Acute and chronic viral hepatitis

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Discovery of aetiological agents of VH

- 1965 Hepatitis B surface antigen (HBsAg) isolated (Blumberg)
- 1973 Hepatitis A virus (HAV) identified (Feinstone)
- 1977 Delta agent (HDV) identified
- (Mario Rizzetto)
- 1985 recombinant DNA technology
- 1989 HCV identified (Houghton)
- 1990 HEV identified (Bradley)
- 1995 HGV (GBV-C) identified

Původce	HAV enterovirus 72	HBV	HCV
Čeleď (Family)	Picornaviridae	Hepadnaviridae	Flaviviridae
Rod (Genus)	Hepatovirus	Orthohepadnavirus	Hepacivirus
Velikost	27-28 nm	42 nm	30-60 nm
Genom	RNA	DNA	RNA
Počet genotypů	4 pouze 1 sérotyp	8 (A až H)	> 6 genotypů > 120 subtypů
Ink. doba (dny)	15-50	30-180	15-150
Přenos: - enterálně	ano	ne	ne
- krví	vzácně	ano	ano
- sexuálně	vzácně	ano	vzácně
- vertikálně	ne	ano	vzácně
Přechod do chronicity	ne	novor. > 90 %, děti do 5 let 25-50 %, dospělí: imunokompetentní < 5 %, imunokompromitovaní > 50 %	55 - 85 %
Laboratorní diagnostika akutní infekce	anti-HAV IgM (možná poz. po akt. imunizaci)	HBsAg HBcAg anti-HBc IgM	anti-HCV HCV RNA
Fulminantní průběh (rozvoj akutního jaterního selhání do 8 týdnů)	0,1 %	0,1 - 1 %	krajně vzácně
Akt. a pas. imunizace	ano	ano	ne

Původce	HDV (delta agens)	HEV swHEV (swine kmeny HEV)	GBV-C (HGV) Nezpůsobuje hepatitidu
Čeleď (Family)		Hepeviridae	Flaviviridae
Rod (Genus)	Deltavirus	Hepevirus	
Velikost	35-37 nm	27-34 nm	
Genom	RNA	RNA	RNA
Počet genotypů (GT)	3 (I až III)	4 základní genotypy (GT)	
Ink. doba (dny)	30-180	15-60	
Přenos: - enterálně	ne	ANO GT 1 a GT 2 kontaminovanou vodou GT 3 a GT 4 zoonotický přenos (vepři, kanci, jelenovití)	ne
- krví	ano	vzácně	ano
- sexuálně	ano	vzácně	
- vertikálně	ano	ano	
Přechod do chronicity	koinfekce < 5 % superinfekce 80-90 %	NE, Chron. průběh bývá u pac. po transplantacích, u malignit, u HIV pozit.	Inhibice HIV replikace - zpomalení progrese
Lab. diagnostika akutní infekce	anti-HDV IgM, HBsAg	anti-HEV IgM a/nebo HEV RNA (ze séra nebo stolice)	anti-HGV, HGV RNA
Fulminantní průběh	u koinfekce 1 % u superinfekce 5 %	1-2 %, 3. trim. grav. kolem 22 % (GT 1 a GT 2)	
Vakcína	proti HB	rekombinantní, v praxi v Číně	ne
Imunoglobulin	proti HB	ne	ne

Virus hepatitidy F

- V prosinci 1994 publikována zpráva o přenosu agens, který způsobuje non-A, non-E hepatitidu u opic
- Virus-like particles o průměru 27-37 nm) byly detekovány ve stolici francouzských pacientů a v játrech a stolicích infikovaných zvířat
- Agens označeno jako hepatitis French virus (HFV) a analýzou virového genomu zjištěna dvojvláknitá DNA

  (Journal of Gastroenterology and Hepatology 2001;16(2):124-131)
- Později existence tohoto viru nebyla potvrzena

HEV resistance on heat

Heating the food to an internal temperature of 71 °C for 20 min is necessary to completely inactivate HEV

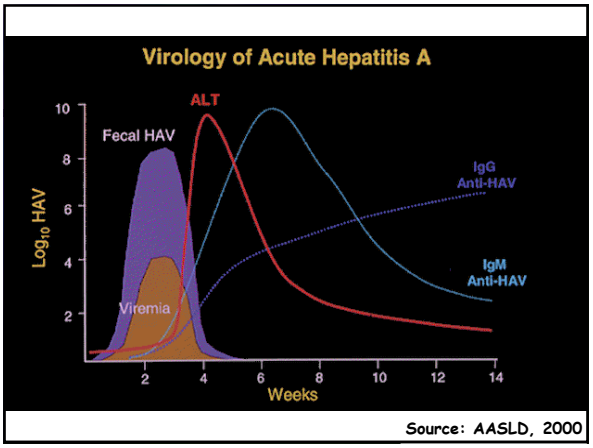
(Barnaud E. et al.: Thermal inactivation of infectious hepatitis E virus in experimentally contaminated food. *Applied and Environmental Microbiology* 2012;78(15):5153-9)

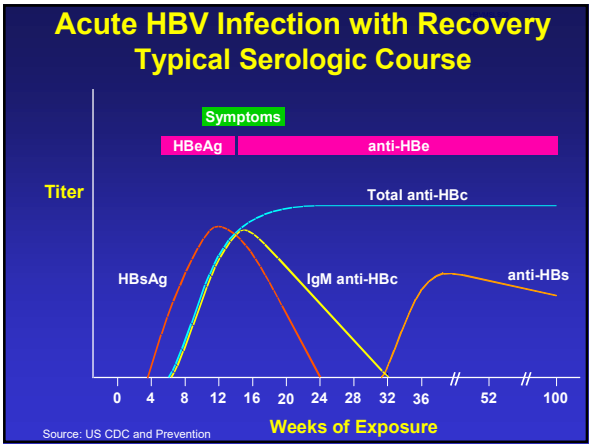
Rezistence HEV na teplo

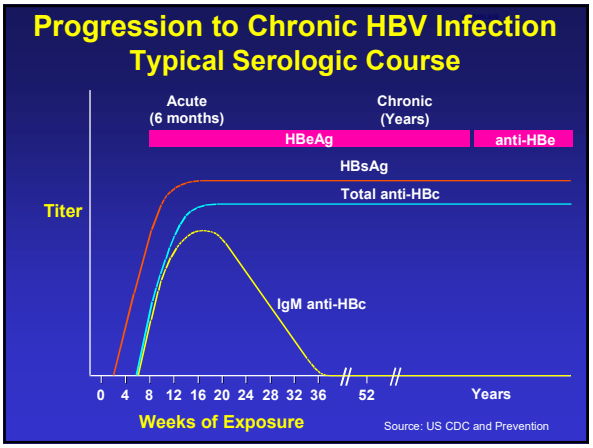
(Feagins AR et al. *Int J Food Microbiol* 2008;123:32-37)

