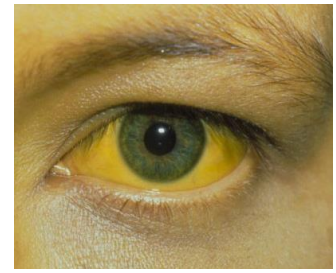
HIV

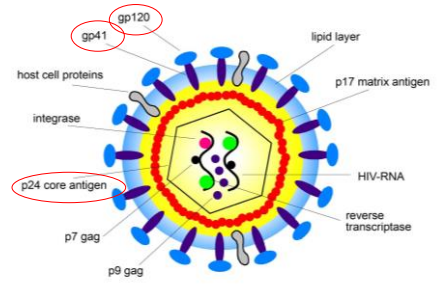
and

hepatitis viruses

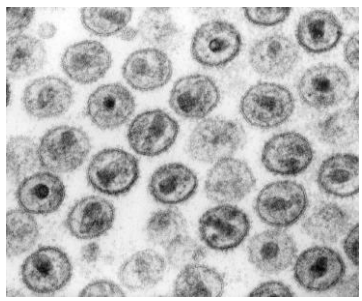


HIV – Human Immunodeficiency virus

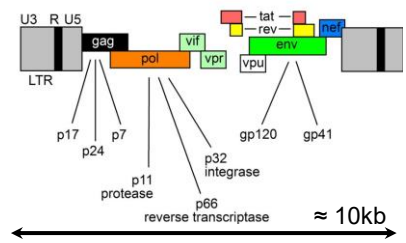
- Retrovirus
- coated ss RNA virus
- diameter 100 - 120 nm
- Not stabile
  in the environment
- Huge genome variability
  - instability



http://hivbook.files.wordpress.com/2011/11/figure-11.jpg?w=482&h=312

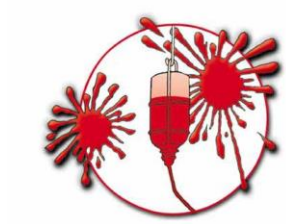


http://upload.wikimedia.org/wikipedia/commons/4/4c/HIV-1_Transmission_electron_micrograph_AIDS02bbb_lores.jpg

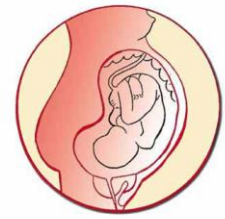


http://hivbook.files.wordpress.com/2011/11/figure-2.jpg?w=435&h=262

Transmission of HIV



Blood and blood derivates



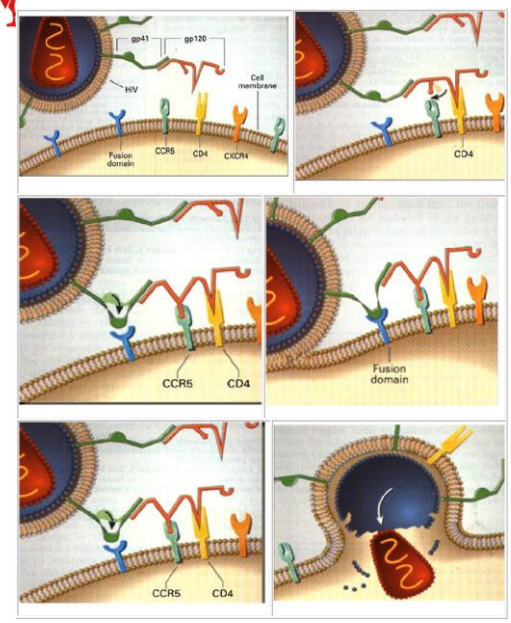
During pregnancy
from mother to child

Sexual intercourse
MSW, MSM, WSW

Blood – injuries, i.v. drug users

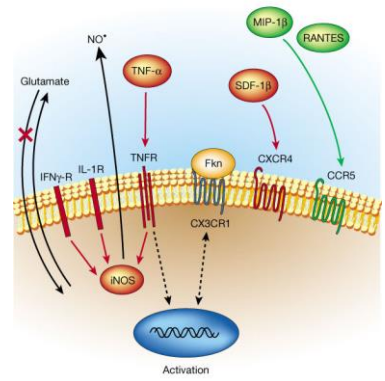
http://health.uml.edu/thc/HealthIssues/HIV%20NP/HIV_PresentationChinaLiuzhou8_061906.jpg

HIV – cell receptor



http://cdn.intechopen.com/pdfs/39816/InTech-Coreceptor_usage_in_hiv_infection.pdf

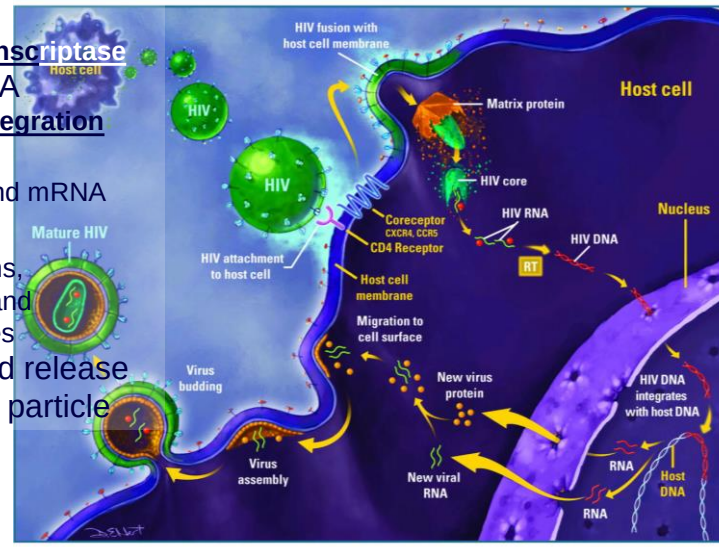
Natural resistance to HIV-1 throught delta 32 mutation in CCR5 (deletion of a part of gene). Homozygotes are resistant to M-tropic strains of HIV-1 infection



http://www.nature.com/nature/journal/v410/n6831/images/410988ac.2.jpg

HIV replication

- viral RNA
  - **reverse transcriptase**
- proviral DNA
  - **genome integration**
- replication
  - viral RNA and mRNA
- translation
  - viral proteins, proteases and glycosidases
- Budding and release of new viral particle



http://home-hiv-tests.com/images/hiv_lifecycle.jpg

HIV replication

- viral RNA
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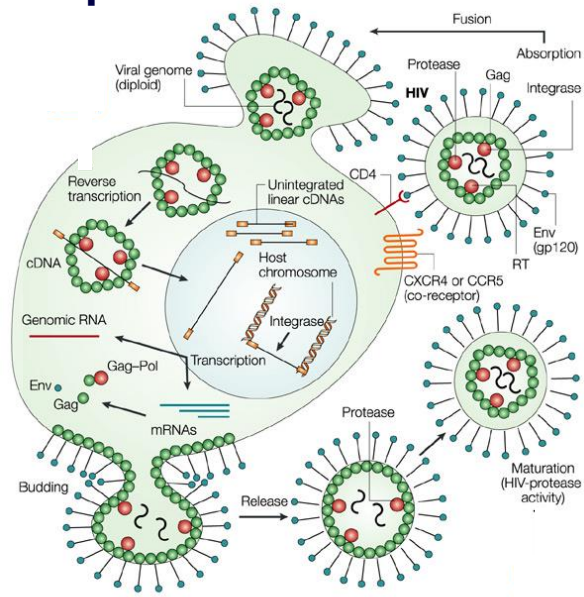


http://www.nature.com/nrc/journal/v4/n11/box/nrc1479_BX1.html

Nature Reviews | Cancer

HIV – infected cells

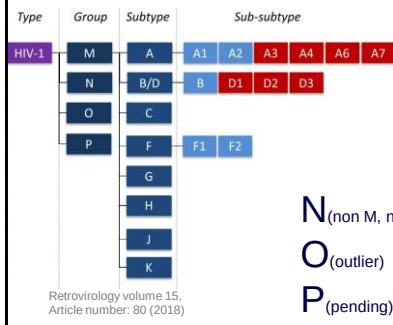
- **helper T cells** (specifically CD4+)
- **macrophages**
- **dendritic cells**
- **1st proliferation in lymphatic tissue – viraemia**
- **Latency**
- **Impact on cells**
  - ↓ counts of CD4+ T cells by:
    - apoptosis of uninfected bystander cells
    - direct viral killing of infected cells
    - killing of infected CD4+ T cells by CD8+ cytotoxic lymphocytes that recognize infected cells

http://www.topnews.in/health/files/hiv2.jpg

Observation of opportunistic infections

Types of HIV

- **HIV -1** M(major) A — West and Central Africa
  - B — Europe, North America, Thailand
  - C — South Africa (especially Kongo), India
  - D — Central Africa
  - E — Central Africa, Thailand, India
  - F — Zaire, Brazil, Romania
  - G — Gabun, Zaire
  - H — Cameroon, Gabun
  - I — complex recombination CRF04_cpx
  - J — North, Central and West Africa, Caribbean
  - K — Democratic Republic of Congo, Cameroon



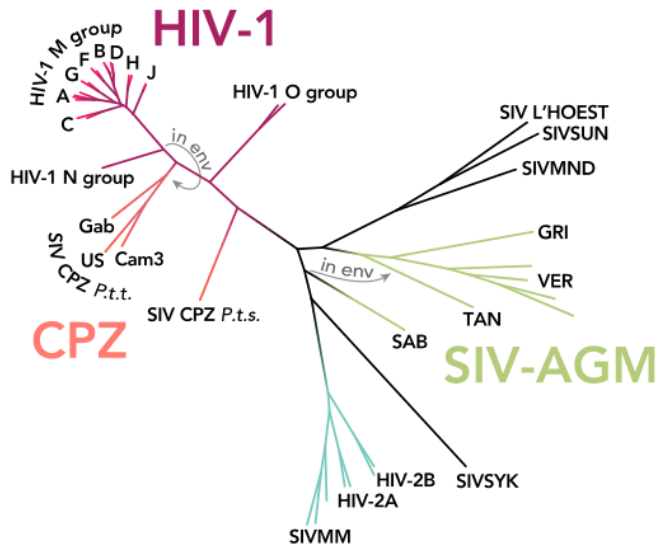
Retrovirology volume 15, Article number: 80 (2018)

- N(non M, non O) — Cameroon
- O(outlier) — Central Africa
- P(pending) — Cameroonian woman from France (similar to SIV (gorillas and chimpanzees)

