AKUT HEPATİT-AKUT ALEVLENME AYRIMI NASIL YAPILMALIDIR?

E. Ediz Tütüncü

IV. UVHS

7 Eylül 2013, Sakarya

Sunum planı

- Epidemiyoloji,
- Viral kinetikler,
- İmmünpatogenez,
  - akut hepatit,
  - kronik hepatit,
  - akut alevlenme,
- Ayırıcı tanı.

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Global epidemiology of hepatitis B virus infection: New estimates of age-specific HBsAg seroprevalence and endemicity

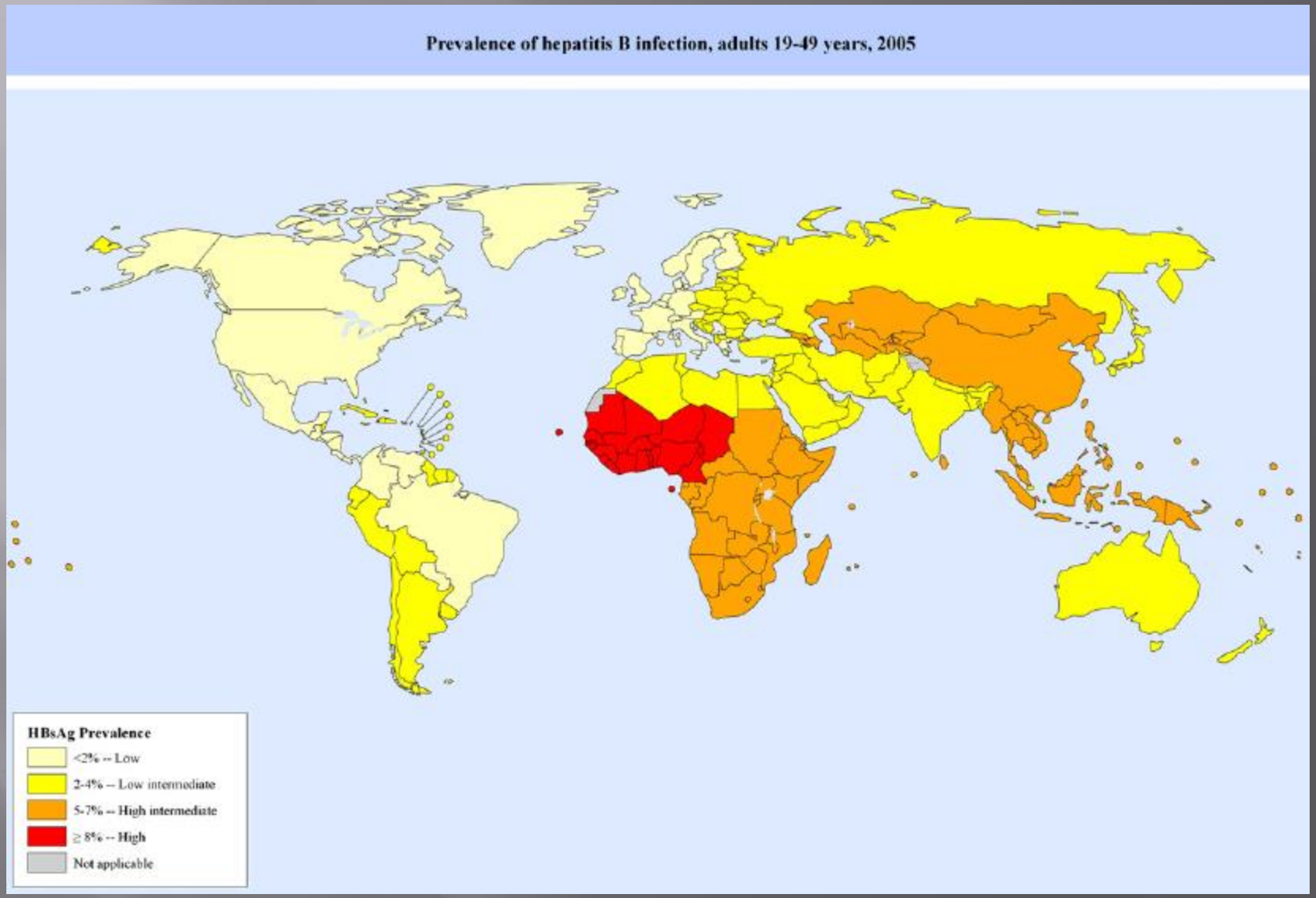
J.J. Ott[a], G.A. Stevens[a], J. Groeger[b], S.T. Wiersma[a,*]

[a] World Health Organization, 20, Avenue Appia, 1211 Geneva 27, Switzerland
[b] Centers for Disease Control and Prevention, Atlanta, GA, USA

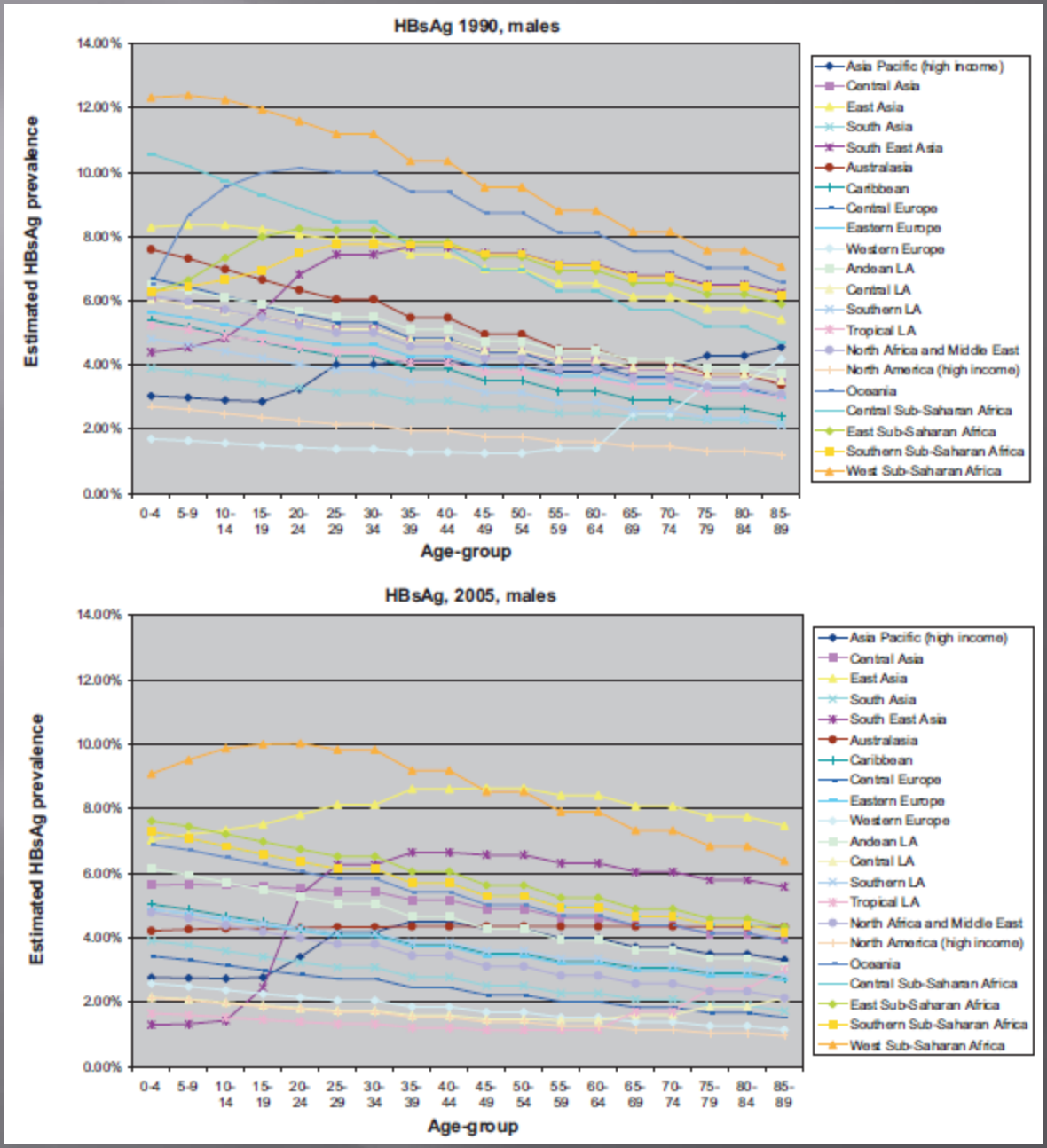
Sistematik derleme

1980-2007 seroprevalans verisi

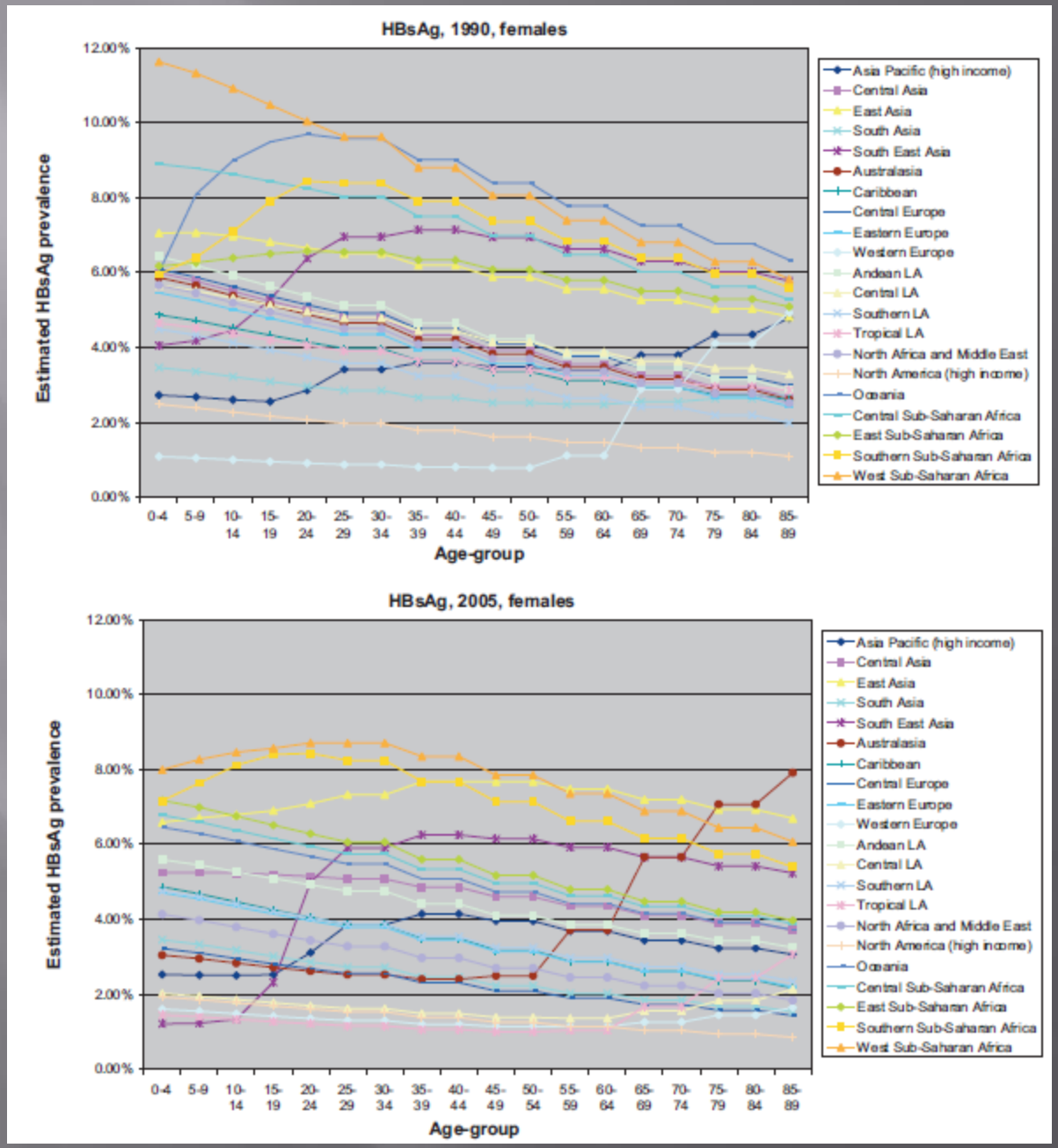
Ott JJ et al. Vaccine 2012;30:2212



Ott JJ et al. Vaccine 2012;30:2212



Ott JJ et al. Vaccine 2012;30:2212



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[b] Centers for Disease Control and Prevention, Atlanta, GA, USA

Table 1
Overview: Global HBsAg and people chronically infected.

Year	Males		Females		Both	
	Persons HBsAg positive	Prevalence	Persons HBsAg positive	Prevalence	Persons HBsAg positive	Prevalence
1990	118 million	4.4	105 million	4.0	223 million	4.2
2005	127 million	3.9	113 million	3.5	240 million	3.7

240 milyon kronik infekte olgu/dünya

Ott JJ et al. Vaccine 2012;30:2212

Published by Oxford University Press 2005
Advance Access publication 25 October 2005

International Journal of Epidemiology 2005;**34**:1329–1339
doi:10.1093/ije/dyi206

INFECTIOUS DISEASES

A mathematical model to estimate global hepatitis B disease burden and vaccination impact

Susan T Goldstein,[1]* Fangjun Zhou,[2] Stephen C Hadler,[2] Beth P Bell,[1] Eric E Mast[1] and Harold S Margolis[1]

HBV ilişkili nedenlerle 620000 ölüm/yıl

580000/yıl kronik infeksiyon ilişkili siroz ve HCC,

40000/yıl akut hepatit B

Goldstein ST et al. Int J Epidemiol 2005;34:1329

Akut hepatit B

- Lokal endemisiteye bağlı olarak insidans
  0.1-120/100000/yıl
- DSÖ 5 milyon/olgu/yıl

WGO Practice Guidelines 2007

National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention
Division of Viral Hepatitis

Disease Burden from Viral Hepatitis A, B, and C in the United States

	Hepatitis B					
	2009	2008	2007	2006	2005	2004
No. of Acute Clinical Cases Reported a	3,371	4,033	4,519	4,758	5,494	6,212
Estimated No. of Acute Clinical Cases b	9,000	12,000	13,000	13,000	15,000	17,000
Estimated No. of New Infections b (current)	38,000	38,000	43,000	46,000	53,000	60,000

Tablo 3.2. Yıllara Göre Bazı Seçilmiş Enfeksiyon Hastalıklarının Vaka Sayıları, Türkiye
Table 3.2. Number of Cases of Some Selected Infectious Diseases by Years, Turkey

	2002	2006	2007	2008	2009	2010
*Kızamık **Measles*	7.810	34	3	4	4	7
Tetanoz *Tetanus*	16	10	14	14	12	25
Neonatal Tetanoz *Neonatal Tetanus*	32	18	5	7	0	2
Boğmaca *Pertussis*	193	57	51	21	10	48
Hepatit B *Hepatitis B*	5.813	6.612	6.451	5.849	5.005	3.099

TCSB Sağlık İstatistikleri Yıllığı 2010

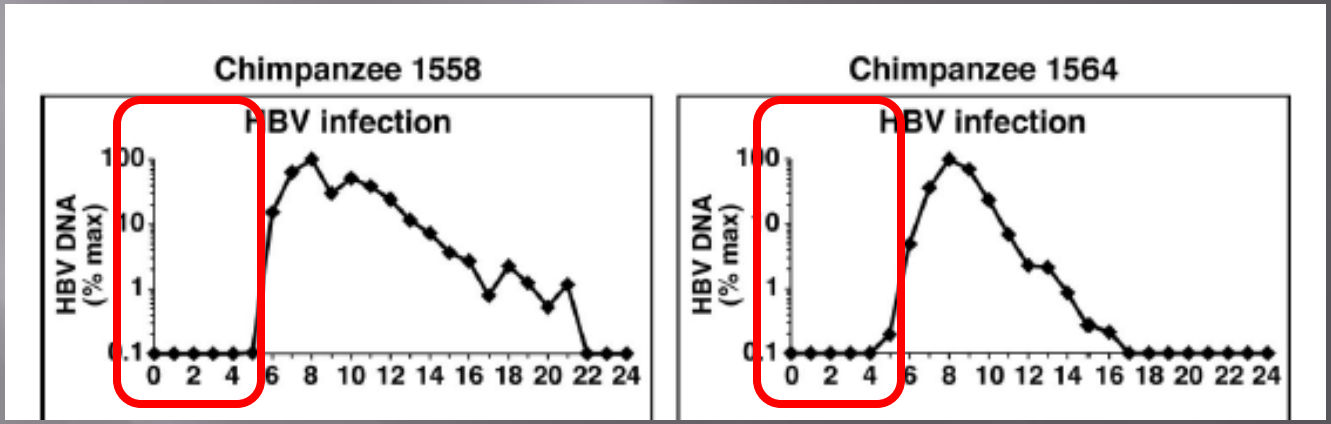
JOURNAL OF VIROLOGY, Aug. 2005, p. 9369–9380 Vol. 79, No. 15
0022-538X/05/$08.00+0 doi:10.1128/JVI.79.15.9369–9380.2005

MINIREVIEW

Stealth and Cunning: Hepatitis B and Hepatitis C Viruses

Stefan F. Wieland and Francis V. Chisari*

Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, California



İnokülasyon sonrası HBV 4-7 hafta kadar etkin bir replikasyona başlamaz (Lag fazı)

Wieland SF et al. J Virology 2005;79:9369

Journal of General Virology (2006), **87**, 1439–1449 DOI 10.1099/vir.0.81920-0

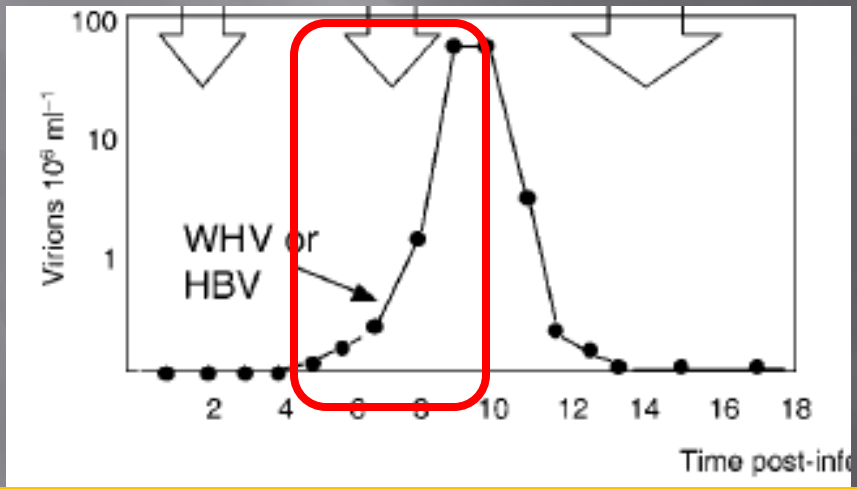
Review

The immune response during hepatitis B virus infection

Antonio Bertoletti and Adam J. Gehring

The UCL Institute of Hepatology, University College of London, 69–75 Chenies Mews, London WC1E 6HX, UK

Correspondence
Antonio Bertoletti
a.bertoletti@ucl.ac.uk



Ardından logaritmik bir ekspansiyon fazı ile hızla yükselerek 10^9-10^{10} kopya/ml düzeylerine ulaşır.