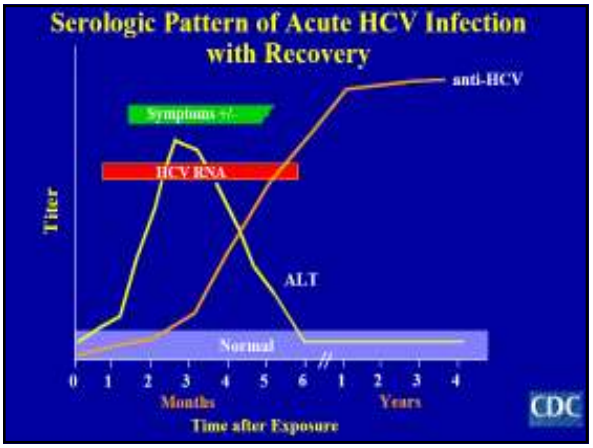
Teplota (ºC)	Čas (min)	Úprava masa	Výsledek
56 ºC	30´- 60´	medium rare	rezistence HEV
60 ºC	60´	medium	reziduální živý HEV
66 ºC	10´- 60´	medium well-cooked	inaktivace HEV
70-71 ºC	10´- 60´	well done	inaktivace HEV

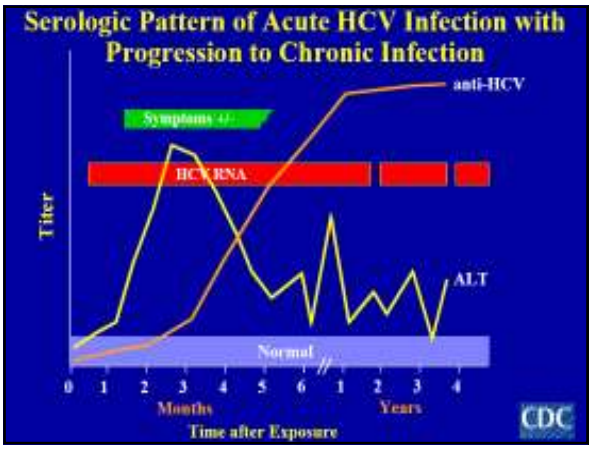
	Anti HAV IgM	HBs Ag	HBe Ag	Anti HBc IgG	Anti HBc IgM	Anti HBs	Anti HCV	Anti HBe	Anti HEV IgM
HA akutní	+	-	-	-	-	-	-	-	-
HB akutní	-	+	+	-	+	-	-	-	-
HB chronická HBeAg pozitivní (dříve infekce divokým typem viru)	-	+	+	+	-	-	-	-	-
HB chronická HBeAg negativní (dříve infekce e-minus mutantou)	-	+	-	+	-	-	-	+	-
St. po vakcinaci proti HB	-	-	-	-	-	+	-	-	-
HC akutní nebo chronická	-	-	-	-	-	-	+ a HCV RNA	-	-
HE akutní	-	-	-	-	-	-	-	-	+ a/nebo HEV RNA

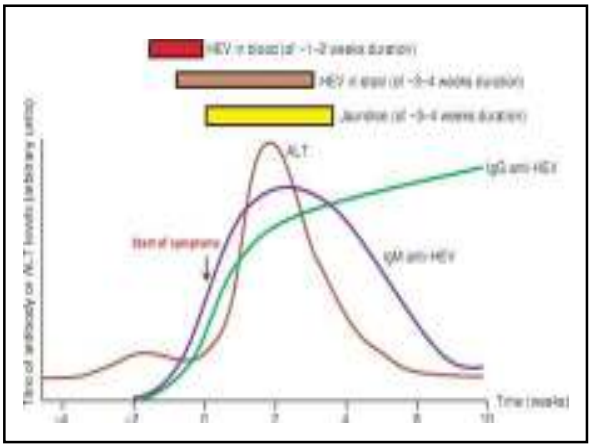


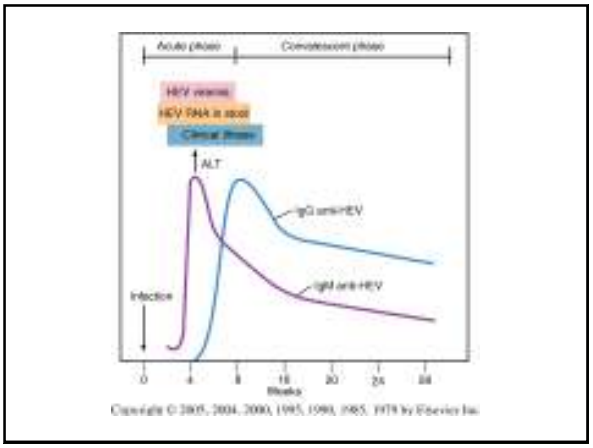












Acute VH in CR (Epidat)

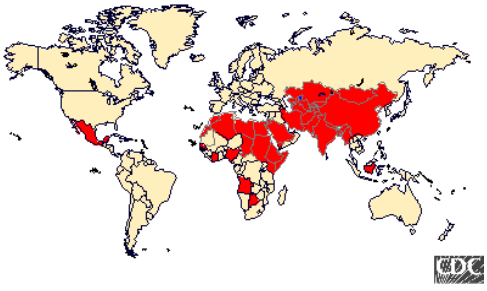
(HC = acute HC + chronic HC firstly diagnosed)

