HDV'DE EPİDEMİYOLOJİ VE GÜNCEL TEDAVİ İLE NEREYE GELİNDİ?

Ediz Tütüncü

Ulusal Viral Hepatit Simpozyumu
1 Ekim 2023, Kayseri

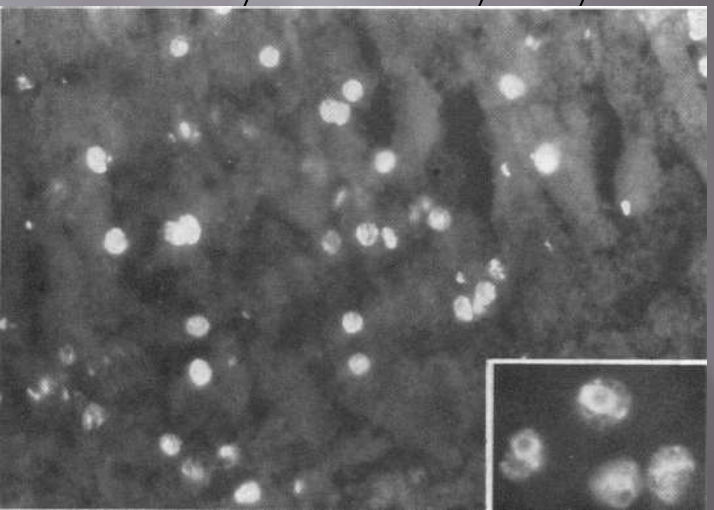
Gut, 1977, **18**, 997-1003

Immunofluorescence detection of new antigen-antibody system (δ/anti-δ) associated to hepatitis B virus in liver and in serum of HBsAg carriers

M. RIZZETTO,[1] M. G. CANESE, S. ARICÒ, O. CRIVELLI, C. TREPO, F. BONINO, AND G. VERME

From the Department of Gastroenterology, Ospedale Mauriziano Umberto I, Turin, Italy, the Electron Microscopy Centre of the Faculty of Medicine, University of Turin, Italy, and INSERM U45, and Laboratory of Hygiene, University Claude Bernard, Lyon, France

- Kronik karaciğer hastalığı olan hepatit B hastalarının hepatosit nükleuslarında direkt immünfloresan yöntemiyle yeni bir Ag-Ak yapısı saptanıyor



the lesion observed in δ positive patients (Nielsen *et al.*, 1973) suggest that the antigen is closely related to the core particle or to the chain of events preceding its assembly or after its clearance. DNA polymerase, circular DNA molecule, and DNA polymerase product are tentative candidates; each of them, however, has been located only inside a mature core envelope (Robinson, 1976), while to be the δ antigen they should exist free and uncovered in the nucleoplasm. Whether this is the case or whether the new antigen is unrelated to any of the known HB virus components is at present under study.

977;18:997

0270-9139/83/0305-0729$02.00/0
HEPATOLOGY

Vol. 3, No. 5, pp. 729–737, 1983
Printed in U.S.A.

The Delta Agent

MARIO RIZZETTO

Division of Gastroenterology, Molinette, Torino 10126, Italy

This review provides a glimpse of the many problems raised by the discovery of the δ agent which need an answer in the future. The most intriguing is the nature of the new pathogen and its ecological niche, where and when it arose and whether other similar pathogens exist, of which δ agent may be a model. The epidemiology of δ agent is largely unknown. It appears to be exotic, yet it is infrequent in regions of Asia where the HBsAg rate is among the highest in the world. Given the mechanism of its spread, δ agent is likely to represent a major epidemiologic risk of hepatitis where the prevalence of HBV is high, as in many parts of the developing world.

Rizzetto M et al. Hepatology 1983;5:729

Hepatitis D

العربية | 中文 | Français | Русский | Español

20 July 2023

Key facts

- Hepatitis D virus (HDV) is a virus that requires hepatitis B virus (HBV) for its replication.
- Hepatitis D virus (HDV) affects globally nearly 5% of people who have a chronic infection with hepatitis B virus (HBV).
- HDV infection occurs when people become infected with both hepatitis B and D simultaneously (co-infection) or get hepatitis D after first being infected with hepatitis B (super-infection).
- Populations that are more likely to have HBV and HDV co-infection include indigenous populations, recipients of haemodialysis and people who inject drugs.
- Worldwide, the number of HDV infections has decreased since the 1980s, due mainly to a successful global HBV vaccination programme.
- The combination of HDV and HBV infection is considered the most severe form of chronic viral hepatitis due to more rapid progression towards liver-related death and hepatocellular carcinoma.
- Hepatitis D infection can be prevented by hepatitis B immunization, but treatment success rates are low.

Related

Global hepatitis report, 2017

World Hepatitis Day

Global health sector strategy on viral hepatitis

News

INFOSAN Quarterly Summary, 2023 #2
14 September 2023

WHO launches "One life, one liver" campaign on World Hepatitis Day

World Health Organization

GLOBAL HEPATITIS REPORT, 2017

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BEYOND THE SCOPE OF THE REPORT: HEPATITIS A, D AND E

HEPATITIS A VIRUS – HAV

Hepatitis A causes only acute hepatitis. HAV is transmitted mostly through exposure to contaminated food or water, or through exposure to infected persons. A safe and effective vaccine is available. WHO estimates that worldwide, hepatitis A caused approximately 11 000 deaths in 2015 (accounting for 0.8% of the mortality

HEPATITIS D VIRUS – HDV

Hepatitis D is caused by an incomplete virus, HDV. It is transmitted mostly through the percutaneous route (exposure to blood). HDV infects only those persons who already have HBV infection. Infection of an HBV-infected person with HDV (a phenomenon referred to as "superinfection") worsens the outcome of HBV infection. Hence, HDV is a cofactor of chronic liver disease. Most experts estimate that 5% of HBV-infected persons are also coinfected with HDV *(10)*. However, there is substantial uncertainty, as in many countries, HBV-infected patients are not tested for HDV infection. In addition, in selected countries, such as Mongolia, up to 60% of HBV-infected persons may also have HDV infection *(11)*. Prevention of HBV infection through vaccination also prevents HDV infection. However, the treatment of HBV–HDV-coinfected patients differs from the treatment of persons with HBV infection alone. Newer antinucleos(t)ides that are highly effective against HBV infection do not work well in HBV–HDV coinfection. Only older, interferon-based treatments can be used, with suboptimal results. WHO does not have estimates of the proportion of deaths due to HBV in which HDV may be a cofactor *(12)*. The distribution of HDV infection varies around the world.

HEPATITIS E VIRUS – HEV

HEV causes mostly acute hepatitis. It is transmitted via the faecal–oral route, principally via contaminated water. Every year, there are an estimated 20 million HEV infections worldwide, leading to an estimated 3.3 million symptomatic cases of acute hepatitis E *(13)*. WHO estimates that hepatitis E caused approximately 44 000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis). Hepatitis E is a usually self-limiting illness, but some patients may progress to acute liver failure. Hepatitis E has a higher case fatality in pregnant women. This leads to maternal mortality that is particularly devastating. Infection with HEV is reported worldwide, but it is most common in East and South Asia. A vaccine to prevent HEV infection has been developed and is licensed in China, but is not yet available in most other countries *(14)*.

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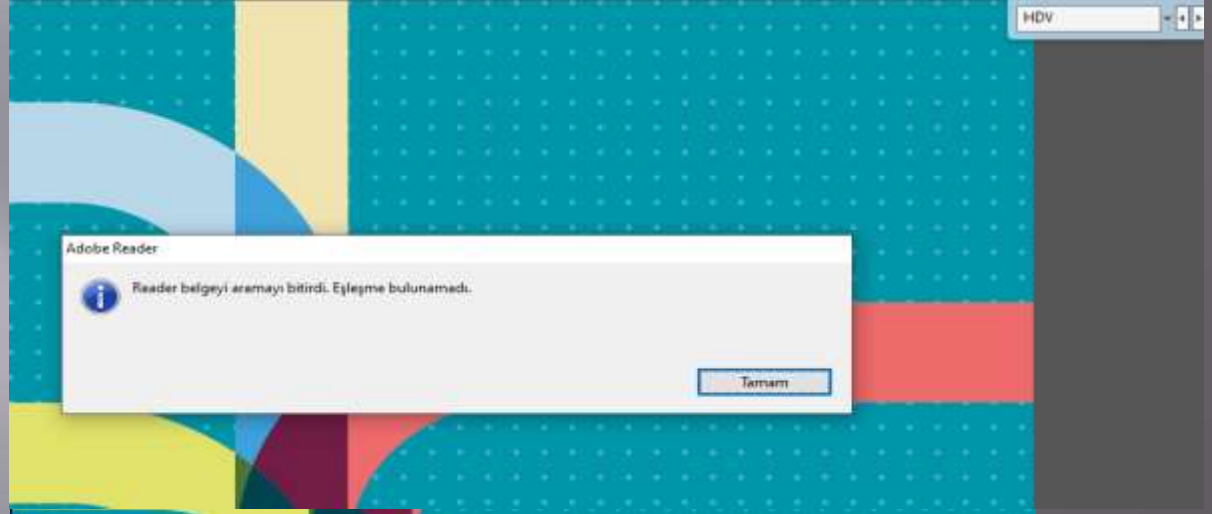

Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022–2030

World Health Organization

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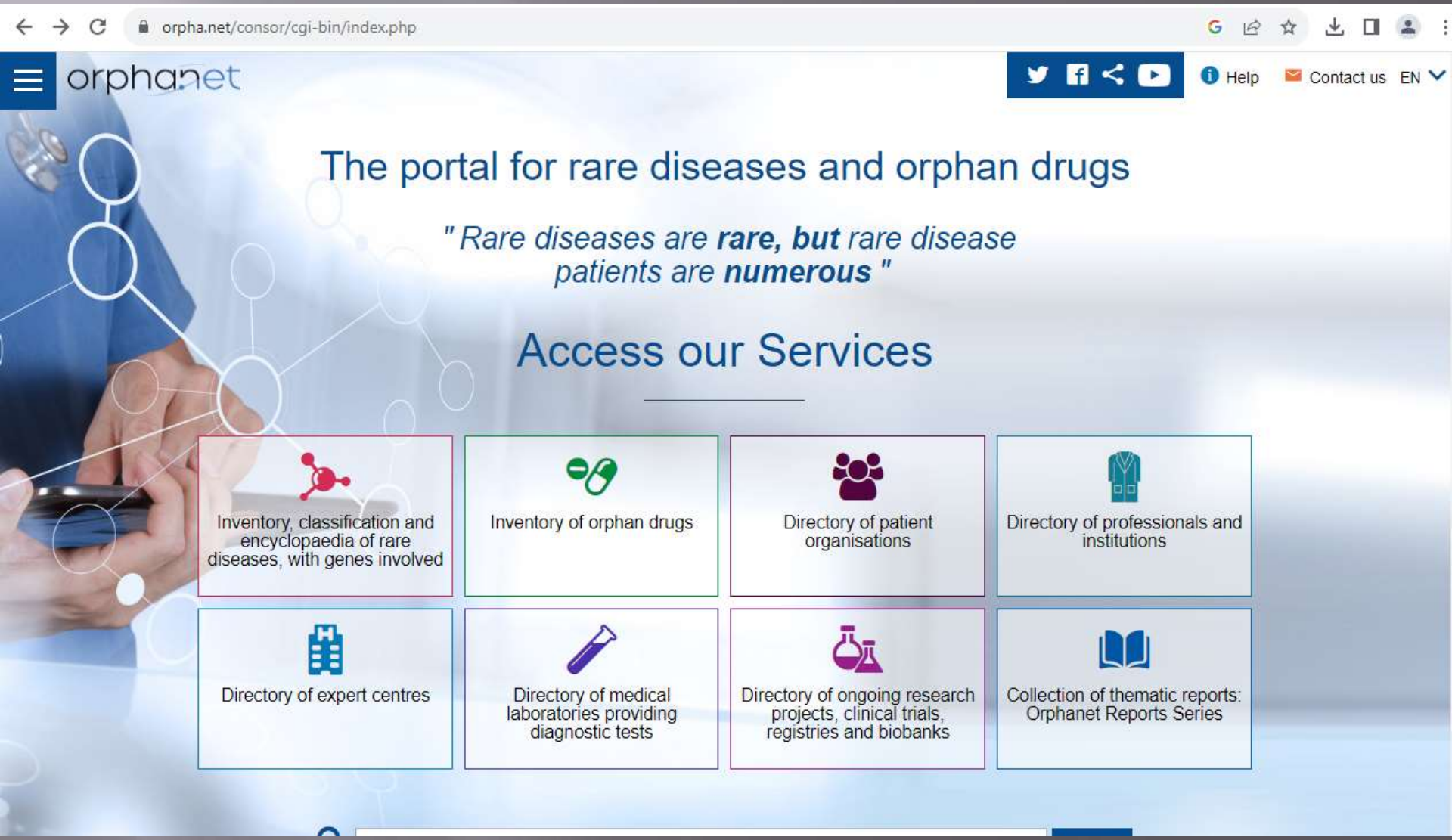