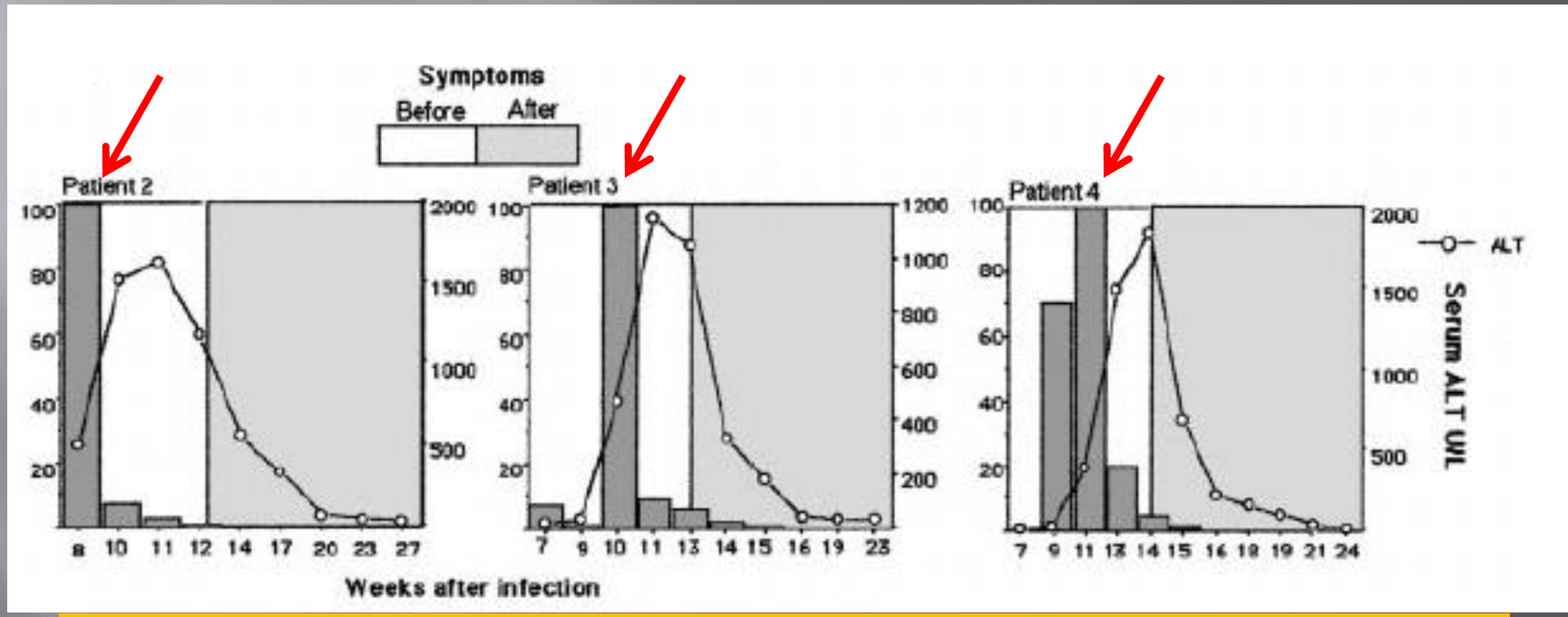
Bertoletti A et al. J Gen Virol 2006;87:1439

Akut infeksiyon sırasında HBsAg düzeyleri de haftalar aylar içinde yükselerek, tipik final konsantrasyonları olan 10000-100000 ng/ml düzeylerine ulaşır (t_d 2-4 gün).

Jindal A et al. Liver Int 2013;33(S1):164

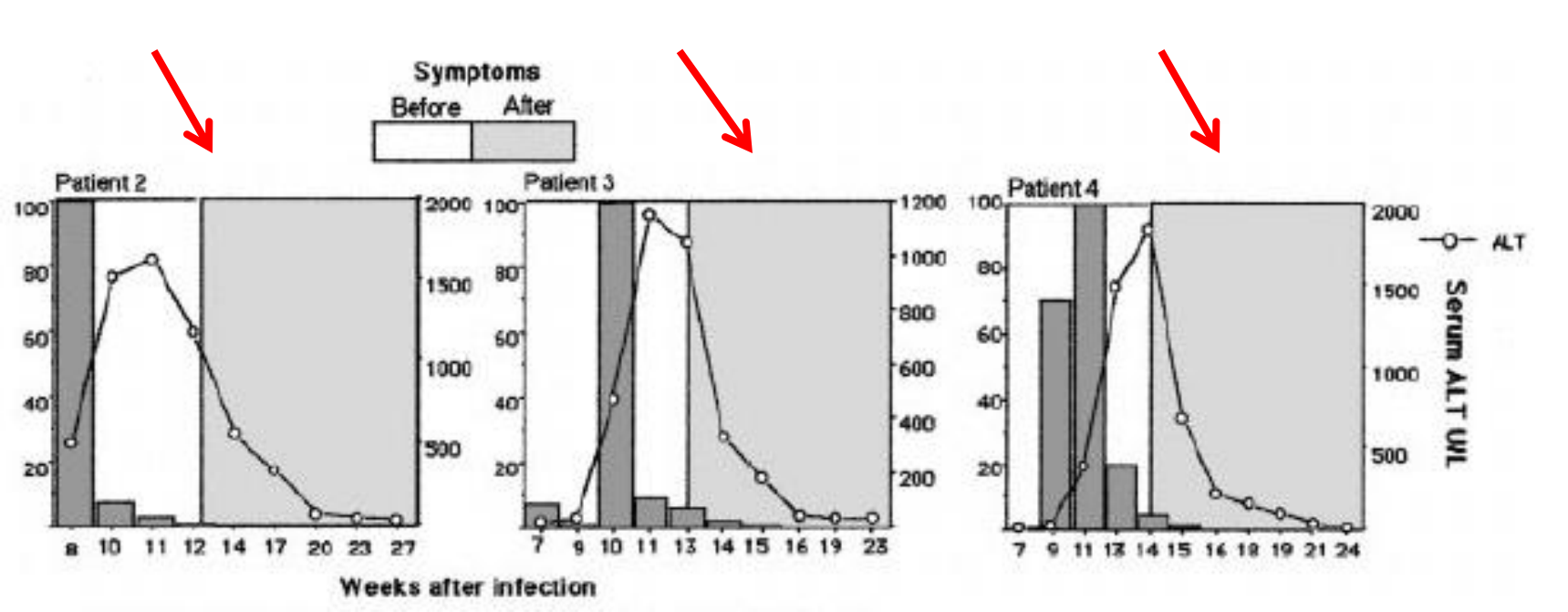
Incubation Phase of Acute Hepatitis B in Man: Dynamic of Cellular Immune Mechanisms

George J. M. Webster,[1] Stephanie Reignat,[4] Mala K. Maini,[4] Simon A. Whalley,[1] Graham S. Ogg,[3] Abigail King,[3] David Brown,[1] Peter L. Amlot,[2] Roger Williams,[4] Diego Vergani,[4] Geoffrey M. Dusheiko,[1] and Antonio Bertoletti[4]



HBV DNA'nın hızla yükseldiği bu dönemde hastalığın klinik semptomları henüz izlenmez.

Webster GJM et al. Hepatology 2000;32:1117



Klinik semptomların başlangıcı, HBV DNA düzeyinin zirve yaptıktan sonra azalmaya başladığı döneme denk gelir.

Webster GJM et al. Hepatology 2000;32:1117

Liver INTERNATIONAL
OFFICIAL JOURNAL OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE LIVER

Liver International ISSN 1478-3223

REVIEW ARTICLE

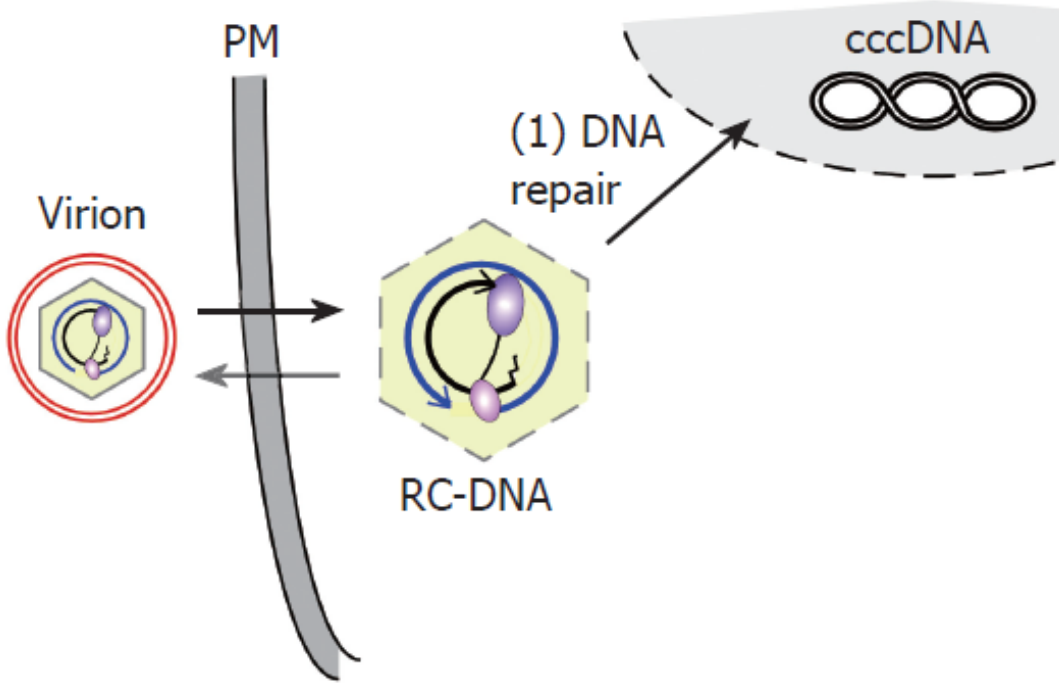
Management of acute hepatitis B and reactivation of hepatitis B

Ankur Jindal, Manoj Kumar and Shiv K. Sarin

Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Haftalar boyu süren viremiye karşın klinik ya da biyokimyasal bulguların olmaması, HBV replikasyonunun tek başına sitopatik olmadığını gösterir.

Jindal A et al. Liver Int 2013;33(S1):164



- İnkomplet Çİ DNA nükleusta→ cccDNA
- nükleusta cccDNA→ viral pregenomik RNA
- nükleokapsid içinde revers transkripsiyon →ssDNA →dsDNA

HBV RNA, RNA/DNA hibridleri, replikatif DNA ara molekülleri tamamen kapsid içinde bulunur

Beck J. World J Gastroenterol 2007;13:48

JOURNAL OF VIROLOGY, Aug. 2005, p. 9369–9380 Vol. 79, No. 15
0022-538X/05/$08.00+0 doi:10.1128/JVI.79.15.9369–9380.2005

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Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, California

HBV inkübasyon döneminin başlangıcında doğal bağışık yanıtı etkin biçimde stimüle etmez.

Bertoletti A et al. J Gen Virol 2006;87:1439

Wieland SF et al. J Virology 2005;79:9369

JOURNAL OF VIROLOGY, Aug. 2005, p. 9369–9380 Vol. 79, No. 15
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HBV hepatositlerin neredeyse tamamını infekte eder, infekte hücrelerde HBV antijenleri yüksek düzeyde eksprese edilir.

Adaptif immün yanıt tarafından daha kolay tanınır.

Wieland SF et al. J Virology 2005;79:9369

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HBV eliminasyonu klinik hastalığın başlangıcından haftalar önce, T hücre bağımlı non-sitolitik mekanizmalar ile başlar.

CTL kaynaklı IFN-γ

Jindal A et al. Liver Int 2013;33(S1):164

JOURNAL OF VIROLOGY, Aug. 2005, p. 9369–9380 Vol. 79, No. 15
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CTL

- IFN-γ salınımı ile HBV gen ekspresyonu non-sitopatik olarak inhibe edilir,
- transkripsiyon kalıbı cccDNA düzeylerini düşürür.

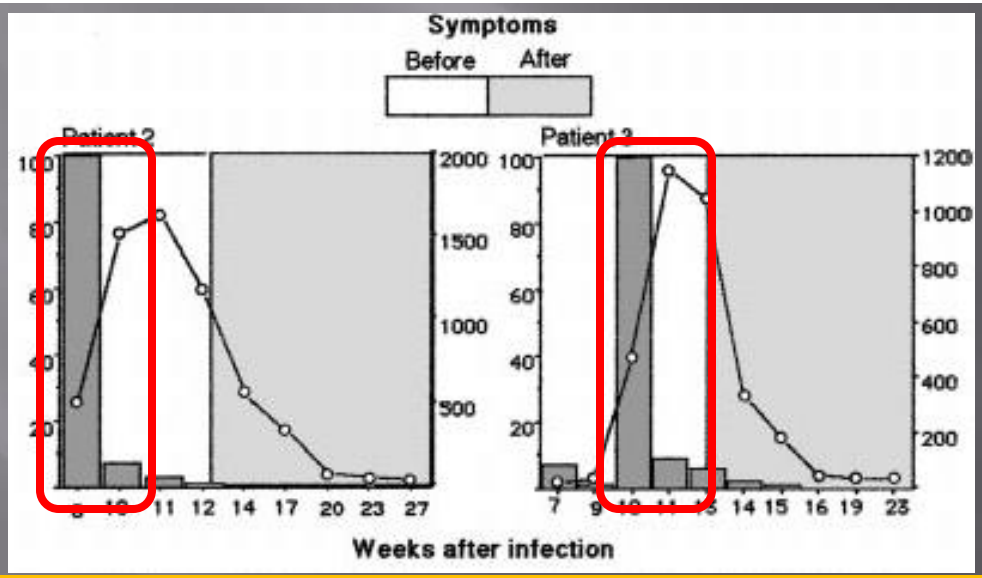
İnfekte hepatositlerin >%90 non-sitolitik mekanizmalar ile temizlenir.

Wieland SF et al. J Virology 2005;79:9369

Kinetics of Acute Hepatitis B Virus Infection in Humans

By Simon A. Whalley,* John M. Murray,§‖ Dave Brown,*
George J.M. Webster,* Vincent C. Emery,‡ Geoffrey M. Dusheiko,*
and Alan S. Perelson§

*From the *Centre for Hepatology, Department of Medicine, Royal Free Campus, and the ‡Department of Virology, Royal Free and University College Medical School, London NW3 2QG, United Kingdom; the §Theoretical Division, Los Alamos National Laboratory, Los Alamos, New Mexico 87545; and the ‖School of Mathematics, University of New South Wales, Sydney NSW 2052, Australia*



HBV DNA'nın hızla düştüğü ilk faz gerçekleşir.

Webster GJM et al. Hepatology 2000;32:1117

Whalley SA et al. J Exp Med 2001;193:847

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Bu dönemde ortalama yarı ömür ($t_{1/2}$) 3.7±1.2 gündür.