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
HA	1195	904	933	614	325	127	114	70	322	132	128	1648	1104	862	264	284	348	673	724	930	772
HB	564	575	636	604	457	413	370	392	361	307	307	306	247	244	192	154	133	105	89	73	85
HC	273	448	634	637	798	858	846	868	844	1022	980	974	836	709	812	794	873	867	956	1104	992
HE	5	17	5	12	13	12	21	36	37	35	43	65	99	72	163	258	218	299	412	339	344

Previous theory about HE prevalance

Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in > 25% of Sporadic Non-ABC Hepatitis

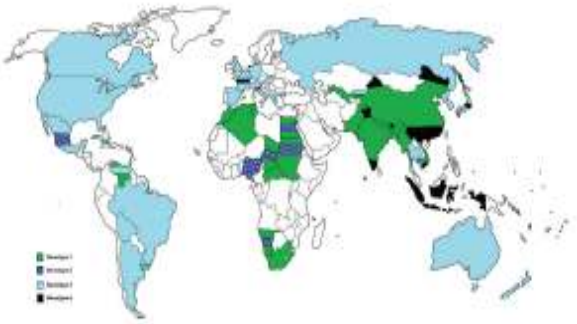


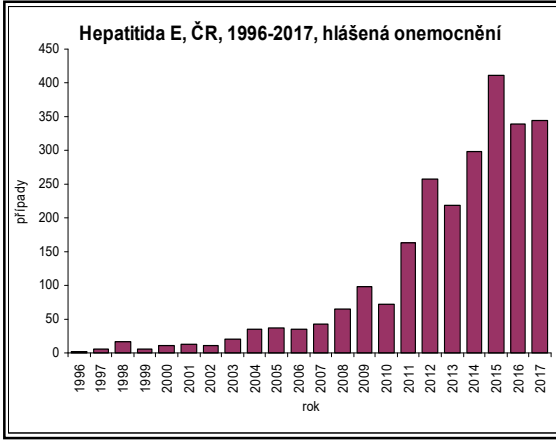
Výskyt HE ve světě

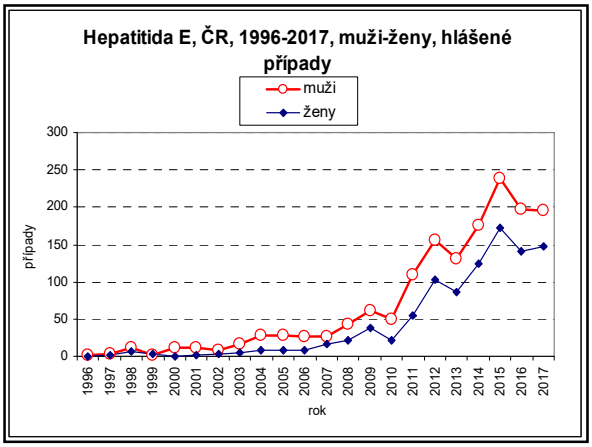
(Epidem. Mikrobiol. Imunol. 2015;64(2):72-78)

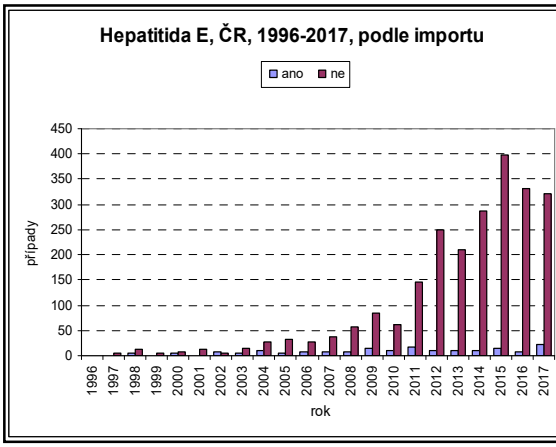
Genotypes of HE in the world

(Hepatic Medicine:Evidence and Research 2014;6:45-59)







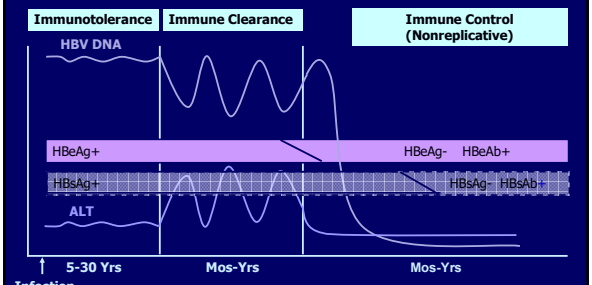


Hepatitis B: Some Sobering Facts

- 350 million people chronically infected
- 2 billion with evidence of past or present infection
- Country of origin is THE major risk factor

World Health Organization. Hepatitis B Fact Sheet. Centers for Disease Control and Prevention. CDC Health Information for International Travel 2012. New York: Oxford University Press; 2012.

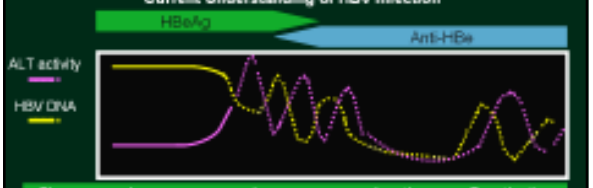
Natural History of Chronic HBV Infection



Yim HJ, et al. Hepatology. 2006;43:S173-S181.

4 Phases of Chronic HBV Infection

Current Understanding of HBV Infection



Phase	Immune Tolerant	Immune Clearance	Inactive Carrier State	Reactivation
Liver	Minimal inflammation and fibrosis	Chronic active inflammation	Mild hepatitis and minimal fibrosis	Active inflammation

Optimal treatment times

Subset of Agents Reported to Cause HBV Reactivation

Class	Agents
Corticosteroids	Dexamethasone, methylprednisolone, prednisolone
Antitumor antibiotics	Actinomycin D, bleomycin, daunorubicin, doxorubicin, epirubicin, mitomycin-C
Plant alkaloids	Vinblastine, vincristine
Alkylating agents	Carboplatin, chlorambucil, cisplatin, cyclophosphamide, ifosfamide
Antimetabolites	Azauridine, cytarabine, fluouracil, gemcitabine, mercaptopurine, methotrexate, thioguanine
Monoclonal antibodies	Alemtuzumab, rituximab
Others	Colaspase, docetaxel, etoposide, fludarabine, folinic acid, interferon, procarbazine

Yeo W, et al. Hepatology. 2008;43:209-220.