- **HIV 2** groups A-H — Central Africa

Not only human – FIV, SIV, …

Types of HIV

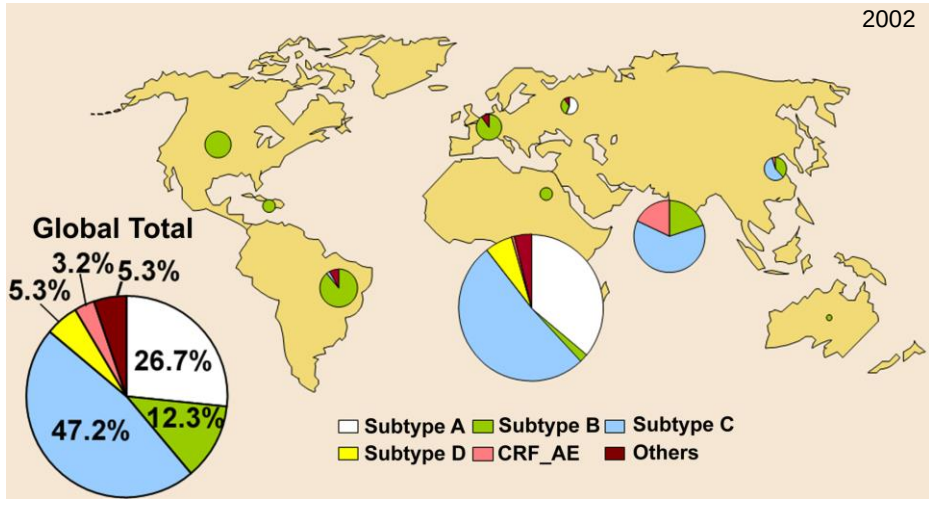


Not only human – FIV, SIV, …

0.10

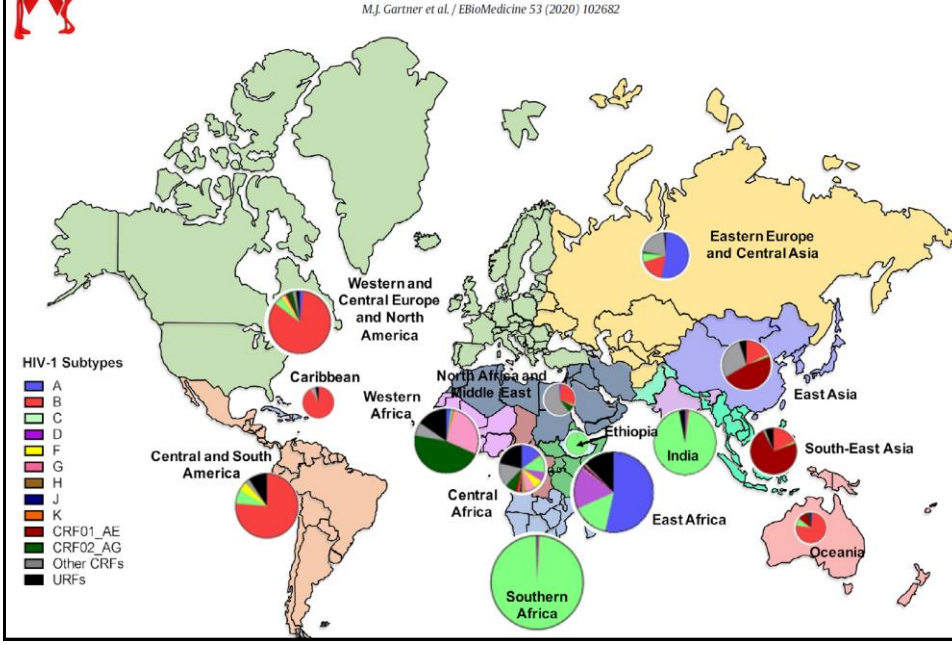
https://upload.wikimedia.org/wikipedia/commons/thumb/f/fb/HIV-SIV-phylogenetic-tree_straight.svg/180px-HIV-SIV-phylogenetic-tree_straight.svg.png

Types of HIV



http://en.wikipedia.org/wiki/File:HIV-1_subtype_prevalence_in_2002.png

Types of HIV - type C is dominating



HIV pathogenesis

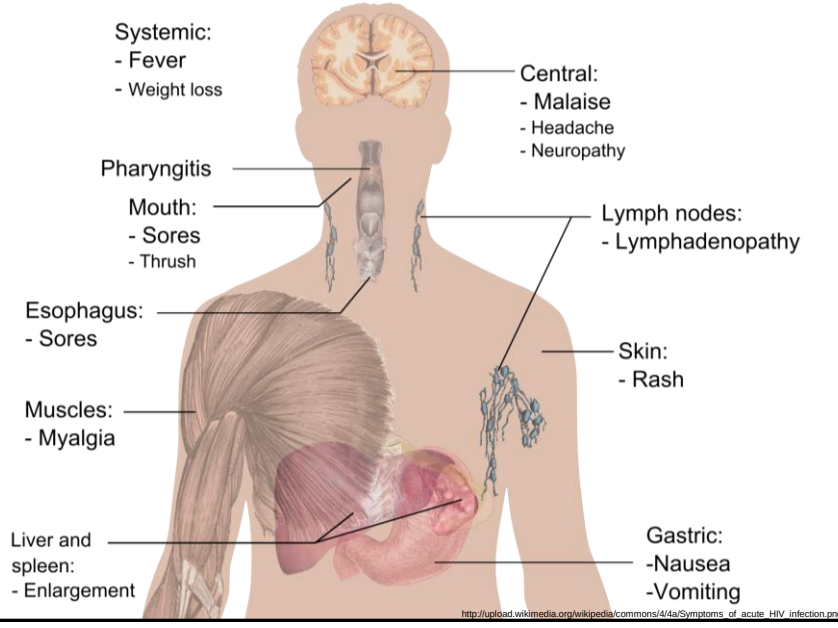
- **Clinical stages**

  Depends on infectious dose and genetic background of the patient

  - **A** - asymptomatic **(CD4+ > 500/µl)**
    (acute infection, benign lymfadenopathy)
  - **B** – light oportunistic infections **(CD4+ 200-500/µl)**
    (oropharyngeal or vulvovaginal candidiasis, diarrhea, „hairy“leucoplaky, peripheral neuropathy)
  - **C** - severe oportunistic infections **(CD4+ < 200/µl)**
    (CMV retinitis,pneumocystis pneumonia, toxoplasmosis or HIV encefalitis, tuberculosis, Kaposhi sarkoma, lymfoma, cryptococcus infection..)

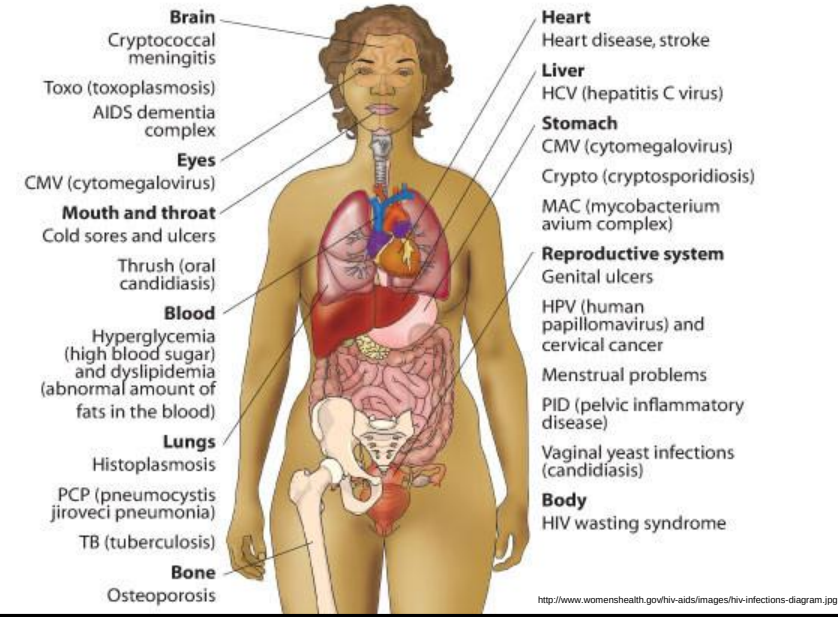
AIDS – Acquired Immunodeficiency Syndrome

Symptoms of acute HIV infection



http://upload.wikimedia.org/wikipedia/commons/4/4a/Symptoms_of_acute_HIV_infection.png

Symptoms of opportunistic infections



http://www.womenshealth.gov/hiv-aids/images/hiv-infections-diagram.jpg

Laboratory diagnostics
general

- Antigen detection **– antigen p24/25**
  - In acute phase
  - During active viral prolipheration
- Antibody detection
  - Basic screening technique **– anti p24/25**
- RNA (quantitative) detection
  - Quantification of viral load
- Detection of proviral integrated DNA

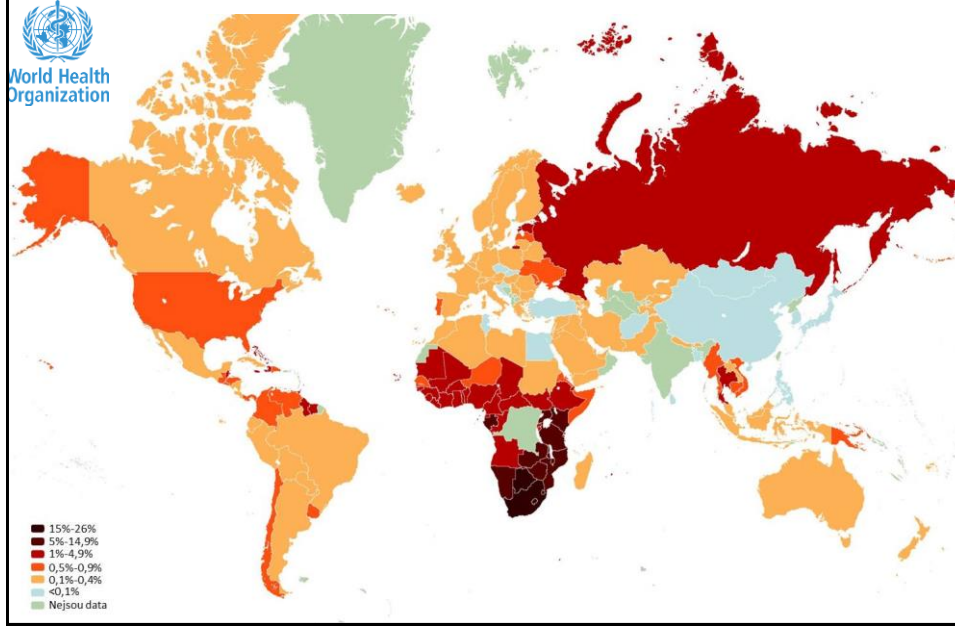
Laboratory diagnostics
detail

- Antibody detection
  - Mainly ELISA tests
  - Screening – necessity of confirmation
  - Positive at about 20 days post infection
- Antibody + antigen detection
  - Screening – necessity of confirmation
  - Positive at about 16-18 days post infection
- All test have to be confirmed

HIV epidemiology

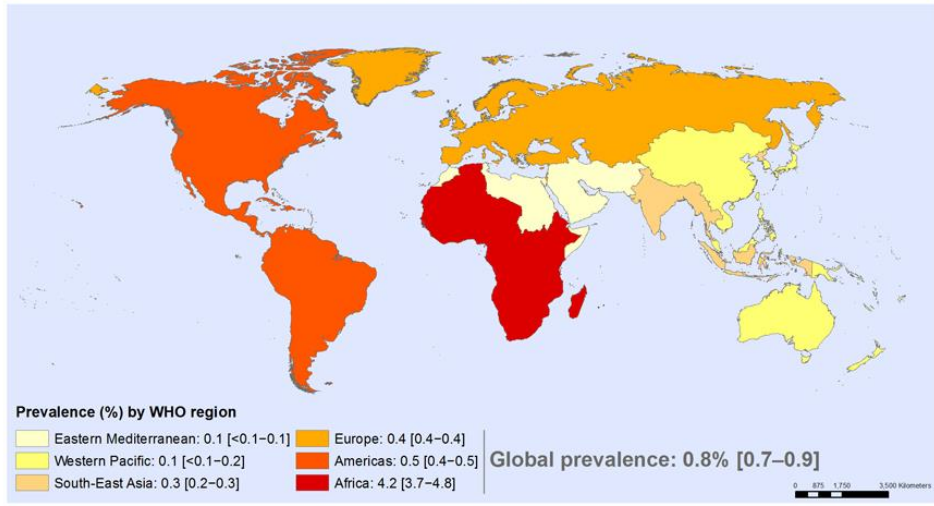
- 1st „wave“
  - Blood transmission, MSM
  - 70-80 % of infected were men
  - North America and Europe
- 2nd „wave“
  - Infection mainly by MSW
  - Ratio of infected men and women 1:1
  - Africa, Asia and spread to other countries

HIV prevalence (2014)



HIV prevalence

Prevalence of HIV among adults aged 15 to 49, 2016
By WHO region



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Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization

