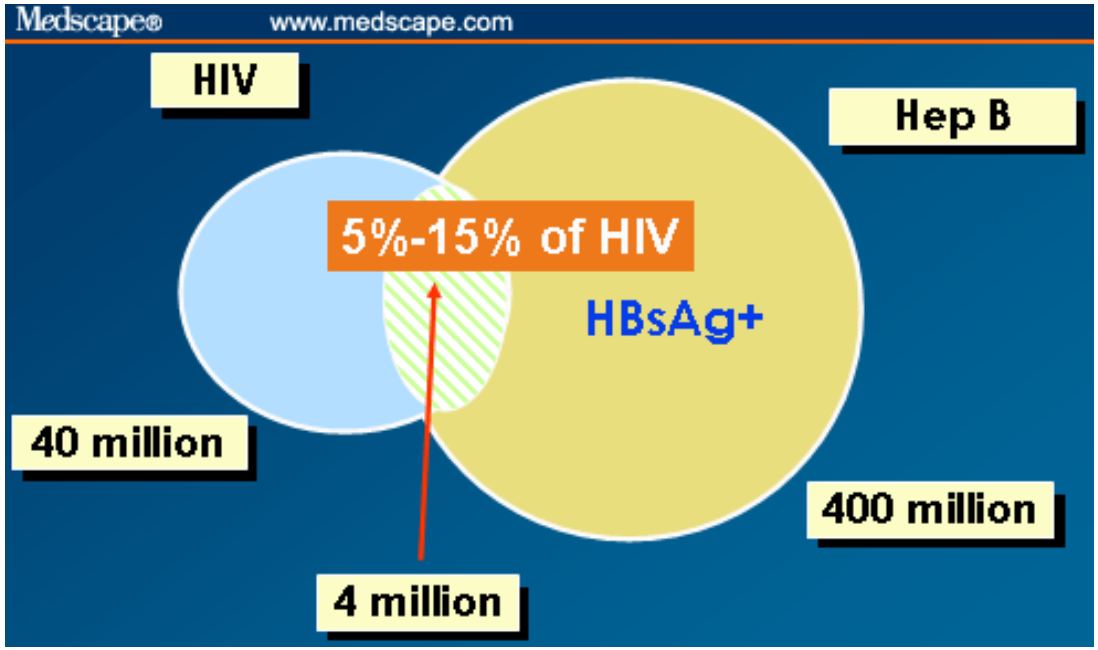
Toplam **11 ülkeden 2105 HIV (+)** olgu

	HIV monoinfected N=1990	HIV-HBV co-infected N=115	*P*
Age (IQR) (years) *	34 (29–40)	34 (30–40)	0.53
Male sex (%)	39	47	0.09

Figure 2b: Multivariable Linear Regression Models



HIV&HBV Koinfeksiyonu Getirileri



HBV → HIV

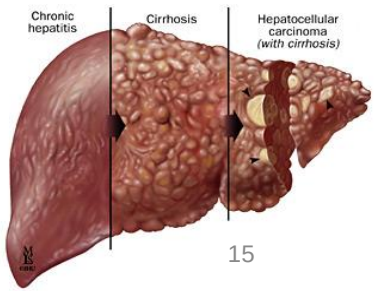
MAJOR ARTICLE HIV/AIDS

Impact of Hepatitis B Virus Infection on the Progression of AIDS and Mortality in HIV-Infected Individuals: A Cohort Study and Meta-Analysis

Georgios K. Nikolopoulos, Dimitrios Paraskevis, Eleni Hatzitheodorou, Zissis Moschidis, Vana Sypsa, Xenophon Zavitsanos, Victoria Kalapothaki, and Angelos Hatzakis

CID 2009:48 (15 June) • HIV/AIDS

- ✓HBV, **CD4** hücrelerinde azalmaya yol açar
- ✓HBV **X** proteini HIV **replikasyon**unu artırır
- ✓Hepatit **ART** tolerabilitesini bozar
- ✓ART yanıtı açısından **fark yok***



HBV ➡ HIV

Hepatitis B virus coinfection in human immunodeficiency virus-infected patients: A review

World J Gastroenterol. 2014; 20:14598-614.

Hsin-Yun Sun, Wang-Huei Sheng, Mao-Song Tsai, Kuan-Yeh Lee, Sui-Yuan Chang, Chien-Ching Hung

- **Primer HIV** infeksiyonu olan hastalarda HBV koinfeksiyonu **immünolojik progresyon** için bağımsız risk faktörü (HR, 3.46)
- ***İsveç çalışması;*** HBsAg'nin ART'nin ilk 3 yılında **CD4** sayısının artışında monoinfekte hastalara göre anlamlı düzeyde **olumsuz etkilediği** gösterilmiş.

 J Infect Dis 2013; 208:1454-8.