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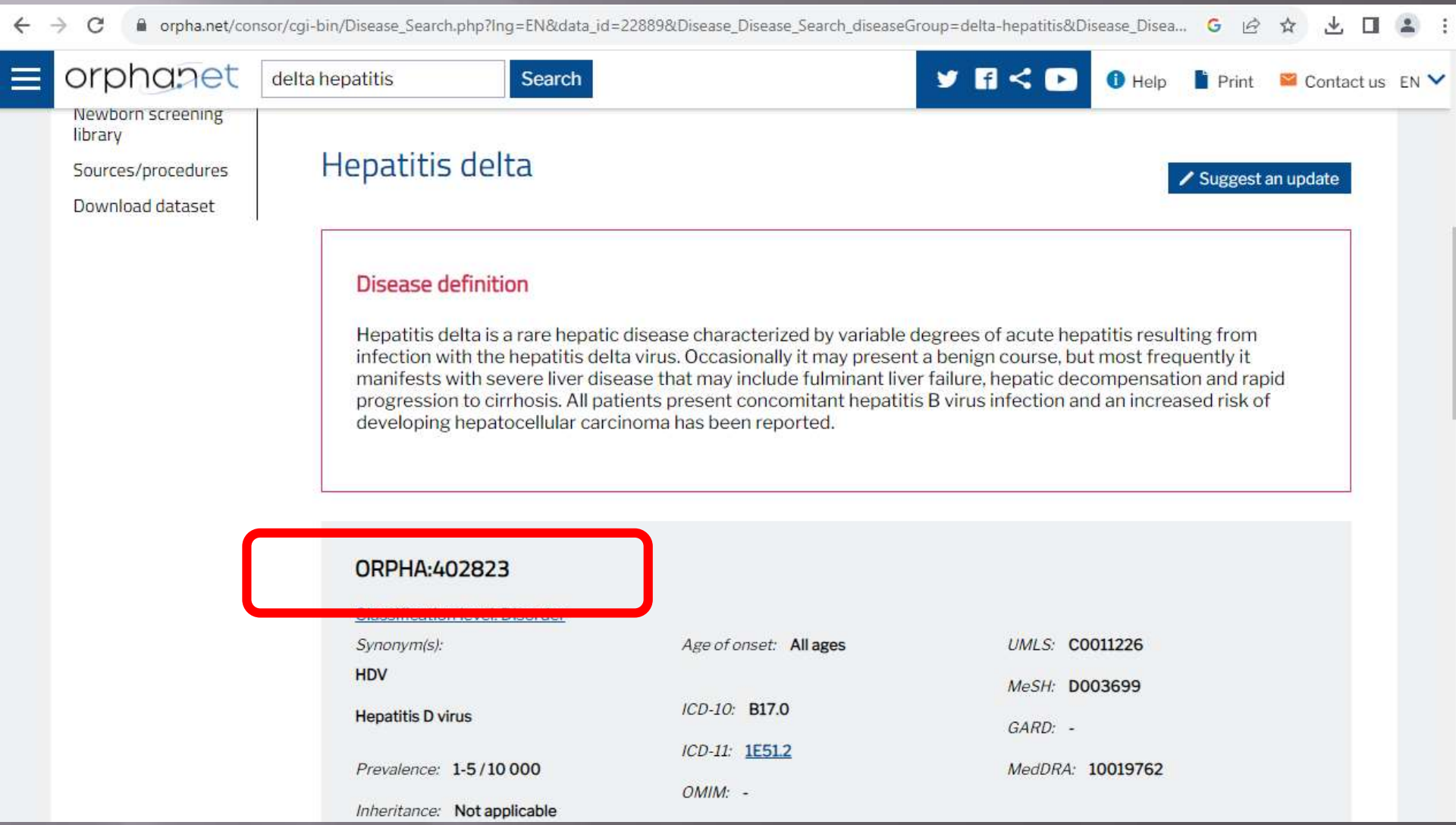

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Review JHEP|Reports

Hepatitis D virus infection: Pathophysiology, epidemiology and treatment. Report from the first international delta cure meeting 2022

Pietro Lampertico,[1,2,*] Elisabetta Degasperi,[1] Lisa Sandmann,[3,4,5] Heiner Wedemeyer [3,4,5], on behalf of the Delta Cure 2022 Working Group[†]

- Yeni tedavi seçeneklerinin gündeme geldiği günümüzde, global prevalans ve klinik hastalık yüküne dair güvenilir tahminlere sahip olmak önem kazanıyor.

Lampertico P et al. JHEP Reports 2023;5:100818

Review JHEP|Reports

Hepatitis D virus infection: Pathophysiology, epidemiology and treatment. Report from the first international delta cure meeting 2022

Pietro Lampertico,[1,2,*] Elisabetta Degasperi,[1] Lisa Sandmann,[3,4,5] Heiner Wedemeyer [3,4,5], on behalf of the Delta Cure 2022 Working Group[†]

- Nüfusa dayalı çalışmalar az sayıda,
- Bazı bölgeler/ülkelerden hiç veri yok,

Lampertico P et al. JHEP Reports 2023;5:100818

Hepatology

ORIGINAL ARTICLE

Prevalence and burden of hepatitis D virus infection in the global population: a systematic review and meta-analysis

Hai-Yan Chen,[1] Dan-Ting Shen,[1] Dong-Ze Ji,[2] Pei-Chun Han,[1] Wei-Ming Zhang,[2] Jian-Feng Ma,[1] Wen-Sen Chen,[3] Hemant Goyal,[4] Shiyang Pan,[1] Hua-Guo Xu[1]

- 1977-2016 arası, 61 ülkeden 182 çalışma,
- Tüm kohortta toplam 40127988 bireye dair veri,
- 94718 HBsAg pozitif birey

Chen HY et al. Gut 2019;68:512

Hepatology

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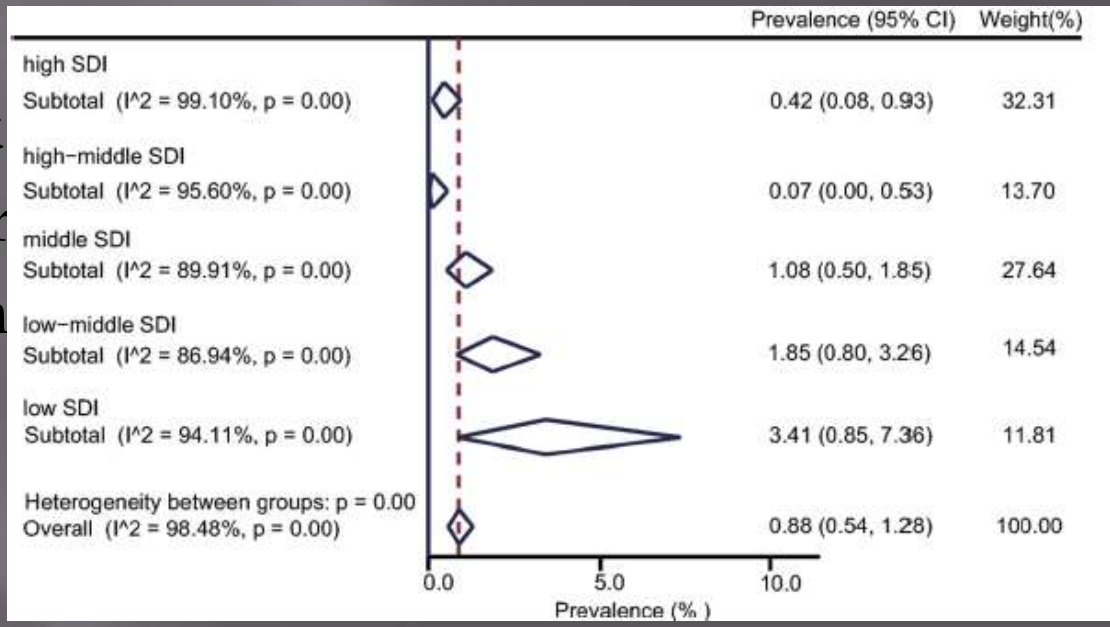
- HDV prevalansı
- Genel popülasyonda %0,98

- Ülkeler arasında çok
  Moğolistan %8, Fr
- Genel popülasyonda
  Avustralya, Kiribati,
  sahip.



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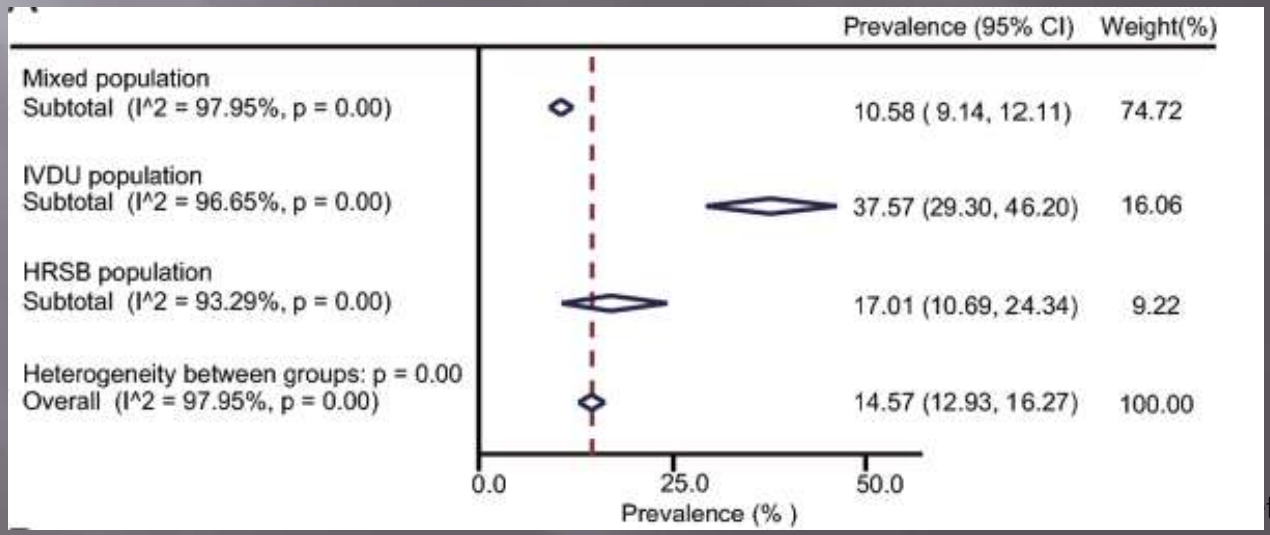
- HBsAg pozitif popülasyonda %14,57

  Risk faktörü olmayan HBsAg pozitif hastalar %10,58

  IVDU %37,57, HRSB %17,01



t al. Gut 2019;68:512

	General population					Mixed population				
Location	No. of studies	Events	Tested (n)	Prevalence (%)	95% CI	Location	No. of studies	Events	Tested (n)	Prevalence (%)	95% CI
Africa										
Benin	2	28	707	3.74	2.44 to 5.29	Benin	2	28	110	24.46	16.75 to 33.05
Ethiopia	1	3	500	0.6	0.20 to 1.75	Ethiopia	1	3	31	9.68	3.35 to 24.90
Gabon	3	55	1932	3.03	0.51 to 7.43	Gabon	3	55	242	21.25	5.26 to 43.74
						Ghana	1	6	53	11.32	5.29 to 22.58
Mauritania	1	49	1966	2.4	1.76 to 3.13	Mauritania	3	137	718	18.99	16.19 to 21.97
Niger	1	12	238	5.04	2.91 to 8.60	Niger	2	17	144	9.88	5.36 to 15.46
						Egypt	2	23	245	8.32	5.10 to 12.19
						Kenya	1	103	653	15.77	13.18 to 18.77
						Somalia	1	26	52	50	36.89 to 63.11
						Zimbabwe	1	21	130	16.15	10.82 to 23.44
						Tunisia	2	77	2155	3.19	2.48 to 3.98
North America											
						Canada	1	0	186	0	0.00 to 2.02
USA	1	0	129	0	0.00 to 2.89	USA	4	182	3303	7.17	2.73 to 13.18
South America											
						Argentina	1	23	1517	1.52	1.01 to 2.26
Brazil	3	83	4028	2.09	0.37 to 5.10	Brazil	6	154	651	21.46	9.07 to 37.11
Colombia	2	19	1558	1.22	0.72 to 1.84	Colombia	2	19	196	7.4	3.90 to 11.76
						Peru	1	57	87	65.52	55.06 to 74.66
Venezuela	1	6	645	0.92	0.28 to 1.86	Venezuela	2	115	404	22.05	11.95 to 34.04
Asia											
Mongolia	1	20	249	8.03	5.26 to 12.08	Mongolia	1	20	24	83.33	64.15 to 93.32
China	7	75	8824	0.45	0.15 to 0.89	China	27	1000	17163	5.57	3.85 to 7.55
						India	7	211	1316	11.09	0.96 to 29.50
Iran	2	9	5540	0.11	0.03 to 0.22	Iran	12	429	6240	6.42	3.90 to 9.48
Japan	3	78	7275	0.73	0.04 to 2.15	Japan	12	397	5417	6.31	3.90 to 9.17
						Korea	1	3	940	0.32	0.11 to 0.93
						Kuwait	1	23	254	9.06	6.11 to 13.22
						Lebanon	2	15	321	2.89	1.21 to 5.14
Pakistan	1	23	946	2.43	1.63 to 3.62	Pakistan	7	2100	10729	34.16	21.34 to 48.27
						Philippine	1	4	42	9.52	3.77 to 22.07
Saudi Arabia	2	78	23 005	0.39	0.06 to 0.95	Saudi Arabia	5	139	1695	7.89	6.61 to 9.26
						Tajikistan	1	12	51	23.53	14.00 to 36.76
Thailand	1	0	37	0	0.00 to 9.41	Thailand	1	0	36	0	0.00 to 9.64
Turkey	1	4	12 423	0.03	0.01 to 0.08	Turkey	6	1085	8304	14.14	5.07 to 26.73
Vietnam	1	2	837	0.24	0.07 to 0.87	Vietnam	2	43	425	8.54	6.03 to 11.42
Yemen	1	2	1074	0.14	0.00 to 0.53	Yemen	1	3	224	0.92	0.00 to 3.03
Europe											
Albania	1	6	1348	0.45	0.20 to 0.97	Albania	1	6	97	6.19	2.87 to 12.84
						Belgium	1	29	757	3.83	2.68 to 5.45
						Denmark	1	9	76	11.84	6.36 to 21.00
France	2	123	39 911 011	0	0.00 to 0.00	France	2	89	4522	1.26	0.89 to 1.68