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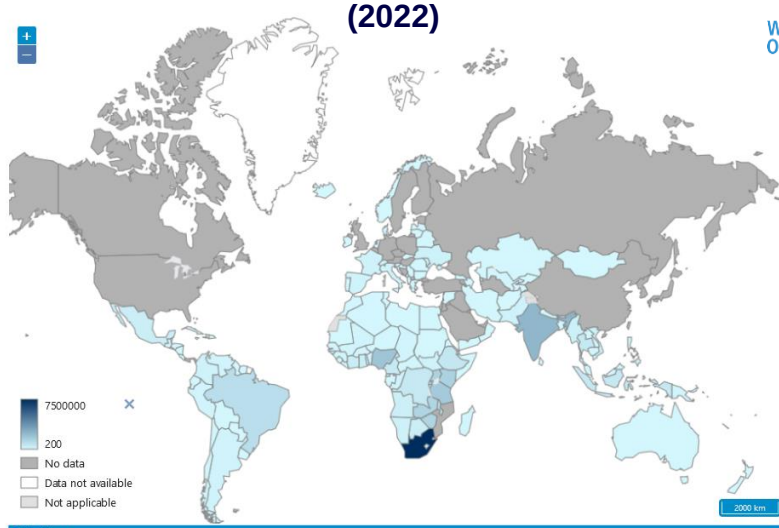
People living with HIV by WHO region (2022)

World Health Organization



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World Health Organization

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Summary of global HIV epidemic

Global HIV epidemic – people living with HIV

2019
Globally
38.0 million
People living with HIV

+24%
Relative to 2010

Source: UNAIDS/WHO estimates

World Health Organization

Summary of global HIV epidemic

2019
Globally
38.0 million
People living with HIV

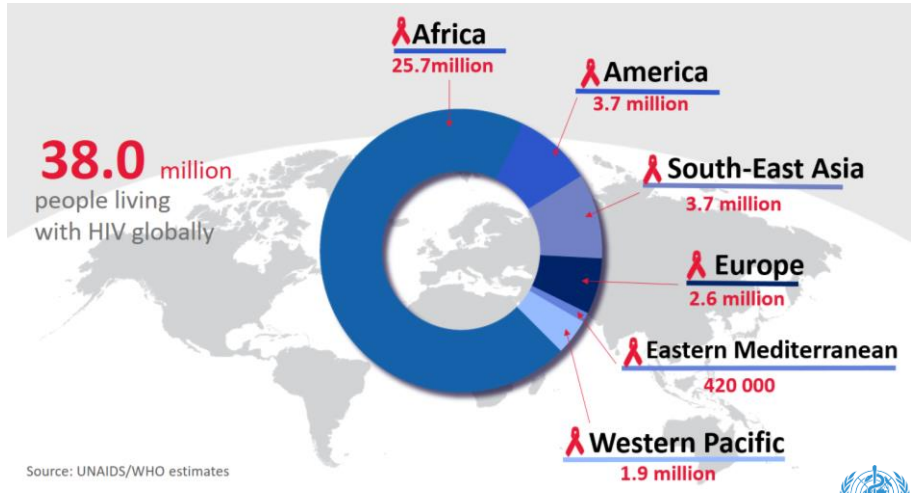
- 23%
New infections annually relative to 2010

- 39%
Deaths annually relative to 2010

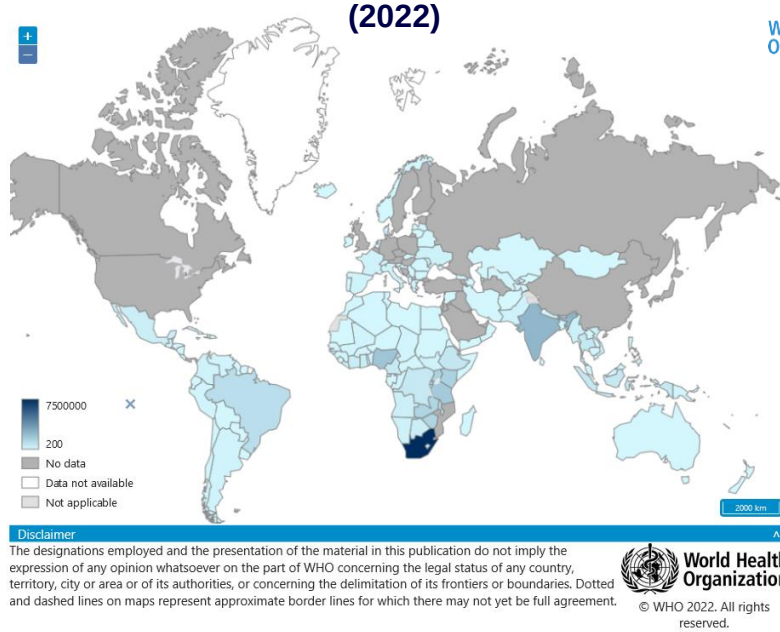
Source: UNAIDS/WHO estimates

World Health Organization

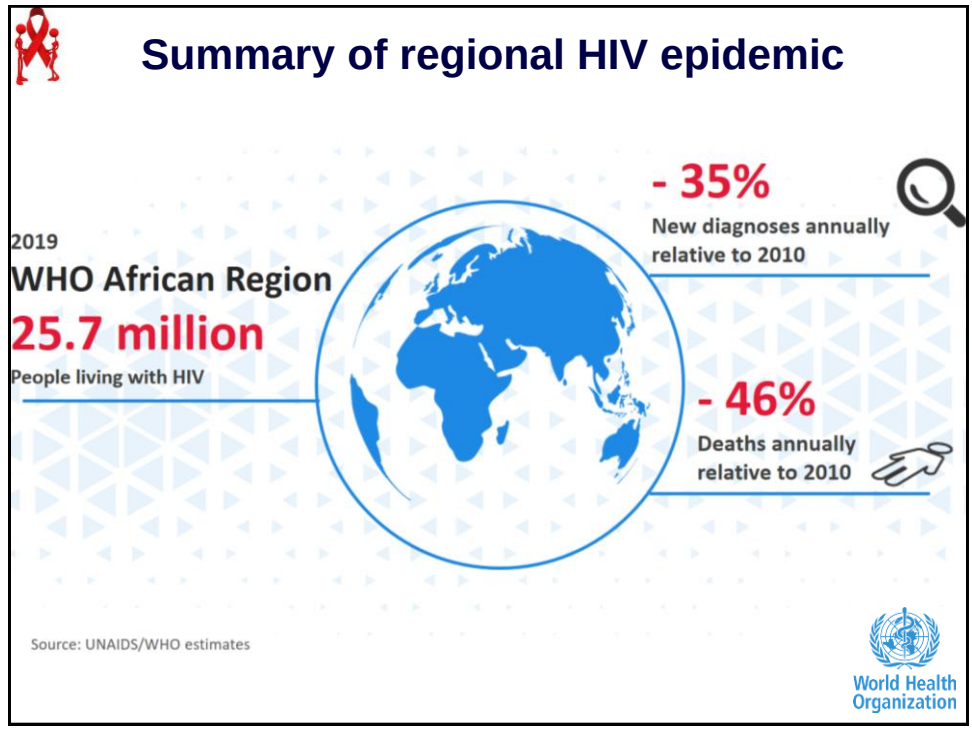
People living with HIV by WHO region
(2019)

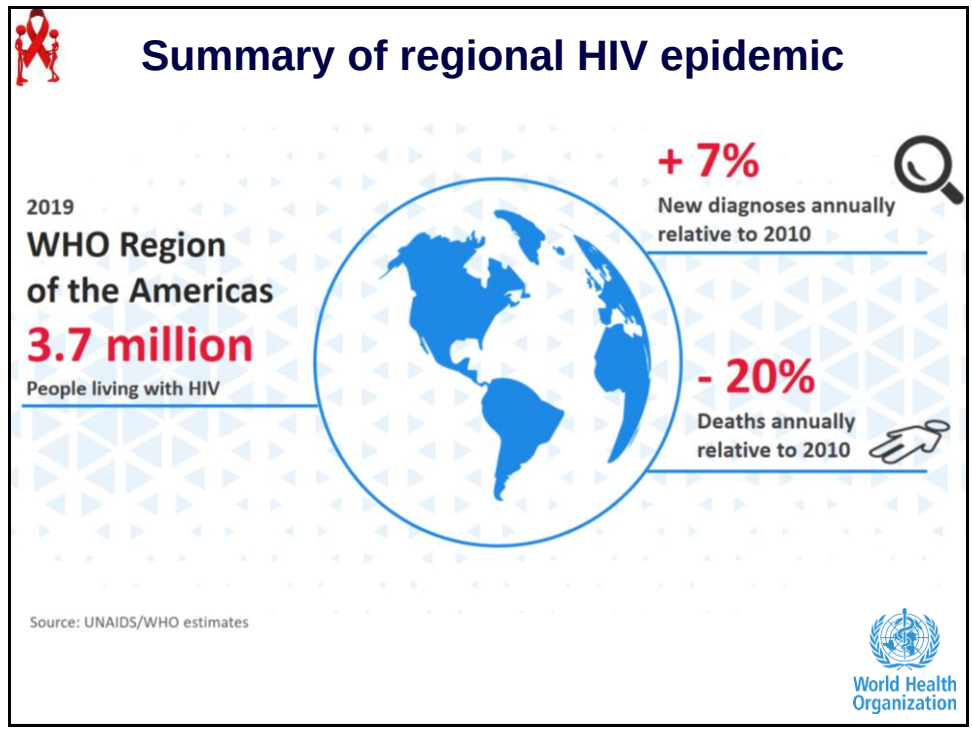


People living with HIV by WHO region
(2022)



World Health
Organization


Summary of regional HIV epidemic
2019
WHO African Region
25.7 million
People living with HIV
- 35%
New diagnoses annually relative to 2010
- 46%
Deaths annually relative to 2010
Source: UNAIDS/WHO estimates
World Health Organization


Summary of regional HIV epidemic
2019
WHO Region of the Americas
3.7 million
People living with HIV
+ 7%
New diagnoses annually relative to 2010
- 20%
Deaths annually relative to 2010
Source: UNAIDS/WHO estimates
World Health Organization

Summary of regional HIV epidemic

2019
WHO South-East Asian Region
3.7 million
People living with HIV

-26%
New diagnoses annually relative to 2010

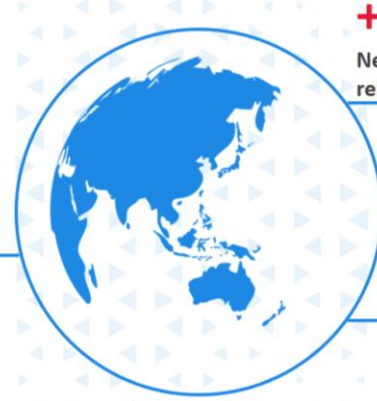
-30%
Deaths annually relative to 2010

Source: UNAIDS/WHO estimates

World Health Organization

Summary of regional HIV epidemic

2019
WHO Western Pacific Region
1.9 million
People living with HIV



+3%
New diagnoses annually relative to 2010

-36%
Deaths annually relative to 2010

Source: UNAIDS/WHO estimates

World Health Organization

Summary of regional HIV epidemic

2019
WHO European Region
2.6 million
People living with HIV

+49%
New diagnoses annually relative to 2010

+14%
Deaths annually relative to 2010

Source: UNAIDS/WHO estimates

World Health Organization

Summary of regional HIV epidemic

2019
WHO Eastern Mediterranean Region
420 000
People living with HIV

+47%
New diagnoses annually relative to 2010

+57%
Deaths annually relative to 2010

Source: UNAIDS/WHO estimates

World Health Organization

Summary of global HIV epidemic (2019)

World Health Organization

	People living with HIV in 2019	People newly infected with HIV in 2019	HIV-related deaths in 2019
Total	38.0 million [31.6 million – 44.5 million]	1.7 million [1.2 million – 2.2 million]	690 000 [500 000 – 970 000 million]
Adults	36.2 million [30.2 million – 42.5 million]	1.5 million [1.1 million – 2.0 million]	600 000 [430 000 – 840 000]
Women	19.2 million [16.4 million – 22.2 million]	790 000 590 000 – 1.1 million]	300 000 [220 000 – 420 000]
Men	17.0 million [13.8 million – 20.4 million]	870 000 630 000 – 1.2 million]	390 000 [280 000 – 560 000]
Children (<15 years)	1.8 million [1.3 million – 2.2 million]	150 000 [94 000 – 240 000]	95 000 [61 000 – 150 000]

Source: UNAIDS/WHO estimates

World Health Organization

Source: UNAIDS/WHO estimates.