HIV ➡ HBV

Hepatitis B Virus Coinfection Negatively Impacts HIV Outcomes in HIV Seroconverters

Helen M. Chun,[1,5] Mollie P. Roediger,[1,7] Katherine Huppler Hullsiek,[1,7] Chloe L. Thio,[3] Brian K. Agan,[1]

- HIV hepatotropik bir virus değil
- Karaciğer hücreleri üzerinde **sitopatik** etkili
- Pro-inflamatuar yanıtta bozukluk ve **apoptozda artış**
- HIV, CD4 hücre harabiyetiyle **HBs antijenemi** artışı
- HIV, akut HBV'nin **kronikleşmesini** artırmakta

Chun HM. *J İnfect Dis*. 2012: 185-93
Sun HY. *World J Gastroenterol*. 2014: 28;20(40): 14598-614

HIV ➡ HBV

Hepatitis B virus coinfection in human immunodeficiency virus-infected patients: A review

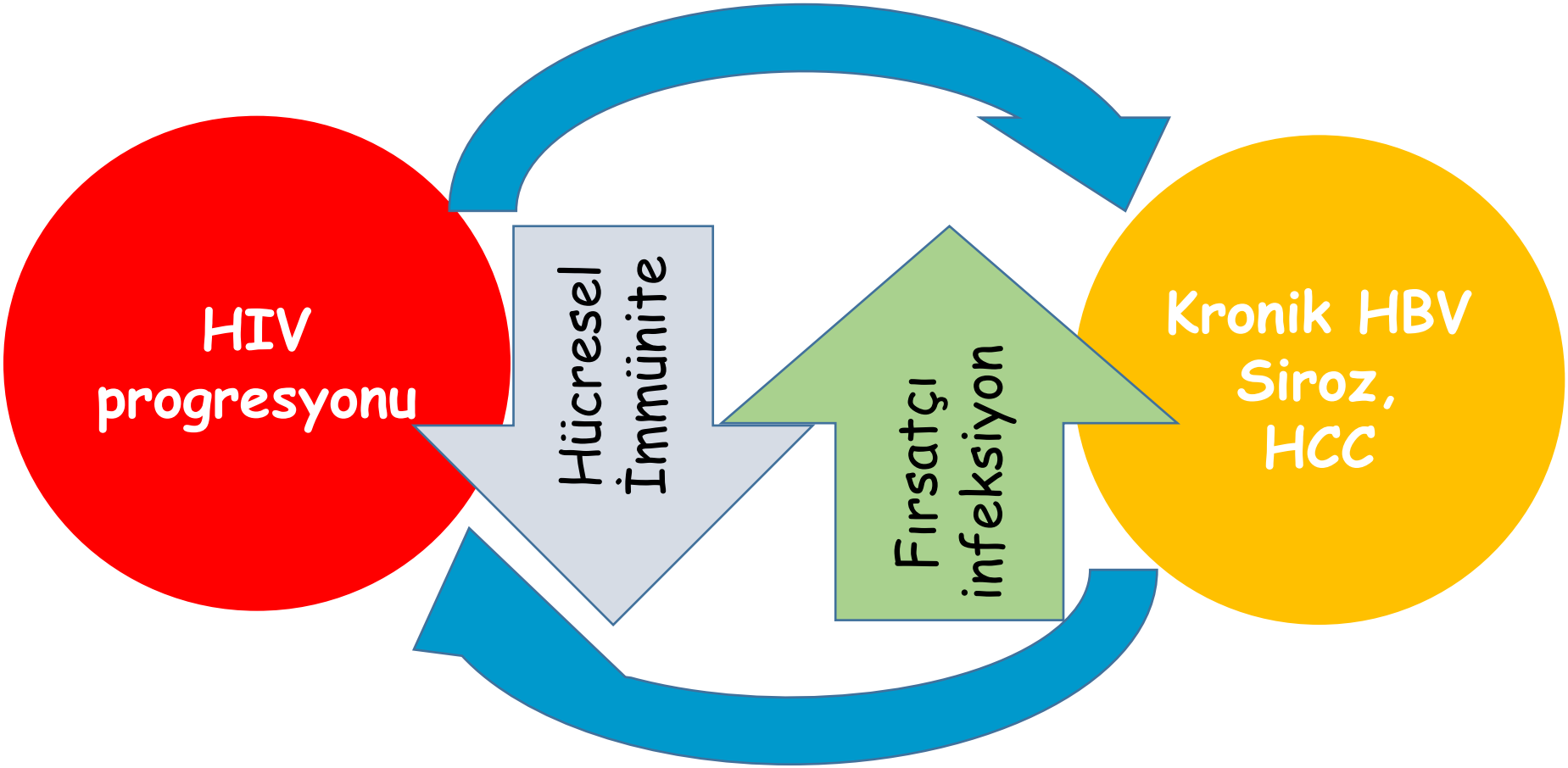
World J Gastroenterol. 2014; 20:14598-614.

Hsin-Yun Sun, Wang-Huei Sheng, Mao-Song Tsai, Kuan-Yeh Lee, Sui-Yuan Chang, Chien-Ching Hung

- HBV/HIV (+) **siroz**, son dönem karaciğer hastalığı ve **HCC** daha **sık**
- HBV **genotip B**, akut hepatit, hepatik **dekompansazyon** ve **mortalite** yüksek
- İleri HIV infeksiyonu, **anti HBs (+)** olguda HBV **aktivasyonuna** yol açabilir

  - Gebede koinfeksiyonda **HBV DNA** pozitifliği ve **HBe Ag seviyeleri** çok daha yüksek