Hepatolo

infection
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g Zhang,[2]
uo Xu[1]

HY et al. Gut 2019;68:512

Hepatology

ORIGINAL ARTICLE

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- Global HDV olgu sayısı 62-72 milyon,
-

2019;68:512

The Journal of Infectious Diseases

MAJOR ARTICLE

Estimating the Global Prevalence, Disease Progression, and Clinical Outcome of Hepatitis Delta Virus Infection

Zhijiang Miao,[1] Shaoshi Zhang,[1] Xumin Ou,[1] Shan Li,[1,2] Zhongren Ma,[3] Wenshi Wang,[1,4] Maikel P. Peppelenbosch,[1] Jiaye Liu,[1] and Qiuwei Pan[1]

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- 634 çalışma,
- Genel popülasyonda 48 ülke, 332155 birey,
- HBsAg pozitif popülasyonda 83 ülke, 271629 birey

Miao Z et al. J Infect Dis 2020;221:1677

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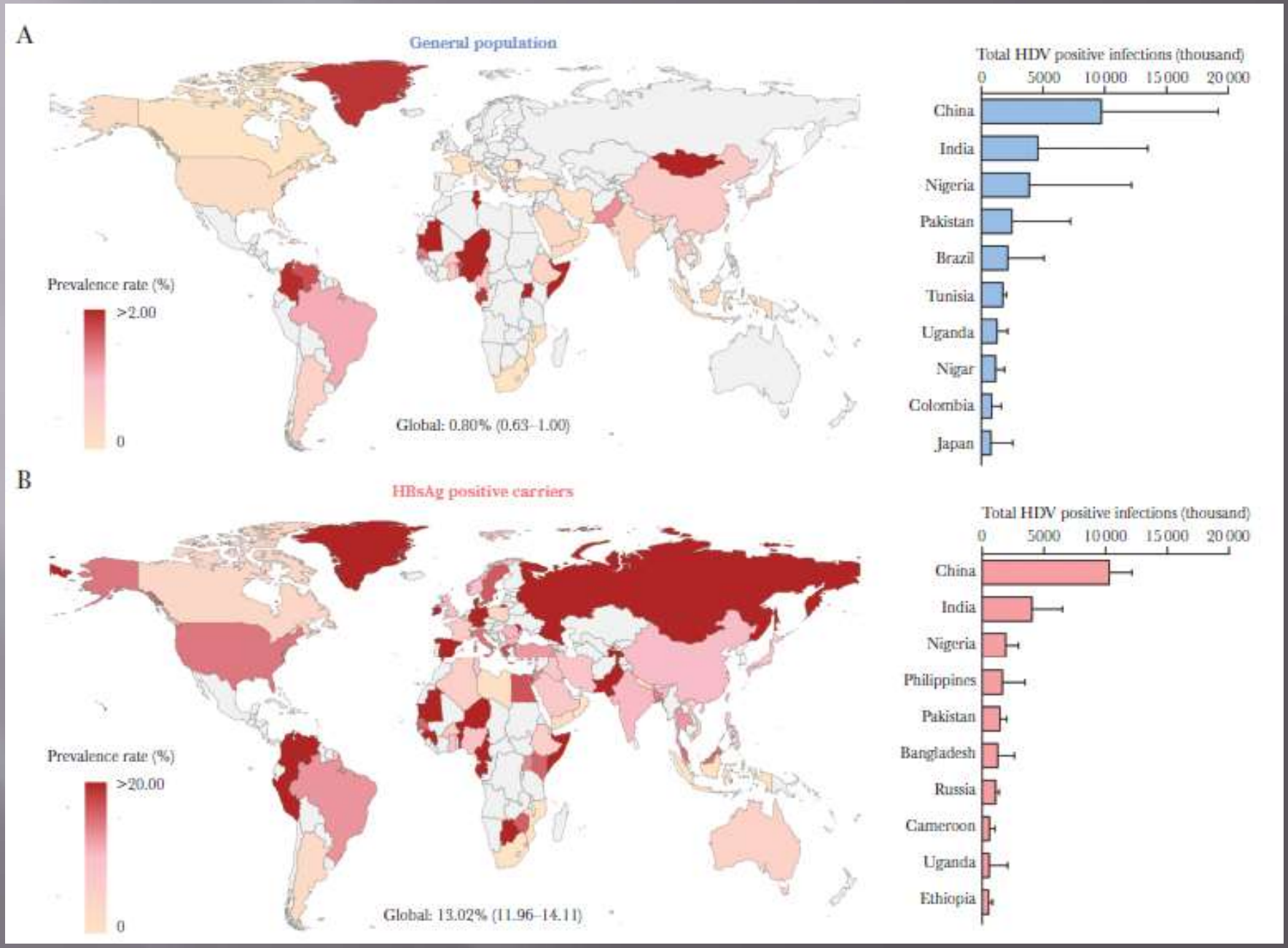
- HDV prevalansı
  - Genel popülasyonda %0,80,
  - HBsAg pozitif popülasyonda %13,02,
  - Global HDV olgu sayısı 48-60 milyon.

Miao Z et al. J Infect Dis 2020;221:1677



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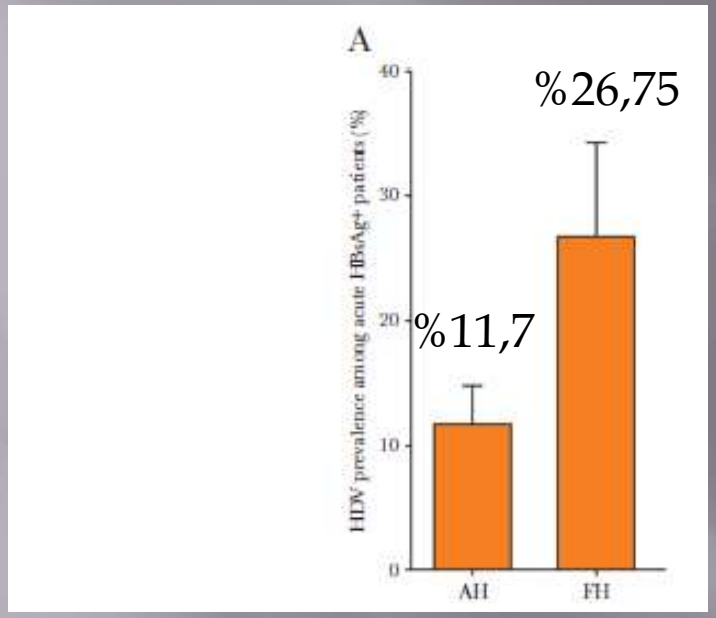
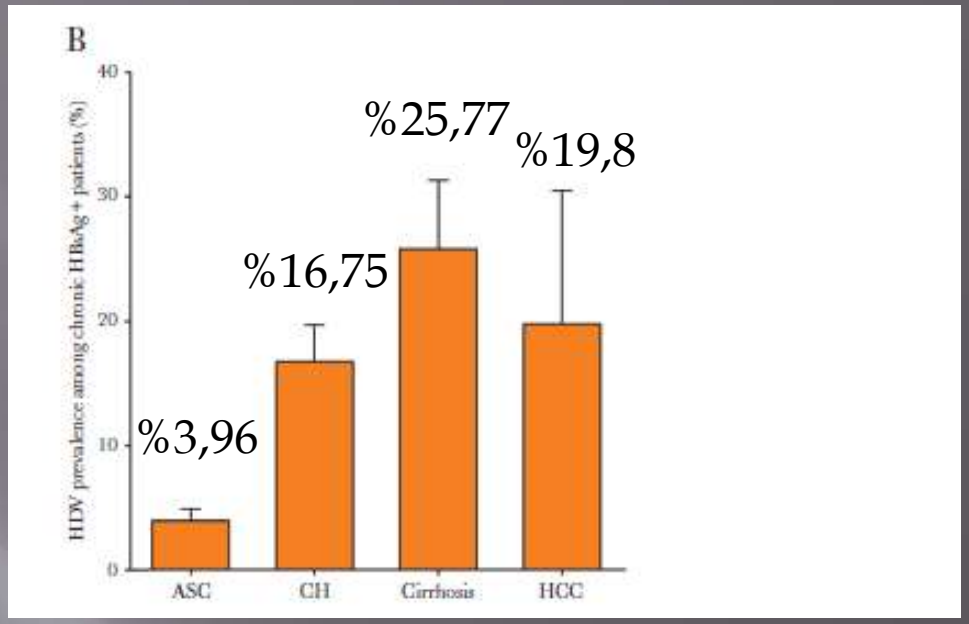
- HDV bulaşı açısından risk faktörleri

IVDU	OR 15,44
HIV	OR 2,99
HCV	OR 3,05

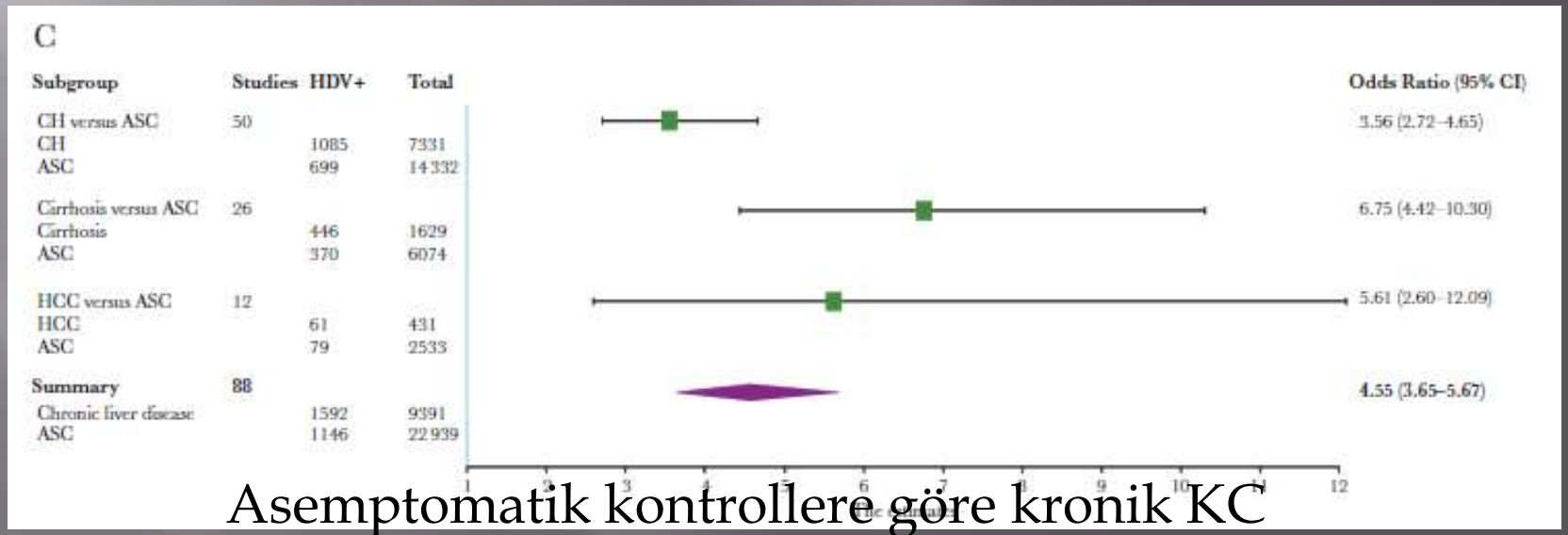
Miao Z et al. J Infect Dis 2020;221:1677



Akut HBV olgularında HDV prevalansı



Kronik HBV olgularında HDV prevalansı



Asemptomatik kontrollere göre kronik KC hastalığı olgularında HDV prevalansı

Miao Z et al. J Infect Dis 2020;221:1677

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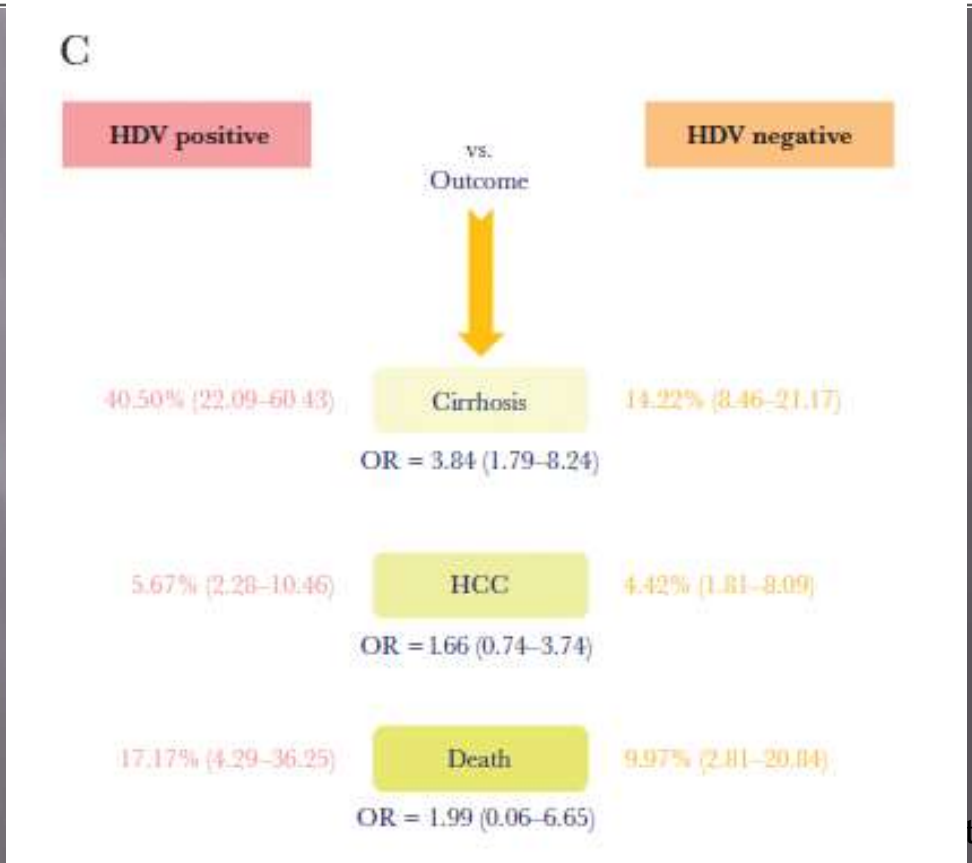

Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

The global prevalence of hepatitis D virus infection: Systematic review and meta-analysis

Alexander J. Stockdale[1,2], Benno Kreuels[3,4], Marc Y.R. Henrion[2,5], Emanuele Giorgi[6], Irene Kyomuhangi[6], Catherine de Martel[7], Yvan Hutin[8], Anna Maria Geretti[1,*]

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- 1998-2019
- 282 çalışma, 95 ülke, 120293 HBsAg pozitif birey

Stockdale AJ et al. J Hepatol 2020;73:523

Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

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- HDV prevalansı
  - HBsAg pozitif popülasyonda %4,5,
  - Hepatoloji kliniklerinde izlenen hastalarda %16,4
  - Genel popülasyonda %0,16,
  - Global HDV olgu sayısı 12 milyon.