Summary of global HIV epidemic (2021)

	People living with HIV in 2021	People acquiring HIV in 2021	People dying from HIV-related causes in 2021
Total	38.4 million [33.9–43.8 million]	1.5 million [1.1–2.0 million]	650 000 [510 000–860 000]
Adults (15+ years)	36.7 million [32.3–41.9 million]	1.3 million [990 000–1.8 million]	560 000 [430 000–740 000]
Women (15+ years)	19.7 million [17.6–22.4 million]	640 000 [480 000–870 000]	240 000 [180 000–320 000]
Men (15+ years)	16.9 million [14.6–19.7 million]	680 000 [500 000–920 000]	320 000 [250 000–430 000]
Children (<15 years)	1.7 million [1.3–2.1 million]	160 000 [110 000–230 000]	98 000 [67 000–140 000]

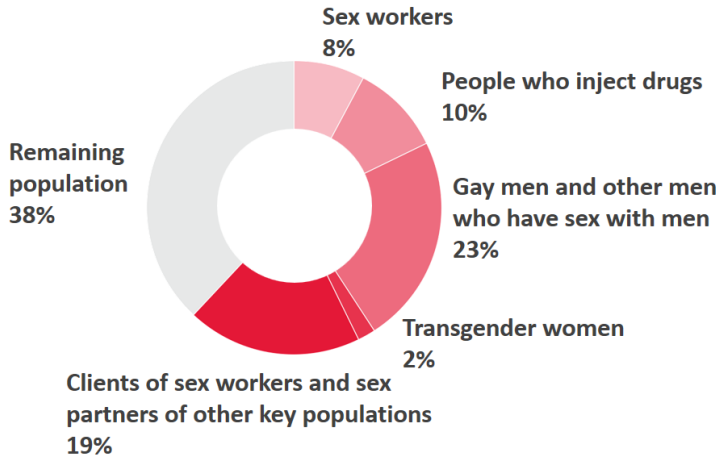
Source: UNAIDS/WHO estimates

Updated: July 2022

World Health Organization

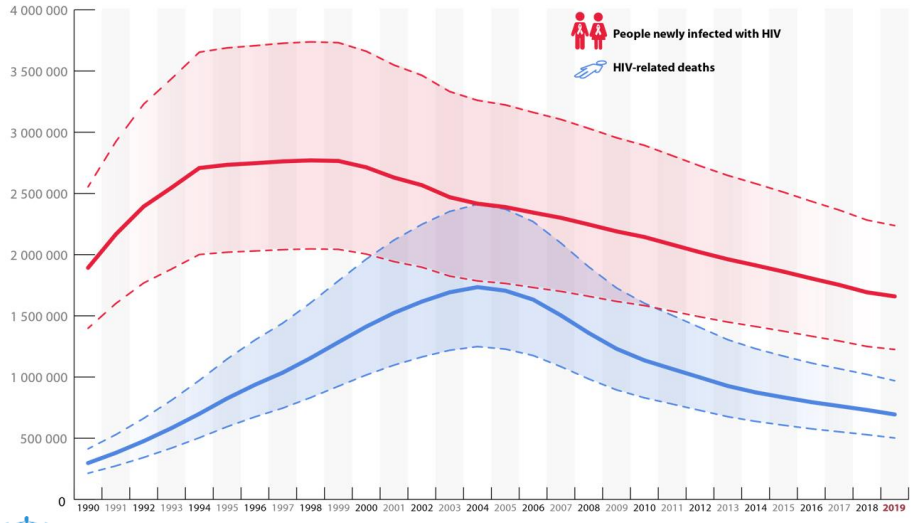
Distribution of new HIV infections by key population, global (2019)

World Health Organization



Source: UNAIDS special analysis, 2020

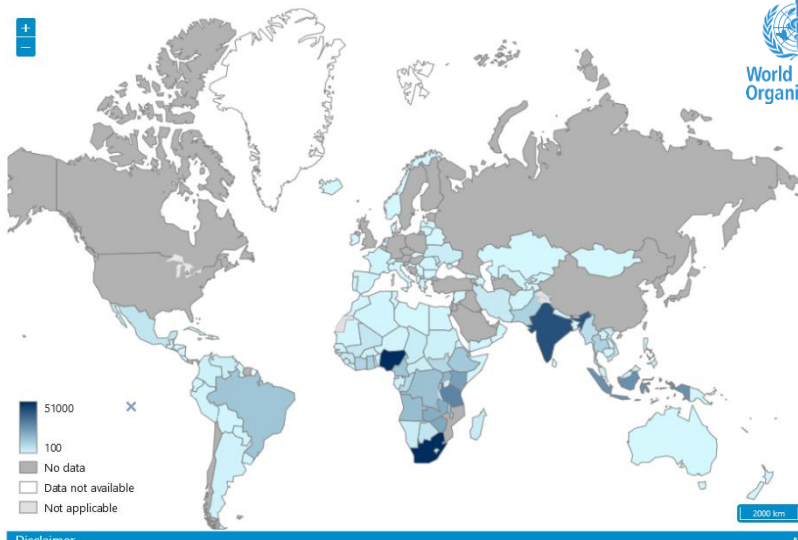
Decline in HIV incidence and mortality over time



World Health Organization

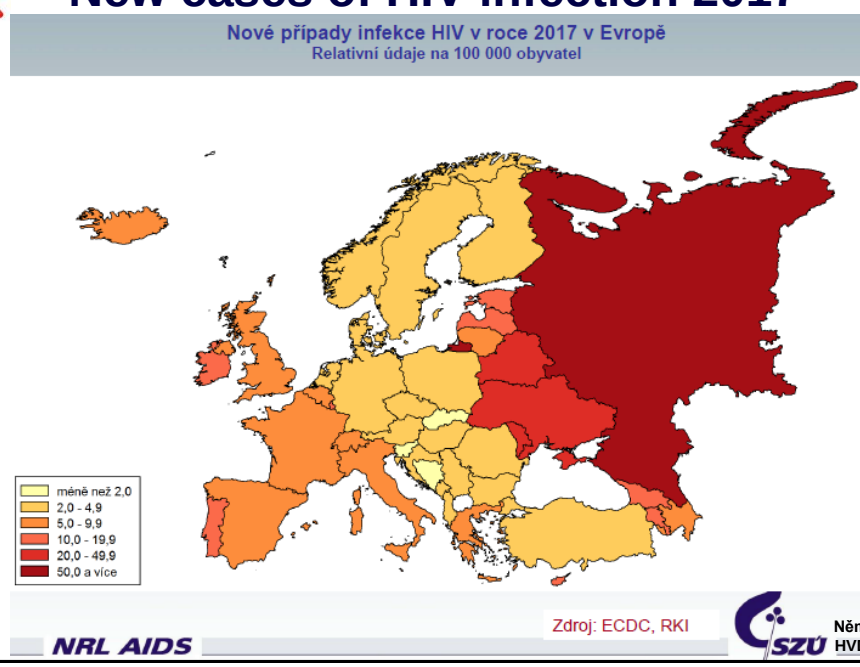
Source: UNAIDS/WHO estimates.

Number of people dying from HIV-related causes



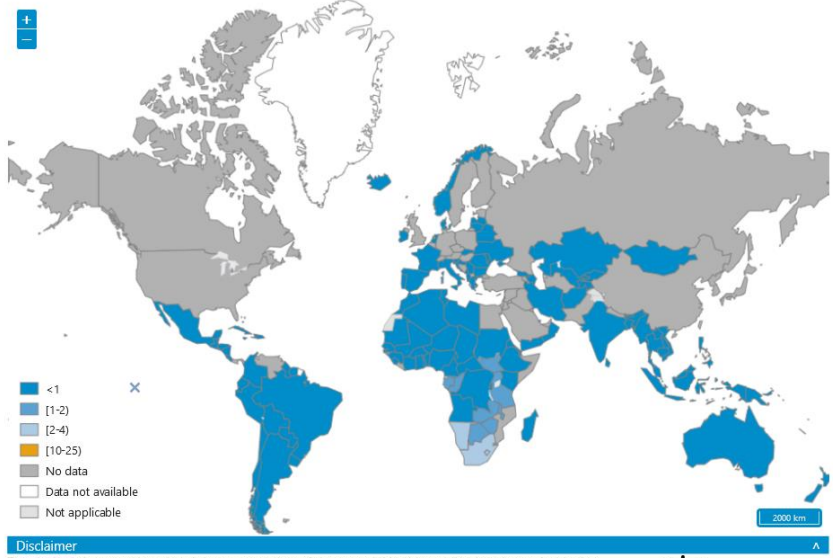
Source: UNAIDS/WHO estimates.

New cases of HIV infection 2017



Němeček
HVD2019

New cases of HIV infection



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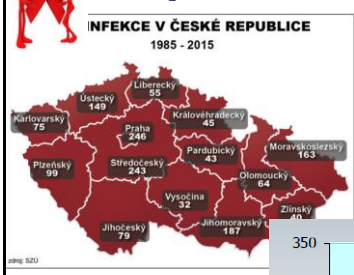
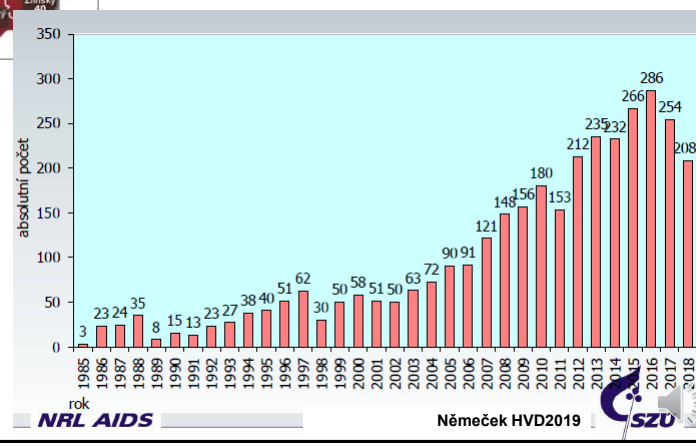
Epidemiological HIV data CR



Cumulative data f new HIV+ cases up to 31.8.2019



NRL AIDS

Němeček HVD2019

SZÚ

Epidemiological HIV data CR
HIV/AIDS 1985-31.8.2019

Total No. of HIV+	**3536**	
	M F	3056 (86.4%) 480 (13.6%)
AIDS (658)	M F	538 (81.8%) 120 (18.2%)
Deceased with AIDS (308)	M F	251 (81.5%) 57 (18.5%)
Deceased from another reason (147)	M F	130 (88.4%) 17 (11.6%)