HIV&HBV Koinfeksiyonu

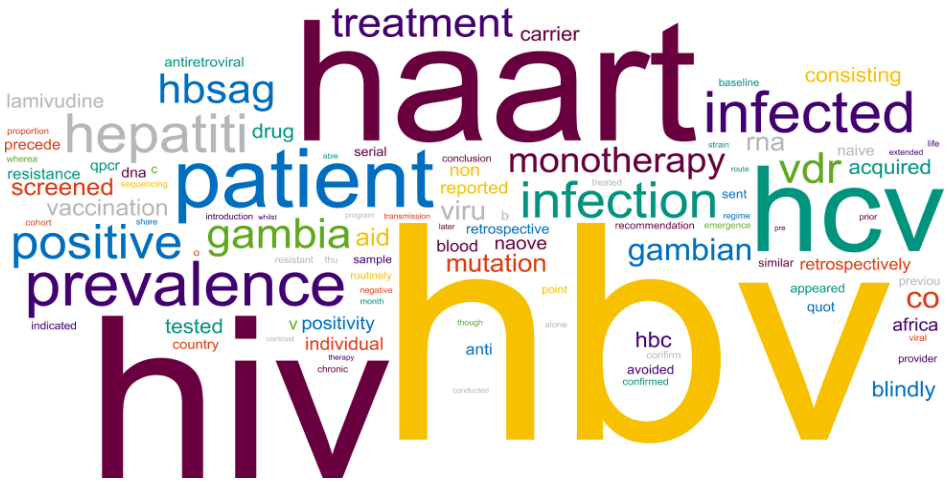


- ✓ ART hepatotoksisiteye yol açabilir
- ✓ Hepatitle ilişkili karaciğer hasarı ART kullanımını güçleştirir

Colin JF. *Hepatology.* 1999;29:1306-10
Thio CL, *Lancet* 2002;360:1921-6
Sulkowski MS,. *JAMA.* 2000;283:74- 80.

HIV&HBV Koinfeksiyonu

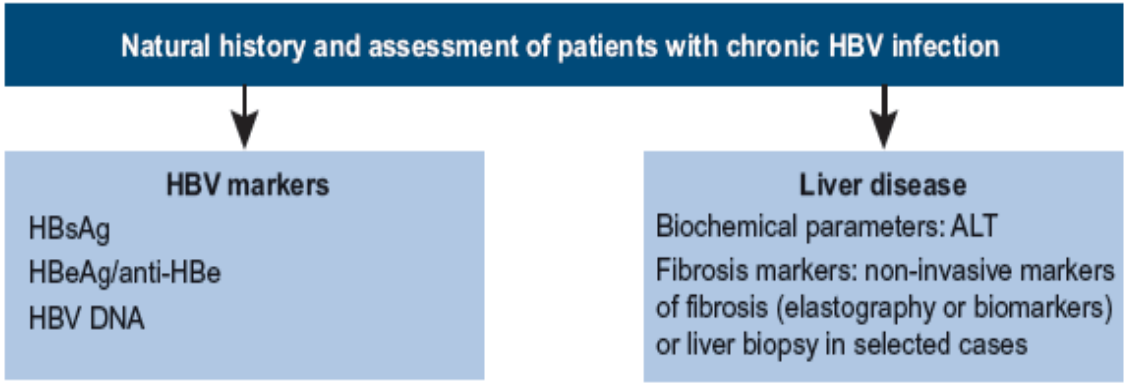
Yönetim



JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*



	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10^7 IU/ml	10^4-10^7 IU/ml	<2,000 IU/ml°°	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management

Recommendations

	Peg	Nucleotide analogues	
	Pegl	TDF	TAF
Dose*	180	245 mg	25 mg
HBV DNA <60–80 IU/ml	19%	93%	94%
ALT normalisation#	59%	76%	83%
HBsAg loss	4%	0%	0%

- All patients with HBeAg-positive or -negative chronic hepatitis B, defined by HBV DNA >2,000 IU/ml, ALT >ULN and/or at least moderate liver necroinflammation or fibrosis, should be treated (Evidence level I, grade of recommendation 1).
- Patients with compensated or decompensated cirrhosis need treatment, with any detectable HBV DNA level and regardless of ALT levels (Evidence level I, grade of recommendation 1).
- Patients with HBV DNA >20,000 IU/ml and ALT >2xULN should start treatment regardless of the degree of fibrosis (Evidence level II-2, grade of recommendation 1).
- Patients with HBeAg-positive chronic HBV infection, defined by persistently normal ALT and high HBV DNA levels, may be treated if they are older than 30 years regardless of the severity of liver histological lesions (Evidence level III, grade of recommendation 2).
- Patients with HBeAg-positive or HBeAg-negative chronic HBV infection and family history of HCC or cirrhosis and extrahepatic manifestations can be treated even if typical treatment indications are not fulfilled (Evidence level III, grade of recommendation 2).

Clinical Practice Guidelines

CrossMark

EASL JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

HIV&HBV

HIV co-infected patients

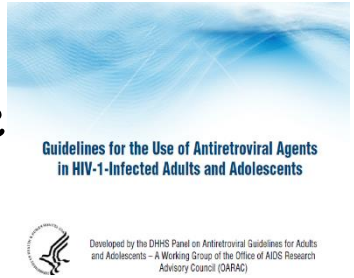
Recommendations

- All HIV-positive patients with HBV co-infection should start antiretroviral therapy (ART) irrespective of CD4 cell count (Evidence level II-2, grade of recommendation 1).
- HIV-HBV co-infected patients should be treated with a TDF- or TAF-based ART regimen (Evidence level I for TDF, II-1 for TAF, grade of recommendation 1).