HBV Reactivation: Overview

- Clinical syndrome characterized by an increase in HBV DNA and ALT/AST with or without symptoms or jaundice
- Occurs in pts with active (HBsAg+) and resolved (HBsAg-, anti-HBc+) HBV infection
- Wide clinical spectrum

  Ranges from silent to acute liver failure (fibrosing cholestatic hepatitis)
- Can occur during treatment with many immunosuppressive agents

  May also occur up to 12 mos after treatment
- Preventable by antiviral prophylaxis

Di Bisceglie AM, et al. Hepatology. 2015;61:703-711.
Perrillo RP, et al. Gastroenterology. 2015;148:221-244.

Slide credit: clinicaloptions.com

Treatment of HCV with direct-acting antivirals (DAAs) may cause reactivation of HBV

Patients fulfilling the standard criteria for HBV treatment should receive NA treatment

HBsAg-positive patients undergoing DAA therapy should be considered for concomitant NA prophylaxis until week 12 post DAA, and monitored closely

HBsAg-negative, anti-HBc positive patients undergoing DAA should be monitored and tested for HBV reactivation

J Hepatol 2017;67:370-98

HBV Reactivation (HBVr) Risk Based on Serologic Status and Immunosuppressive Potency

Risk Level (anticipated incidence of HBVr)	Serological Risk Status	Immunosuppressive Agent Risk Status
High (>10% of cases)	HBsAg+, high HBV DNA, or HBeAg+	▪ B-cell–depleting agents (are used in pts with leukemias, non-Hodgkin lymphoma, cryoglobulinemia, rheumatoid arthritis, idiopathic thrombocytopenic purpura) – rituximab (anti-CD20), ofatumumab ▪ Systemic chemotherapy ▪ Moderate/high-dose corticosteroids
Intermediate (1% to 10% of cases)	HBsAg-, anti-HBc+, anti-HBs-	▪ TNF inhibitors – etanercept, adalimumab, certolizumab, infliximab ▪ Tyrosine kinase inhibitors – imatinib, nilotinib ▪ Other cytokine and integrin inhibitors – abatacept,ustekinumab,natalizumab,vedolizumab ▪ Transarterial chemoembolization ▪ Low/moderate/high-dose corticosteroids
Low (<1% of cases)	HBsAg-, anti-HBc+, anti-HBs+ (anti-HBs positivity may provide additional protection against HBVr)	▪ Methotrexate ▪ Azathioprine ▪ 6-mercaptopurine ▪ Low-dose corticosteroids

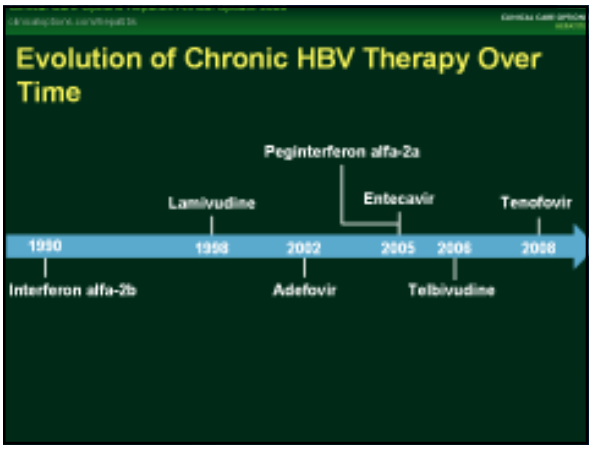
high-dose corticosteroids (> 20 mg prednisone daily or equivalent) for ≥ 4 weeks or moderate-dose corticosteroids (10-20 mg prednisone daily or equivalent) for ≥ 4 weeks or low-dose corticosteroids (< 10 mg prednisone daily or equivalent) for ≥ 4 weeks.

Slide credit: clinicaloptions.com

Nová nomenklatura chronické HBV infekce (*J Hepatol 2017;67:370-98*)

- Chronická HBV infekce je dynamickým procesem odrážejícím interakce mezi replikací HBV a imunitním systémem
- Ne všichni pacienti s chronickou HBV infekcí mají chronickou hepatitidu B:

1. HBeAg pozitivní chronická HBV infekce (dříve imunotolerantní fáze)
2. HBeAg pozitivní chronická hepatitida B
3. HBeAg negativní chronická HBV infekce (dříve inaktivní nosičství)
4. HBeAg negativní chronická hepatitida B
5. HBsAg negativní fáze (také okultní infekce HBV)



Effects of interferon alfa

- IFN alfa inhibits the synthesis of viral nucleid acids and structural and nonstructural viral proteins
- Immunomodulatory effect:
  IFN alfa increases the activity of cytotoxic T lymphocytes (CTLs) and NK cells, stimulates T lymphocytes and macrophages to the production and secretion of next cytokines
- IFN alfa increases the expression of HLA antigens of the 1st class on the health and viral inficated cells and therefore inficated hepatocytes are then more sensitive to CTLs

Indication for the treatment of HBV infection

(EASL 2017 Clinical Practice Guidelines)

- HBV DNA >2,000 IU/ml
- Elevated ALT and/or at least moderate histological lesions
  (i.e. markers of inflammation = HBeAg-positive or HBeA-negative chronic HB)
- All cirrhotic patients with detectable HBV DNA
- The prevention of mother to child transmission in pregnant women with high viremia (i.e. > 200 000 IU/ml) – *Czech recommendation (from SEP 2017) is to use tenofovir (TDF) from 24th-28th week of gravidity and stop this prophylaxis during the next 12 weeks after the birth*
- Prevention of HBV reactivation in patients requiring immunosuppression or chemotherapy
- Patients with HBeAg-positive chronic HBV infection with normal ALT and high HBV DNA (i.e. previously termed „immune tolerant" phase) if they are older than 30 years
- Patients with severe acute HB, characterised by coagulopathy or protracted course, should be treated with nucleos(t)ide analogue (NA) therapy and considered for liver transplantation
- Tenofovir (TDF) is recommended for pregnant women with CHB and advanced fibrosis or cirrhosis