Stockdale AJ et al. J Hepatol 2020;73:523

Research Article
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Germany; [5]Liverpool School of Tropical Medicine, Liverpool
University of Lancaster, Lancaster, United Kingdom; [7]Internati
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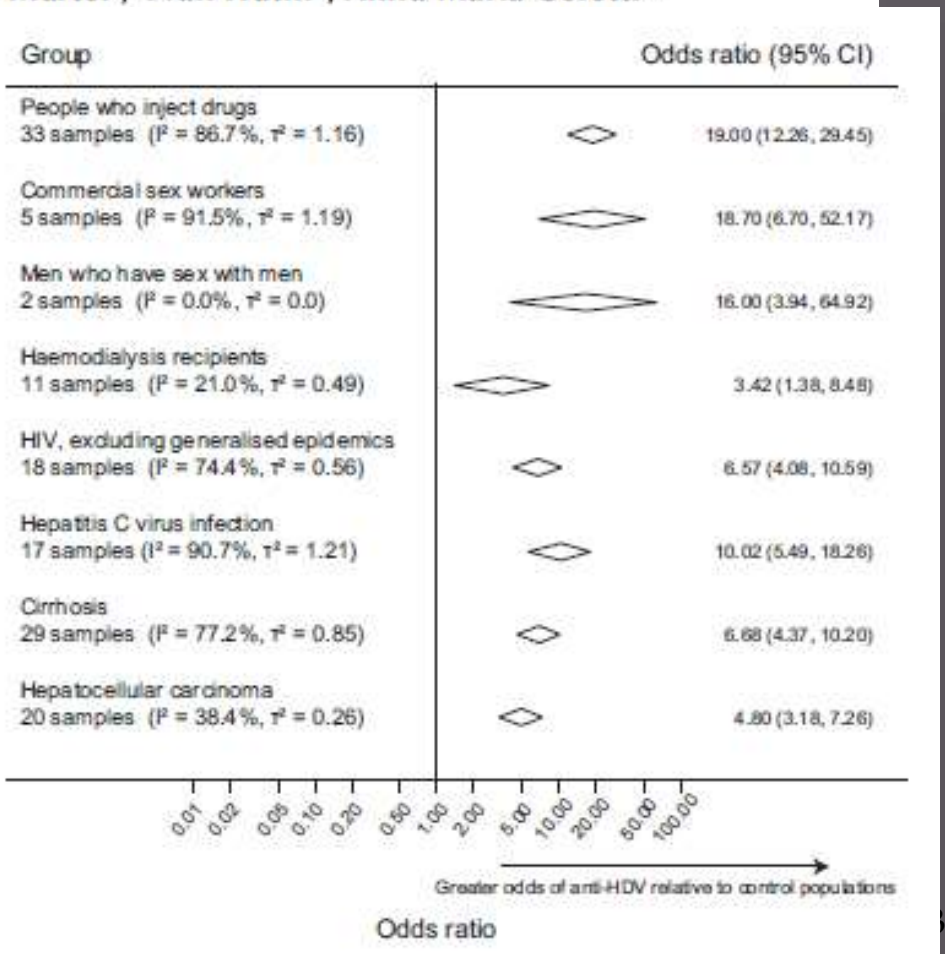
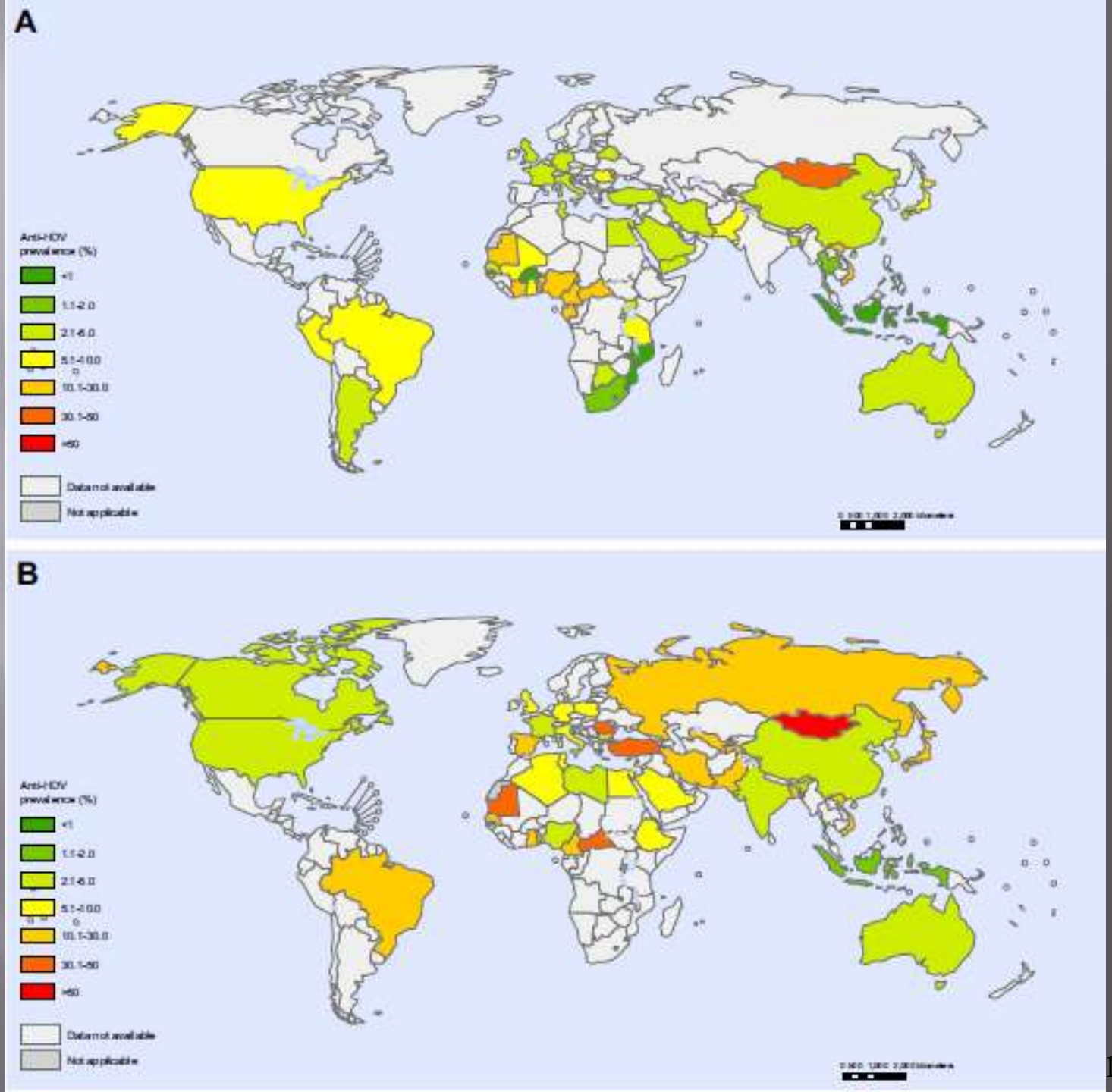
HDV bulaşı
açısından risk faktörleri




A
Anti-HDV prevalence (%)
<1
1.1-2.0
2.1-5.0
5.1-10.0
10.1-30.0
30.1-50
>50
Data not available
Not applicable
B
Anti-HDV prevalence (%)
<1
1.1-2.0
2.1-5.0
5.1-10.0
10.1-30.0
30.1-50
>50
Data not available
Not applicable

	Chen, 2019[10]	Miao, 2020[13,14]	Stockdale, 2020[16]
Databases searched	PubMed, Embase, Cochrane Library, China knowledge Integrated databases	Embase, Medline, Ovid, Cochrane, China knowledge Integrated database	PubMed, Embase, Scopus and grey literature
Language of Studies included	English, Chinese	English, Chinese	All languages
Time period of publication of studies included	01/01/1977 - 31/12/2016	01/01/1982 - 01/02/2019	01/01/1998 - 28/01/2019
Inclusion Criteria	Available data on HDV seroprevalence, patient selection methods, geographical and clinical setting included in the analysis	Studies with data on prevalence and outcome of HDV. The prevalence of HDV was defined by the detection of HDV antibodies (anti-HDV IgG and/ or anti-HDV IgM), supplemented by the additional detection of HDAg and HDV RNA.	Studies that examined geographic and clinical setting of participants with HBsAg and applied a systematic selection method to anti-HDV testing, where all/random selection of eligible participants was tested.
Exclusion criteria	Data on infants of children	Studies with fewer than 100 subjects from general population or 20 HBsAg carriers	
Patient groups where HDV prevalence was	General population from 1977 to 1996 and 1997 to 2016, Mixed population (HBsAg carriers without risk factors)	General population, HBsAg carriers; Blood donors, IVDUs, people with HBSB, HIV and/or HCV, frequent blood	General HBsAg-positive populations, comprising people tested in community
Records identified in literature search	2717	3518	2104
Studies included in meta-analysis	182	634	282
Number of subjects included	40 127 988 general population subjects from 61 countries (one study from France: 39 911 011 subjects); 101 363 HBsAg-positive cases from 51 countries	332 155 general population subjects from 48 countries 271 629 HBsAg-positive cases from 83 countries	24 025 000 general population subjects from 50 countries; 120 293 HBsAg-positive cases from 95 countries
Global HDV prevalence	0.98% in general population; 14.6% in HBsAg-positive cases	0.80% in general population; 13.0% in HBsAg-positive cases	0.16% in general population; 4.5% in HBsAg-positive cases of general population; 16.4% in HBsAg-positive cases of Hepatology clinics
Estimated global number of HDV cases	Approximately 72 million	48-60 million; revised to 32-61 million	12 (8.7-18.7) million

Liver International ISSN 1478-3223

CLINICAL STUDIES

Seropositivity for delta hepatitis in patients with chronic hepatitis B and liver cirrhosis in Turkey: a meta-analysis

Halil Değertekin[1], Kendal Yalçın[2], Mustafa Yakut[2] and Cihan Yurdaydin[3]

1 Department of Gastroenterology, Ufuk University School of Medicine, Ankara, Turkey
2 Department of Gastroenterology, Dicle University School of Medicine, Diyarbakır, Turkey
3 Department of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey

- 5231 kronik hepatit, 1503 siroz, toplam 6734 hasta

Degertekin H et al. Liver int 2008;28:494

Liver International ISSN 1478-3223

CLINICAL STUDIES

Seropositivity for delta hepatitis in patients with chronic hepatitis B and liver cirrhosis in Turkey: a meta-analysis

Hali

1 Dep
2 Dep
3 Dep

Table 1. AntiHDV positivity in patients with chronic hepatitis B in Turkey

Region	Year	Researcher	No.	Anti-HDV (%)	Anti-HDV *n*
West Turkey					
Istanbul	1997	Ökten *et al.* (6)	526	4.5	24
Istanbul	2001	Tabak *et al.* (10)	423	7.0	30
Istanbul	2003	Ökten *et al.* (8)	296	2.9	9
Bursa	1997	Nak *et al.* (11)	579	3.5	20
Izmir	1999	Ersöz *et al.* (12)	1551	4.7	73
Izmir	2001	Akarca *et al.* (13)	526	6.1	32
Total			3901	4.8	188
Central Turkey (< 1995)					
Ankara	1991	Erbaş *et al.* (14)	191	31.5	60
Ankara	1992	Okçu *et al.* (15)	51	21.8	11
Ankara	1993	Özyılkan *et al.* (6)	123	28.4	35
Total			365	29.0	106
Central Turkey (> 1995)					
Ankara	2000	Görenek *et al.* (16)	89	8.6	8
Eskişehir	1999	Us *et al.* (6)	77	15.6	12
Total			166	12.1	20
Southeast Turkey (< 1995)					
Diyarbakır	1994	Canoruc *et al.* (17)	100	30.0	30
Diyarbakır	1995	Turfan *et al.* (6)	54	51.7	28
Total			154	37.7	58
Southeast Turkey (> 1995)					
Diyarbakır	1998	Değertekin *et al.* (18)	120	20.0	24
Diyarbakır	2003	Yalçın *et al.* (19)	168	32.1	54
Total			288	27.1	78
East Turkey					
Elazig	2001	Yalniz *et al.* (19)	209	16.5	35
Elazig	2003	Türkdoğan *et al.* (19)	148	33.3	49
Total			357	23.5	84

int 2008;28:494

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2 Department of Gastroenterology, Dicle University School of Medicine, Diyarbakır, Turkey
3 Department of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey

Table 2. AntiHDV positivity in patients with liver cirrhosis in Turkey

Region	Year	Researcher	No.	Anti-HDV (%)	Anti-HDV *n*
West Turkey (< 1995)					
Istanbul	1988	Okten *et al.* (6)	73	34.2	25
Izmir	1985	Batur *et al.* (6)	110	41.0	45
Total			183	38.3	70
West Turkey (> 1995)					
Izmir	1996	Kuruüzüm *et al.* (6)	107	14.0	15
Izmir	2001	Akarca *et al.* (14)	141	25.8	36
Istanbul	2003	Okten *et al.* (11)	316	19.6	62
Total			564	20.0	113
Central Turkey					
Ankara	1989	Emri *et al.* (6)	59	44.4	26
Southeast Turkey (< 1995)					
Diyarbakir	1989	Degertekin *et al.* (6)	60	74.0	44
Diyarbakir	1995	Turfan *et al.* (6)	50	58.0	29
Total			110	66.4	73
Southeast Turkey (> 1995)					
Diyarbakır	2004	Yalcin *et al.* (19)	179	46.3	83
East Turkey					
Elazig	2004	Koca *et al.* (20)	120	30.0	36
Van	2001	Tuncer *et al.* (21)	115	20.8	24
Van	2003	Turkdogan *et al.* (19)	75	45.3	34
Van	2004	Uygan *et al.* (22)	157	23.0	36
Total			467	27.8	130

Liver International ISSN 1478-3223

CLINICAL STUDIES

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1 Department of Gastroenterology, Ufuk University School of Medicine, Ankara, Turkey
2 Department of Gastroenterology, Dicle University School of Medicine, Diyarbakır, Turkey
3 Department of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey

Table 4. Change in delta hepatitis prevalence among patients with chronic hepatitis B in different regions of Turkey

	Disease group	< 1995 *n* (%)	> 1995 *n* (%)	*P* value
Central Turkey	CHB	106/365 (29.0%)	20/166 (12.1%)	< 0.001
Southeast Turkey	CHB	58/154 (37.7%)	78/288 (27.1%)	< 0.001
Western Turkey	LC	70/183 (38.3%)	113/564 (20.0%)	< 0.001
Southeast Turkey	LC	73/110 (66.4%)	83/179 (46.4%)	< 0.001

Degertekin H et al. Liver int 2008;28:494

Liver International ISSN 1478-3223

CLINICAL STUDIES

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2 Department of Gastroenterology, Dicle University School of Medicine, Diyarbakır, Turkey
3 Department of Gastroenterology, Ankara University School of Medicine, Ankara, Turkey

- Delta hepatit, doğu ve güneydoğu bölgelerinde batıya göre daha yaygın,
- Son dekatta daha önceki döneme göre sıklığı azalıyor ancak hala önemli bir sorun.

Degertekin H et al. Liver Int 2008;28:494

Frequency of Hepatitis Delta Virus in Hepatitis B Surface-antigen-positive Patients

Hepatit B Yüzey Antijeni-pozitif Hastalarda Hepatit Delta Virüsünün Sıklığı

Ayfer Yolcu[1], Nuran Karabulut[1], Sema Alaçam[1], Mustafa Önel[1], Melek Büyük[2], Mine Güllüoğlu[2], Ali Ağaçfidan[1]

[1]Istanbul University, Istanbul Faculty of Medicine, Department of Medical Microbiology, Division of Virology and Fundamental Immunology, Istanbul, Turkey
[2]Istanbul University, Istanbul Faculty of Medicine, Department of Pathology, Istanbul, Turkey

- Nisan 2015-Mart 2017, İstanbul
- 2089 HBsAg pozitif hasta
- Antidelta seroprevalansı %4,1

Yolcu A et al. Viral Hepat J 2019;25:14

Investigating the Prevalence of Hepatitis Delta and Assessment of Treatment Response

Delta Hepatit Sıklığının Araştırılması ve Tedavi Yanıtının Değerlendirilmesi

Pınar Ergen, Fatma Yılmaz Karadağ, Özlem Aydın

İstanbul Medeniyet University, Göztepe Training and Research Hospital, Infectious Diseases and Clinical Microbiology, İstanbul, Turkey

- Ocak 2015-Aralık 2019, İstanbul
- 2548 HBsAg pozitif hasta
- Antidelta seroprevalansı %2,9

Ergen P et al. Viral Hepat J 2020;26:135

Annals of Medical Research

DOI: 10.5455/annalsmedres.2021.06.459

Original Article

Anti-HDV seroprevalence in patients with decompensated liver cirrhosis due to hepatitis B

Nergiz Ekmen[1], Sami Cifci[2]

[1]Department of Gastroenterology, Faculty of Medicine, Gazi University, Ankara, Turkey
[2]Clinic of Gastroenterology, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey

- HBV'ye bağlı dekompanse siroz (n=147)
- antiHDV pozitif %31,3

Ekmen N et al. Annals Med Res 2021;28:1771

REVIEW ARTICLE

JVH WILEY

The changing epidemiology of delta hepatitis in Türkiye over three decades: A systematic review

Suleyman Uraz[1] | Zeynep Deniz[2] | Esra Yerlikaya Zerdali[3] | Adel Araslanova[4] | Veysel Tahan[5] | Fehmi Tabak[6] | Resat Ozaras[7]

- Son 35 yılda delta hepatit, 111 çalışma
  - Periyod 1, 1999 ve öncesi,
  - Periyod 2, 2000-2009,
  - Periyod 3, 2010 ve sonrası

Uraz S et al. J Viral Hepat 2023;30:588

REVIEW ARTICLE

JVH WILEY

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Suleyman Uraz[1] | Zeynep Deniz[2] | Esra Yerlikaya Zerdali[3] | Adel Araslanova[4] | Veysel Tahan[5] | Fehmi Tabak[6] | Resat Ozaras[7]

TABLE 3 Cumulative data of hepatitis D virus prevalence in hepatitis B virus-infected patients.

	1999 and before	2000–2009	2010 and after	*p*
Inactive carriers	102/2079 (4.9%)	224/4697 (4.8%)	89/1726 (5.2%)	.8
Chronic hepatitis B	367/2047 (17.9%)	646/12,397 (5.2%)[a]	870/12,625 (6.9%)[a]	<.00001
All HBsAg-positive patients	655/9372 (7.0%)	83/2739 (3.0%)[a]	978/20,662 (4.7%)[b]	<.00001
Total	1124/13,498 (8.3%)	953/19,833 (4.8%)[a]	1937/35013 (5.5%)[c]	<.00001

- HBV taşıyıcıları ve kronik hepatitlerde %5-8,
- Sirotik hastalarda %9-22,
- HCC olgularında %13-18

Uraz S et al. J Viral Hepat 2023;30:588

REVIEW ARTICLE

JVH WILEY

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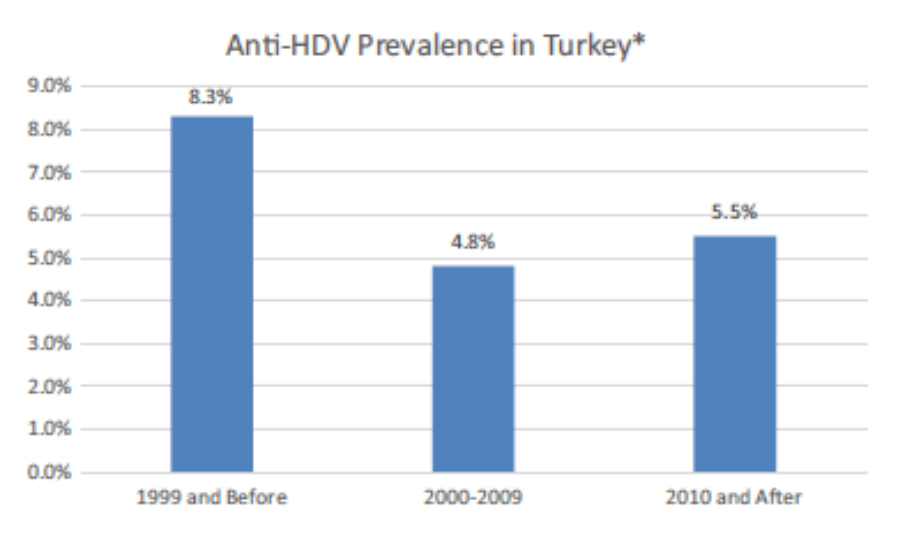

REVIEW ARTICLE

Liver INTERNATIONAL WILEY

New epidemiology of hepatitis delta

Jiannis Vlachogiannakos | George V. Papatheodoridis

- HDV epidemiyolojisinde coğrafik değişkenlikler sıktır,
  Orta ve Batı Afrika, Akdeniz havzası, Orta Doğu, Doğu Avrupa, Kuzey Asya, Amazon bölgesi gibi kimi yüksek prevalans bölgeleri tanımlanmıştır,

- IVDU, HRSB, MSM, HIV ya da HCV ile infekte hastalarda HDV infeksiyonu riski daha yüksektir,

Vlachogiannakos J et al. Liver Int 2020;40(S1):48

REVIEW ARTICLE

Liver INTERNATIONAL WILEY

New epidemiology of hepatitis delta

Jiannis Vlachogiannakos | George V. Papatheodoridis

- HDV epidemiyolojisi halen tam olarak anlaşılamamıştır ve global prevalans tam olarak bilinmemektedir.

Vlachogiannakos J et al. Liver Int 2020;40(S1):48

Review JHEP|Reports

Hepatitis D virus infection: Pathophysiology, epidemiology and treatment. Report from the first international delta cure meeting 2022

Pietro Lampertico,[1,2,*] Elisabetta Degasperi,[1] Lisa Sandmann,[3,4,5] Heiner Wedemeyer [3,4,5], on behalf of the Delta Cure 2022 Working Group[†]

- Nüfusa dayalı çalışmalar az sayıda,
- Bazı bölgeler/ülkelerden hiç veri yok,
- Tarama stratejileri değişkenlik gösteriyor,
- Farkındalık eksikliği,
- Test yöntemleri standardize değil.

Lampertico P et al. JHEP Reports 2023;5:100818

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 *

Initial assessment of subjects with chronic HBV infection

The initial evaluation of a subject with chronic HBV infection should include a complete history, a physical examination, assessment of liver disease activity and severity and markers of HBV infection (Fig. 1). In addition, all first degree relatives and sexual partners of subjects with chronic HBV infection should be advised to be tested for HBV serological markers (HBsAg, anti-HBs, anti-HBc) and to be vaccinated if they are negative for these markers.

(6) Co-morbidities, including alcoholic, autoimmune, metabolic liver disease with steatosis or steatohepatitis and other causes of chronic liver disease should be systematically excluded including co-infections with hepatitis D virus (HDV), hepatitis C virus (HCV) and HIV.

(7) Testing for antibodies against hepatitis A virus (anti-HAV) should be performed, and patients with negative anti-HAV should be advised to be vaccinated against HAV.

EASL CPG. J Hepatol 2017;67:370

Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update

S. K. Sarin[1] · M. Kumar[1] · G. K. Lau[2,27] · Z. Abbas[3] · H. L. Y. Chan[4] · C. J. Chen[5] · D. S. Chen[6] · H. L. Chen[7] · P. J. Chen[8] · R. N. Chien[9] · A. K. Dokmeci[10] · Ed Gane[11] · J. L. Hou[12] · W. Jafri[13] · J. Jia[14] · J. H. Kim[15] · C. L. Lai[16] · H. C. Lee[17] · M. Al Mahtab[20] · R. Moha · B. C. Sharma[25] · J. Sollano · S. S. Zheng[31] · J. H. Kao[32]

3.3 Recommendations (assessment of persons with chronic HBV infection)

3.3.1 The initial evaluation of an individual with HBV infection should include assessment of the level of viremia, degree of inflammation and the presence and stage of liver disease. A detailed history to investigate the possible source of HBV transmission, as well as physical examination, biochemical tests [including aspartate aminotransferase (AST) and ALT, gamma-glutamyl transpeptidase (GGT), alkaline phosphatase, bilirubin, and serum albumin and globulins, and prothrombin time], complete blood count and hepatic ultrasound should be performed (A1).

3.3.2 Measurement of HBV DNA is essential for the diagnosis, assessment for initiating treatment and subsequent monitoring of infected subjects (A1).

3.3.3 Other causes of chronic liver disease should be looked for, including coinfections with HDV, HCV and/or HIV (A1).

3.3.4 Comorbidities, including alcoholic, autoimmune, metabolic liver disease with steatosis or steatohepatitis should be assessed (A1).