HIV&HBV TEDAVİ

Hızla ART Başlanması Gereken Durumlar

- Akut/erken infeksiyon (akut retroviral sendrom)
- Gebelik
- **HIV/hepatitis B–C koinfeksiyonu**
- AIDS tanımlayıcı hastalık, HIV-ilişkili demans ve AIDS-ilişkili malignite
- Fırsatçı infeksiyonlar
- Düşük CD4 sayısı (<200 /mm^3)
- HIV ilişkili nefropati (HIVAN)



HBV'ye Etkili Antivirallerin HIV ile İnfekte Hastalardaki Etkileri

Characteristics	Interferon alfa-2b[1]	Pegylated interferon alfa-2a[1]	Lamivudine	Emtricitabine	Adefovir	Entecavir	Telbivudine	Tenofovir diso-proxil fumarate
Antiviral effect	Immune modulation	Immune modulation	Interference of HBV DNA synthesis	Interference of HBV DNA synthesis	Interference of HBV DNA synthesis	Interference of HBV DNA synthesis	Interference of HBV DNA synthesis	Interference of HBV DNA synthesis
HIV-1 activity	No	No	Yes	Yes	No, at low dose[2]	Yes	No[7]	Yes
Dosage and administration	10 million IU SC or IM 3 times a week	180 mg SC once a week	300 mg/d oral	200 mg/d oral	10 mg/d oral	0.5 mg/d oral[5]	600 mg/d oral	300 mg/d oral
Defined treatment duration	48 wk	48 wk	Indefinite	Indefinite	Indefinite	Indefinite	Indefinite	Indefinite
Undetectable HBV DNA	-	-	40%-84% at 1 yr	53% at 2 yr	8.6% and 5.7% at 36 wk 36 and 48, respectively[8]	38% by the end of study (mean follow-up, 74 wk)[9]	-	Up to 91% at 5 yr
HBeAg seroconversion	0%-20%	0%-20%	22%-35% at 1 yr	14% at 48 wk	9% at 144 wk	-	-	50% of TDF use; 57% of TDF plus FTC use at 5 yr

Sun HY. *World J Gastroenterol.* 2014: 28;20: 14598-614

Guidelines HIV. http://www.**aidsinfo.nih.gov**/ContentFiles/AdultandAdolescentGL.pdf.

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Virus Coinfection (Last updated October 17, 2017; last reviewed October 17, 2017)

- ART başlamadan önce HBsAg (+) tüm hastalarda **HBV DNA** ölçülmelidir **(AIII)**.
- **FTC, 3TC, TDF** ve **TAF** hem HBV hem de HIV'e etkilidirler. ART bel kemiği NRTI olarak bunları içermelidir (**AI**).
- TDF veya TAF verilemiyorsa **entekavir** eklenmeli **(BI)**.
- **Entekavir, HIV'e etkili ancak** ART olmadan verilirse **M184** mutasyon seçimi olabilir, HIV'in 3TC ve FTC direnci **(AII)**.
- Özel hastalarda **PegIFN-α** monoterapisi değerlendirilebilir **(CII)**.

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Virus Coinfection (Last updated October 17, 2017; last reviewed October 17, 2017)

❖**Adefovir** tek başına veya **3TC** ya da **FTC** ve **telbivudin** HBV/HIV koinfeksiyonunda **önerilmez (CII)**.

❖HBV tedavisinin kesilmesi reaktivasyona yol açabileceğinden **kesmemeleri** ve HBV açısından da **takip** edilmeleri gerekliliği **(AII)**.

❖HIV'e karşı gelişen **virolojik başarısızlık** durumunda ART modifiye edilecekse **HBV tedavisine devam** edilmelidir **(AIII)**.

EACS European AIDS Clinical Society

October 2017. Version 9.0.

Treatment of HBV/HIV Co-infection

1. TDF intoleransı yoksa, **TDF** veya **TAF** başlanmalıdır.
2. Koinfekte hastalarda **kemik mineral yoğunluğu** değişiklikleri takip edilmelidir.
3. TDF veya TAF kesinlikle verilemiyorsa, 3TC kullanma öyküsü yoksa güçlü bir ART'ye **entekavir** eklenmeli
4. **KC sirozu** ve **düşük CD4** sayısı olanlar ART ilk aylarında **İRİS** ve **dekompanzasyon** dikkat

EACS European AIDS Clinical Society

October 2017. Version 9.0.

Treatment of HBV/HIV Co-infection

5. Düşük potent (3TC gibi) bir HBV etkili ilaca geçerken **YMDD** mutasyonlarına karşı dikkatli olunmalıdır
6. HBV tedavisi **hayat boyu** verilmelidir.
7. HBeAg veya HBsAg **serokonversiyonu** olursa en az **1 yıl** daha HBV tedavisi verilmeli. **Sirozlu** hastalarda asla **kesilmeme**lidir.
8. **KT** veya **immün süpresif** (**ritüksimab** gibi) tedavi alan HBsAg pozitif hastalara HBV-DNA seviyesinden bağımsız olarak **TDF/TAF profilaksisi** mutlaka eklenmelidir.

EACS European AIDS Clinical Society

October 2017. Version 9.0.

Treatment of HBV/HIV Co-infection

9. Yüksek immün süpresif (lenfoma KİT gibi) alan **anti-HBc pozitif HBV DNA** ve **HBsAg** takip edilmeli, edilemeyecekse hastalara, **TDF/TAF profilaksisi**

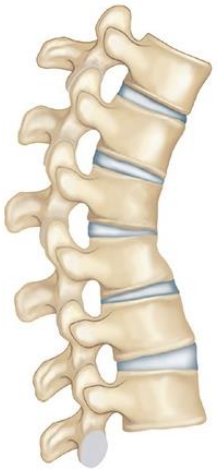
10. HBV **aşılaması** yapılan ancak **antikor oluşmayan** hastalarda ART, **TDF/TAF** içermelidir.