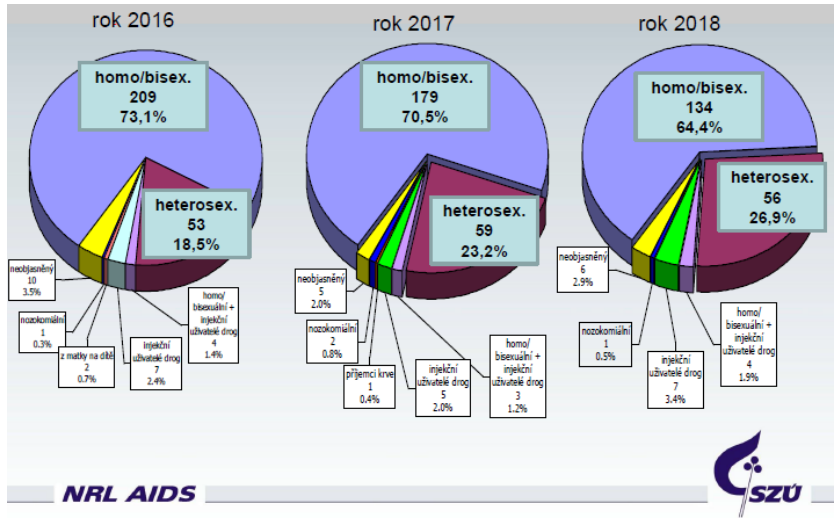
NRL AIDS

SZÚ

Němeček
HVD2019

Epidemiological HIV data CR

New cases according to the transmission 2016-2019



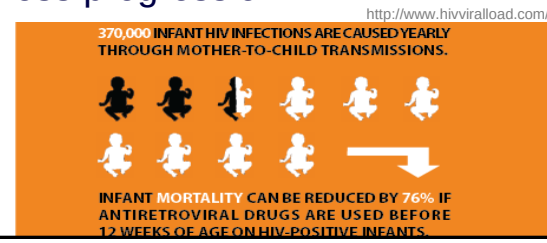
NRL AIDS

SZÚ

Němeček HVD2019

HIV prevention

- Prevention of exposition
  - Health education for people
  - Control of blood and blood derivates
  - Babies of the HIV+ mothers
- Stop of spreading of the infection in the body
  - Vaccines (so far in development)
  - Limitation of Mother to child transmission
- Decrease of the illness progression
  - Virostatic treatment



Possible HIV vaccines

- Typ of vaccine
  - Surface antigen (subunit)
  - Control of blood and blood derivates
- Attenuated virus
- Poxvirus expressing the HIV antigens

- Possible problems
  - Virus variability
  - Long time for development of immunity
  - Risky for children

HIV treatment

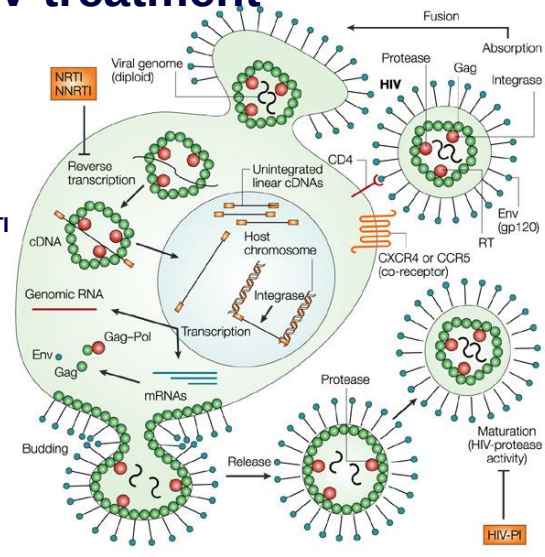
- Receptor neutralisation — Solution of anti-CD4; Neutralizing antibody; CD4+ imunoadhesins
- Reverse transcriptase inhibitors (RTIs) — AZT(Retrovir), ddI(Videx) 3TC(Epivir)…
- Inhibitors of integrase
- Inhibitors of transcription — Ribavirine
- Protease inhibitors (PI) — Saqinavir, Ritonavir...
- Antiglycosidase

HAART – Highly Active AntiRetroviral Therapy

usual HAART regimen combines 3 or more different drugs such as 2 nucleoside RTIs and PI, 2 nucleoside RTIs and a non-nucleoside reverse transcriptase inhibitor (NNRTI) or other such combinations

HIV treatment

- Receptor neutralisation
- Reverse transcriptase inhibitors (RTIs) – **NRTI a NNRTI**
- Inhibitors of integrase
- Inhibitors of transcription
- Protease inhibitors (PI)
- Antiglycosidase

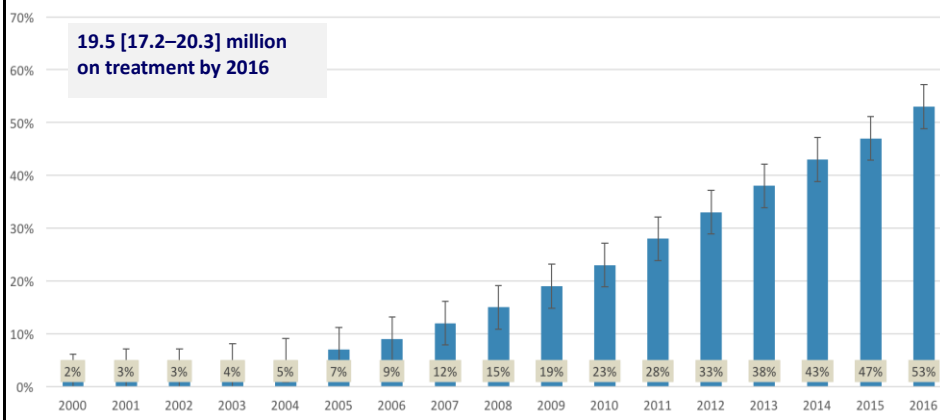


HAART

usual HAART regimen combines 3 or more different drugs such as 2 nucleoside RTIs and PI, 2 nucleoside RTIs and a non-nucleoside reverse transcriptase inhibitor (NNRTI) or other such combinations

ART coverage over time

World Health Organization



Source: UNAIDS/WHO estimates.

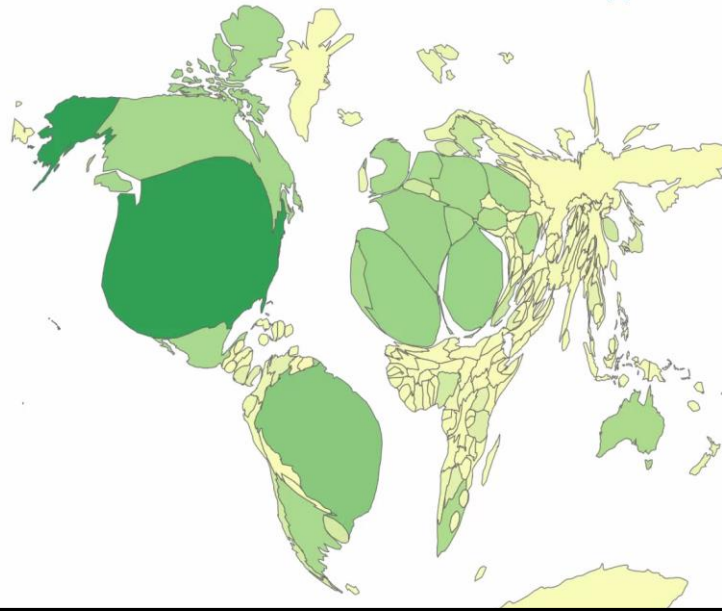
19.5 millions (17 in 2015) of people had access to antiretroviral therapy

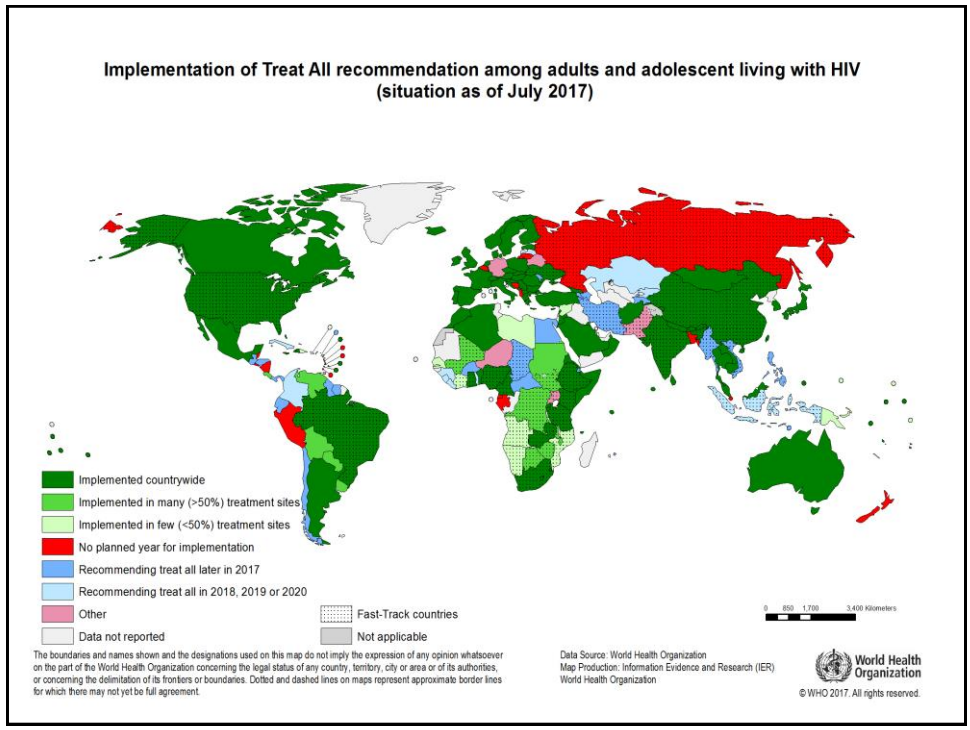
HAART

- 2 nucleoside RTIs and PI
- 2 nucleoside RTIs and a NNRTI
- …

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

World Health Organization




Implementation of Treat All recommendation among adults and adolescent living with HIV
(situation as of July 2017)
Implemented countrywide
Implemented in many (>50%) treatment sites
Implemented in few (<50%) treatment sites
No planned year for implementation
Recommending treat all later in 2017
Recommending treat all in 2018, 2019 or 2020
Other
Data not reported
Fast-Track countries
Not applicable
0 850 1,700 3,400 Kilometers
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization
World Health Organization
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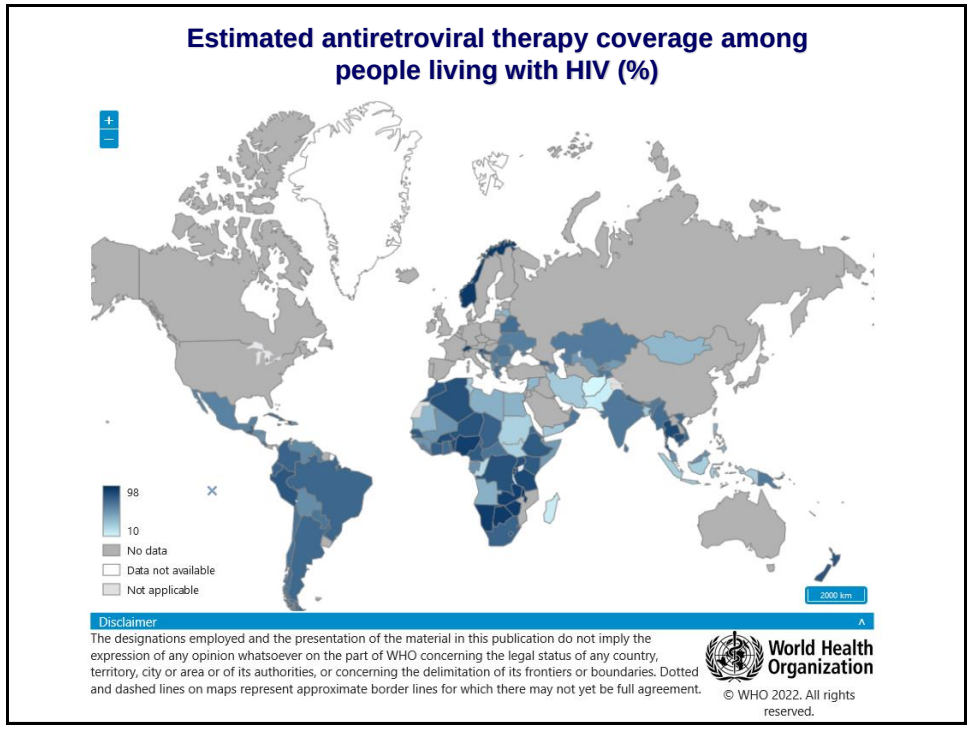
Estimated antiretroviral therapy coverage among people living with HIV (%)
98
10
No data
Data not available
Not applicable
2000 km
Disclaimer
The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
World Health Organization
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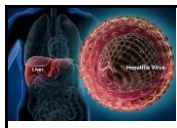
Factors influencing the survival

- ↓ of viral load – primoinfection therapy
- Treatment of the opportunistic infections
- Careful use of common vaccines
- Treatment during decrease of CD4 lymfocyte count

After HAART
IRIS –
Immune Reconstitution Inflammatory Syndrome can be observed.