Update on Prevention, Diagnosis, and Treatment and of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance

NA Terrault,
Division of Gastroenterology/Hepatology, University of California San Francisco, San Francisco, CA

AS Lok,
Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI

BJ McMahon,
Live

Guidance Statements for Treatment of Patients with HBV and HCV Coinfection

1. All HBsAg-positive patients should be tested for HCV infection using the anti-HCV test.
2. HCV treatment is indicated for patients with HCV viremia (113).
3. HBV treatment is determined by HBV DNA and ALT levels as per the AASLD HBV guidelines for monoinfected patients (1).
4. HBsAg-positive patients are at risk of HBV DNA and ALT flares with HCV DAA therapy, and monitoring of HBV DNA levels every 4 to 8 weeks during treatment and for 3 months posttreatment is indicated in those who do not meet treatment criteria for monoinfected patients (per AASLD–Infectious Diseases Society of America HCV Guidance).
5. HBsAg-negative, anti-HBc positive patients with HCV are at very low risk of reactivation with HCV DAA therapy. ALT levels should be monitored at baseline, at the end of treatment, and during follow-up, with HBV DNA and HBsAg testing reserved for those whose ALT levels increase or fail to normalize during treatment or posttreatment.

atology 2018;67:1560

Update on Prevention, Diagnosis, and Treatment and of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance

NA Terrault,
Division of Gastroenterology/Hepatology, University of California San Francisco, San Francisco, CA

AS Lok,
Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI

BJ McMahon,
Liver Diseases and Hepatitis Program, Alaska NativeTribal Health Consortium, Anchorage, AK

Guidance Statements for Management of Patients With HDV Infection

1. Anti-HDV screening is recommended in HIV-positive persons, persons who inject drugs, men who have sex with men, those at risk for sexually transmitted diseases, and immigrants from areas of high HDV endemicity. Patients with low HBV DNA levels and elevated ALT levels may be considered for HDV screening. If there is any uncertainty regarding the need to test, an initial anti-HDV test is recommended.
2. For those at risk for HDV acquisition, periodic retesting is recommended.
3. Anti-HDV–positive patients should have periodic assessment of HDV RNA and HBV DNA.

Terrault NA et al. Hepatology 2018;67:1560

Delta Hepatitis within the Veterans Affairs Medical System in the United States: Prevalence, Risk Factors, and Outcomes

Tatyana Kushner[1], **Marina Serper**[1,2], and **David E. Kaplan**[1,2]

[1]Division of Gastroenterology, University of Pennsylvania, Philadelphia PA

[2]Department of Medicine Philadelphia VA Medical Center, Philadelphia PA

- Ulusal retrospektif çalışma,
- Ekim 1999-Aralık 2013 arasında HBsAg pozitifliği saptanan 25603 hasta

- HDV testi yapılan hasta sayısı 2008 (%7,8)
- Yüksek riskli profile sahip olanlarda test yapılmayanlar %80 (1181/1468)

Kushner T et al. J Hepatol 2015;63:586

Delta Hepatitis within the Veterans Affairs Medical System in the United States: Prevalence, Risk Factors, and Outcomes

Tatyana Kushner[1], **Marina Serper**[1,2], and **David E. Kaplan**[1,2]

[1]Division of Gastroenterology, University of Pennsylvania, Philadelphia PA

[2]Department of Medicine Philadelphia VA Medical Center, Philadelphia PA

- Gastroenteroloji ya da infeksiyon hastalıkları uzmanlarınca görülen hastalarda test yapılma olasılığı daha yüksek (OR 3,3, %95 CI 3,0–3,6)
- ABD'de KHB hastalarında HDV test oranları kabul edilemeyecek derecede düşüktür.

Kushner T et al. J Hepatol 2015;63:586

Contents lists available at ScienceDirect

Virus Research

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

Short communication

Hepatitis D diagnostics:Utilization and testing in the United States

Parham Safaie[1], Sanam Razeghi[2], Susan D. Rouster, Isaac Privitera, Kenneth E. Sherman*

Division of Digestive Diseases, University of Cincinnati College of Medicine, Cincinnati, OH, United States

- Üçüncü basamak akademik merkez
- 2012-2016 arasında saptanan tüm HBsAg pozitif hastalar (n=1007)

- HDV koinfeksiyonu açısından test edilen hasta sayısı 121 (%12)

Safaie P et al. Virus Res 2018;250:114

Contents lists available at ScienceDirect

Virus Research

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

Short communication

Hepatitis D diagnostics:Utilization and testing in the United States

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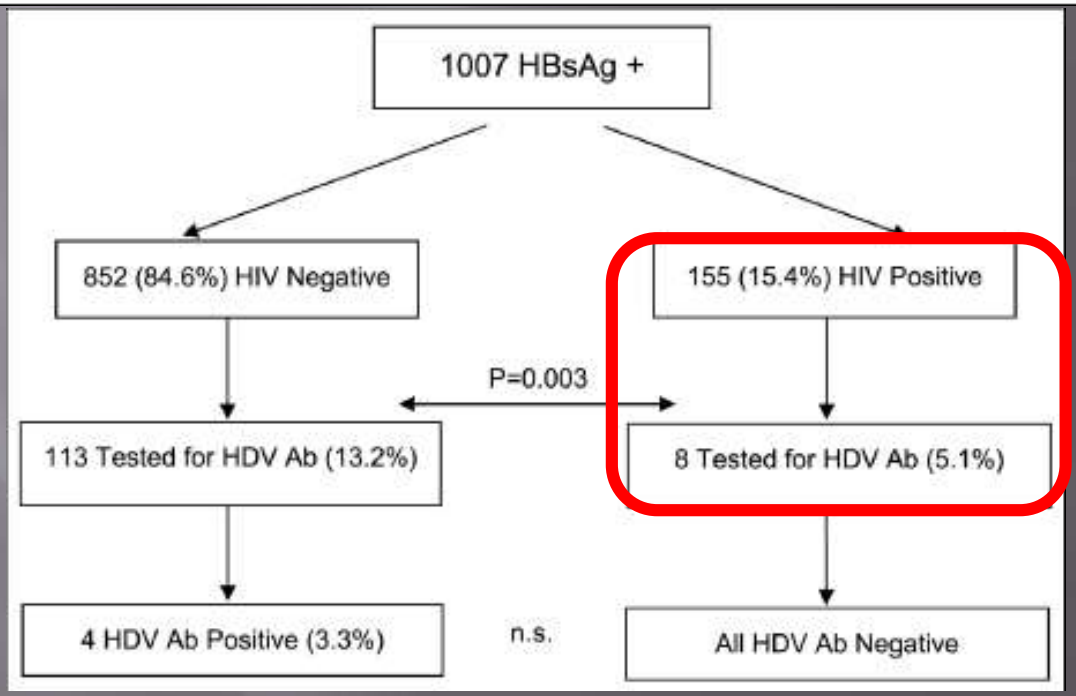
Division of Digestive Diseases, University of Cincinnati College of Medicine, Cincinnati, OH, United States



Safaie P et al. Virus Res 2018;250:114

Prevalence and clinical course of hepatitis delta infection in Greece: A 13-year prospective study

Emanuel K. Manesis[1,*], Georgia Vourli[2], George Dalekos[3], Themistoclis Vasiliadis[4], Nina Manolaki[5], Athina Hounta[6], Sotirios Koutsounas[7], Irini Vafiadis[8], Georgia Nikolopoulou[9], Gregory Giannoulis[10], George Germanidis[11], George Papatheodoridis[12], Giota Touloumi[2]

[1]*Division of Internal Medicine, Athens University Medical School, Greece;* [2]*Department of Hygiene, Epidemiology & Medical Statistics, Athens University Medical School, Greece;* [3]*Department of Medicine and Research Laboratory of Internal Medicine, Thessaly University Medical School, Larissa, Greece;* [4]*2nd Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Hippokration Hospital, Thessaloniki, Greece;* [5]*2nd Department of Pediatrics, Agia Sophia Children's Hospital, Agia Sophia Hospital, Goudi, Athens, Greece;* [6]*4th Academic Department of Internal Medicine and Infectious Diseases, Attikon University General Hospital, University of Athens Medical School, Greece;* [7]*Hepatology Service, Foundation of Social Insurance (IKA), Athens, Greece;* [8]*Department of Propedeutic Medicine, Athens University Medical School, "Laikon" Hospital, Athens, Greece;* [9]*Greek National Center for Disease Control (KEELPNO), Athens, Greece;* [10]*2nd Department of Internal Medicine, General Hospital "Tzaneion", Piraeus, Greece;* [11]*1st Department of Internal Medicine, General Hospital "AXEΠA", Thessaloniki, Greece;* [12]*2nd Department of Internal Medicine, Athens University Medical School, Greece*

- Hep-Net.Greece kohort çalışmasından prospektif veri,
- Ocak 1997-Ağustos 2010 arasında prospektif olarak izlenen 4673 kronik hepatit B olgusu

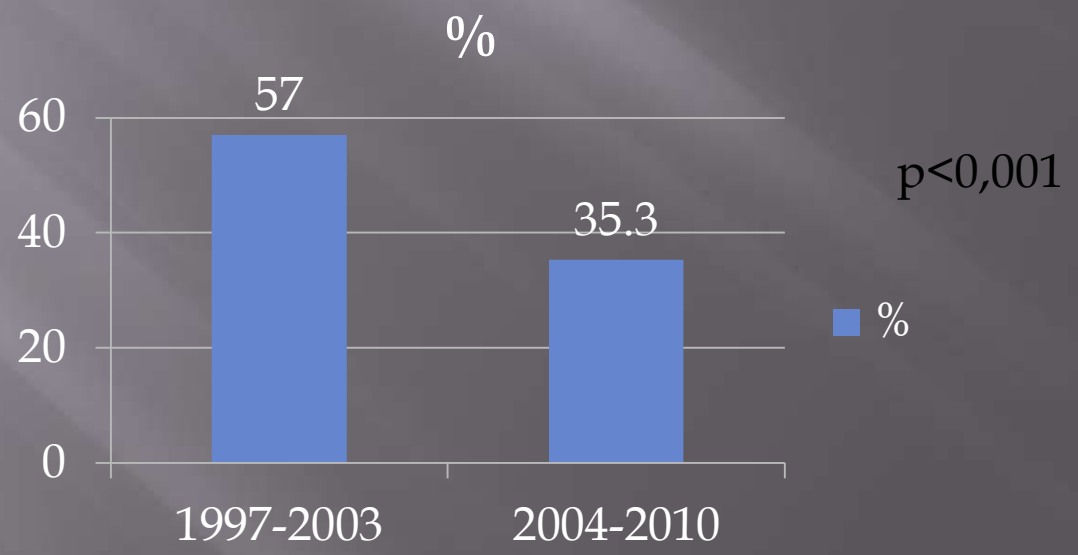
- HDV testi yapılan hasta sayısı 2137 (%45,7)

Manesis EK et al. J Hepatol 2013; 59:949

Prevalence and clinical course of hepatitis delta infection in Greece: A 13-year prospective study

Emanuel K. Manesis[1,*], Georgia Vourli[2], George Dalekos[3], Themistoclis Vasiliadis[4], Nina Manolaki[5], Athina Hounta[6], Sotirios Koutsounas[7], Irini Vafiadis[8], Georgia Nikolopoulou[9], Gregory Giannoulis[10], George Germanidis[11], George Papatheodoridis[12], Giota Touloumi[2]

[1]*Division of Internal Medicine, Athens University Medical School, Greece;* [2]*Department of Hygiene, Epidemiology & Medical Statistics, Athens University Medical School, Greece;* [3]*Department of Medicine and Research Laboratory of Internal Medicine, Thessaly University Medical School, Larissa, Greece;* [4]*2nd Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Hippokration Hospital, Thessaloniki, Greece;* [5]*2nd Department of Pediatrics, Agia Sophia Children's Hospital, Agia Sophia Hospital, Goudi, Athens, Greece;* [6]*4th Academic Department of Internal Medicine and Infectious Diseases, Attikon University General Hospital, University of Athens Medical School, Greece;* [7]*Hepatology Service, Foundation of Social Insurance (IKA), Athens, Greece;* [8]*Department of Propedeutic Medicine, Athens University Medical School, "Laikon" Hospital, Athens, Greece;* [9]*Greek National Center for Disease Control (KEELPNO), Athens, Greece;* [10]*2nd Department of Internal Medicine, General Hospital "Tzaneion", Piraeus, Greece;* [11]*1st Department of Internal Medicine, General Hospital "ΑΧΕΠΑ", Thessaloniki, Greece;* [12]*2nd Department of Internal Medicine, Athens University Medical School, Greece*



Manesis EK et al. J Hepatol 2013; 59:949

ORIGINAL ARTICLE

JVH WILEY

The Delta Delta: Gaps in screening and patient assessment for hepatitis D virus infection

Rohit Nathani[1] | Randy Leibowitz[1] | Dewan Giri[2] | Carolina Villarroel[2] | Sidra Salman[1] | Mantej Sehmbhi[1] | Bo Hyung Yoon[3] | Amreen Dinani[4] | Ilan Weisberg[5]

- Ocak 2016-Aralık 2021 arasında 11190 KHB hastası

- HDV için taranan hasta sayısı 1444 (%12,9)
- HDV RNA PCR doğrulaması %80,5

Nathani R et al. J Viral Hepat 2023;30:195

REVIEW

Hepatitis D infection: from initial discovery to current investigational therapies

Ben L. Da [1], Theo Heller[2] and Christopher Koh[2,*]

[1]Digestive Diseases Branch, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, Bethesda, MD, USA; [2]Liver Diseases Branch, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, Bethesda, MD, USA

*Corresponding author. Liver Diseases Branch, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, 10 Center Drive, Bldg. 10, Room 5-2740, Bethesda, MD 20892, USA. Tel: +1-301-451-1721; Fax: +1-301-402-0491; Email: Christopher.koh@nih.gov

Diagnostic test	Detection	Significance	Comments
Liver HDAg	Detects HDV antigen on liver histology via immunohisto-chemical staining	Indicates active infection	Lack of availability. Poor sensitivity
Serum HDAg	Detects HDV antigen in the serum	Indicates active infection but disappears quickly	Rarely performed. May be unde-tectable in chronic HDV
Anti-HDV IgM	Detects the presence of IgM antibodies against HDV in the serum	Indicates active infection, usually found in acute but can be found in chronic HDV	Often negative in chronic HDV but can be positive during periods of increased HDV replication
Anti-HDV IgG	Detects the presence of IgG antibodies	Usually indicates previous infection or chronic HDV	Appears late in acute HDV but persistent in chronic HDV
HDV RNA PCR (Qualitative)	Detects HDV RNA in the serum	Indicates active infection, can be found in acute or chronic HDV	LLOD depends on the assay. Useful for diagnosis
HDV RNA PCR (Quantitative)	Quantifies HDV RNA in the serum	Indicates active infection, can be found in acute or chronic HDV	LLOQ depends on the assay. Useful for treatment monitoring
HDV genotyping	Determines HDV genotype	Distinguish specific HDV genotype (1–8) with possible prognostic significance	Not commercially available

Da BL et al. Gastroenterol Rep 2019;7:231

Review JHEP|Reports

Hepatitis D virus infection: Pathophysiology, epidemiology and treatment. Report from the first international delta cure meeting 2022

Pietro Lampertico,[1,2,*] Elisabetta Degasperi,[1] Lisa Sandmann,[3,4,5] Heiner Wedemeyer [3,4,5], on behalf of the Delta Cure 2022 Working Group[†]

- Anti HDV serolojisinde kullanılan kitlerin tanısal performanslarında (duyarlılık, özgüllük) dikkat çekici değişkenlikler söz konusudur.