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B (HBV)/HIV Coinfection

(Last updated: July 14, 2016; last reviewed: July 14, 2016)



Initial Combination Regimen for ART-naïve Adult HIV-positive Persons

A) Recommended regimens (one of the following to be selected)[1,**]

Regimen	Dosing	Food requirement	Caution
2 NRTIs + INSTI			
ABC/3TC/DTG[(i,l)]	ABC/3TC/DTG 600/300/50 Triumeq	None	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before). DTG 50 mg bid with rifampicin.
TAF/FTC[(k)] or TDF/FTC[(k,v)] + DTG	TAF/FTC TDF/FTC (Truvada; Hivend) + DTG (tivicay)	None	
TAF/FTC/EVG/c[(k)] or TDF/FTC/EVG/c[(k,v)]	TAF/FTC/EVG/c 10/200/150/150 mg, 1 tablet qd or , 1 tablet qd	With food	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h or 6h before).
TAF/FTC[(k)] or TDF/FTC[(k,v)] + RAL	TAF/FTC 25/2 mg, 1 tablet qd or RAL (isentress)	Nor	administration of antacids taining Al or Mg not recom-nded. RAL 400 or 800 mg bid rifampicin.
2 NRTIs + NI			
TAF/FTC/RP TDF/FTC/RP	TAF/FTC TDF/FTC EVG © Genvoya Stribild	Wit req	y if CD4 count > 200 cells/μL HIV-VL < 100,000 copies/mL. contra-indicated; H2 antago-s to be taken 12h before or 4h r RPV.
2 NRTIs + PI/r or P			
TAF/FTC[(k)] or TDF/FTC[(k,v)] + DRV/c or + DRV/r	TDF/FTC 300/200 mg, 1 tablet qd DRV/c 800/150 mg, 1 tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	With food	Monitor in persons with a known sulfonamide allergy.

HBV'ye etkili iki ilaç

1. Her iki virusta gelişebilecek **direnç** sorununu
2. HBV ye karşı **IRIS** gelişme riskini azaltır

"Immune Reconstitution Inflammatory Syndrome" (IRIS)

➢ **IRIS**: ART sonrası immün sistem iyileşmesiyle HBV ile ilişkili KC hastalığının alevlenmesi

- ART başlanmasından **6-12.** haftadan sonra CD4 sayısındaki yükselmeyle **ALT**'nin yükselmesi
- **Akut hepatit B** semptom ve bulguları
- Sirotik olgularda alevlenme **daha ağır**
- IRIS'in ART ilişkili hepatotoksisite ve diğer viral infeksiyonların ayrımı zor

HIV&HBV Koinfekte Son Dönem Karaciğer Hastaları

- Bu olgularda monoinfekte olgularda olduğu gibi **interferon kontrindike** ancak nükleozid analogları güvenlidir
- Olgular hepatologla konsülte edilmeli
- Gereğinde **transplantasyona** hazırlanmalıdır

*World J Gastroenterol.*2014;20(2):414-24.

Orthotopic Liver Transplantation in Human-Immunodeficiency-Virus-Positive Patients in Germany

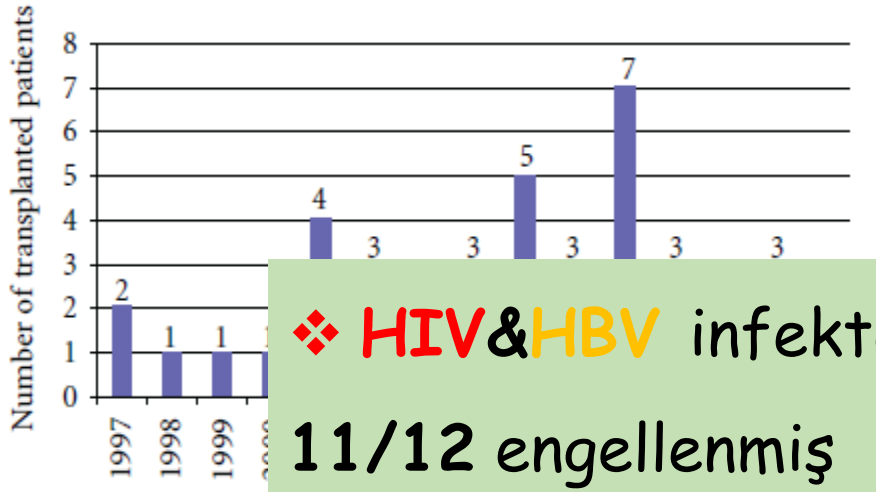


FIGURE 1: Thirty-eigh
infected patients from

- ❖ **HIV&HBV** infekte hastalarda rekürrens
- **11/12** engellenmiş
- ❖ HIV&**HCV** hepsi **nüks**

TABLE 4: Recurrence and prevention of hepatitis B in HIV-positive patients after OLT.