Webster GJM et al. Hepatology 2000;32:1117

Whalley SA et al. J Exp Med 2001;193:847

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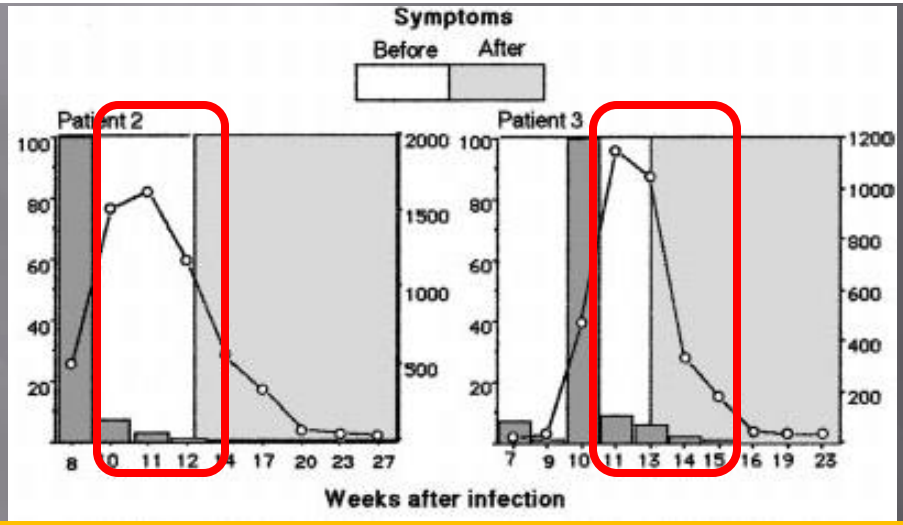

Ardından CTL aracılı sitolitik yanıt gelişir, cccDNA içeren hepatositlerin yıkımı ile akut hepatit semptomları oluşur.

Webster GJM et al. Hepatology 2000;32:1117

Jindal A et al. Liver Int 2013;33(S1):164

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ALT zirvesi DNA zirvesinden 12±6 gün sonra izlenir. ALT ↑ / DNA↓

Viral temizlenmenin ikinci fazında ortalama yarı ömür değişkendir ($t_{1/2}$) 4.8±284 gün

İnfekte hepatositlerin ortadan kaldırılma hızı ile ilişkilidir.

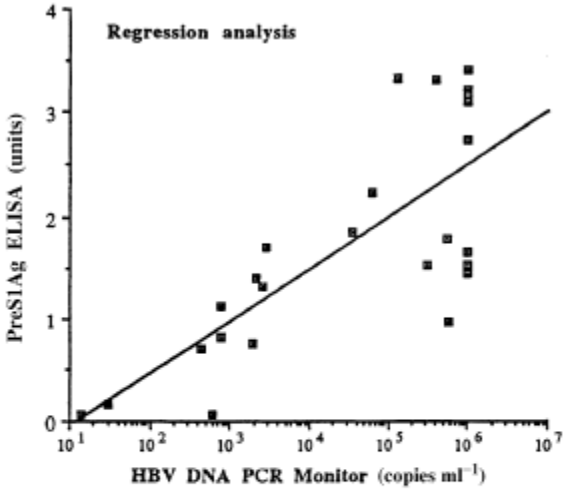
Webster GJM et al. Hepatology 2000;32:1117

Whalley SA et al. J Exp Med 2001;193:847

Journal of Viral Hepatitis, 2000, 7, 387–392

Evaluation of an enzyme-linked immunosorbent assay for detection and quantification of hepatitis B virus PreS1 envelope antigen in serum samples: comparison with two commercial assays for monitoring hepatitis B virus DNA

D. Buffello-Le Guillou,[1] J. C. Duclos-Vallée,[1] F. Eberle,[2] F. Capel[1] and M. A. Petit[1] [1]*Centre Hépato-Biliaire, INSERM E99-41 and UPRES 1596, Hôpital Paul Brousse, Villejuif and* [2]*Roche Diagnostics, Grenoble, France*



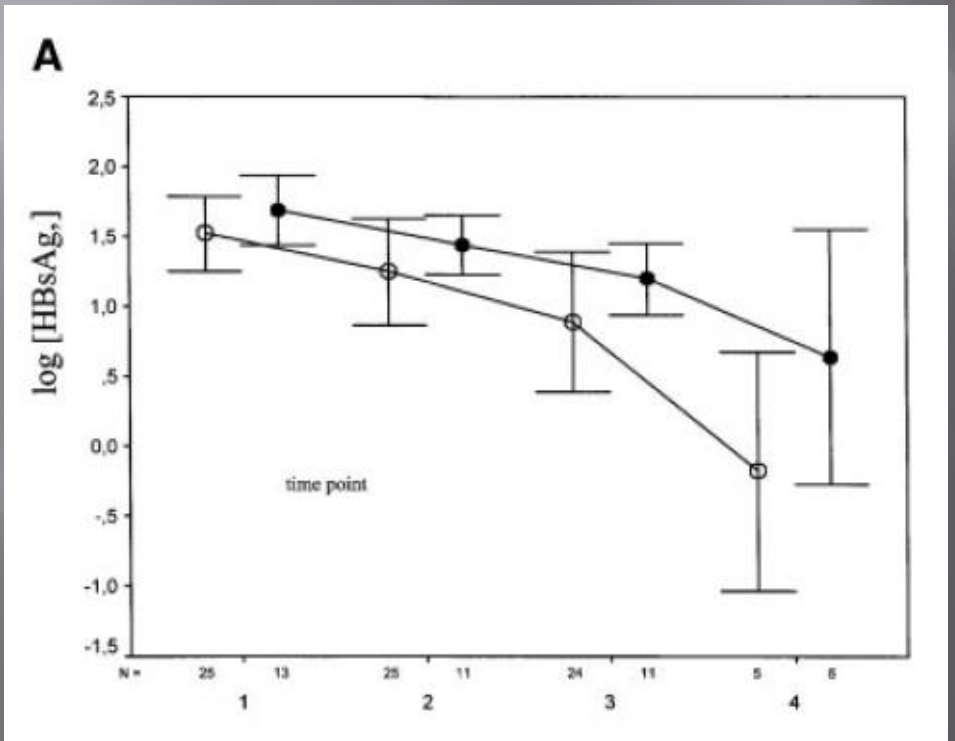
PreS1Ag : (units)	**< 0.25**	**0.25 < x < 1**	**1 < x < 2**	**2 < x < 3**	**> 3**
HBV DNA : (copies ml $^{-1}$)	**< 400**	**400 < x < 10^3**	**10^3 < x < 10^5**	**10^5 < x < 10^7**	**> 10^7**
HBV replication:	**Negative**	**Very low**	**Low**	**Moderate**	**High**

Le Guillou DB et al. J Viral Hep 2000;7:387

Journal of Medical Virology 69:313–323 (2003)

Kinetics of HBV DNA and HBsAg in Acute Hepatitis B Patients With and Without Coinfection by Other Hepatitis Viruses

Vladimir P. Chulanov,[1,2] German A. Shipulin,[1] Stephan Schaefer,[2] and Wolfram H. Gerlich[2]*
[1]*Central Research Institute of Epidemiology, Russian Federal Aids Center Moscow, Russia*
[2]*Institute of Medical Virology, Justus Liebig University Giessen, Germany*



Chulanov VP et al. J Med Virol 2003;69:313

CONCISE REVIEW IN MECHANISMS OF DISEASE

Kinetics of the Immune Response During HBV and HCV Infection

Antonio Bertoletti[1] and Carlo Ferrari[2]

HBV infeksiyonlarının kendiliğinden iyileştiği olgularda, erken, kuvvetli, poliklonal ve birden çok viral epitopa karşı multispesifik CD4 ve CD8 T lenfosit yanıtı ile Th-1 tipi sitokin profili olduğu gösterilmiştir.

Bertoletti A. Hepatology 2003;38:4

Journal of General Virology (2006), **87**, 1439–1449 DOI 10.1099/vir.0.81920-0

Review

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a.bertoletti@ucl.ac.uk

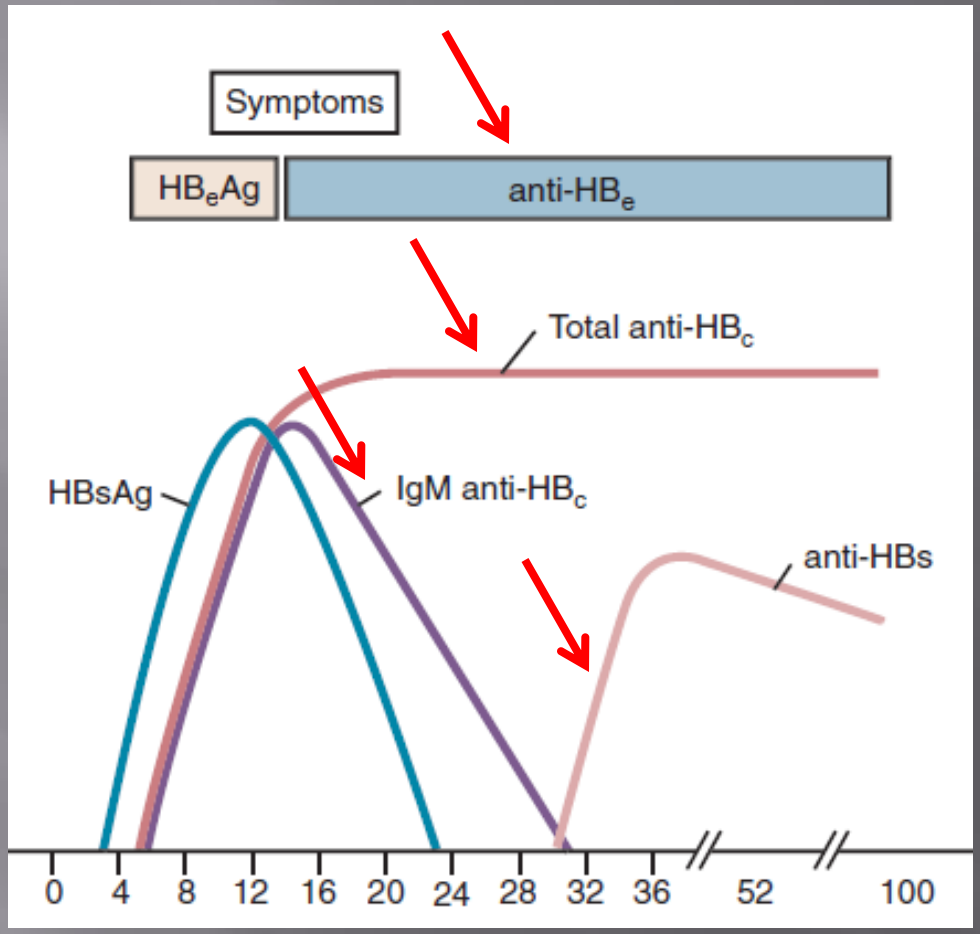
Eşzamanlı olarak, humoral immün yanıt da gelişir ve infeksiyonun kontrolünde rol oynar.

core antijeni,

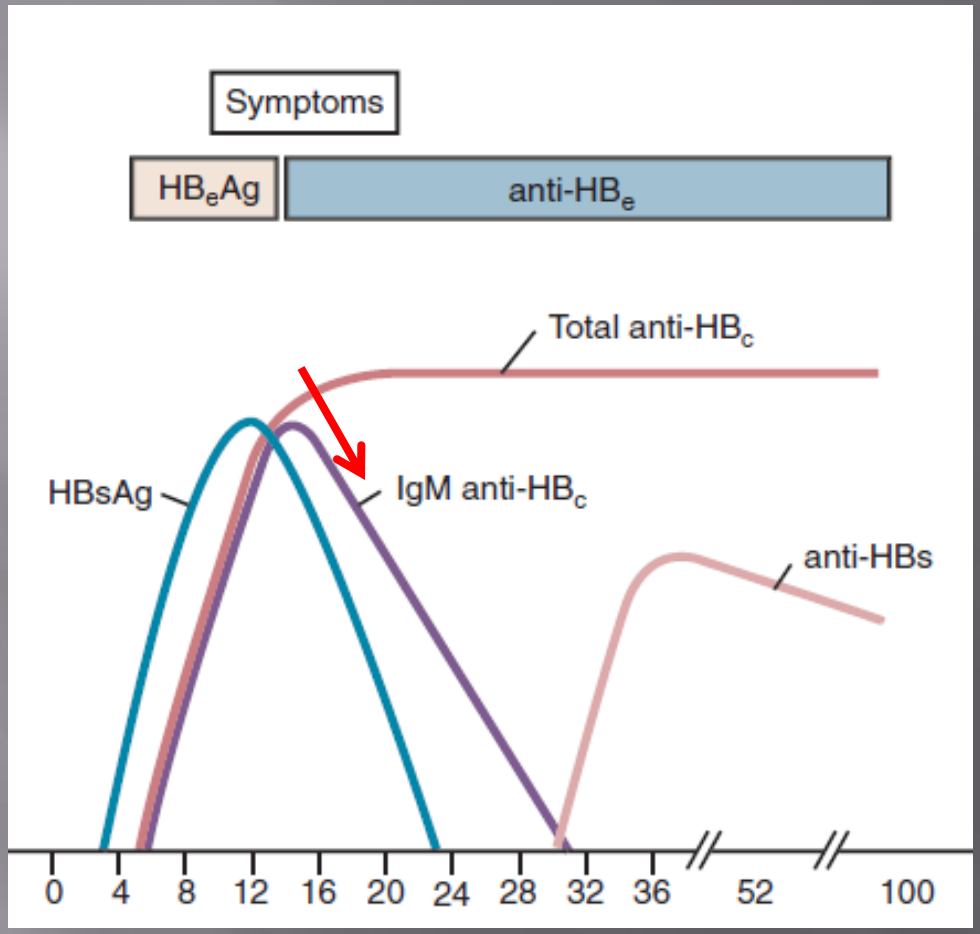
HBe antijeni,

HBs antijeni

Bertoletti A et al. J Gen Virol 2006;87:1439



antiHBc yanıtı kısmen T hücrelerinden bağımsızdır, dolayısıyla etkin bir immün yanıt geliştiremeyen hastalarda da saptanabilir.

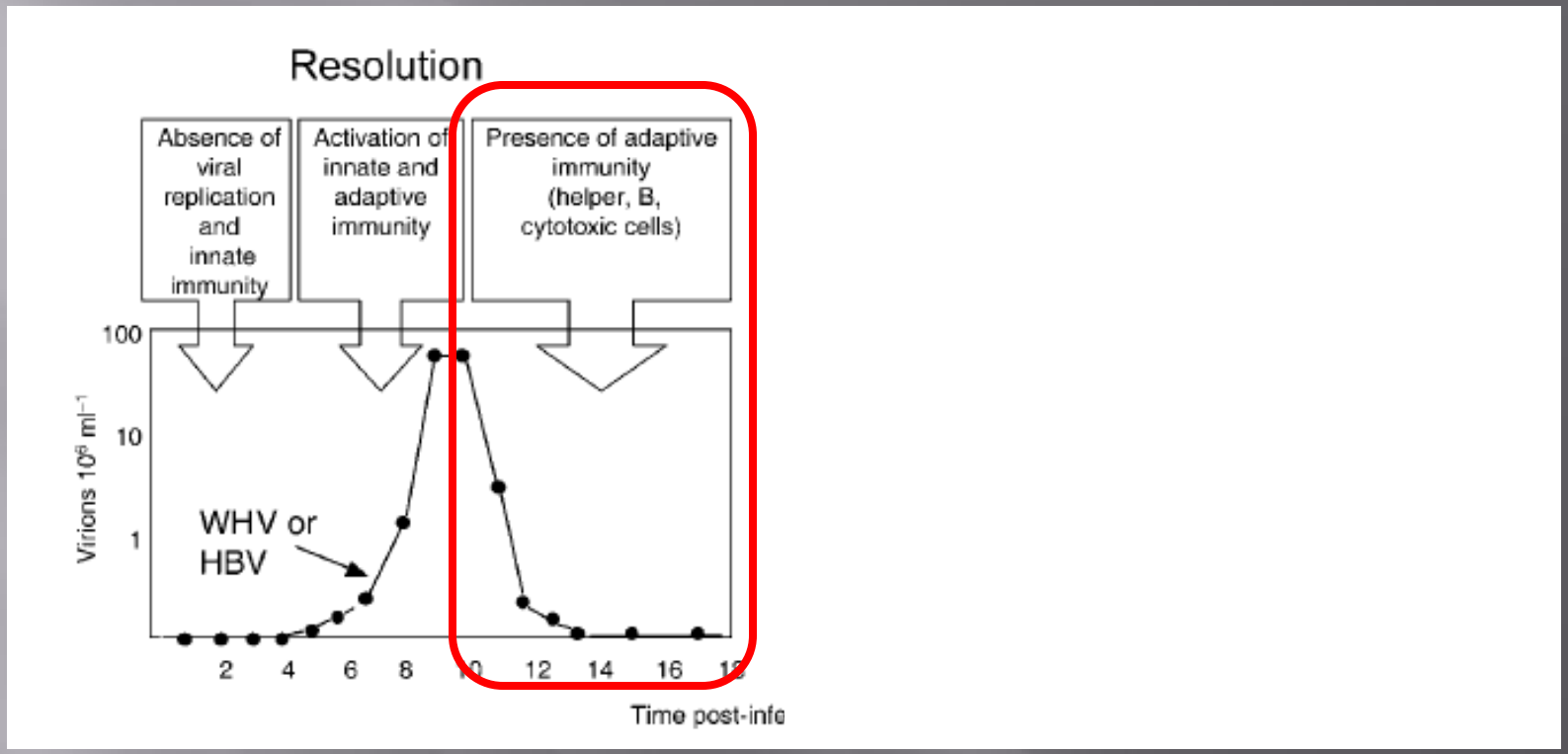


antiHBcIgM, HBsAg'nin saptanmasından sonra ~1 ay içinde belirir.