Viral hepatitis

- A RNA virus Picornaviridae /Heparnavirus
- B DNA virus Hepadnaviridae/Hepadnavirus
- C RNA virus Flaviviridae/Flavivirus
- D RNA virus HBV dependent/Deltavirus
- E RNA virus Hepeviridae
- G RNA virus Flaviviridae
- TTV DNA virus Anelloviridae

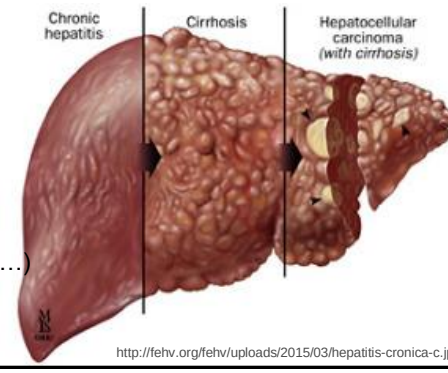


Hepatitis

Hepatitis is a disease of the liver characterized by the presence of inflammatory cells in the tissue of the organ. Hepatitis may occur without symptoms, but can lead to jaundice (a yellow discoloration of the skin, mucous membranes, and conjunctiva of the eyes), poor appetite, and fatigue. (Wikipedia)

- acute – chronic
- cirhosis – fibrosis
- potencially lethal

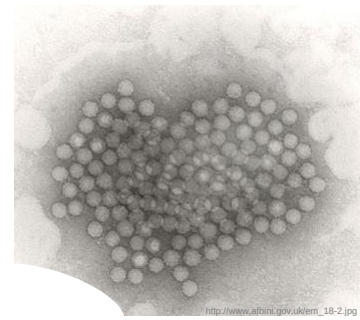
- treatment
  - hepatoprotective drugs
  - liver-protective food (no/low fat…)



http://fehv.org/fehv/uploads/2015/03/hepatitis-cronica-c.jpg

Hepatitis A Virus (HAV)

- small RNA virus (27-30 nm)
- non-enveloped - Picornavirus
- genetically homogenous
- resistant to environment
- transmission fecal-oral route through GIT
- release in stool
- human restricted pathogen

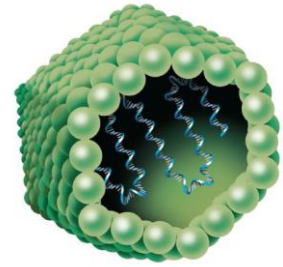


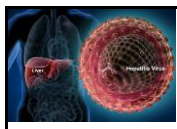
http://www.afbini.gov.uk/em_18-2.jpg

http://www.healthsym.com/wp-content/uploads/2013/01/JAUNDICE.jpg

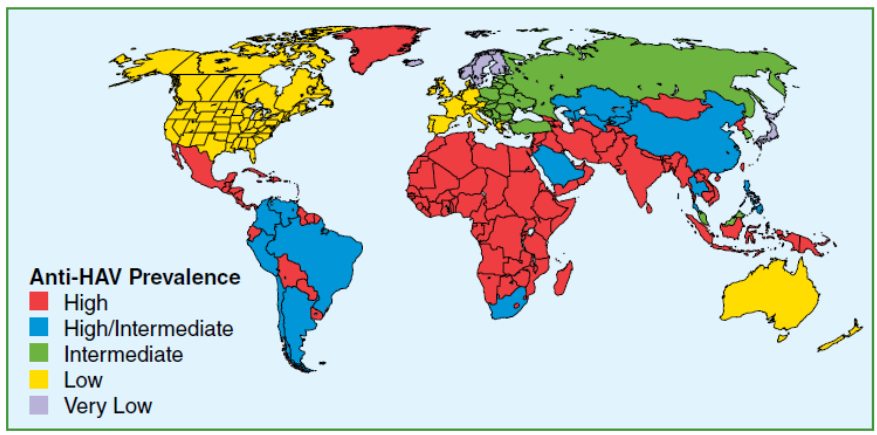
Hepatitis A Virus (HAV) Pathogenesis

- Incubation period 15-45 days
- Primary proliferation in enterocytes
- Short viremia
- Subsequently infects hepatocytes and release to the stool through bile
- No ability to chronic infection





Hepatitis A Virus (HAV) Geographic distribution

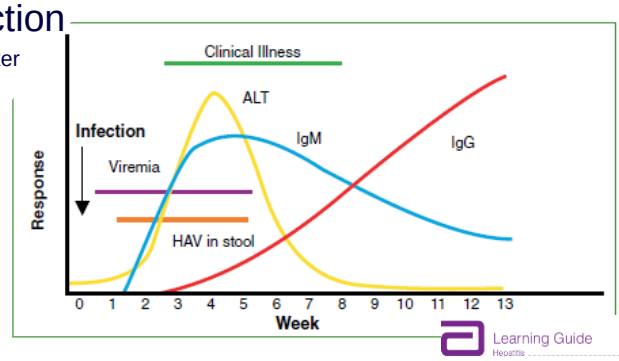


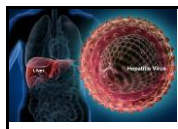
*Note: This map has been generalized from available data.

Learning Guide
Hepatitis

Hepatitis A Virus (HAV) Diagnostics

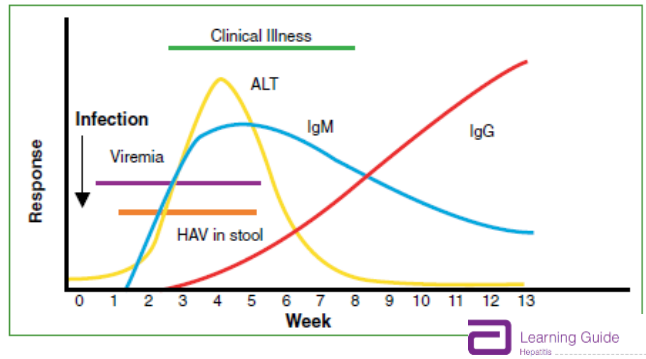
- Electronmicropy in stool
  - In the 2nd part of incubation period, shortly after start of the clinical symptoms
- Antigen and RNA detection
  - In stool, similar to EM
- Antibody detection
  - Main diagnostic marker

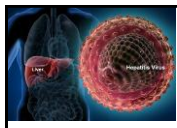




Hepatitis A Virus (HAV) Diagnostics - antibody

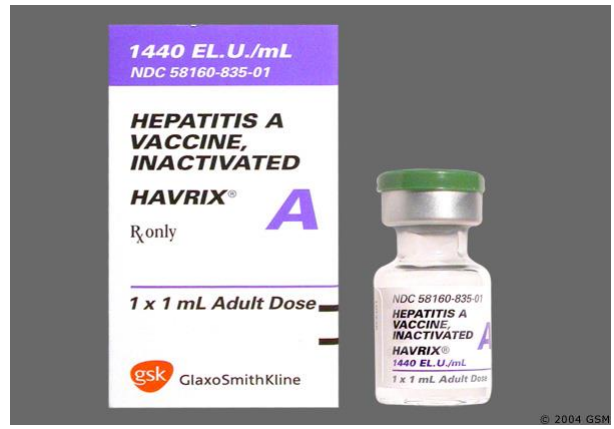
- Total Immunoglobuline (Ig)
  - Acute infection
  - Post infection immunity
  - Post vaccination immunity
- Specific IgM
  - Acute infection
  - Convalescence (even > 1 yr)

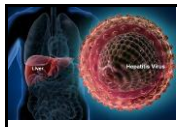




Hepatitis A Virus (HAV) Therapy and prevention

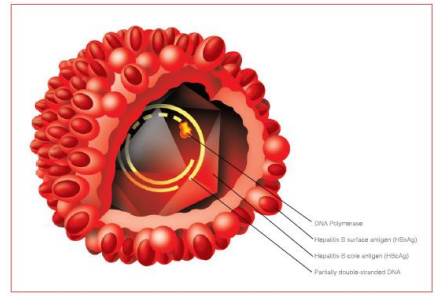
- No specific treatment
- Prophylaxis with human immunoglobuline
- Vaccination
  - (Havrix..)

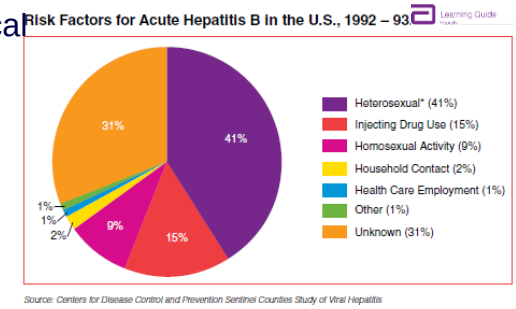




Hepatitis B Virus (HBV)

- DNA virus with complicated life cycle
- enveloped
- genus – Hepadnavirus
- Antigen structures important for diagnostics
- HBV subtypes without clinical importance
- Sensitive to environmental conditions
- Blood and sexually transmitted
- human restricted pathogen

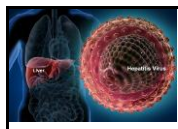




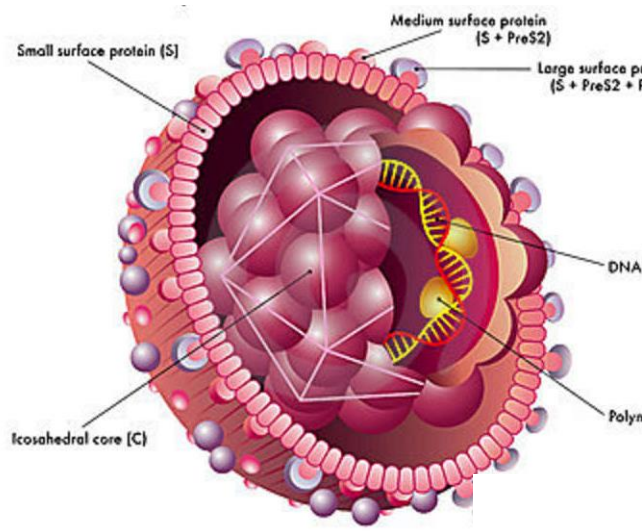
Hepatitis B Virus (HBV) Genome structure

- circular DNA, not fully double-stranded
- one end of the full length strand linked to the viral DNA polymerase
- genome 3020–3320 nucleotides long (full-length strand) and 1700–2800 nucleotides long (short length-strand)

http://upload.wikimedia.org/wikipedia/commons/thumb/0/00/HBV_Genome.svg/425px-HBV_Genome.svg.png



Hepatitis B Virus (HBV) Viral structure

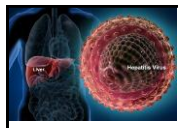


HBsAg – surface antigen

HBeAg – enhanced infectivity

HBcAg – core antigen

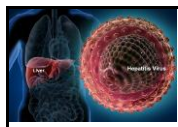
http://thumbs.dreamstime.com/z/hepatitis-b-virus-22144156.jpg