Viral hepatitis	HBV therapy	HBV virus
		negative
		negative
		negative
		negative
		negative
		negative
		negative
		negative
		iremia
HBV	TDF	HBsAg negative
HBV/HCV	TDF, HBs-Ig	HBsAg negative
HBV	3TC	HBsAg negative

Reasons for OLT	
HCV coinfection	19 (1 ETOH, 5 HCC)
HCV+HBV coinfection	1 (1 HCC)
HBV coinfection	10 (1 ETOH, 1 HCC)
HBV+HCV+HDV coinfection	1
Budd-Chiari syndrome	1

AIDS Research & Treatment.2012. ID 197501

*World J Gastroenterol.*2014;20(2):414-24.

Outcomes and management of viral hepatitis and human immunodeficiency virus co-infection in liver transplantation

HIV (+) Karaciğer Transplantasyonu adayın karşılaması gereken ölçütler

- ✓ **CD4 > 100** h/μL (fırsatçı infeksiyon öyküsü varsa CD4 >200)
- ✓ **HIV RNA<50** k/mL
- ✓ **AIDS** tanımlayıcı hastalığının olmaması
- ✓ **IRIS** tablosunun bulunmaması
- ✓ PML, intestinal kriptosporidiozis, primer **SSS lenfoması olmaması**

Table 2 Summary of outcomes post orthotopic liver transplant in hepatitis B virus/human immunodeficiency virus co-infection

Ref.	Study period	Country	*n*	Median follow-up (mo)	Survival	Graft survival	Comments
Coffin *et al*[49]	2001-2007	United States	22	42	85% 1 yr 85% 3 yr	85% 1 yr 85% 3 yr	About 50% had detectable HBV pre transplant
Tateo *et al*[97]	1999-2007	France	13	3[illegible]	100%	100%	1 co-infected with HDV, 2 with HCV, 4 with HCV and HDV
Anadol *et al*[96]	1997-2011	Germany	10	61[1]	90% 1 yr 80% 5 yr	NR	
Schreibman *et al*[98]	1999-2006	United States	8	NR	75% 1 yr [illegible]% 3 yr	NR	2 co-infected with HCV, 1 fulminant hepatic failure
Norris *et al*[99]	1995-2003	United Kingdom	4	22	100% [illegible] yr	NR	

*World J Gastroenterol.*2014;20(2):414-24.

Outcomes and management of viral hepatitis and human immunodeficiency virus co-infection in liver transplantation

Table 4 Drug-drug interactions: Antiretrovirals and immunosuppressants[54,102]

	Steroids	Calcineurin inhibitors (cyclosporine/tacrolimus)	mTOR inhibitors (sirolimus, everolimus)	Antimetabolites (mycofenylate mofitl)
PI	Significant increase	Significant increase in immunosuppression levels in general. Calcineurin inhibitor levels may increase or decrease with exposure to either amprenavir or fosamprenavir	Significant increase in immunosuppression levels	Generally no effect; levels may decrease with nelfinavir, lopinavir/ritonavir
NNRTI	Mild decrease in level	Mild decrease in level	Mild decrease in level	No effect on immunosuppressant levels. May decrease nevirapine levels
NRTI	No effect	No effect	No effect	May be increased with zidovudine
Integrase inhibitors	No effect	Increased with elvitegravir	Increased with elvitegravir	Increased with elvitegravir
CCR5-agonists			No effect	
Fusion inhibitors			No effect	

HIV&HBV koinfekte hastalar nakil sonrası **ömür boyu**;

***Anti-HBs > 100 IU/L => HBIG + tenofovir** veya **entekavir**

HBV Serolojisi Negatif HIV olguları

❖HBV bulaşı açısından riskli davranışlar ve bulaşı önleme yolları anlatılmalı

- ➢Cinsel temas sırasında alınması gereken önlemler
- ➢ IV uyuşturucu bağımlılarının enjektör paylaşımının önlenmesi
- ➢ Dövme ve piersingden kaçınma