Nucleos(t)ide analogues

*famciklovir – *analogue of deoxygunosin*

*lamivudine (3TC, LAM) – *analogue of deoxycytidin (Zeffix™)*

*adefovir dipivoxil (ADV) – *analogue of dAMP (Hepsera™)*

*tenofovir – *similar as ADV*
TDF = *tenofovir disoproxil fumarate (Viread™)*
TAF = *tenofovir alafenamide (Vemlidy™)*

*entecavir (ETC) –*analogue of deoxyguanin (Baraclude™)*

*emtricitabine (FTC) – *analogue of cytosinu*

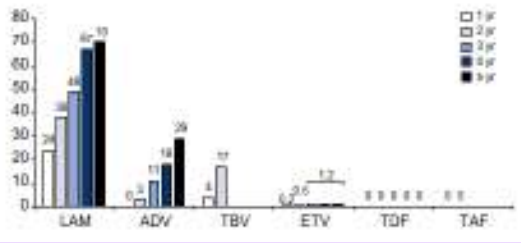
*clevudine (LFMAU) –*analogue of pyrimidin*

*telbivudine (LdT) – *analogue of L-deoxythymidin*

Duration of the therapy of chronic HB

	HBeAg pos.	HBeAg neg.
PEG-IFN alfa	48 wks	48 wks
Nucleos(t)ide analogues (LAM,ADV,TDF,ETC)	To HBeAg disappearance and next 12 months	To HBsAg disappearance X HBsAg persistency very often to the end of the life
Initiation of antiviral therapy	HBV DNA >2 000 IU/mL (>10^4 copies/mL)	HBV DNA >2 000 IU/mL (>10^4 copies/mL)

Cumulative incidence of HBV resistance for lamivudine (LAM), adefovir (ADV), telbivudine (TBV), entecavir (ETV), tenofovir (TDF) and tenofovir alafenamide (TAF) in pivotal trials in nucleos(t)ide-naïve patients with chronic HB (*Hepatology 2014;60:313A-317A*)



Long-term Oral HBV Therapy is Highly Effective

- Suppresses HBV DNA[1,2]
- Normalizes ALT[2,3]
- Prevents fibrosis progression[3,4]
- Promotes fibrosis regression, even in cirrhosis[4]
- Prevents and even reverses hepatic decompensation[1]
- ***Reduces, but does not eliminate, the risk of HCC[1,5]***
- ***Long-term therapy is effective . . . but low rates of HBsAg loss[6]***

1. Lim YS, et al. Gastroenterology. 2014;147:152-161.2. Chang TT, et al. Hepatology. 2010;51:422-430. 3. Zoutendijk R, et al. Gut. 2013;62:760-765. 4. Marcellin P, et al. Lancet. 2013;381:468-475. 5. Papatheodoridis GV, et al. J Hepatol. 2015;62:363-370. 6. Papatheodoridis GV, et al. Hepatol. 2016;63:1481-1492.

Slide credit: clinicaloptions.com

Long-term Oral HBV Therapy: Downsides

- Toxicity
  - Potential for renal, bone complications with TDF
- Resistance
  - High with lamivudine (not preferred by guidelines)[1]
  - Very low with entecavir—unless already LAM resistant[2]
  - None with TDF in clinical trials (similar expected with TAF)[3]
- Cost
- Adherence

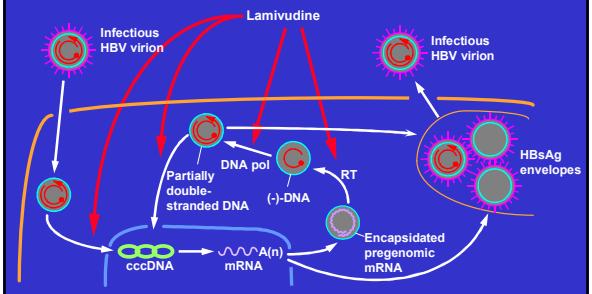
1. Hadziyannis SJ, et al. Hepatology. 2000 ;32:847-51.
2. 2. Gish SR, et al. Gastroenterology. 2007;133:1437-44. 3. Buti M, et al. Dig Dis Sci. 2015;60:1457-1464.

Slide credit: clinicaloptions.com

Budoucnost v léčbě HBV infekce

- Probíhající klinické studie:
  - inarivir + tenofovir
  - GS-4774 tepelně inaktivovaná, T-buňky stimulující vakcína (rekombinantní, kvasinková)
- Optimální by bylo antivirotikum, umožňující degradaci a eliminaci cccDNA (covalently closed circular DNA)
- V případě dosažení inhibice či destrukce cccDNA – by nedošlo k reaktivaci

HBV Replication: Inhibition by Lamivudine



Lai *et al.*, *J Med Virol* 2000

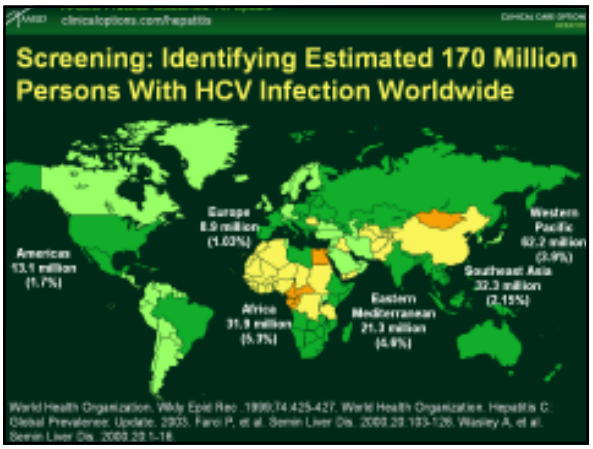
cccDNA covalently closed circular DNA (kovalentně uzavřená cirkulární DNA)