Hepatitis B Virus (HBV) Clinical symptoms

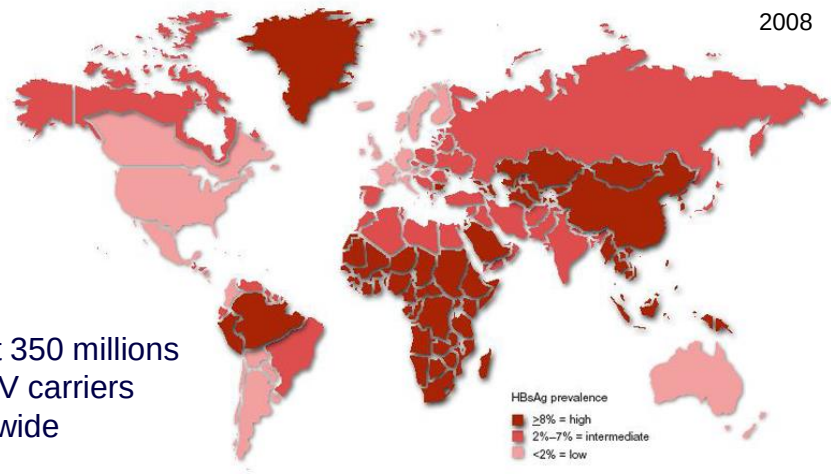
- acute illness
- history of blood administration
- incubation period 2-6 months
- long lasting infection
- switch to chronicity in 5-10%
  - Hepatic fibrosis

http://www.google.cz/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&cad=rja&docid=rQwLNq8-Wn1SeM&tbnid=STc4TtPRL8qMYM:&ved=&url=http%3A%2F%2Faquilathp.blogspot.com%2F2013%2F08%2Fcirrhosis.html&ei=N_9WUqycJIeS5ATqqYCoAw&bvm=bv.53899372,d.bGE&psig=AFQjCNG575vNjxajKUy5GPU0YNHCYVq4tQ&ust=1381519543978090



Hepatitis B Virus (HBV) Geographic distribution

2008

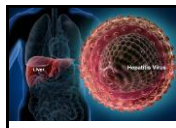


About 350 millions of HBV carriers worldwide

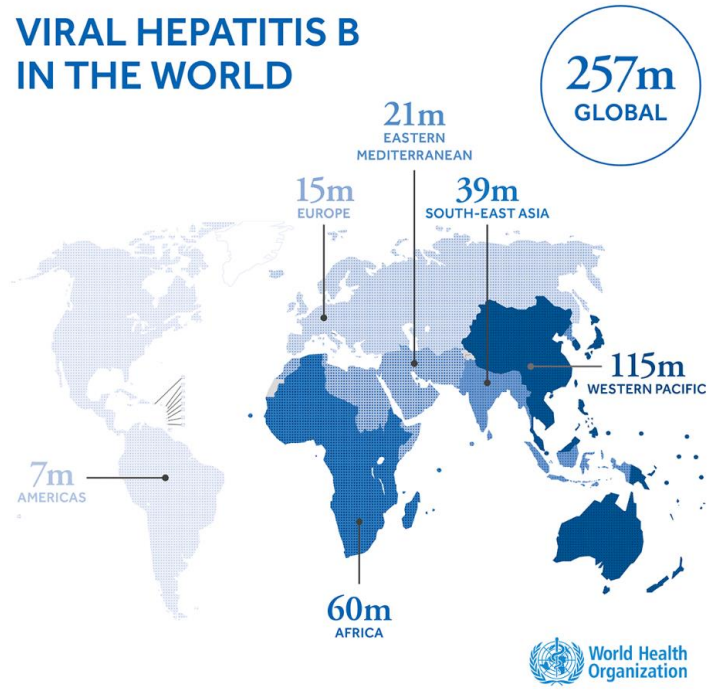
* For multiple countries, estimates of prevalence of hepatitis B surface antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg prevalence might vary within countries by subpopulation and locality.

Source: CDC. Travelers' health; yellow book. Atlanta, GA: US Department of Health and Human Services, CDC; 2008. Available at http://wwwn.cdc.gov/travel/yellowbookch4-HepB.aspx.

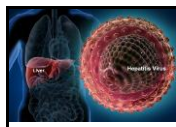
http://img.medscape.com/fullsize/migrated/editorial/casecme/2008/17750/figure.png



VIRAL HEPATITIS B IN THE WORLD



2017



Hepatitis B Virus (HBV) Diagnostic markers

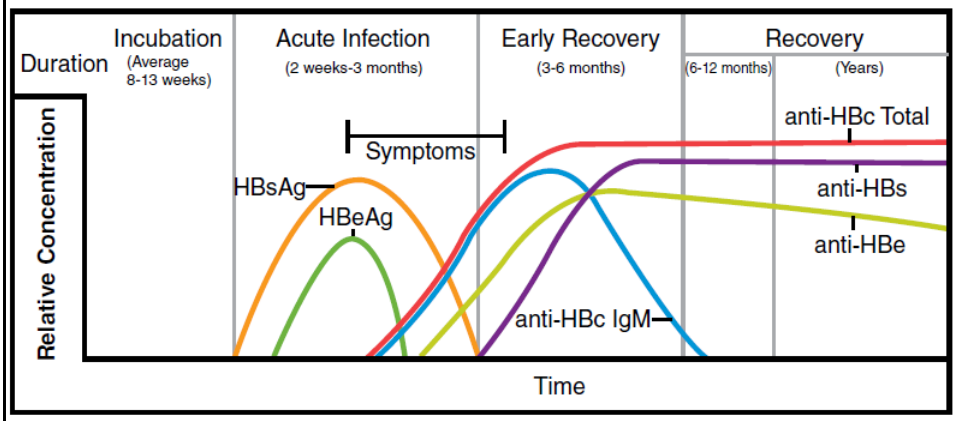
- Antigens
- HBs Ag
  - high amounts
  - in acute and chronic
  - sign of carrier
- HBe Ag
  - marker of acute and active infection
- DNA
  - Qualitative
  - Quantitative

    (treatment monitoring)

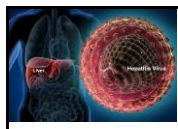
- Antibodies
- anti HBs
  - in convalescence
  - after vaccination
- anti HBe
  - in convalescence
- anti HBc
  - lifelong evidence of infection

Hepatitis B Virus (HBV) Antibody response

Acute Hepatitis B Diagnostic Profile

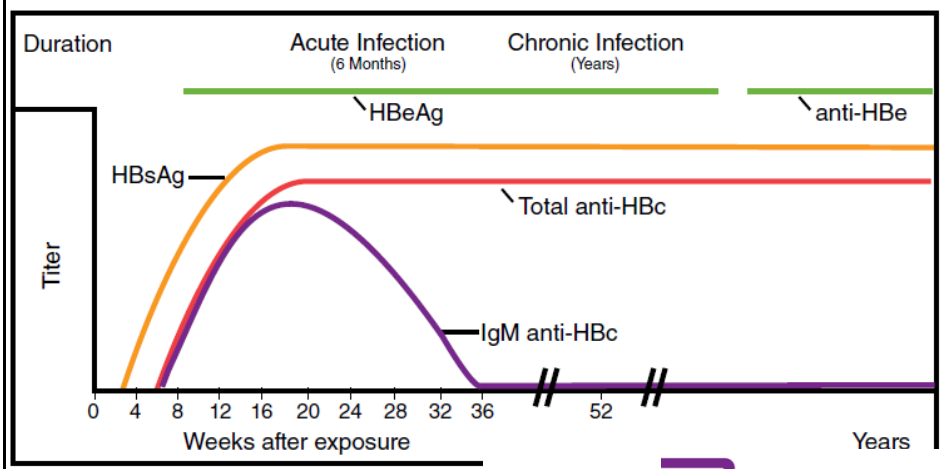


Learning Guide
Hepatitis



Hepatitis B Virus (HBV) Antibody response

Progression to Chronic HBV Infection Typical Serologic Course

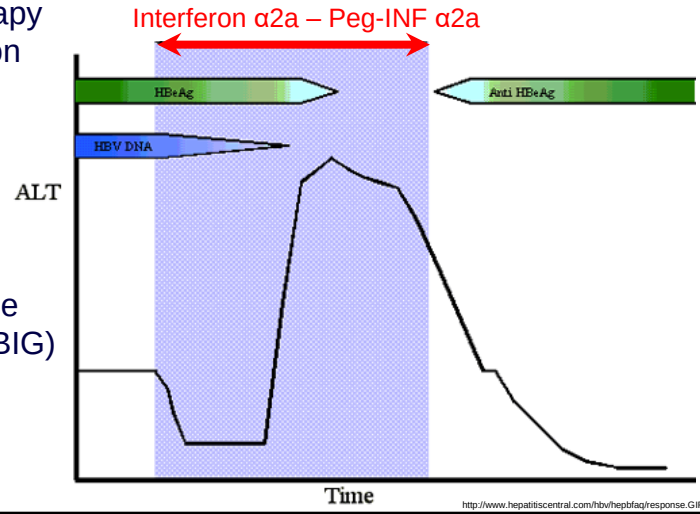


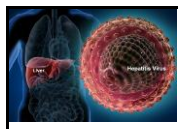
Learning Guide
Hepatitis

Hepatitis B Virus (HBV) Therapy and prevention

- Immunotherapy with interferon
- Virostatics (lamivudine, adefovir)
- Vaccine
  - Engerix..
- Hyperimmune globuline (HBIG)

BUT…

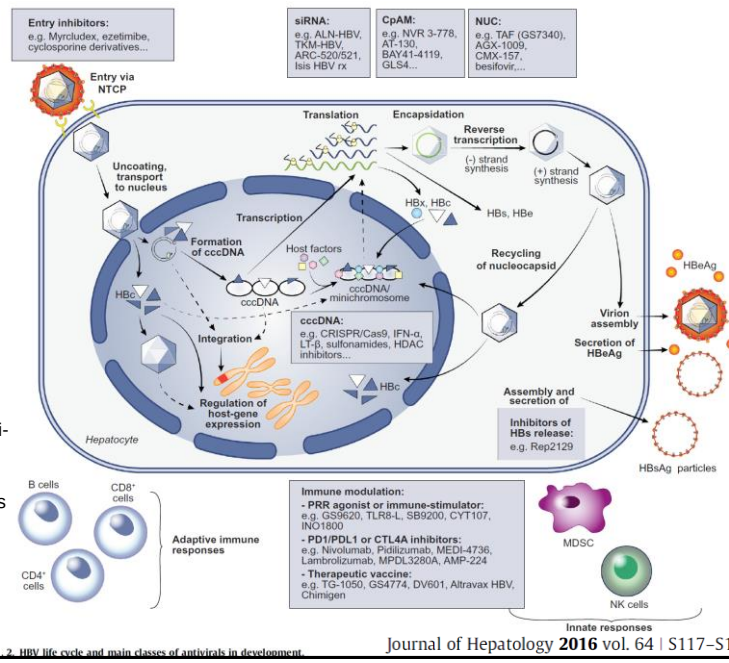




Hepatitis B Virus (HBV) New therapy

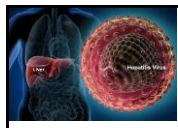
DAA

inhibitors of viral entry
new polymerase inhibitors
capsid and assembly inhibitors
virus release blockers
disruptors of cccDNA formation and transcription
Agents enhancing anti-HBV specific immune responses
including TLR agonists
checkpoint inhibitors
therapeutic vaccines



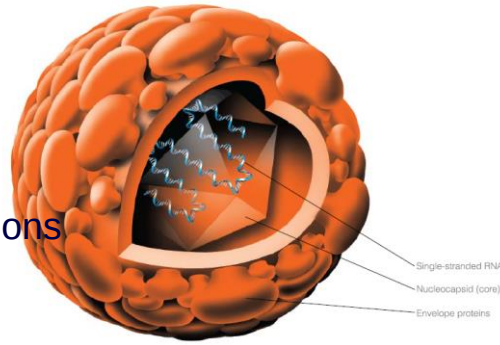
2. HBV life cycle and main classes of antivirals in development.