Aile desteği

Sosyal destek

Alkol ve uyuşturucu kullanımı

Depresyon durumu

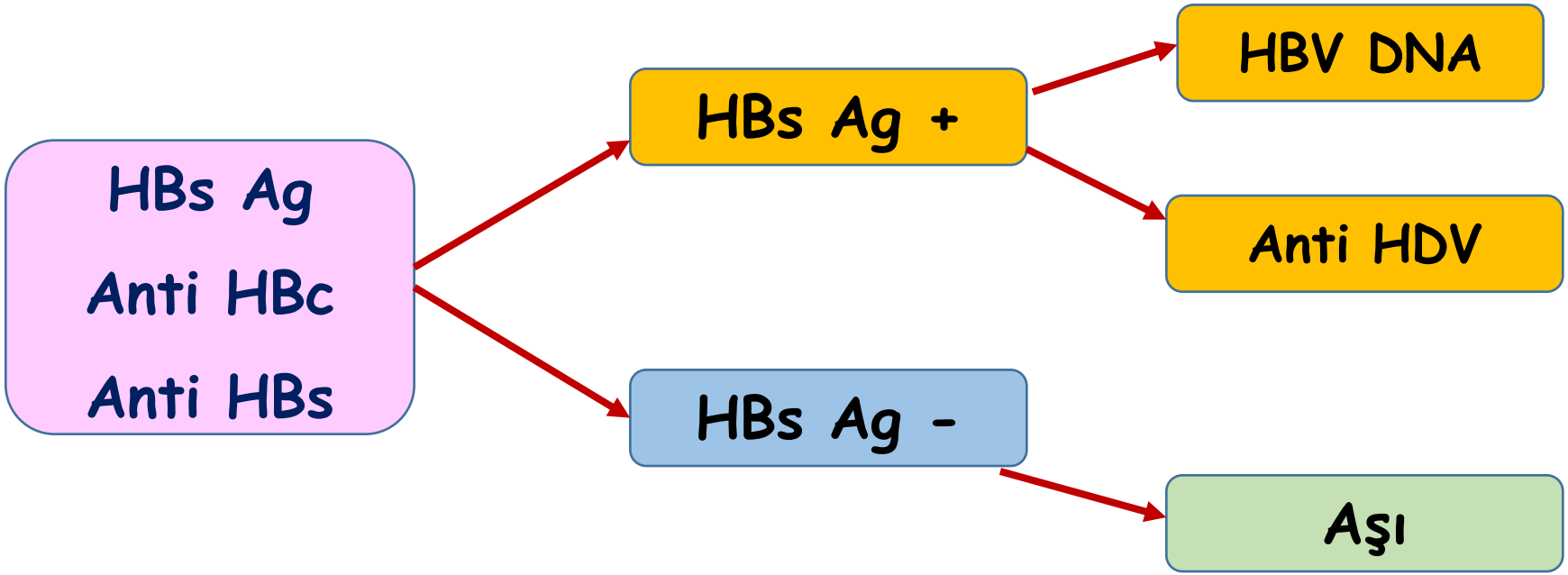
Kognitif fonksiyonları

Meslek

Sağlık güvencesi

https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

HBV Serolojisi Negatif HIV olguları



HIV (+) olgularda hepatit **aşının** immünijenitesi düşüktür

- CD4 sayısı düşük
- HIV RNA'sı saptanabilir düzeyde
- HCV koinfeksiyonu varlığı aşıya yanıtı düşürmekte
- CD4 sayısı **200 altında** olduğunda yanıt **%25**

Original Article

Immune Response to Standard Hepatitis B Vaccination in HIV-Infected Patients

Amitis Ramezani[1], Minoo Mohraz[2], Mohammad Banifazl[3], Maryam Foroughi[2], Ali Eslamifar[1], Arezoo Aghakhani[1*]

1 Department of Clinical Research, Pasteur Institute of Iran, Tehran, Iran.
2 Iranian Research Center for HIV/AIDS, Tehran, Iran.
3 Iranian Society for Support of Patients with Infectious Diseases, Tehran, Iran.

Accepted Mar. 02, 2015

Abstract

Introduction: Due to their similar routes of transmission, human immunodeficiency virus (HIV) and hepatitis B virus (HBV) co-infection occurs considerably. HBV infection progresses more rapidly in HIV-infected patients. Therefore, HBV vaccination of all non-immune HIV infected patients is recommended. On the other hand, HIV-infected subjects have suboptimal responses to HBV vaccine. In this study, we aimed to determine the immune responses to standard HBV vaccination in HIV-infected patients. **Methods:** Fifty-six HIV infected patients who lacked evidence of either prior HBV infection or immunity were subjected to standard HBV vaccination, as 3 intramuscular injections of the standard dose (20 µg) of recombinant HBV vaccine at months 0, 1 and 6. Hepatitis B surface antibody (anti-HBs) titers were checked in all cases one month after the vaccination. A protective antibody response was defined as an anti-HBs titer of ≥10 IU/L. **Results:** HBV seroprotection was observed in 56.6% of HIV-infected patients. There was no significant difference between cases with and without seroprotection regarding age, sex, possible route of HIV acquisition, CD4 count, receiving antiretroviral therapy (and its duration) and HCV infection. **Conclusion:** Our study confirms previous reports that HIV-infected patients have a lower response rate to the standard HBV vaccination compared to general population. So other strategies are needed to improve the HBV vaccine response rate in HIV cases.

Keywords: Human Immunodeficiency Virus(HIV), Hepatitis B Virus(HBV), Vaccination.

AIDSinfo
A Service of the U.S. Department of Health and Human Services

Recommended Immunizations for HIV Positive Adults

Immunization Name	Associated Disease	Dosage	Comments and Warnings
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.

Ref.	Year	Schedules/ administration	Age, median, yr	CART	HIV-1 VL, RNA copies/ mL < 10000	CD4, median, cells/μL	Response rate	Predictors
Irungu *et al*[139]	2013	0, 1 to 3, 6 mo, IM	31		HIV-1 uninfected		85.7%	CD4 > 500 cells/μL; female
				0%	65.7%	557	64.2%	
Alternative strategies								
Fonseca *et al*[140]	2005	0, 1, 6 mo, IM	37	85.1%	80.9%	≥ 350, 59.6%	94%	CD4 > 350 cells/μL; HIV-1 VL <
				87.8%	75.5%	≥ 350, 57.1%	47% ($P = 0.07$)	10000 copies/mL
Cornejo-Juárez *et al*[147]	2006	0, 1, 6 mo, IM	35.6	56.4%	≤ 20000, 56.6%	≥ 200, 48.8%	61.5%	CD4 ≥ 200 cells/μL
			34.1	72.5%	≤ 20000, 55.6%	≥ 350, 47.5%	60% ($P = 0.89$)	
Potsch *et al*[148]	2010	0, 1, 2, 6 mo, IM	36	79%	< 80, 70%	402	89%	HIV-1 VL < 80 copies/mL
Launay *et al*[146]	2011	0, 1, 6 mo, IM	43	86%	< 50, 79%	516	65% (95%CI: 56-72)	Young age; four-dose
		0, 1, 2, 6 mo, IM	42	80%	< 50, 77%	509	82% (95%CI: 77-88)	
		0, 1, 2, 6 mo, ID	43	86%	< 50, 78%	482	77% (95%CI: 56-72)	