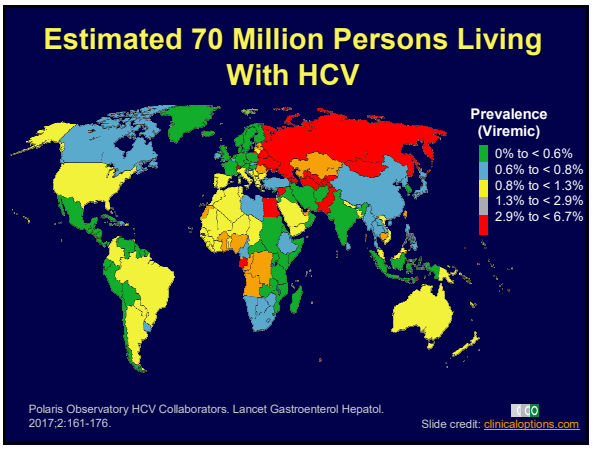
PegIFN vs Nucleos(t)ide Analogues

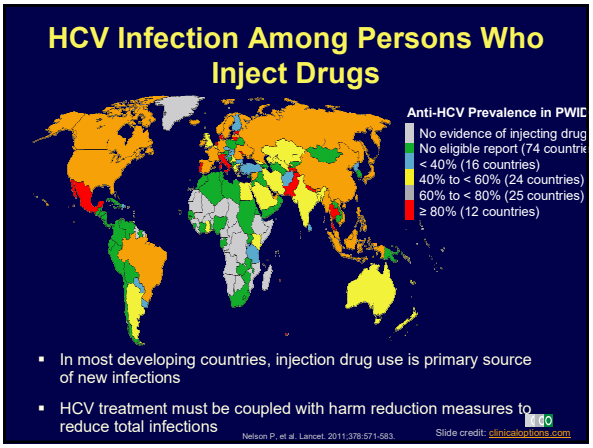
PegIFN		Nucleos(t)ide Analogues	
Pro	Con	Pro	Con
• Finite course of therapy • No resistance • Higher rate of HBeAg loss in 1 yr • Higher rate of HBsAg loss with short duration therapy*	• SQ administration • Frequent AEs • Contraindicated in patients with cirrhosis, in pregnancy, with acute hepatitis B, and who are immunosuppressed	• PO administration • Infrequent AEs • Safe at all stages of disease, including decompensated cirrhosis† • Safe in immuno-compromised populations • Selected drugs probably safe in pregnancy	• Need for long-term or indefinite therapy • Potential for drug resistance

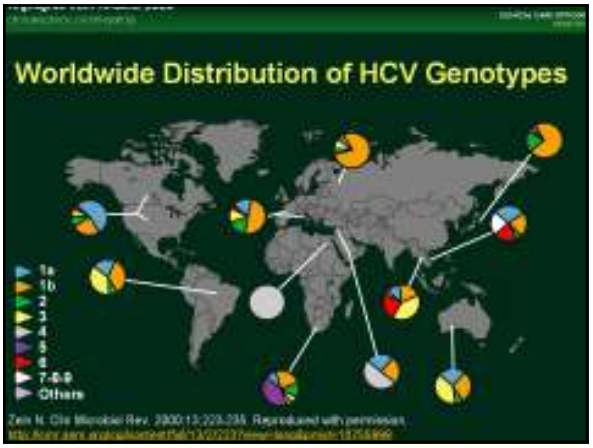
*Particularly for HBeAg-positive patients with genotype A infection.
†Recent case report of lactic acidosis in severe liver failure.

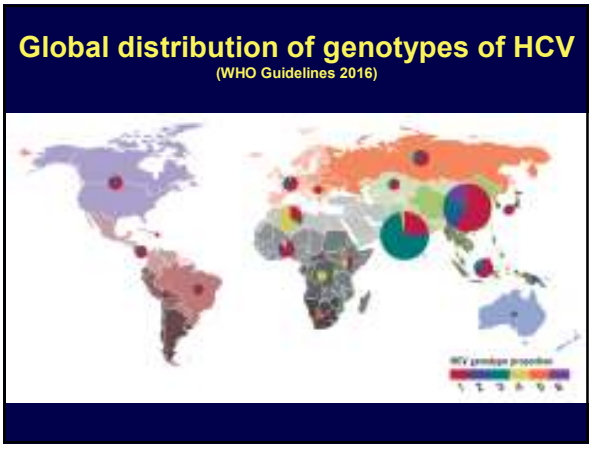
Lok AS, et al. Hepatology. 2007;45:507-539. Lok AS, et al. Hepatology. 2009;50:661-662. Lok AS. Hepatology. 2010;52:743-747. Buster EH, et al. Gastroenterology. 2008;135:459-467. Lange CM, et al. Hepatology. 2009;50:2001-2006.

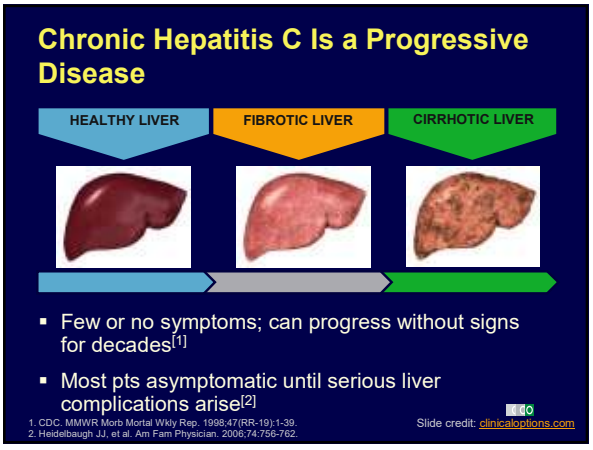

clinicaloptions.com/hepatitis
Screening: Identifying Estimated 170 Million Persons With HCV Infection Worldwide
Europe
8.9 million
(1.03%)
Western Pacific
62.2 million
(3.9%)
Americas
13.1 million
(1.7%)
Southeast Asia
32.3 million
(2.15%)
Africa
31.9 million
(5.7%)
Eastern Mediterranean
21.3 million
(4.8%)
World Health Organization. Wkly Epid Rec. 1999;74:425-427. World Health Organization. Hepatitis C: Global Prevalence: Update. 2003. Farci P, et al. Semin Liver Dis. 2000;20:193-126. Wasley A, et al. Semin Liver Dis. 2000;20:1-16.