  Fransa'da IgM testleri arasındaki uyum %43-100.

Lampertico P et al. JHEP Reports 2023;5:100818

World Health Organization

WHO/BS/2013.2227
ENGLISH ONLY

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION
Geneva, 21 to 25 October 2013

Collaborative Study to Establish a World Health Organization International Standard for Hepatitis D Virus RNA for Nucleic Acid Amplification Technique (NAT)-Based Assays

Michael Chudy[1], Kay-Martin Hanschmann[1], Mithat Bozdayi[2], Julia Kreß[1], C. Micha Nübling[1] and the Collaborative Study Group*

- HDV RNA NAT test protokollerinin optimizasyonu ve standardizasyonu için HDV G1 temelli uluslararası standartlar

Chudy M et al. Collaborative study to establish a World Health Organization International Standard for HDV RNA for nucleic acid amplification technique (NAT)-based assays. WHO; 2013

First International External Quality Assessment for Hepatitis Delta Virus RNA Quantification in Plasma

Frédéric LE GAL [1,2], Ségolène BRICHLER [1,2,3], Roland SAHLI [4], Sylvie CHEVRET [5,6,*], Emmanuel GORDIEN [1,2,3,*]

[1] Laboratoire de Bactériologie, Virologie, Hygiène, Hôpital Avicenne, Assistance Publique - Hôpitaux de Paris, Université Paris 13, Bobigny, France

[2] Centre national de référence des hépatites B, C et Delta (laboratoire associé pour le virus de l'hépatite Delta)

[3] Unité INSERM U955, équipe n° 18, Créteil, France Université Paris Est

- 17 ülke, 28 laboratuvar
- Panel A: Farklı viral yük ve genotiplerde 20 klinik örnek
- Panel B: DSÖ standart dilüsyonları

Le Gal F et al. Hepatology 2016;64:1483

First International External Quality Assessment for Hepatitis Delta Virus RNA Quantification in Plasma

Frédéric LE GAL [1,2], Ségolène BRICHLER [1,2,3], Roland SAHLI [4], Sylvie CHEVRET [5,6,*], Emmanuel GORDIEN [1,2,3,*]

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[3] Unité INSERM U955, équipe n° 18, Créteil, France Université Paris Est

- 13 (%46,3) laboratuvar tüm örnekleri doğru olarak kuantifiye etti,
- 16 (%57,1) laboratuvar 1 ila 10 örnekte doğru sonuç veremedi,
- Birkaç laboratuvar G1, G5-8 için >3 log IU/ml düşük sonuç verdi.

Le Gal F et al. Hepatology 2016;64:1483

First International External Quality Assessment for Hepatitis Delta Virus RNA Quantification in Plasma

Frédéric LE GAL [1,2], Ségolène BRICHLER [1,2,3], Roland SAHLI [4], Sylvie CHEVRET [5,6,*], Emmanuel GORDIEN [1,2,3,*]

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[3] Unité INSERM U955, équipe n° 18, Créteil, France Université Paris Est

- HDV RNA NAT test yöntemlerinin tanısal performansları arasında çok yüksek heterojenite vardır.

Le Gal F et al. Hepatology 2016;64:1483

First International External Quality Assessment for Hepatitis Delta Virus RNA Quantification in Plasma

Frédéric LE GAL [1,2], Ségolène BRICHLER [1,2,3], Roland SAHLI [4], Sylvie CHEVRET [5,6,*], Emmanuel GORDIEN [1,2,3,*]

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- Standardize, full otomatize, real time yöntemler ticari olarak erişilebilir olana dek, ardışık hasta örneklerinde kantitatif HDV RNA monitorizasyonu, aynı laboratuvarda aynı kit ve yöntemle yapılmalıdır.

Le Gal F et al. Hepatology 2016;64:1483

Implementation of anti-HDV reflex testing among HBsAg-positive individuals increases testing for hepatitis D

Adriana Palom,[1,2,†] Ariadna Rando-Segura,[3,†] Judit Vico,[1] Beatriz Pacín,[3,4] Elena Vargas,[1,2] Ana Barreira-Díaz,[1,2,5] Francisco Rodríguez-Frías,[3,4,5] Mar Riveiro-Barciela,[1,2,5] Rafael Esteban,[1,2,5] Maria Buti[1,2,5,*]

[1]Liver Unit, Internal Medicine Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2]Department of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain; [3]Microbiology Department, Clinical Laboratories, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [4]Department of Biochemistry and Molecular Biology, Universitat Autònoma de Barcelona, Barcelona, Spain; [5]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain

- Ocak 2018-Aralık 2021 retrospektif, prospektif çalışma
  - Ocak 2018-Aralık 2020 retrospektif
  - Ocak 2021-Aralık 2021 prospektif
- Yeni saptanan HBsAg pozitif 2236 hasta

Palom A et al. JHEP Rep 2022;4:100547

Implementation of anti-HDV reflex testing among HBsAg-positive individuals increases testing for hepatitis D

Adriana Palom,[1,2,†] Ariadna Rando-Segura,[3,†] Judit Vico,[1] Beatriz Pacín,[3,4] Elena Vargas,[1,2] Ana Barreira-Díaz,[1,2,5] Francisco Rodríguez-Frías,[3,4,5] Mar Riveiro-Barciela,[1,2,5] Rafael Esteban,[1,2,5] Maria Buti[1,2,5,*]

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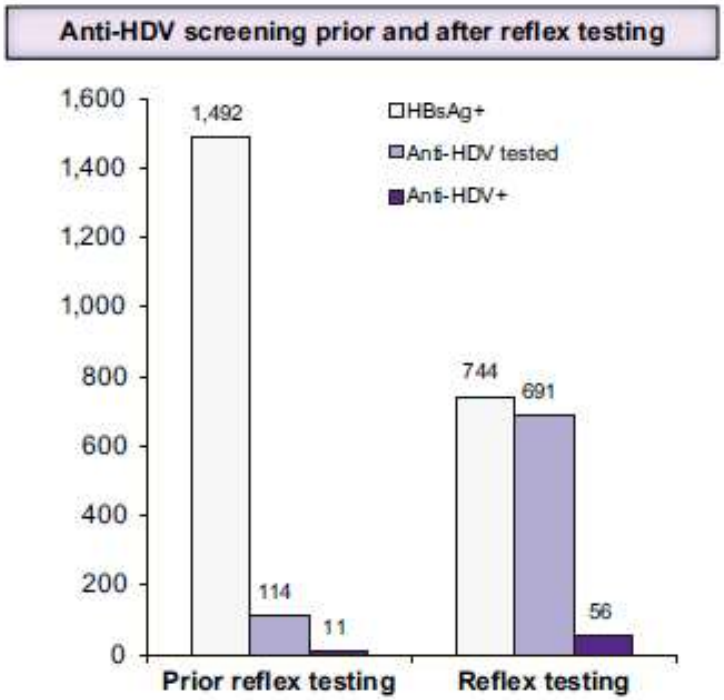
Retrospektif
(n=1492)
AntiHDV
%7,6
AntiHDV (+)
n=11 (%9,6)



Prospektif
(n=744)
AntiHDV
%93
AntiHDV (+)
n=56 (%8,1)

Palom A et al. JHEP Rep 2022;4:100547

Implementation of anti-HDV reflex testing among HBsAg-positive individuals increases testing for hepatitis D

Adriana Palom,[1,2,†] Ariadna Rando-Segura,[3,†] Judit Vico,[1] Beatriz Pacín,[3,4] Elena Vargas,[1,2] Ana Barreira-Díaz,[1,2,5] Francisco Rodríguez-Frías,[3,4,5] Mar Riveiro-Barciela,[1,2,5] Rafael Esteban,[1,2,5] Maria Buti[1,2,5,*]

[1]Liver Unit, Internal Medicine Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2]Department of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain; [3]Microbiology Department, Clinical Laboratories, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [4]Department of Biochemistry and Molecular Biology, Universitat Autònoma de Barcelona, Barcelona, Spain; [5]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain

- HDV ardışık test uygulaması, yeni tanı konan delta hepatit olgu sayısını 5 kat arttırdı.
- AntiHDV pozitif saptanan olguların %60'ında risk faktörü tanımlanmıyordu.

Palom A et al. JHEP Rep 2022;4:100547

Public Health Corner

JOURNAL OF HEPATOLOGY

Hepatitis D double reflex testing of all hepatitis B carriers in low-HBV- and high-HBV/HDV-prevalence countries

Homie A. Razavi[1,*], Maria Buti[2], Norah A. Terrault[3], Stefan Zeuzem[4], Cihan Yurdaydin[5], Junko Tanaka[6], Alessio Aghemo[7,8], Ulus S. Akarca[9], Nasser M. Al Masri[10], Abduljaleel M. Alalwan[11], Soo Aleman[12], Abdullah S. Alghamdi[13], Saad Alghamdi[14], Waleed K. Al-Hamoudi[15], Abdulrahman A. Aljumah[16], Ibrahim H. Altraif[17], Tarik Asselah[18], Ziv Ben-Ari[19,20], Thomas Berg[21], Mia J. Biondi[22], Sarah Blach[23], Wornei S.M. Braga[24], Carlos E. Brandão-Mello[25,26], Maurizia R. Brunetto[27,28], Joaquin Cabezas[29,30], Hugo Cheinquer[31], Pei-Jer Chen[32], Myeong-Eun Cheon[33], Wan-Long Chuang[34], Carla S. Coffin[35], Nicola Coppola[36], Antonio Craxi[37], Javier Crespo[38,39], Victor De Ledinghen[40], Ann-Sofi Duberg[41], Ohad Etzion[42,43], Maria Lucia G. Ferraz[44], Paulo R.A. Ferreira[45], Xavier Forns[46], Graham R. Foster[47], Giovanni B. Gaeta[48], Ivane Gamkrelidze[1], Javier García-Samaniego[49], Liliana S. Gheorghe[50,51], Pierre M. Gholam[52], Robert G. Gish[53], Jeffrey Glenn[54], Julian Hercun[55], Yao-Chun Hsu[56], Ching-Chih Hu[57], Jee-Fu Huang[58], Naveed Janjua[59], Jidong Jia[60], Martin Kåberg[61], Kelly D.E. Kaita[62], Habiba Kamal[12], Jia-Horng Kao[63], Loreta A. Kondili[64], Martin Lagging[65,66], Pablo Lázaro[67], Jeffrey V. Lazarus[68], Mei-Hsuan Lee[69], Young-Suk Lim[70], Paul J. Marotta[71], Maria-Cristina Navas[72], Marcelo C.M. Naveira[1], Mauricio Orrego[73,74], Carla Osiowy[75], Calvin Q. Pan[76], Mário G. Pessoa[77], Giovanni Raimondo[78], Alnoor Ramji[79], Devin M. Razavi-Shearer[1], Kathryn Razavi-Shearer[1], Cielo Y. Ríos-Hincapié[80], Manuel Rodríguez[81], William M.C. Rosenberg[82], Dominique M. Roulot[83], Stephen D. Ryder[84], Rifaat Safadi[85], Faisal M. Sanai[86], Teresa A. Santantonio[87], Christoph Sarrazin[88,89], Daniel Shouval[85], Frank Tacke[90], Tammo L. Tergast[91], Juan Miguel Villalobos-Salcedo[92], Alexis S. Voeller[1], Hwai-I Yang[69,93,94,95], Ming-Lung Yu[96,97,98], Eli Zuckerman[99], on behalf of the Polaris Observatory

- Ulusal düzeyde HDV prevalansına dair doğru öngörüde bulunabilmek için en etkin yöntem
- Tüm HBsAg pozitif hastalarda antiHDV; tüm antiHDV pozitif hastalarda HDV RNA

Razavi HA et al. J Hepatol 2023;79:576

Public Health Corner

JOURNAL
OF HEPATOLOGY

Hepatitis D double reflex testing of all hepatitis B carriers in low-HBV- and high-HBV/HDV-prevalence countries

Homie A. Razavi[1,*], Maria Buti[2], Norah A. Terrault[3], Stefan Zeuzem[4], Cihan Yurdaydin[5], Junko Tanaka[6], Alessio Aghemo[7,8], Ulus S. Akarca[9], Nasser M. Al Masri[10], Abduljaleel M. Alalwan[11], Soo Aleman[12], Abdullah S. Alghamdi[13], Saad Alghamdi[14], Waleed

- Günümüzde farklı ülkelerde kullanılan antiHDV ve HDV RNA PCR testlerine erişim kısıtlıdır, standardizasyonları sorunludur ve DSÖ onaylı testler mevcut değildir.