3 × 20

3 × 40

3 × 20

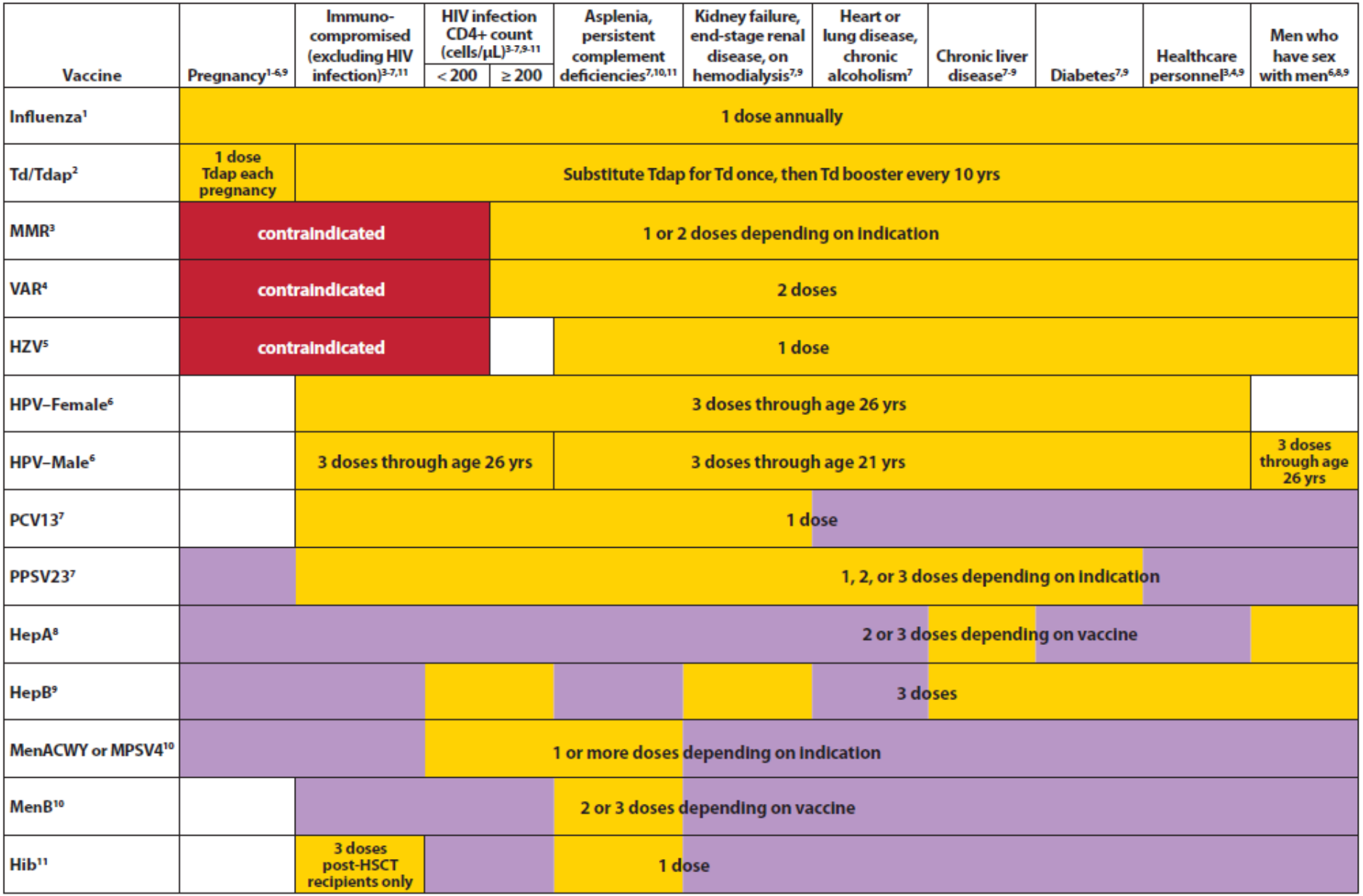
HBV aşıları HIV (+):

- ✓ CD4 ≥ 350 ab yanıtı yüksek
- ✓ Güvenli
- ✓ Hastalık ilerlemesinde etkileri yok
- ✓ Yeni adjuvanlar denenmekte (GM-CSF/***CPG 7909***)

İnsan B ve dendritic hücreleri uyarıyor

Sun HY. *World J Gastroenterol.* 2014: 28;20: 14598-614

Figure 2. Recommended immunization schedule for adults aged 19 years or older by medical condition and other indications, United States, 2017



Sonuç

- **HIV pozitifliği** saptanan tüm olgular **HBV koinfeksiyonu** açısından araştırılmalıdır
- Olgularda **HAV, HCV ve Delta virus** serolojisine bakılmalı,
- HBV serolojik göstergeleri **negatif** olan olgular HBV aşısıyla **bağışıklanmalı**dır
- Seronegatif olgulara **HAV aşısı** yapılmalıdır

Sonuç olarak

- Tedavi gerektiren kronik HBV infeksiyonu olan HIV olgularında **CD4 düzeyine bakılmaksızın** hemen **HAART** başlanmalı
- Başlanacak olan **HAART rejimi HBV 'ye etkili en az iki** ilaç içermelidir

Sağlıklı günler...