~%20 olguda 2 yıla kadar pozitif saptanır.

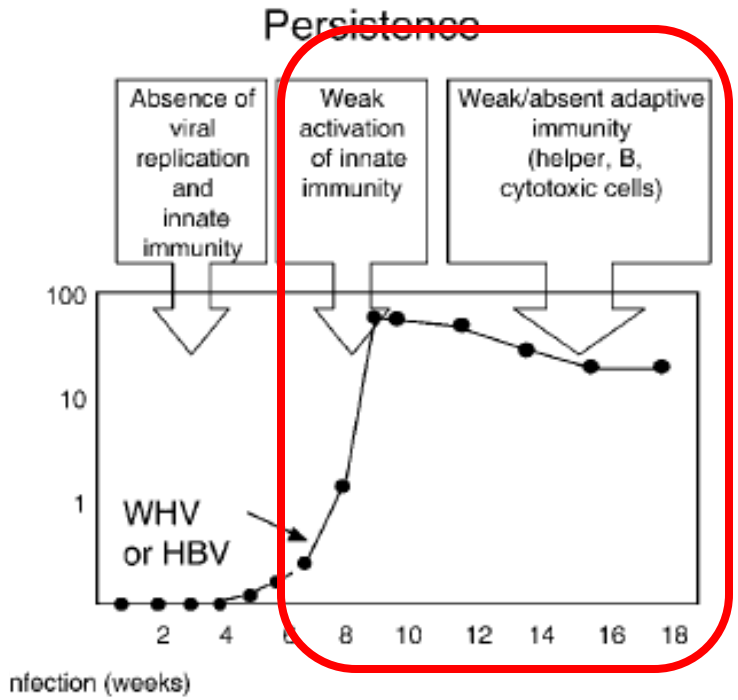
Sonuç olarak HBV infeksiyonunun kontrolü için adaptif immün yanıtın hem hücresel hem de humoral kollarının aktivasyonu gerekmektedir.

Bertoletti A et al. J Gen Virol 2006;87:1439



HBV ve HCV infeksiyonunun kontrolünde esas sorumlu mekanizma, etkin ve sürekli bir hücresel immün yanıt geliştirme yeteneğidir.

Bertoletti A et al. J Gen Virol 2006;87:1439



Bu yanıtın yetersiz olması kronikleşme ile sonuçlanır.

Bertoletti A et al. J Gen Virol 2006;87:1439

JOURNAL OF VIROLOGY, Aug. 2005, p. 9369–9380 Vol. 79, No. 15
0022-538X/05/$08.00+0 doi:10.1128/JVI.79.15.9369–9380.2005

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Mutasyonel kaçak

Kronik HBV infeksiyonunda B ve T hücre epitoplarında mutasyonel inaktivasyon gösterilmiştir.

T hücre epitop mutasyonları antijen sunumunu engeller.

Wieland SF. J Virol 2005;79:9369

Precore protein

tolerojendir,

HBcAg'e T hücre ve antikor yanıtını baskılar,

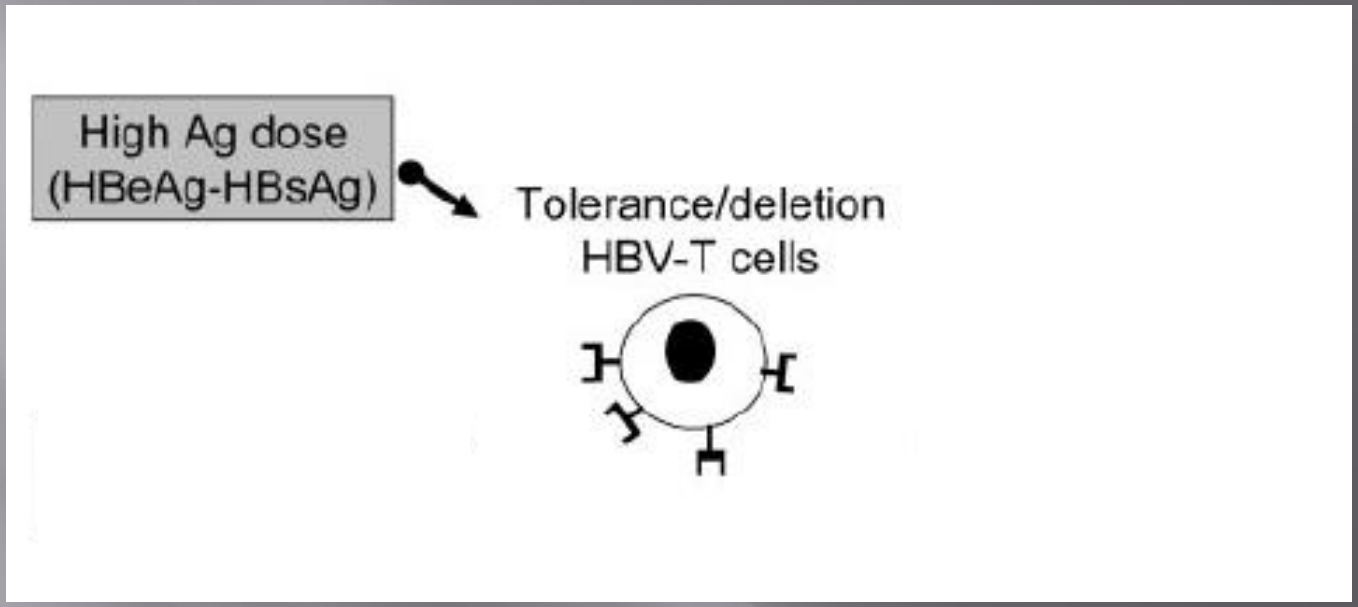
HBcAg/HBeAg çapraz-reaktif T hücre anerjisi.

HBeAg üretimini sonlandıran mutasyonlar, sıklıkla karaciğer hastalığında alevlenme ve bazen de viral temizlenme ile ilişkilidir.

HBeAg

transgenik farelerde Th-1 hücrelerin delesyonu ve Th-2 sitokinlerin üretimini indükler.

Wieland SF. J Virol 2005;79:9369

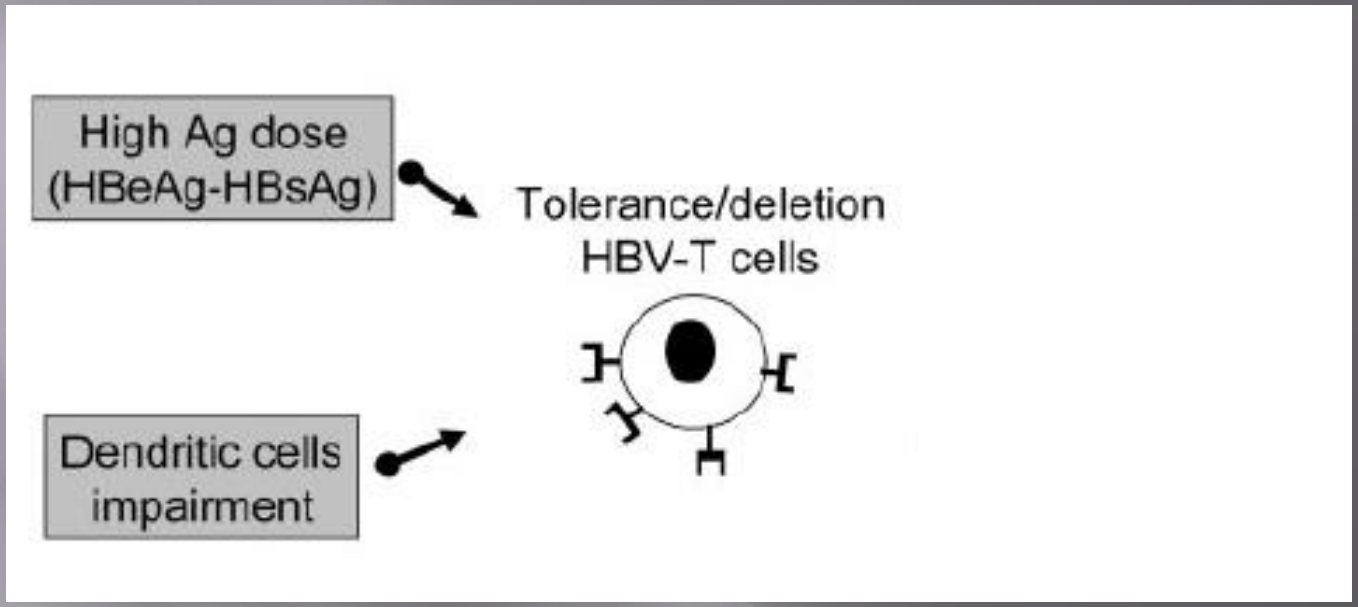


HBeAg'nin tolerojen etkisi

HBsAg'nin aşırı miktarda üretimi

virionların 10^3-10^6 katı HBsAg partikülü

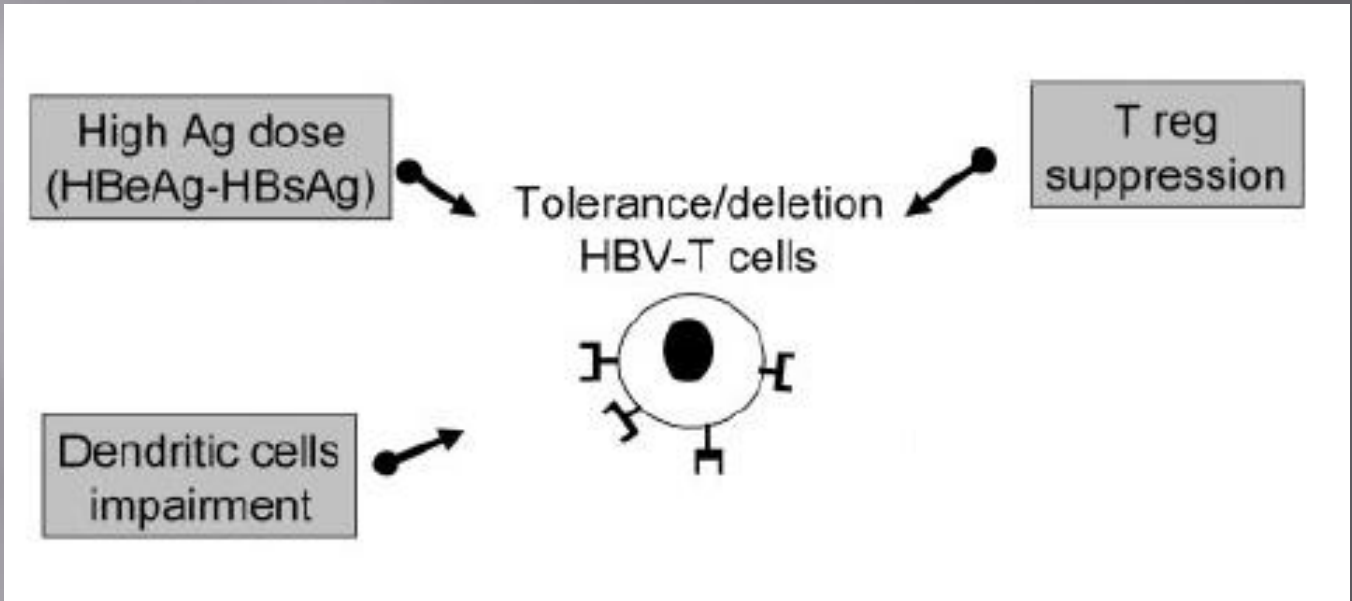
Bertoletti A et al. J Gen Virol 2006;87:1439



APC dendritik hücre fonksiyon bozuklukları

CD4+ T lenfosit yanıtsızlığına yol açar

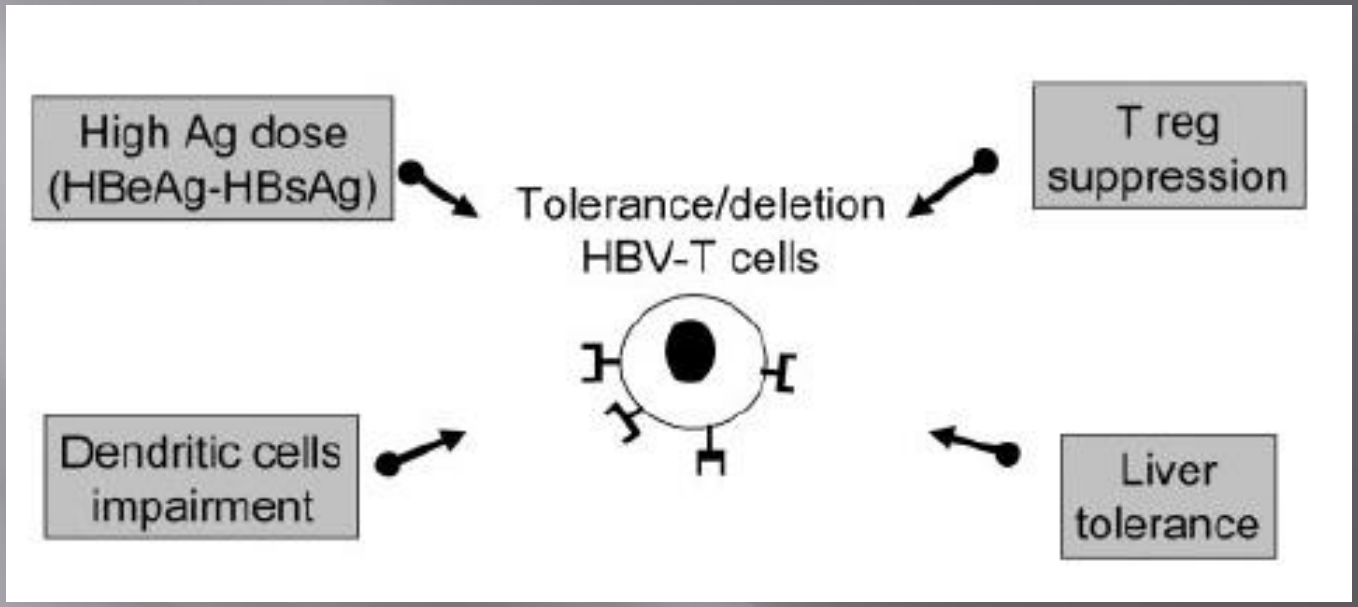
Bertoletti A et al. J Gen Virol 2006;87:1439



CD4+ CD25+ Tregs

HBV spesifik CD8+ T hücre fonksiyonlarını inhibe ederek immün aracılı hepatosit hasarını sınırlandırmaya çalışırlar

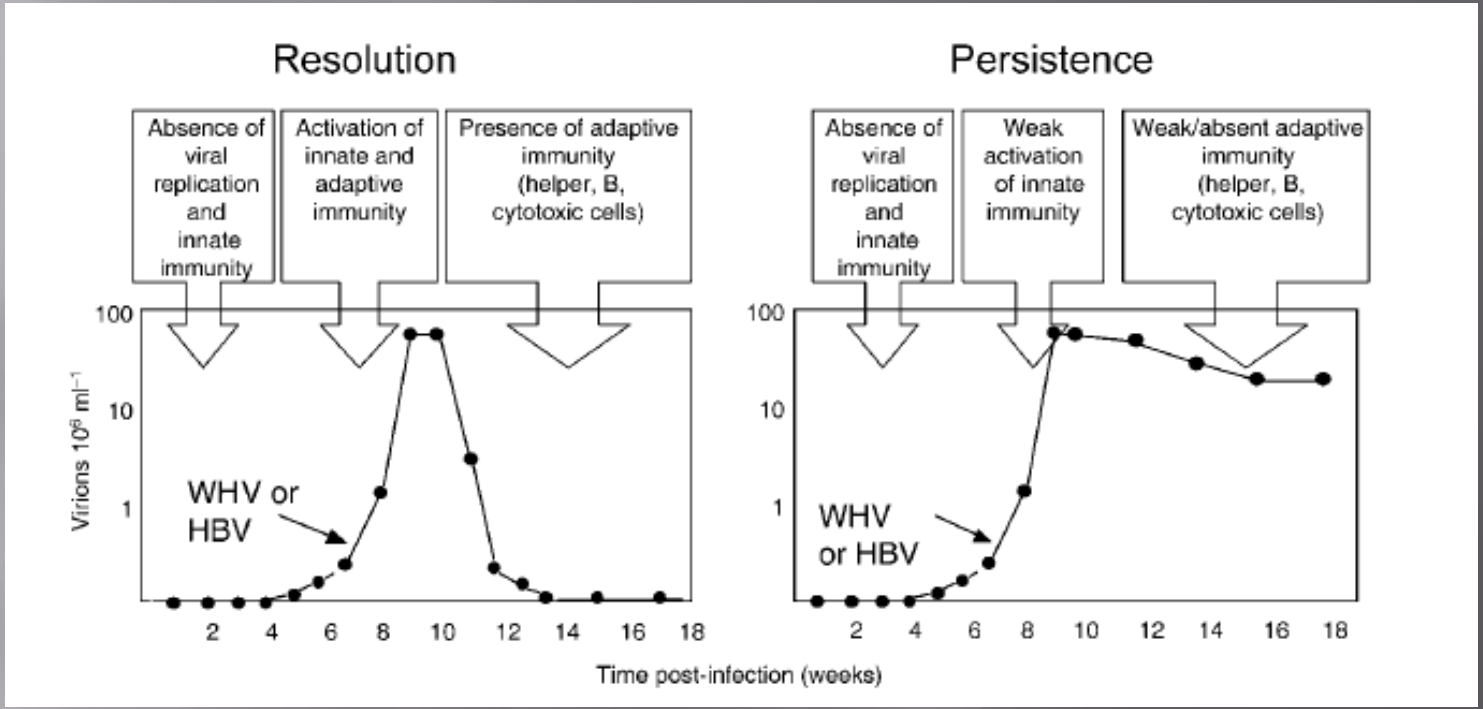
Bertoletti A et al. J Gen Virol 2006;87:1439