- Ardışık test stratejisi ile tanısal testler üreten firmaların ticari yatırım yapabilmesi, kalite ve fiyat rekabeti yaratılması ve HDV tanı testlerinde standardizasyon sağlanarak yaygınlaştırılması sağlanabilir.

Razavi HA et al. J Hepatol 2023;79:576

Tedavi

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 *

- PegIFNα for at least 48 weeks is the current treatment of choice in HDV-HBV co-infected patients with compensated liver disease (Evidence level I, grade of recommendation 1).
- In HDV-HBV co-infected patients with ongoing HBV DNA replication, NA therapy should be considered (Evidence level II-2, grade of recommendation 1).
- PegIFNα treatment can be continued until week 48 irrespective of on-treatment response pattern if well tolerated (Evidence level II-2, grade of recommendation 2).

EASL CPG. J Hepatol 2017;67:370

Contents lists available at ScienceDirect

Antiviral Research

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

Effectiveness of pegylated interferon monotherapy in the treatment of chronic hepatitis D virus infection: A meta-analysis

Aigerim Abdrakhman [a], Aiymkul Ashimkhanova [a], Wassim Y. Almawi [a,b,*]

[a] School of Medicine, Nazarbayev University, Nur Sultan (Astana), Kazakhstan
[b] College of Health Sciences, Abu Dhabi University, Abu Dhabi, United Arab Emirates

- Peginterferon alpha-2a ya da -2b ile tedavi edilmiş 475 hastanın yer aldığı 13 çalışmanın metaanalizi,
  - SVR %29
  - BR %33
- PegIFN HDV tedavisinde sınırlı etkinliğe sahiptir.

Abdrakhman A et al. Antiviral Res 2021;185:104995

HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases

Late HDV RNA Relapse After Peginterferon Alpha-Based Therapy of Chronic Hepatitis Delta

Benjamin Heidrich,[1,2,11] Cihan Yurdaydın,[3] Gökhan Kabaçam,[3] Boris A. Ratsch,[4] Kalliopi Zachou,[1,5] Birgit Bremer,[1] George N. Dalekos,[5] Andreas Erhardt,[6] Fehmi Tabak,[7] Kendal Yalcin,[8] Selim Gürel,[9] Stefan Zeuzem,[10] Markus Cornberg,[1,11] C.-Thomas Bock,[4] Michael P. Manns,[1,2,11] Heiner Wedemeyer,[1,2,11] for the HIDIT-1 Study Group

- PegIFN ile tedavi edilen ve SVR kabul edilen 16 hasta median 4,5 yıl takip,
- 9 hastada uzun dönemde HDV RNA pozitifliği saptanıyor…
- HDV infeksiyonunda SVR terimi kullanılmamalıdır.

Heidrich B et al. Hepatology 2014;60:87

BRIEF DEFINITIVE REPORT

Liver INTERNATIONAL WILEY

Residual low HDV viraemia is associated HDV RNA relapse after PEG-IFNa-based antiviral treatment of hepatitis delta: Results from the HIDIT-II study

Birgit Bremer[1] | Olympia E. Anastasiou[2] | Svenja Hardtke[3,14] | Florin Alexandru Caruntu[4] | Manuela G. Curescu[5] | Kendal Yalcin[6] | Ulus S. Akarca[7] | Selim Gürel[8] | Stefan Zeuzem[9] | Andreas Erhardt[10] | Stefan Lüth[11] | George V. Papatheodoridis[12] | Monica Radu[4] | Ramazan Idilman[13] | Michael P. Manns[1,14] | Markus Cornberg[1,14] | Cihan Yurdaydin[13,15] | Heiner Wedemeyer[1,14,16]

- Daha önceden in-house HDV RNA yöntemiyle çalışılan örnekler, daha duyarlı bir yöntemle tekrar çalışılmış.
- In house Cobas TaqMan LOD 930 IU/ml
- RoboGene HDV RNA LOD 14 IU/ml

Bremer B et al. Liver Int 2021;41:295

BRIEF DEFINITIVE REPORT

Liver INTERNATIONAL WILEY

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- Negatif olarak kaydedilen örneklerin %31'i pozitif saptanmış.
- 48-96. haftada saptanan düşük düzey HDV viremisi relaps açısından yüksek riskli.

Bremer B et al. Liver Int 2021;41:295

Peginterferon alfa-2a plus tenofovir disoproxil fumarate for hepatitis D (HIDIT-II): a randomised, placebo controlled, phase 2 trial

Heiner Wedemeyer, Cihan Yurdaydin*, Svenja Hardtke, Florin Alexandru Caruntu, Manuela G Curescu, Kendal Yalcin, Ulus S Akarca, Selim Gürel, Stefan Zeuzem, Andreas Erhardt, Stefan Lüth, George V Papatheodoridis, Onur Keskin, Kerstin Port, Monica Radu, Mustafa K Celen, Ramazan Idilman, Kristina Weber, Judith Stift, Ulrike Wittkop, Benjamin Heidrich, Ingmar Mederacke, Heiko von der Leyen, Hans Peter Dienes, Markus Cornberg, Armin Koch, Michael P Manns, for the HIDIT-II study team†*

- PegIFN ileTDF kombinasyonu tedavi sonu yanıtı artırmaz.

Wedemeyer H et al. Lancet Infect Dis 2019;19:275

Journal of Viral Hepatitis, 2007, **14**, 812–816 doi:10.1111/j.1365-2893.2007.00875.x

A pilot study of 2 years of interferon treatment in patients with chronic delta hepatitis

C. Yurdaydın,[1,2] H. Bozkaya,[1] H. Karaaslan,[1] F. O. Önder,[1] Ö. E. Erkan,[2] K. Yalçın,[3] H. Değertekin,[3] A. M. Bozdayı[1,2] and Ö. Uzunalimoğlu[2] [1]*Gastroenterology Section, University of Ankara Medical School;* [2]*Hepatology Institute, University of Ankara, Ankara; and* [3]*Gastroenterology Section, Dicle University Medical School, Diyarbakır, Turkey*

Received September 2006; accepted for publication January 2007

- Tedavi süresinin iki yıla uzatılması ile SVR artmıyor.

Yurdaydın C et al. J Viral Hep 2007;14:812

Long term therapy of chronic delta hepatitis with peginterferon alfa

Theo Heller[1,*], Yaron Rotman[1,*], Christopher Koh[1,*], Shauna Clark[1], Vanessa Haynes-Williams[1], Rebecca McBurney[2], Peter Schmid[3], Jeffrey Albrecht[3], David E. Kleiner[4], Marc G. Ghany[1], T. Jake Liang[1], and Jay H. Hoofnagle[1]

[1]Liver Diseases Branch, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, Bethesda, Maryland [2]Clinical Center, National Institutes of Health, Bethesda, Maryland [3]National Genetics Institute, Los Angeles, California [4]Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

- Tedavi süresinin beş yıla kadar uzatılması ile SVR artmıyor.

Heller T et al. Aliment Pharmacol Ther. 2014;40:93

Antiviral treatment and liver-related complications in hepatitis delta

Anika Wranke[1], Beatriz Calle Serrano[1], Benjamin Heidrich[1,2], Janina Kirschner[1], Birgit Bremer[1], Patrick Lehmann[1], Svenja Hardtke[1,2], Katja Deterding[1], Kerstin Port[1], Max Westphal[3], Michael P. Manns[1,2,4], Markus Cornberg[1,2], Heiner Wedemeyer[1,2,4]

[1]*Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany,*

- IFN alfa tedavisi uzun dönemde daha düşük KC ilişkili komplikasyonlar ile ilişkili.

Wranke A et al. Hepatology 2017;65:414

Sonuç olarak

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The Delta Agent

MARIO RIZZETTO

Division of Gastroenterology, Molinette, Torino 10126, Italy

This review provides a glimpse of the many problems raised by the discovery of the δ agent which need an answer in the future. The most intriguing is the nature of the new pathogen and its ecological niche, where and when it arose and whether other similar pathogens exist, of which δ agent may be a model. The epidemiology of δ agent is largely unknown. It appears to be exotic, yet it is infrequent in regions of Asia where the HBsAg rate is among the highest in the world. Given the mechanism of its spread, δ agent is likely to represent a major epidemiologic risk of hepatitis where the prevalence of HBV is high, as in many parts of the developing world.

and depends on external help to initiate and maintain replication. Experimental evidence consistently indicates that the necessary helper function is provided only by HBV infection, and extensive epidemiologic studies confirm that the δ antigen-antibody system is expressed only in subjects with circulating HBsAg, except in occasional individuals with anti-δ who have recently recovered from HBsAg/δ hepatitis. The symbiosis materializes in the form of δ agent identified in blood, a hybrid particle whose interior contains δ genome and antigen, and whose exterior is coated by HBsAg.

Because of the obligatory association with HBV, the biological expression of the new pathogen occurs only if concomitant HBs antigenemia is present, and the outcome of δ infection is modulated by the type and course of the background HBV infection. This concept is crucial in understanding the natural history of δ infection and the mechanisms for its varied pathology.

Address reprint requests to: Mario Rizzetto, M.D., Division of Gastroenterology, Molinette, Corso Bramante 88, Torino 10126, Italy.

IgG is destroyed in formalin-fixed sections, which can be stained by direct and indirect immunohistological methods.

Serum δ antigen and anti-δ are determined by sensitive solid-phase radio- and enzyme-linked immunoassays (6–8). Assays for anti-δ were developed using δ antigen obtained from human liver (6). The antigen is extracted with strong dissociating agents (urea or guanidine at high molarity). It is a protein of approximately 68,000 daltons molecular weight, resistant to heating and a variety of chemical treatments (6). Assays for anti-δ are competitive, based on blocking by anti-δ in test serum of δ antigen fixed on a solid phase which is then not available for reaction with radioiodinated or enzyme-labeled IgG anti-δ.

A specific test for anti-δ of the IgM type was also developed based on capture of IgM in test serum by anti-human μ linked to a solid phase (9).

δ antigen obtained from acute phase sera of patients with δ hepatitis was also recently used to develop an ELISA for anti-δ (10). This test is more sensitive than

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journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative Review

Treatment of hepatitis D: an unmet medical need

G.P. Caviglia, M. Rizzetto*

Department of Medical Sciences, University of Turin, Turin, Italy

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ABSTRACT

Background: Therapy of chronic hepatitis D (CHD) is still based on interferon alpha (IFNα), introduced in clinical practice 30 years ago; results are modest and better therapies are an urgent medical need.
Aims: This article provides a critical overview of the new therapies under investigation for CHD.
Sources: Review of the recently published medical literature.
Content: New therapeutic efforts aim to deprive the hepatitis D virus (HDV) of functions provided to its life cycle by the hepatitis B virus (HBV) or by the host. Three therapeutic strategies are in evaluation: a) Myrcludex B, a myristoylated lipopeptide of the pre-S1 domain of the HBsAg that blocks the entry of the HDV into hepatocytes and controls infection by preventing the spreading of the virus to liver cells not infected by the HBV; b) Lonafarnib, an inhibitor of a host farnesyltransferase that hinders morphogenesis of the HDV by preventing the farnesylation of the large HD-antigen, necessary for virion assembly; c) REP 2139, a nucleic acid polymer that prevents export of the mature HDV by the presumed inhibition of the synthesis of subviral HBsAg particles with which the virion is coated. Myrcludex B and Lonafarnib increase therapeutic efficacy in combination with Peg-IFNα. In a pilot study, REP 2139 in combination with Peg-IFNα induced the clearance of serum HDV RNA and of the HBsAg in about half of 12 treated patients.
Implications: Long-term therapies with either Myrcludex B or Lonafarnib in combination with Peg-IFNα are required to achieve clinical control of CHD. However, with prolonged therapies tolerance becomes a problem; studies are on the way to determine whether Peg-IFN lambda may be better tolerated that Peg-IFNα. The promising preliminary data of REP 2139 in combination with Peg-IFNα await confirmation of the original pilot study. **G.P. Caviglia, Clin Microbiol Infect 2020;26:824**
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Introduction

Chronic hepatitis D (CHD) is the most severe form of viral hepatitides, rapidly leading to cirrhosis, liver dysfunction and hepatocellular carcinoma [1].

Infection with hepatitis D virus (HDV) was estimated to occur worldwide in 15–20 million out of the 300 million chronic carriers of the hepatitis B virus (HBV), but its medical burden may be significantly higher; a recent metanalysis has calculated that the global prevalence of HDV among HBsAg carriers may be as high as 13.02%, corresponding to 48–60 million infections [2].

There is as yet no efficient treatment for HDV infections. Therapy still relies on interferon alpha (IFNα) which was empirically introduced in clinical practice more than 30 years; the efficacy is poor and the addition of antivirals against the partner HBV, such as Adefovir (ADV), Entecavir (ETV) and Tenofovir (TDF), is of no avail [3]. In the largest trial of CHD, the Hep-Net International Delta Hepatitis Intervention Trial (HIDIT-I), the cumulative rate of sustained viral response (clearance of serum HDV maintained 6 months after stopping treatment) was 28% using Pegylated (Peg)-IFN either in monotherapy or in combination with ADV [4]; however, relapses were frequent post-therapy [5].

New therapies against hepatitis D are an urgent need but the challenge is daunting. With an RNA genome of only about 1700 nucleotides, the HDV does not code for proteins like the viral polymerases and proteases of the HBV and hepatitis C virus; it depends for dissemination and replication on the helper HBV and the host replicative machinery [6], and can not therefore be targeted by conventional antivirals, such as those currently used to control the HBV or cure hepatitis C.

* Corresponding author. M. Rizzetto, Department of Medical Sciences, University of Turin, Via San Massimo 24, 10100 Turin, Italy.
E-mail address: marcohdv88@gmail.com (M. Rizzetto).

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