Estimated 70 Million Persons Living With HCV
Prevalence (Viremic)
0% to < 0.6%
0.6% to < 0.8%
0.8% to < 1.3%
1.3% to < 2.9%
2.9% to < 6.7%
Polaris Observatory HCV Collaborators. Lancet Gastroenterol Hepatol. 2017;2:161-176.
Slide credit: clinicaloptions.com


HCV Infection Among Persons Who Inject Drugs
Anti-HCV Prevalence in PWID
No evidence of injecting drug
No eligible report (74 countries)
< 40% (16 countries)
40% to < 60% (24 countries)
60% to < 80% (25 countries)
≥ 80% (12 countries)
In most developing countries, injection drug use is primary source of new infections
HCV treatment must be coupled with harm reduction measures to reduce total infections
Nelson P, et al. Lancet. 2011;378:571-583.
Slide credit: clinicaloptions.com

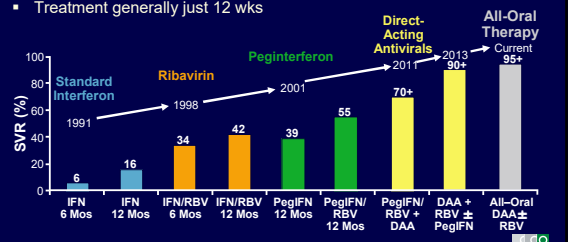

Worldwide Distribution of HCV Genotypes
1a
1b
2
3
4
5
6
7-8-9
Others


Global distribution of genotypes of HCV
(WHO Guidelines 2016)


Chronic Hepatitis C Is a Progressive Disease
HEALTHY LIVER
FIBROTIC LIVER
CIRRHOTIC LIVER
Few or no symptoms; can progress without signs for decades[1]
Most pts asymptomatic until serious liver complications arise[2]
1. CDC. MMWR Morb Mortal Wkly Rep. 1998;47(RR-19):1-39.
2. Heidelbaugh JJ, et al. Am Fam Physician. 2006;74:756-762.
Slide credit: clinicaloptions.com

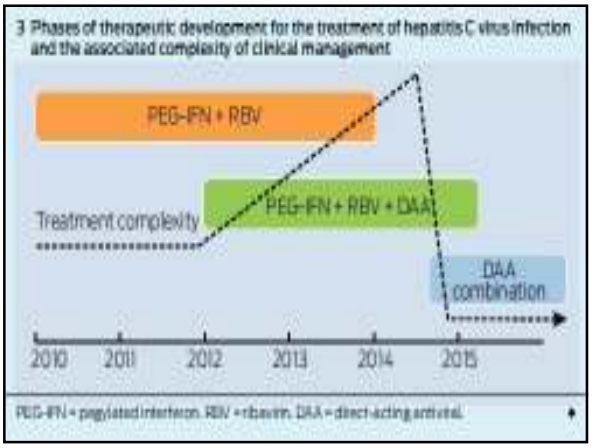
Nearly Everyone With HCV Can Now Be Treated Successfully

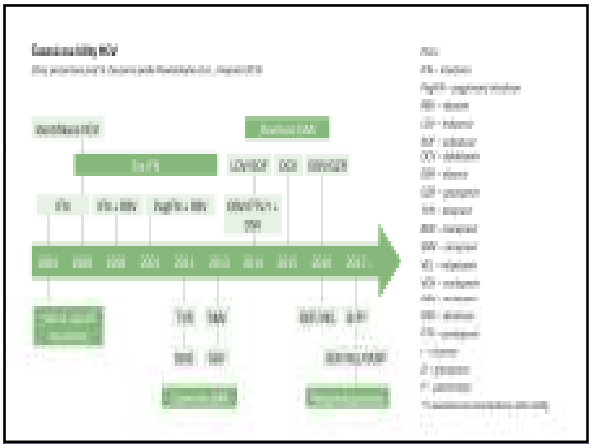
- Very high SVR rates; therapies highly tolerable
- All-oral therapy for almost every pt
- Treatment generally just 12 wks

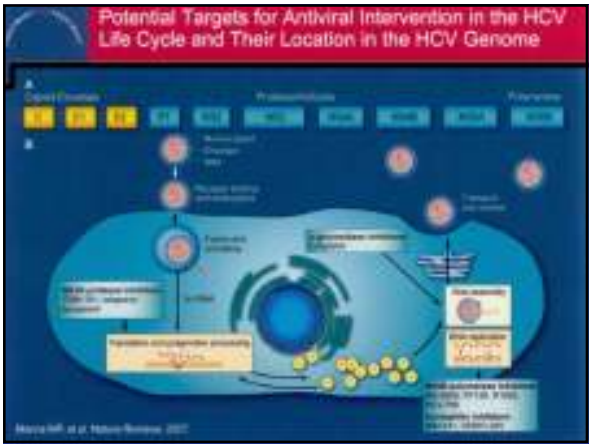


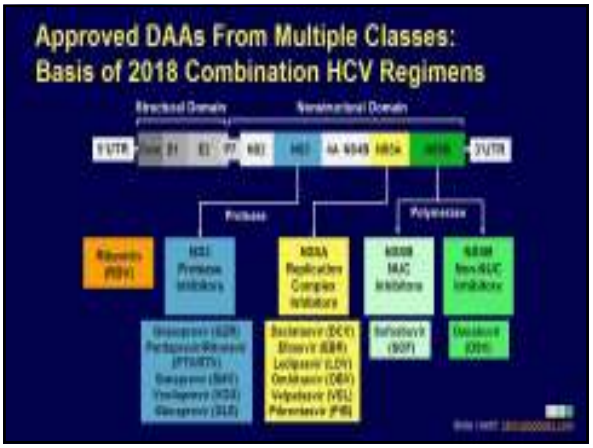
References in slidenotes.