Karaciğer toleransı

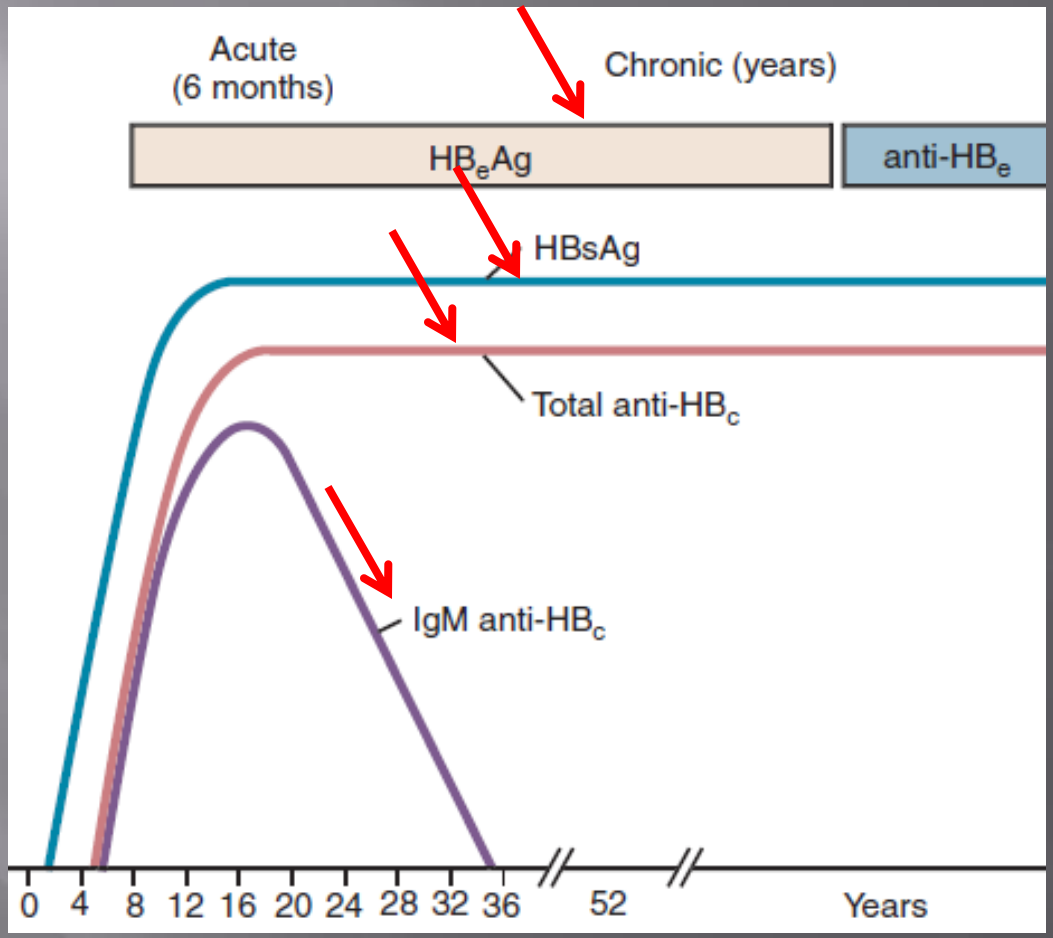
hepatositler düşük düzeyde MHC-Class I eksprese ederler ve benzer sayıda CD8+ T hücresi stimüle etmek için, diğer APC'den, 100 kat daha fazla peptid konsantrasyonu gerekir.

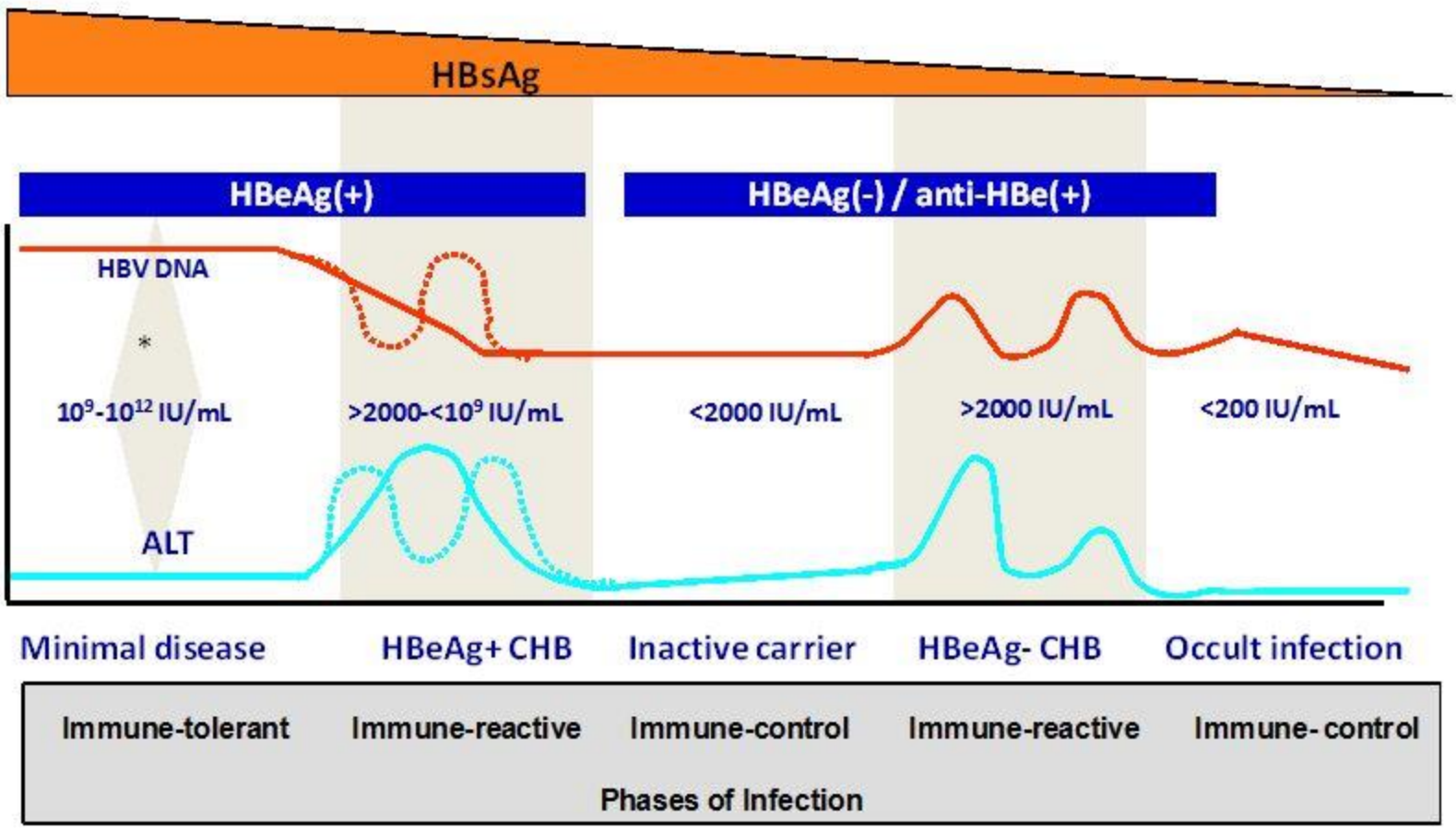
Hepatositlerdeki patojenler CD8+ T hücreleri tarafından daha güç tanınır.



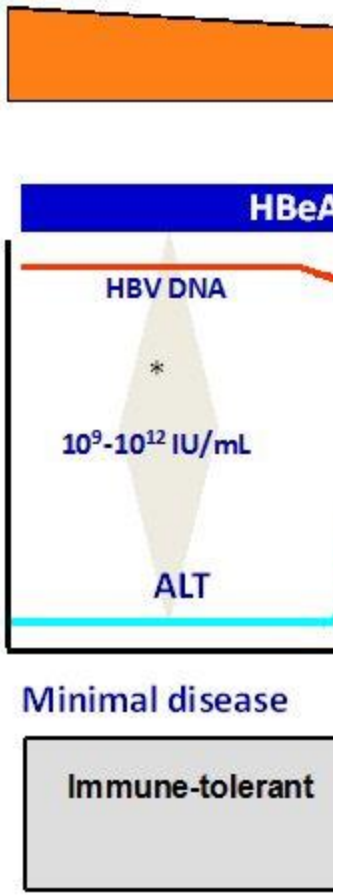
T hücre yanıtsızlığı ya da HBV spesifik T hücre ekspansiyonunun erken dönemde azalması kronikleşme ile ilişkilidir.

Bertoletti A et al. J Gen Virol 2006;87:1439

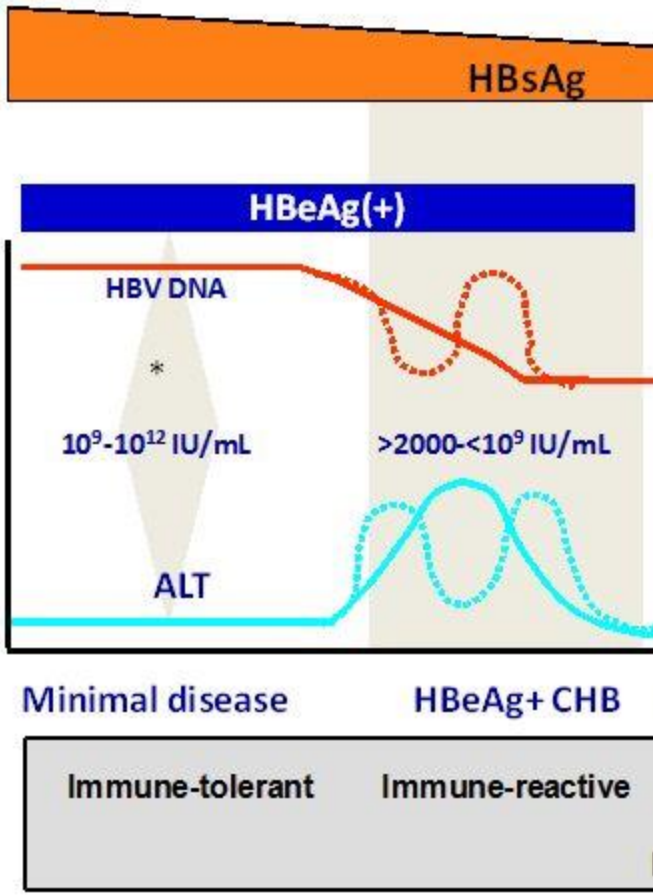

Acute
(6 months)
Chronic (years)
HBeAg
anti-HBe
HBsAg
Total anti-HBc
IgM anti-HBc
0 4 8 12 16 20 24 28 32 36 52
Years



Kronik hepatit B’nin doğal seyrinde 4 evre



Kronik hepatit B’nin doğal seyrinde 4 evre



Kronik hepatit B’nin doğal seyrinde 4 evre

GASTROENTEROLOGY 2001;120:1009–1022

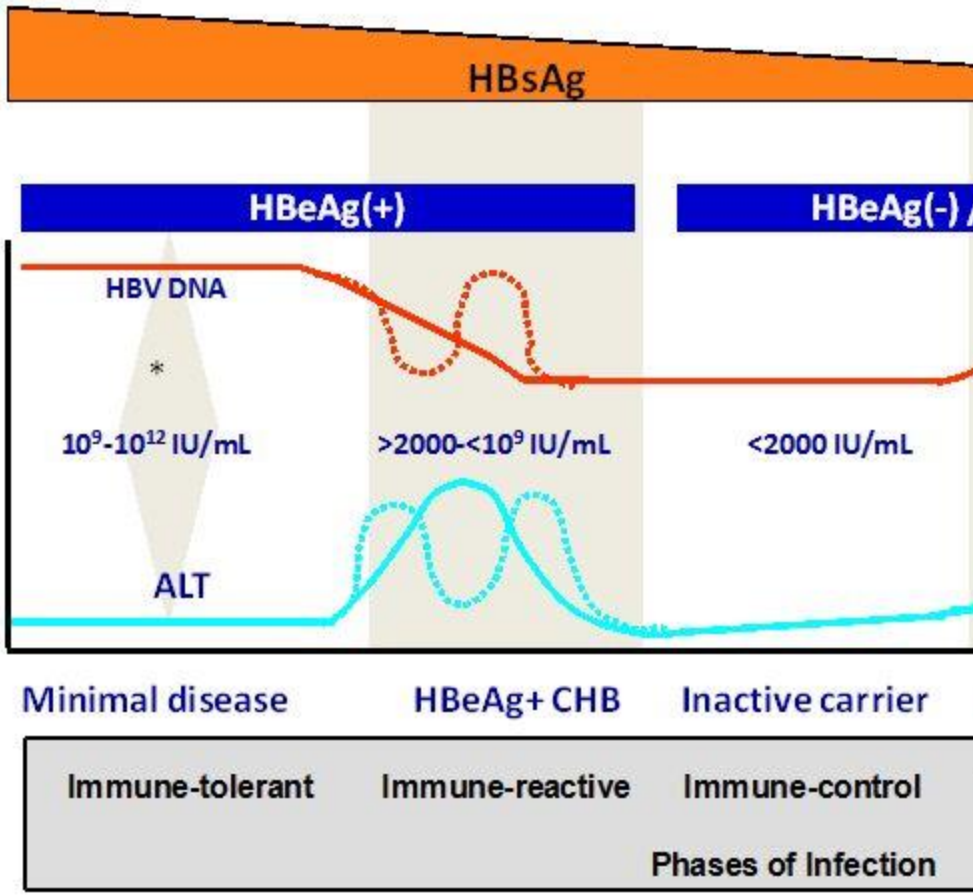
Acute Flares in Chronic Hepatitis B: The Natural and Unnatural History of an Immunologically Mediated Liver Disease

ROBERT P. PERRILLO
Section of Gastroenterology and Hepatology, Ochsner Clinic and Alton Ochsner Medical Foundation, New Orleans, Louisiana

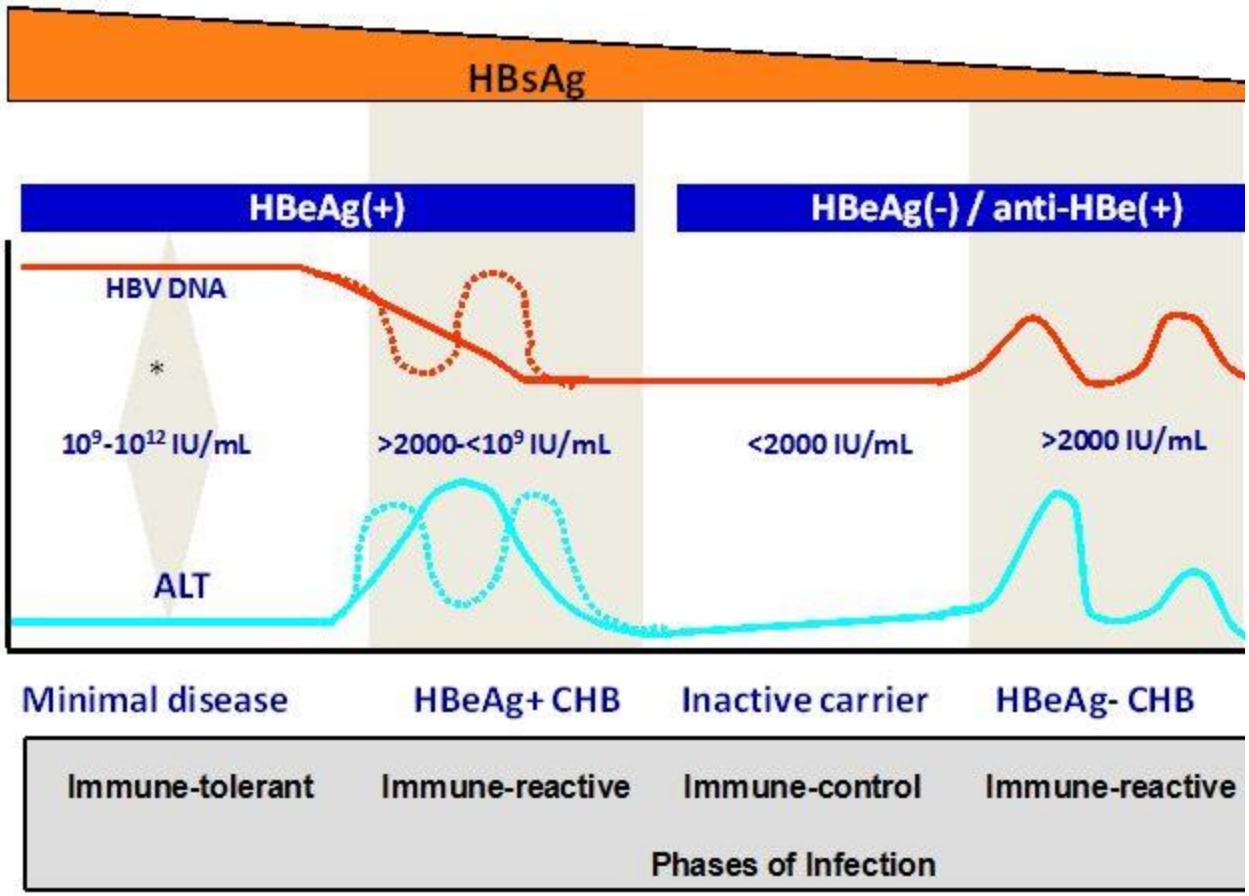
Alevlenme epizodları serokonversiyon için başarılı olabilen / olamayan denemelerdir.

İmmün reaktif fazdaki alevlenmeler HBeAg (+) hastaların %40-50'sinde görülür

Perillo RP et al. Gastroenterology 2001;120:1009



Kronik hepatit B’nin doğal seyrinde 4 evre



Kronik hepatit B’nin doğal seyrinde 4 evre

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Klinik olarak saptanan alevlenmelerin çoğu, düşük replikatif fazda yaşanır.

HBeAg (-) dönemdeki hastaların %15-30'unda görülür.

Perillo RP et al. Gastroenterology 2001;120:1009

GASTROENTEROLOGY 2001;120:1009–1022

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ROBERT P. PERRILLO
Section of Gastroenterology and Hepatology, Ochsner Clinic and Alton Ochsner Medical Foundation, New Orleans, Louisiana

Akut alevlenmelerin sıklığı açısından Asya ve Avrupa hastaları arasında dikkat çekici farklılıklar vardır.

Asya kökenli hastalarda HBeAg (-) dönemde reaktivasyon ve serolojik dalgalanmalar daha sıktır.

Perillo RP et al. Gastroenterology 2001;120:1009

GASTROENTEROLOGY 2001;120:1009–1022

Acute Flares in Chronic Hepatitis B: The Natural and Unnatural History of an Immunologically Mediated Liver Disease

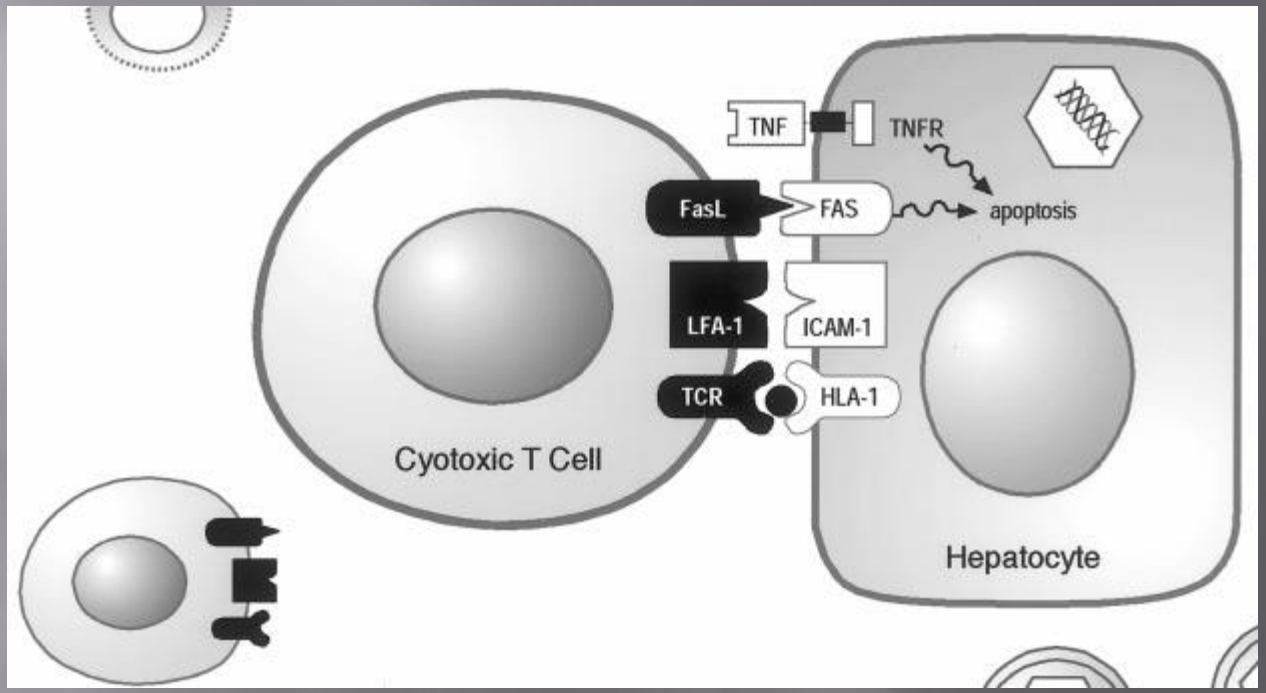
ROBERT P. PERRILLO
Section of Gastroenterology and Hepatology, Ochsner Clinic and Alton Ochsner Medical Foundation, New Orleans, Louisiana

Akut alevlenmelerin spontan olduğu kabul edilir.

HBV replikasyonunda artış ya da mutant HBV T hücre yanıtını uyarabilir.

HBV'ye karşı immün yanıtta kuvvetlenme anlamına gelir.

Perillo RP et al. Gastroenterology 2001;120:1009



Akut alevlenmelerde nekroinflamatuvar reaksiyon alanlarındaki hücresel infiltrasyonu esas olarak CD8+ CTL oluşturur.

TNF-α, fas ligand, perforin aracılı

Perillo RP et al. Gastroenterology 2001;120:1009

Kronik HBV infeksiyonunda HBV spesifik T hücre yanıtı ve sitolitik aktivite, hepatositlerden virüsü eradike edecek kadar iyi değildir ama hepatosit hasarına yol açacak kadar da kuvvetlidir.

Online Submissions: wjg.wjgnet.com
wjg@wjgnet.com
doi:10.3748/wjg.14.7133

World J Gastroenterol 2008 December 14; 14(46): 7133-7137
World Journal of Gastroenterology ISSN 1007-9327

CASE REPORT

Acute hepatitis B or exacerbation of chronic hepatitis B-that is the question

Efrat Orenbuch-Harroch, Liran Levy, Eldad Ben-Chetrit

Endemik bölgelerde akut hepatit B klinik tablosu ile başvuran hastaların %50'si aslında kronik hepatitin akut alevlenmesidir.

Orenbuch-Harroch E et al. World J Gastroenterol 2008;14:7133

Ciddi reaktivasyonun tipik klinik tablosu, yüksek ALT düzeyleri ve sarılıkla karakterizedir

	Akut hepatit	Akut alevlenme
ALT	↑	↑
DNA	↑	↑
Bilirubin	↑	↑

Semptomlar, fizik inceleme ya da biyokimyasal parametrelerle “KHB akut alevlenme” ile “akut hepatit B”yi ayırt etmek olanaklı değildir.

Akut alevlenme tablosu ile başvuran hastaların %10-15'inde antiHBcIgM pozitifliği saptanır.

Öykü/Özgeçmiş

- sarılık öyküsü,
- kronik hepatit B için aile öyküsü,
- kan transfüzyonu,
- operasyon,
- dental girişim,
- perkütan yaralanma,
- korunmasız cinsel ilişki.

Akut hepatit seyrinde

antiHBcIgM pozitifleşir,
antiHBcIgG pozitifleşir,
HBV DNA ↓,
HBsAg ↓,
HBeAg serokonversiyonu

Digestive Diseases and Sciences, Vol. 51, No. 3 (March 2006), pp. 594–599 (© 2006)
DOI: 10.1007/s10620-006-3175-2

Differentiating Acute Hepatitis B from the First Episode of Symptomatic Exacerbation of Chronic Hepatitis B

MANOJ KUMAR, MD, SANJAY JAIN, MD, BARJESH CHANDER SHARMA, MD, DM, and SHIV KUMAR SARIN, MD, DM

Akut hepatit semptomları olan 79 hasta
49 akut hepatit B (AHB)
30 akut alevlenme (AE)

Kumar M et al. Dig Dis and Sci 2006;51:594

TABLE 2. CLINICAL PRESENTATION

Parameters	*Group 1* (n = 49) n(%)	*Group 2* (n = 30) n(%)	P
Prodrome			
Fever	35 (71.4%)	16 (53.3%)	.08
Fatigue	35 (71.4%)	21 (70%)	.54
Anorexia	33 (67.3%)	20 (66.7%)	.57
Jaundice	49 (100%)	30 (100%)	—
Abdominal discomfort	17 (34.7%)	8 (26.7%)	.31
Itching	13 (26.5%)	9 (30%)	.46
Loose stools	2 (4.1%)	1 (3.3%)	.67
Clay stools	5 (10.2%)	1 (3.3%)	.25
Hepatomegaly	12 (24.5%)	6 (20%)	.43
Splenomegaly	5 (9.9%)	3 (10%)	.41
Pedal edema	1 (1.9%)	0	.62
Clinical ascites	0	0	—

TABLE 3. BIOCHEMICAL PROFILE

Parameters	*Group 1* (n = 49)	*Group 2* (n = 30)	p
Serum bilirubin median	8.2	9.8	.264
(mg/dL) range	(2.7–72.9)	(3.0–37.2)	
Mean ± SD	10.7 ± 10.6	11.1 ± 6.8	
ALT levels (median)	1085	923	.103
Range	(400–6920)	(400–2900)	
Mean ± SD	1541.9 ± 1232.8	1127 ± 692	
5–10 × ULN	1 (2%)	2 (6.7%)	
10–20 × ULN	12 (24.5%)	10 (33.3%)	
>20 × ULN	36 (73.5%)	18 (60%)	
PT prolongation (median) (sec)	3.0	4.4	.689
Range	(0–32)	(0–16)	
Mean ± SD	5.2 ± 5.5	5.1 ± 4.2	
Serum albumin (g/dL) (median)	3.70	3.75	.887
Range	(2.9–4.6)	(2.7–4.5)	
Mean ± SD	3.72 ± 0.36	3.69 ± 0.49	
Serum globulin (g/dL)			
Median	2.90	3.10	.105
Range	(2.0–3.8)	2.0–5.0	
Mean ± SD	3.0 ± 0.42	3.20 ± 0.61	
Albumin/globulin (median)	1.20	1.09	.070
Ratio (range)	(0.94–1.85)	(0.77–2.00)	
Mean ± SD	1.26 ± 0.22	1.18 ± 0.28	

Kumar M et al. Dig Dis and Sci 2006;51:594

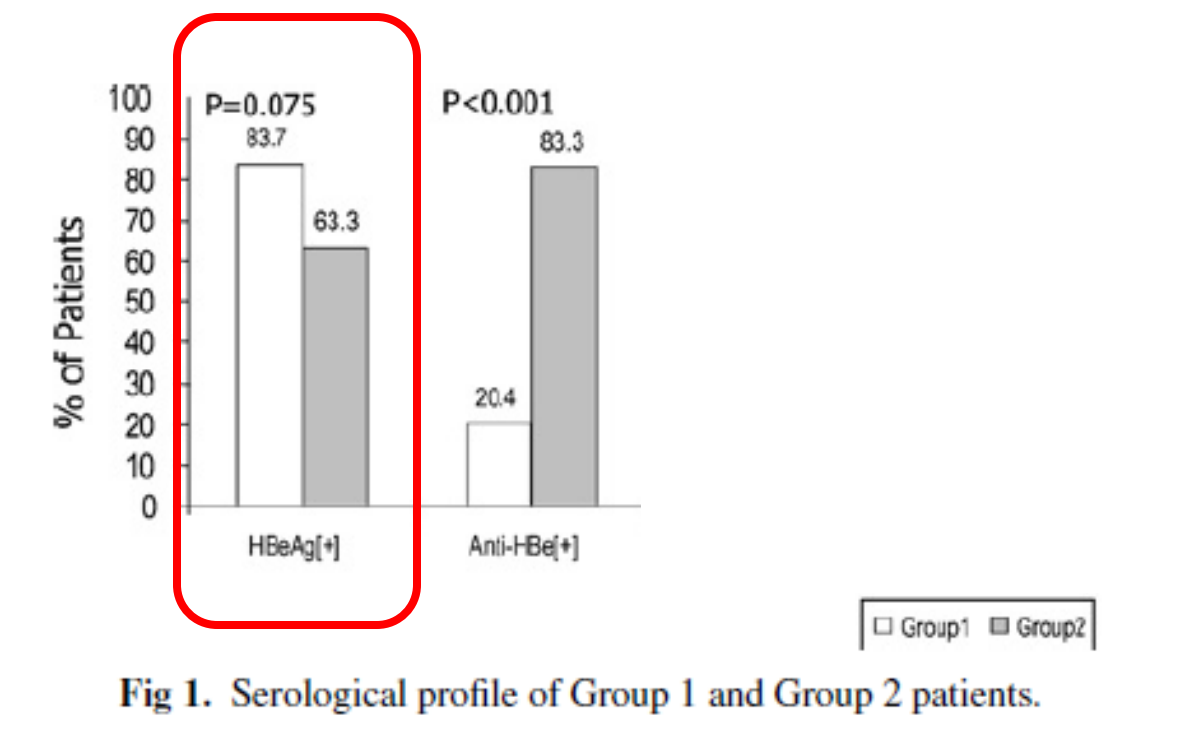


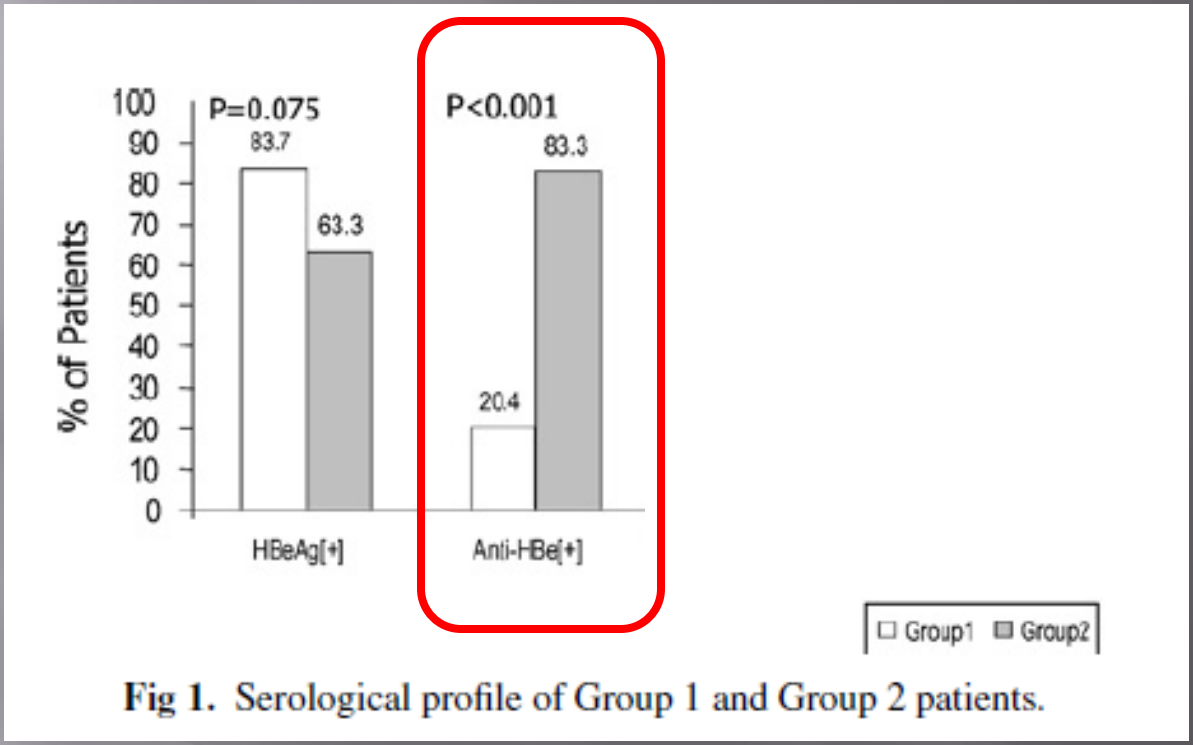
Fig 1. Serological profile of Group 1 and Group 2 patients.