Slide credit: clinicaloptions.com









EASL 2018 HCV Treatment Guidelines

- Recommendations for treatment-naive patients and patients previously treated with pegIFN/RBV ± SOF or SOF + RBV, ± compensated cirrhosis

HCV Genotype	SOF/VEL (Epclusa™)	GLE/PIB (Maviret™)	SOF/VEL/ VOX (Vosevi™)	LDV/SOF (Harvoni™)	EBR/GZR (Zepatier™)	OBV/PTV/ RTV + DSV (Viekirax™ + Exviera™)
1a	Yes	Yes	No*	Yes†	Yes‡	No
1b	Yes	Yes	No*	Yes	Yes	Yes
2	Yes	Yes	No*	No	No	No
3	Yes¶	Yes	Yes§	No	No	No
4	Yes	Yes	No*	Yes†	Yes#	No
5 or 6	Yes	Yes	No*	Yes†	No	No

*Triple combination effective but not needed because double combinations comparably effective. †Tx naive ± compensated cirrhosis. ‡Tx naive or tx experienced without cirrhosis or with compensated cirrhosis and HCV RNA ≤ 800,000 IU/mL. §Tx naive or tx experienced without cirrhosis. ¶Tx naive or tx experienced with compensated cirrhosis. #Treatment naive without cirrhosis or with compensated cirrhosis and HCV RNA ≤ 800,000 IU/mL.

EASL HCV Guidelines. 2018. In press.

Slide credit: clinicaloptions.com

Dostupné varianty IFN-free režimů pro jednotlivé genotypy HCV (*DP ČHS ČLS JEP 2017*)

kombinace	genotyp HCV				
	GT 1	GT 2	GT 3	GT 4	GT 5 a 6
	ano	ne	ne	ano	ano
	ano	ano	ano	ano	ano
	ano	ne	ne	ne	ne
	ne	ne	ne	ano	ne
	ano	ne	ne	ano	ne
	ano	ano	ano	ano	
	ano	ne	ne	ano	ne

sofosbuvir+ledipasvir = HARVONI™ (Gilead)
sofosbuvir+velpatasvir = EPCLUSA™ (Gilead)
ombitasvir+paritaprevir = VIEKIRAX™ (AbbVie)
dasabuvir = EXVIERA™ (AbbVie)
(r) = ritonavir
grazoprevir+elbasvir = ZEPATIER™ (MSD)
asunaprevir = SUNVEPRA™ (BMS)

sofosbuvir = SOVALDI™ (Gilead)
daclatasvir = DAKLINZA™ (BMS)
simeprevir = OLYSIO™ (Janssen)
sofosbuvir+velpatasvir+voxilaprevir = VOSEVI™ (Gilead)
glecaprevir+pibrentasvir = MAVYRET™ (AbbVie) - US
glecaprevir+pibrentasvir = MAVIRET™ (AbbVie)-EU, Japan

SVR12 a SVR24

Cílem terapie je vyléčení HCV infekce = dosažení trvalé eliminace viru. Eliminace viru brání rozvoji jaterních i mimojaterních komplikací HCV infekce, včetně pokročilé jaterní fibrózy, CIH, dekompenzované CIH a HCC.

Eliminací infekce je myšleno dosažení setrvalé virologické odpovědi (SVR, sustained viral response) = dosažení negativní HCV RNA v séru ve 12. nebo 24. týdnu po skončení protivirové léčby (SVR12 a SVR24).
SVR12 a SVR24 spolu korelují v 99 % případů.

Podle dlouhodobých studií znamená dosažení SVR v 99 % případů trvalé vyléčení HCV infekce, tj. u osob se SVR nedochází k pozdním relapsům onemocnění.

HBV Testing/Monitoring During HCV DAA Therapy

- Test all pts initiating HCV therapy for HBsAg, anti-HBc, and anti-HBs
  - Vaccinate if no HBV markers; follow flow chart below if HBV markers present

Pro případy selhání DAA léčby

Pangenotypální režimy:

Epclusa™ (Gilead)
= sofosbuvir + velpatasvir

Vosevi™ (Gilead)
= sofosbuvir + velpatasvir + voxilaprevir

Maviret™ (AbbVie)
= glecaprevir + pibrentasvir

University of Liverpool hepatitis drug interactions website (*HEP Drug Interaction Checker*)

http://www.hep-druginteractions.org/

Management of Pts With HCV Who Achieved SVR

- SVR associated with myriad clinical benefits
- Mandatory to continue HCC surveillance post SVR in pts with F3/F4 fibrosis; ultrasound every 6 mos
  - Consider assessing AFP levels as well for these pts
  - Less evidence to support continued screening of F0-F2 but remains a theoretical concern
- Indefinite screening for varices not warranted if varices absent at baseline: 1 more exam after SVR?
  - Surveillance of small varices if no other liver disease present requires further study but advisable
  - Large varices require ongoing management and surveillance
- Routine monitoring for fibrosis regression not the standard of care; further studies may change this
- For pts with ongoing risk for HCV infection after SVR, counsel and test HCV RNA annually

Slide credit: clinicaloptions.com

Main extrahepatic manifestations in pts with HCV infection

(Ther Adv Infect Dis 2016;3(1):3-14)

Immune-related extrahepatic manifestations

- Mixed cryoglobulinemia
- Cryoglobulinemic vasculitis
- B-cell non-Hodgkin's lymphoma
- Sicca syndrome (Sjögren´s syndrome)
- Arthralgia/myalgia
- Autoantibody production (i.e. cryoglobulins, rheumatoid factor, and antinuclear, anticardiolipin, antithyroid and anti-smooth muscle antibodies)
- Polyarteritis nodosa
- Monoclonal gammopathies
- Immune thrombocytopenia

Inflammatory-related extrahepatic manifestations

- Type 2 diabetes mellitus type 2
- Insulin resistance
- Glomerulonephritis (membranoproliferative)
- Renal insufficiency
- Fatigue
- Cognitive impairment
- Depression
- Impaired quality of life
- Polyarthritis/fibromyalgia
- Cardiovascular disorders (i.e. stroke, ischemic heart disease)