HBeAg pozitifliği

AHB %83.7

AE %63.3

Kumar M et al. Dig Dis and Sci 2006;51:594



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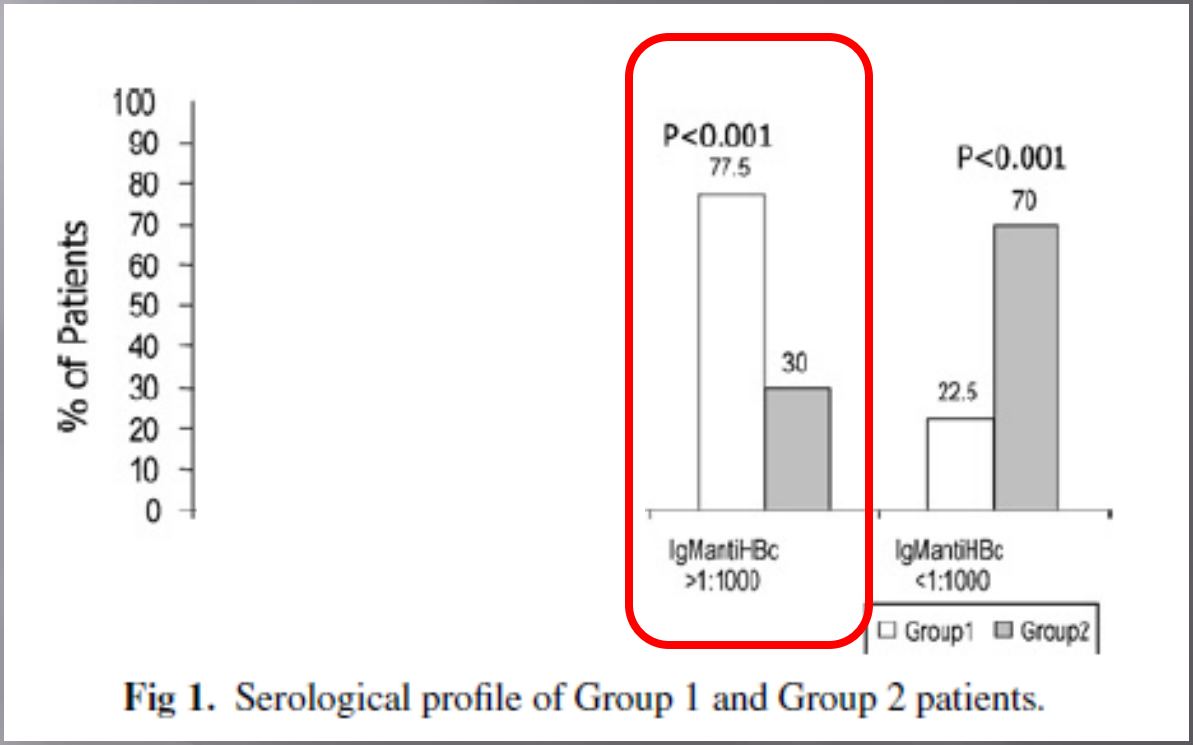


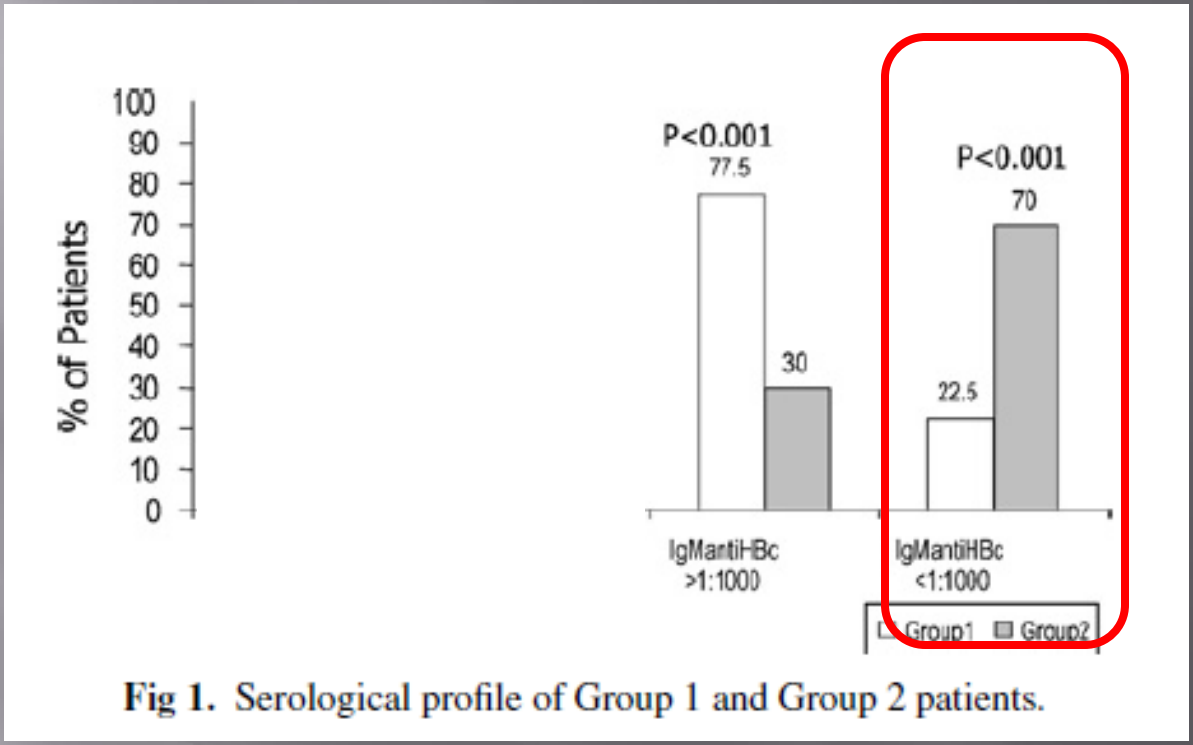
Fig 1. Serological profile of Group 1 and Group 2 patients.

antiHBcIgM >1:1000

AHB %77.5

AE %30 p<0.001

Kumar M et al. Dig Dis and Sci 2006;51:594



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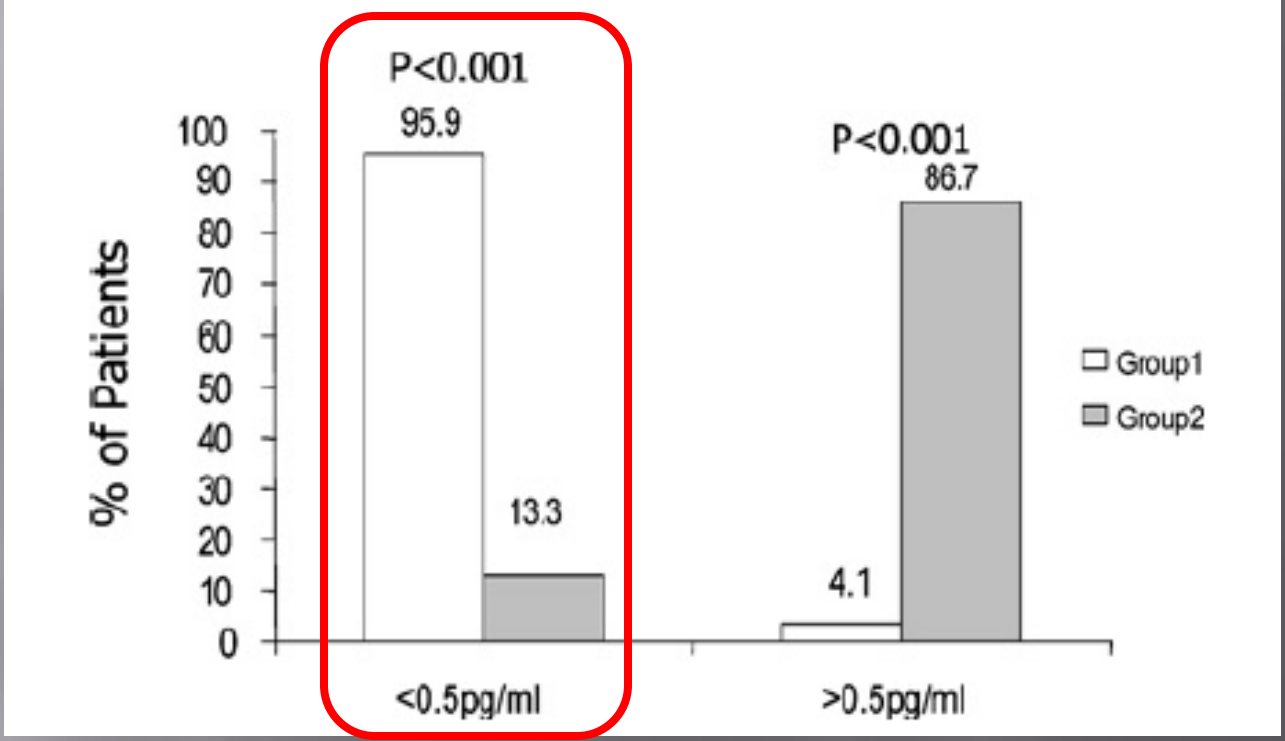


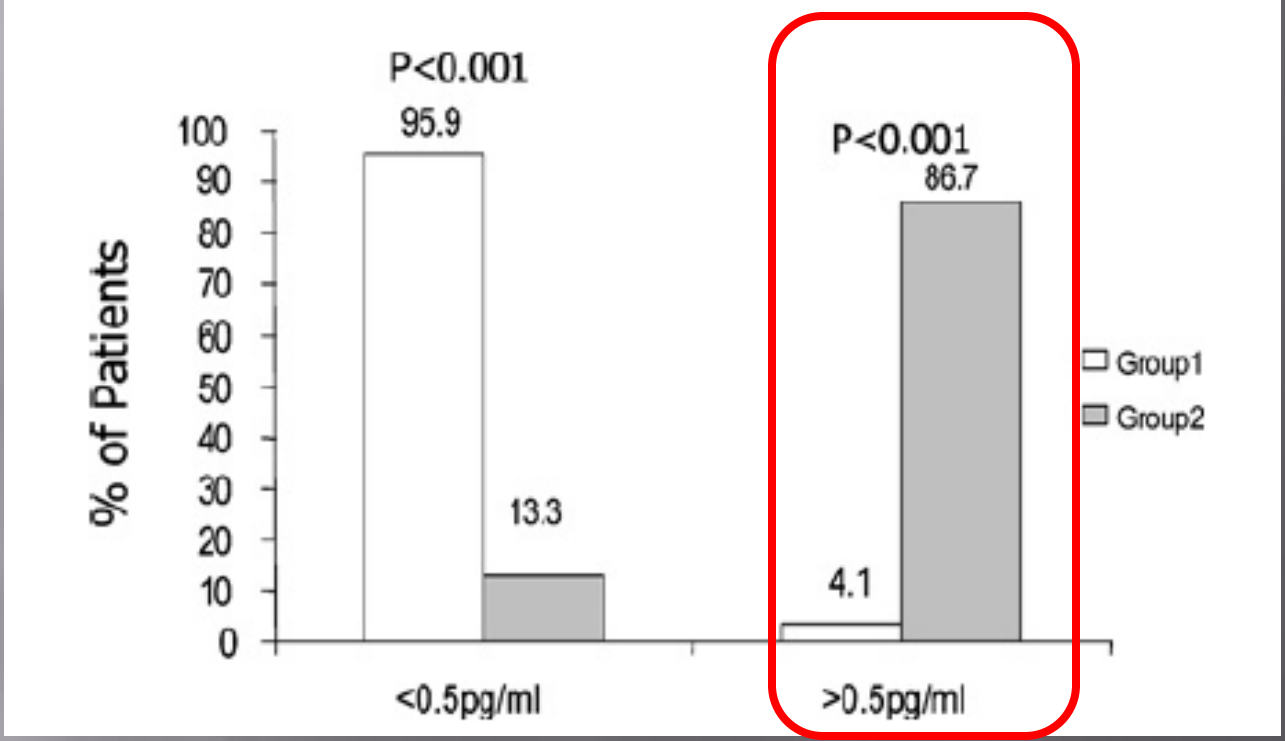
HBV DNA <0.5 pg/ml*

AHB %95.9

AE %13.3 p<0.001

*141500 kopya/ml

Kumar M et al. Dig Dis and Sci 2006;51:594



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*141500 kopya/ml

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Akut infeksiyon seyrinde antiHBc IgM titrelerinin, kronik infeksiyonun akut alevlenmesinde saptanan düzeylere göre daha yüksek olduğu gösterilmiştir.

AHB tanısı için antiHBcIgM >1:1000
duyarlılık %77.6
özgüllük %70

Kumar M et al. Dig Dis and Sci 2006;51:594

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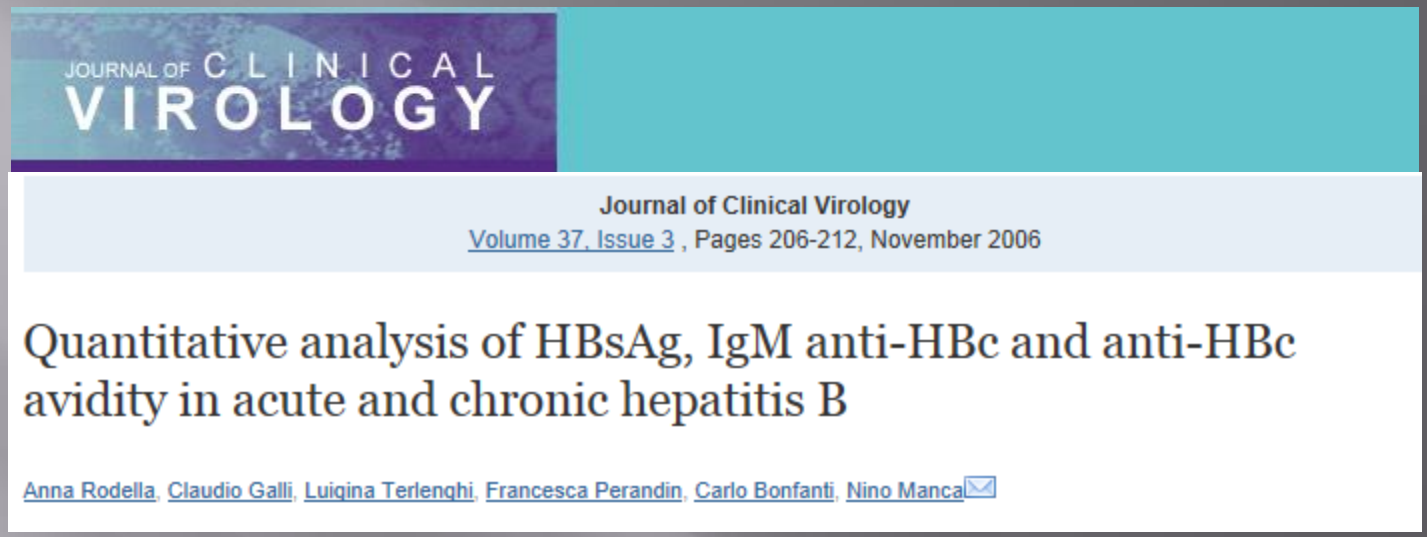
AE tanısı için
antiHBcIgM <1:1000 ve HBV DNA> 0.5 pg/ml
duyarlılık %100
özgüllük %97.9

antiHBe (+)

Kumar M et al. Dig Dis and Sci 2006;51:594



Örnek /cutoff oranı (S/CO)

	Akut hepatit	Akut alevlenme	
antiHBcIgM	%100	%32,85	
S/CO	25,96	2,95	p<0,005

antiHBcIgM S/CO >10
AHB için PPV %99,1

Rodella A et al. J Clin Virol 2006;37:206

IgG avidite testi

Avidite=Fonksiyonel afinite,

“Farklı” antikor popülasyonlarının antijeni bağlama gücünü ifade eder.

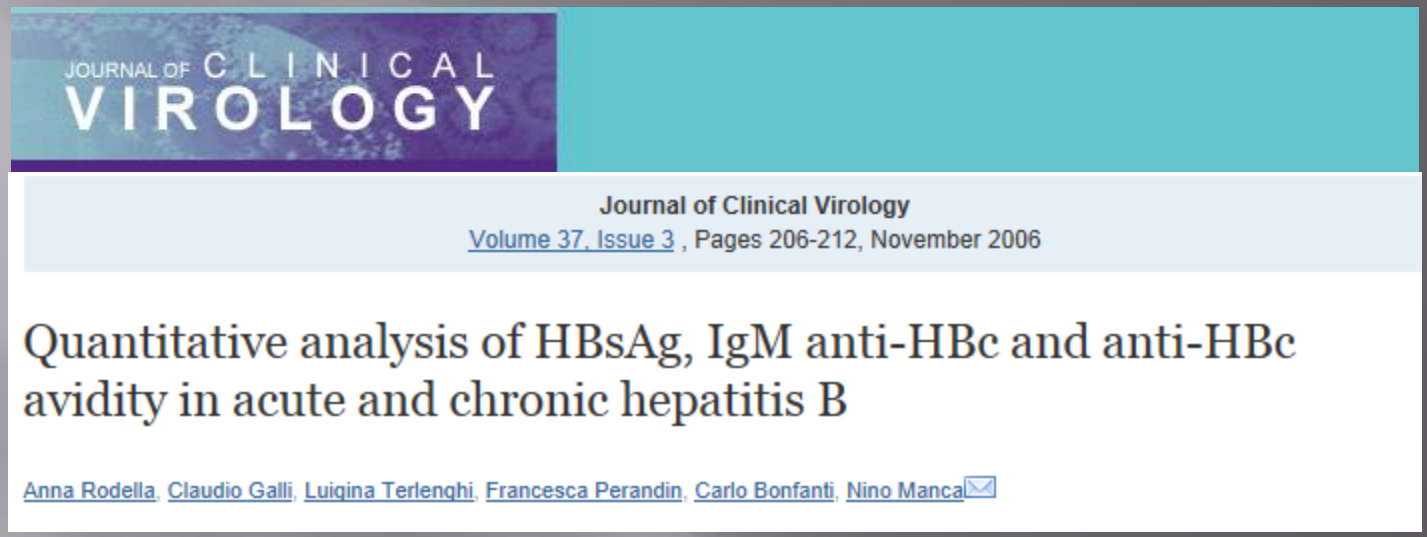
Spesifik IgG antikorlarının fonksiyonel afinitesi, başlangıçta düşüktür,

B lenfosit seleksiyonu ile, izleyen haftalar-aylar içerisinde yükselir.

IgG avidite testi

üre gibi protein denatüre edici ajanlar kullanılarak, antijen-antikor kompleksleri ayrıştırılır.

Sonuçta, düşük aviditeli antikorlar tamamen çözünür/Ag'den ayrılırlarken, yüksek aviditeli antikorlar bağlı kalmaya devam ederler.



antiHBcIgG Avidite indeksi >0.7

AE 2/193 (%1,04)

Rodella A et al. J Clin Virol 2006;37:206

Journal of Medical Virology 51:189–197 (1997)

Relative Functional Affinity of Specific Anti-Core IgG in Different Categories of Hepatitis B Virus Infection

H.I.J. Thomas*
Department of Virology, Preston Public Health Laboratory, Royal Preston Hospital, Preston, United Kingdom

Serum dietilamin ile işlem görmeden önce ve sonraki OD değerleri saptanıyor,

AI=(DEA OD/normal OD)x100

Thomas HIJ et al. J Med Virol 1997;51:189

Journal of Medical Virology 51:189–197 (1997)

Relative Functional Affinity of Specific Anti-Core IgG in Different Categories of Hepatitis B Virus Infection

H.I.J. Thomas*
Department of Virology, Preston Public Health Laboratory, Royal Preston Hospital, Preston, United Kingdom

Avidite indeksi

<%30	düşük antiHBcIgG AI
>%30-<50	equivocal
>%50	yüksek antiHBcIgG AI

Thomas HIJ et al. J Med Virol 1997;51:189

TABLE I. HBc-Specific IgG Avidity Results in Relation to HBsAg Status in Sera From Cases of Acute, Resolving HBV Infection

Anti-HBc IgG avidity	HBsAg + (n = 88)	HBsAg +/– (n = 1)	HBsAg – (n = 40)
AI +	76 (86.4)	1	10 (25)
AI +/–	3 (3.4)		11 (27.5)
AI –	9 (10.2)		18 (45)

AI(+) Düşük antiHBcIgG AI
AI(-) Yüksek antiHBcIgG AI

Akut hepatit B olgularında
HBsAg (+) iken AI(+)___ avidite düşük
HBsAg (-) iken AI(-)___ avidite yüksek

KHB olgularında %87.3 AI(-)

Thomas HIJ et al. J Med Virol 1997;51:189

HEPATOLOGY

Clinical, biochemical, immunological and virological profiles of, and differential diagnosis between, patients with acute hepatitis B and chronic hepatitis B with acute flare

Yongnian Han, Qun Tang, Wei Zhu, Xiaoqing Zhang and Longying You

Research Unit of Liver Disease, Shanghai No. 8 People's Hospital, Shanghai, China

AHB tanısı için antiHBcIgM >1:1000

duyarlılık %77,6

özgüllük %70

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Han Y et al. J Gastroenterol Hepatol 2008;23:1728

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	Akut hepatit	Akut alevlenme	
HBsAg S/CO<50	%46.4	%23.3	p<0.001
HBeAg S/CO<20	%42.7	%13.5	
S/CO>20	%8	%40.6	

HBsAg ve HBeAg düzeyleri akut hepatit olgularında daha düşük saptanmış.

Han Y et al. J Gastroenterol Hepatol 2008;23:1728

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	Akut hepatit	Akut alevlenme	
HBeAg			
S/CO<20	%42.7	%13.5	
S/CO>20	%8	%40.6	
Negatif	%49.3	%45.9	
HBeAg S/CO<20	%92	%59.4	p<0.001
HBeAg serokonversiyonu	%26.1	%11.3	p<0.05

Han Y et al. J Gastroenterol Hepatol 2008;23:1728

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	Akut hepatit	Akut alevlenme	
antiHBcIgM			
Negatif	%0	%76.9	
1:1000	%3.8	%16.2	
1:10000	%96.2	%6.9	p<0.001

Han Y et al. J Gastroenterol Hepatol 2008;23:1728

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	Akut hepatit	Akut alevlenme	
HBV DNA			
Negatif	%22.1	%6.2	
log_{10} kopya/ml	4.53	6.59	p<0.001

Han Y et al. J Gastroenterol Hepatol 2008;23:1728

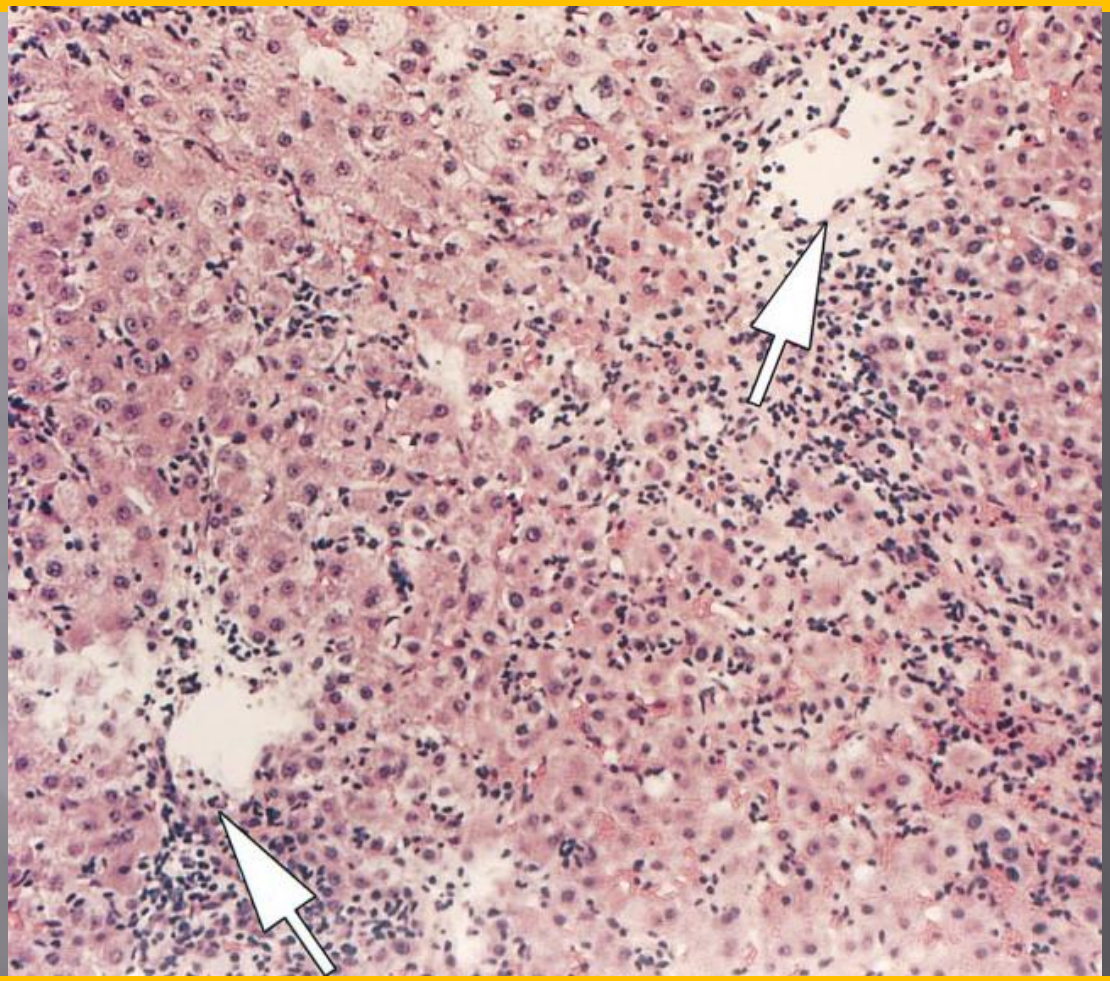
Table 4 Diagnostic performance of laboratory tests for ASL-HB

Laboratory tests	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
Positive IgM anti-HBc at 1:10 000	96.2	93.1	94.6	93.3	96.0
HBV-DNA <10^5 copies/mL	75.4	79.2	77.0	78.4	75.7
HBeAg S/CO <20†	86.6	57.1	66.8	63.8	75.0
IgM anti-HBc at 1:10 000 plus AFP <5× URL	100.0	89.4	97.1	96.2	100.0
IgM anti-HBc at 1:10 000 plus HBeAg S/CO <20†	100.0	90.7	97.0	95.8	100.0
IgM anti-HBc at 1:10 000 plus HBV-DNA <10^5 copies/mL	98.3	95.6	96.6	96.3	98.9
IgM anti-HBc at 1:10 000 plus HBV-DNA <10^5 copies/mL plus HBeAg S/CO <20†	100.0	97.9	99.3	98.9	100.0
IgM anti-HBc at 1:10 000 plus HBeAg S/CO <20† plus AFP <5× URL	100.0	89.5	98.2	98.3	100.0
IgM anti-HBc at 1:10 000 plus HBV-DNA <10^5 copies/mL plus AFP <5× URL	100.0	100.0	100.0	100.0	100.0

antiHBcIgM 1:10000,
HBV DNA<10^5 kopya/ml,
HBeAg S/CO<20

Han Y et al. J Gastroenterol Hepatol 2008;23:1728

Karaciğer biyopsisi

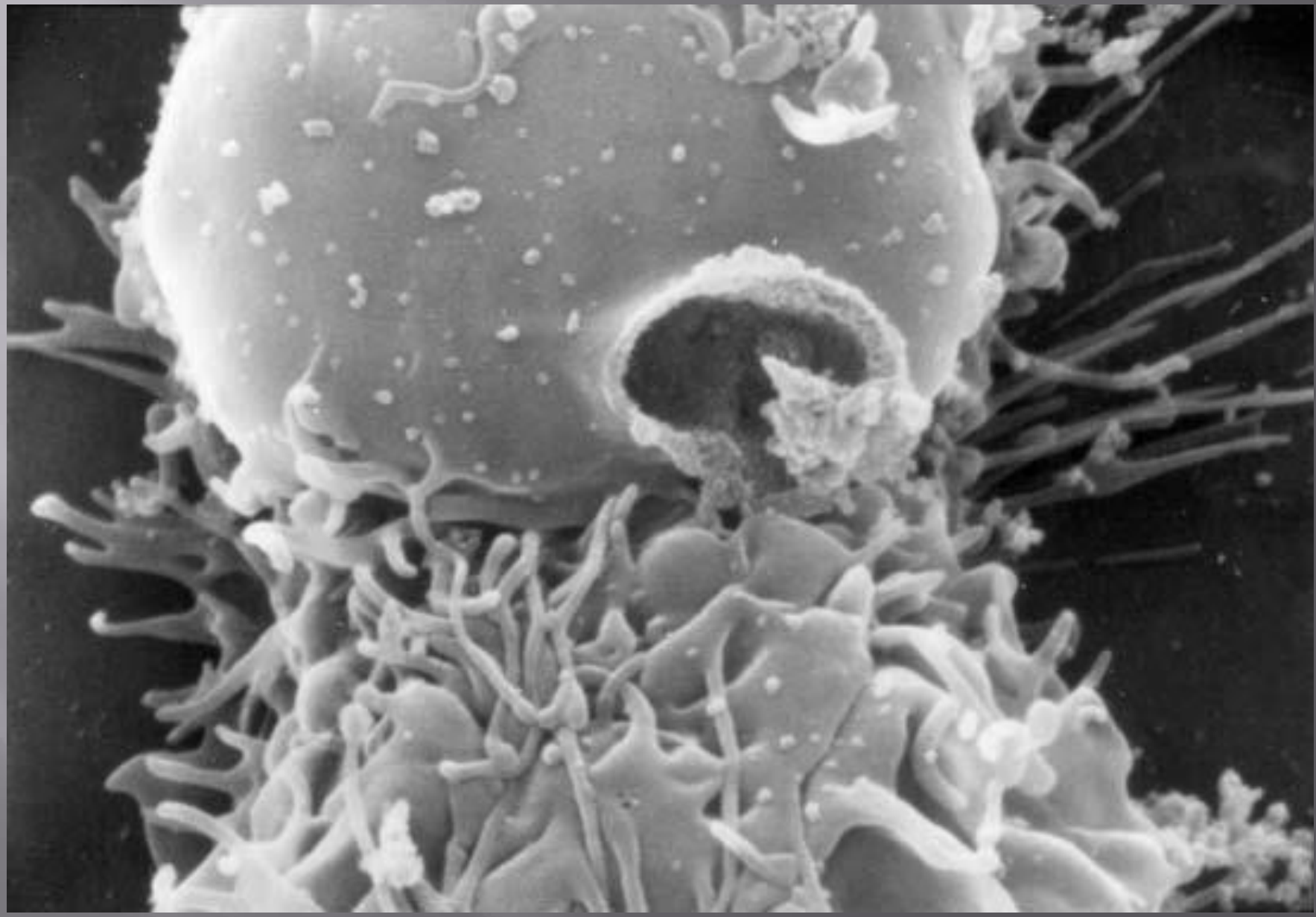


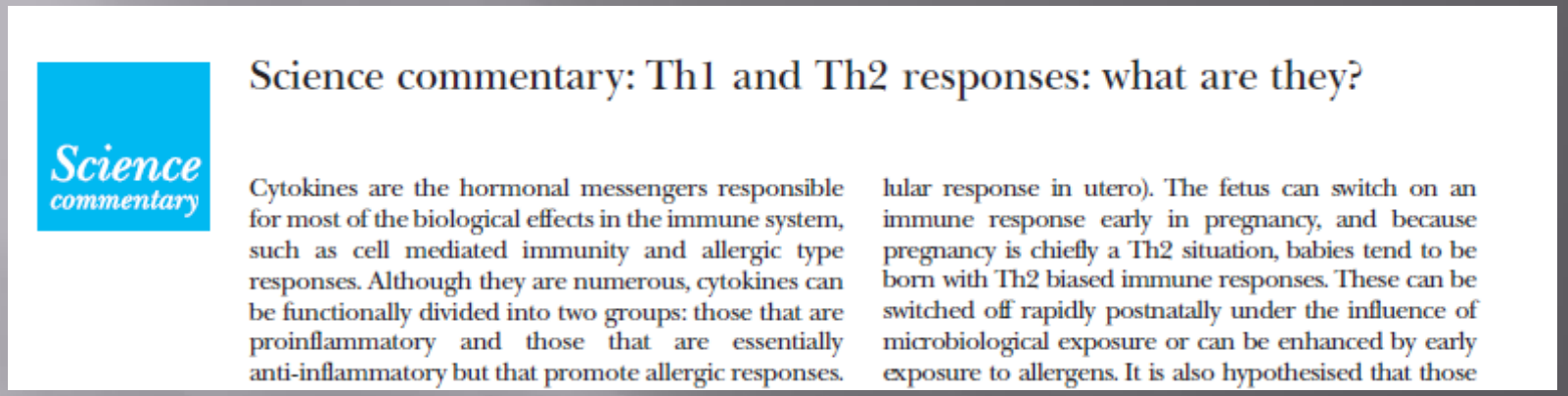
Kronik viral hepatite bağlı değişikliklerin üzerine eklenmiş akut lobüler hepatit

Perillo RP et al. Gastroenterology 2001;120:1009

Akut hepatitli hastalarda

- antiHBcIgM düzeyleri daha yüksek,
- antiHBcIgG avidite indeksi,
- HBV DNA,
- HBeAg,
- HBsAg düzeyleri daha düşüktür.





Science commentary

Science commentary: Th1 and Th2 responses: what are they?

Cytokines are the hormonal messengers responsible for most of the biological effects in the immune system, such as cell mediated immunity and allergic type responses. Although they are numerous, cytokines can be functionally divided into two groups: those that are proinflammatory and those that are essentially anti-inflammatory but that promote allergic responses.

lular response in utero). The fetus can switch on an immune response early in pregnancy, and because pregnancy is chiefly a Th2 situation, babies tend to be born with Th2 biased immune responses. These can be switched off rapidly postnatally under the influence of microbiological exposure or can be enhanced by early exposure to allergens. It is also hypothesised that those

Th1 sitokinler

IFN-γ, IL-2

Hücresel bağışık yanıt
Sitotoksik CD8 T lenfosit

İyileşme

Th2 sitokinler

IL-4, 5, 6, 10, 13

Antikor stimülasyonu
B lenfositler

Kronikleşme