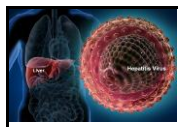
Journal of Hepatology **2016** vol. 64 | S117–S131



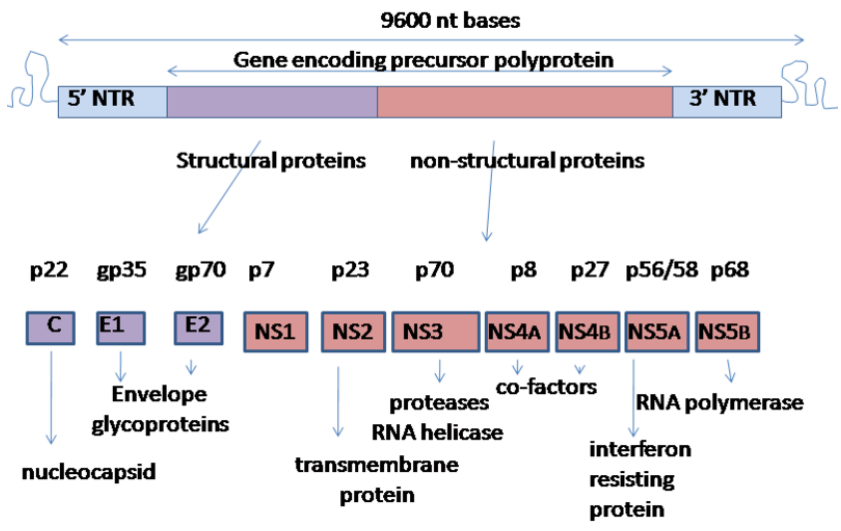
Hepatitis C Virus (HCV)

- ss RNA virus (uncultivateable)
- Flavivirus
- 6 types and about 40 subtypes
- Sensitive to environmental conditions
- Blood and sexually transmitted
- Human restricted pathogen

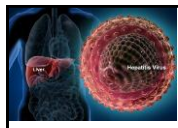




Hepatitis C Virus (HCV) Genome structure

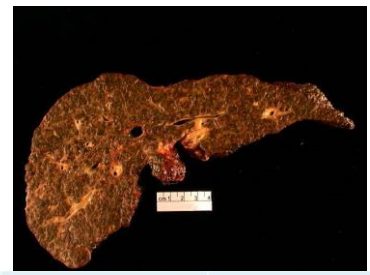


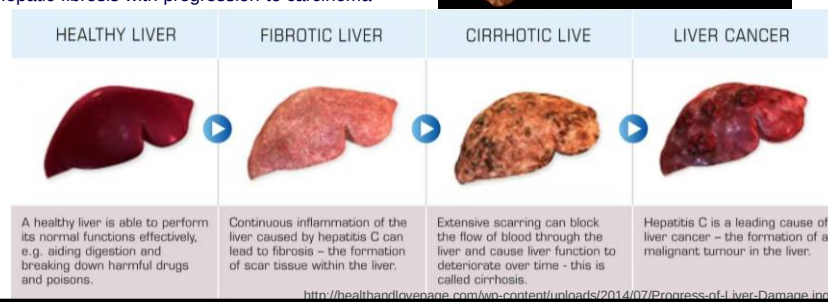
http://upload.wikimedia.org/wikipedia/commons/thumb/c/c0/HCV_genome.png/800px-HCV_genome.png



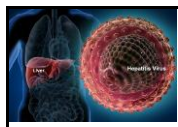
Hepatitis C Virus (HCV) Clinical symptoms

- discreet start of illness
- often unicteric form 60-70%
- incubation period 2-7 wks (2-26 wks)
- long lasting infection
- switch to chronicity up to 80%
  - Hepatic fibrosis with progression to carcinoma



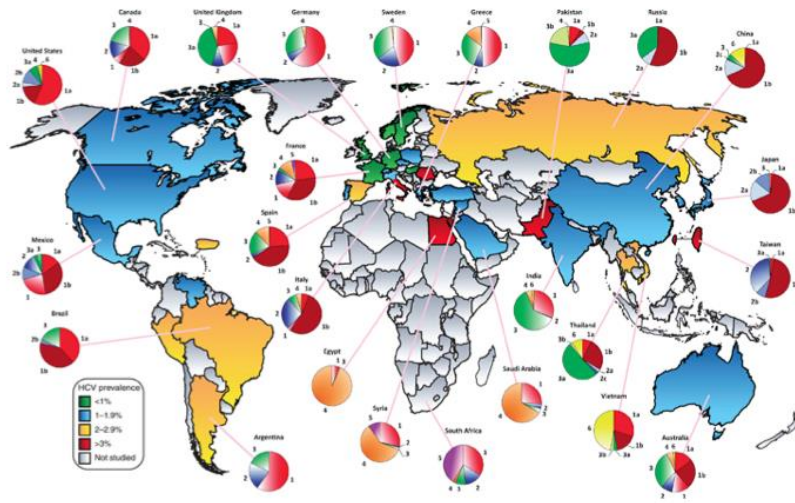


http://healthandlovepage.com/wp-content/uploads/2014/07/Progress-of-Liver-Damage.jpg



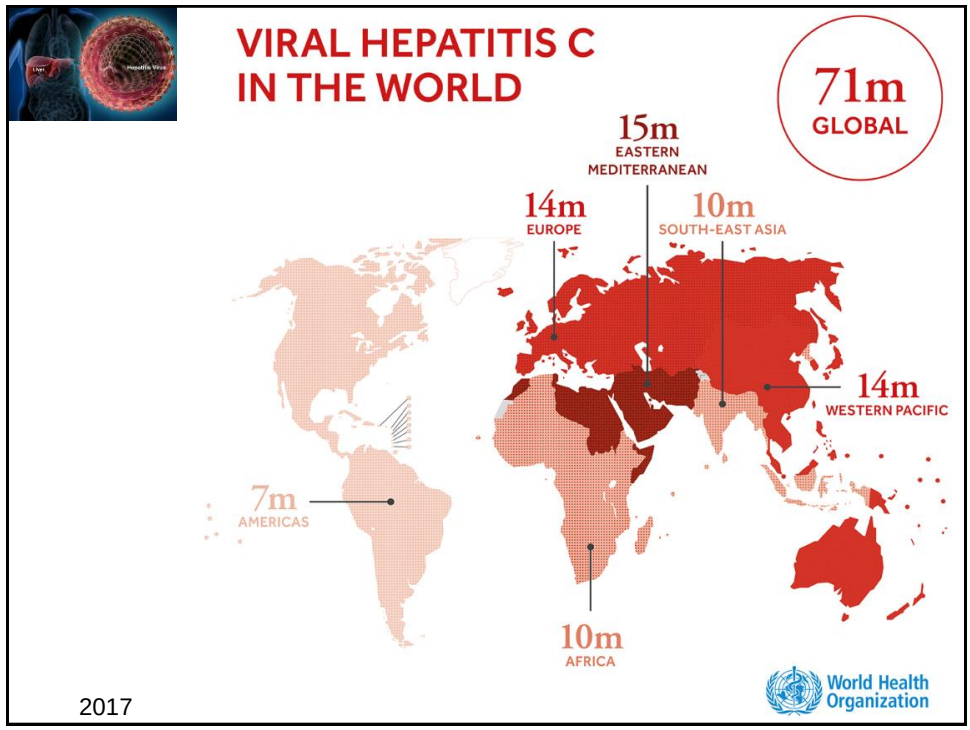
Hepatitis C Virus (HCV) Geographic distribution

2011



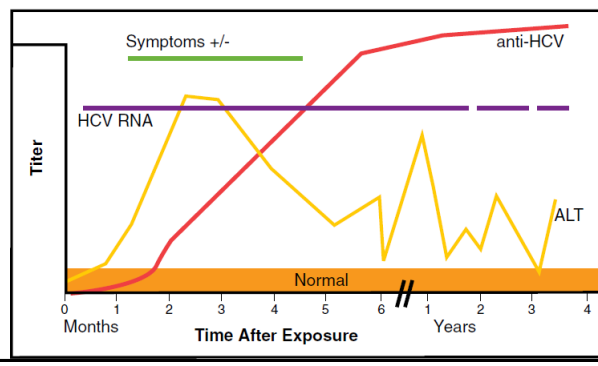
About 170 millions of HCV carriers worldwide

http://lloydbelcher.files.wordpress.com/2011/07/hcv-global-prevalence.png



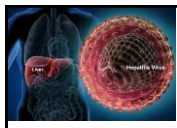
Hepatitis C Virus (HCV) Diagnostics

- RNA
  - Qualitative or quantitative
    (treatment monitoring)
- Antibody detection anti-HCV (ELISA)
  - in infection and convalescence
    - < 3 months



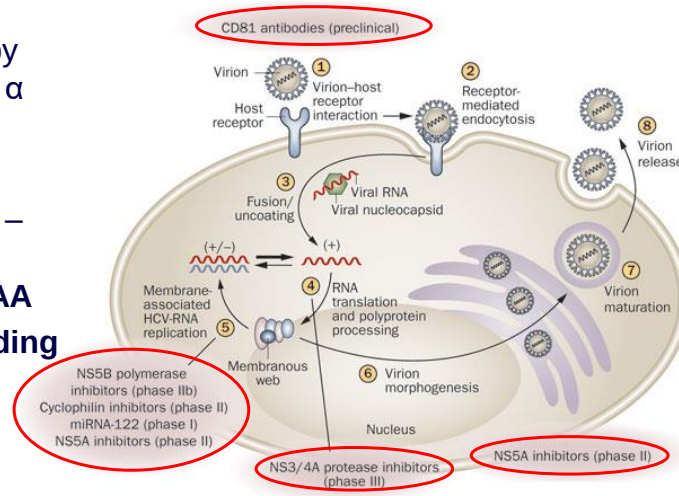
Serologic Pattern of Acute HCV Infection With Progression to Chronic Infection

Learning Guide
Hepatitis



Hepatitis C Virus (HCV) Therapy and prevention

- Immunotherapy with interferon α
- Virostatics (ribavirine)
- Combined Th. – **Direct acting antivirals - DAA**
- **Differs according to the type of HCV**
- No Vaccine



http://www.nature.com/nrgastro/journal/v8/n2/images/nrgastro.2010.219-f1.jpg

Hepatitis C Virus (HCV) Therapy and prevention

- **Direct acting antivirals – DAA**
  - nonstructural proteins 3/4A (NS3/4A) protease inhibitors (PIs) **telaprevir** a **boceprevir**
  - NS5B nucleoside polymerase inhibitors (NPIs) **grazoprevir**, **paritaprevir** a **simeprevir**, **sofosbuvir**
  - NS5B non-nucleoside polymerase inhibitors (NNPIs) **dasabuvir**
  - NS5A inhibitors **edipasvir**, **ombitasvir**, **elbasvir** a **daclatasvir**
  - **In some drugs, there are fixed combination of virostatics**

STANDARDNÍ DIAGNOSTICKÝ

A TERAPEUTICKÝ POSTUP

CHRONICKÉ INFEKCE VIREM

HEPATITIDY C (HCV)

Pracovní skupina pro virové hepatitidy České hepatologické společnosti České lékařské společnosti Jana Evangelisty Purkyně

Pracovní skupina pro virové hepatitidy Společnosti infekčního lékařství České lékařské společnosti Jana Evangelisty Purkyně

Autoři

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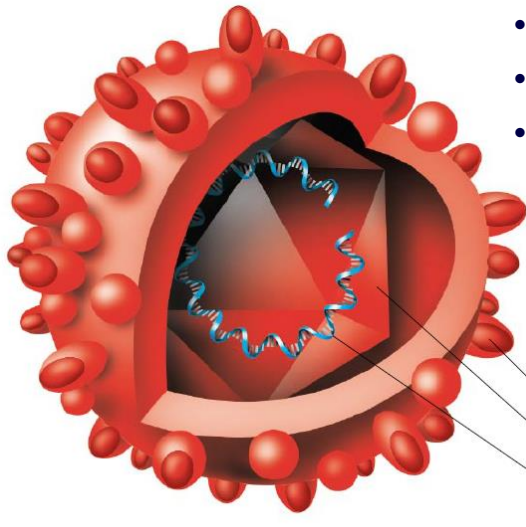
Doc. MUDr. Luděk Rožnovský, CSc.
MUDr. Petr Kümpel

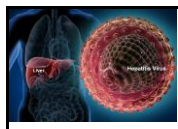
www.ces-hep.cz
www.infekce.cz

Datum: 29.10. 2014

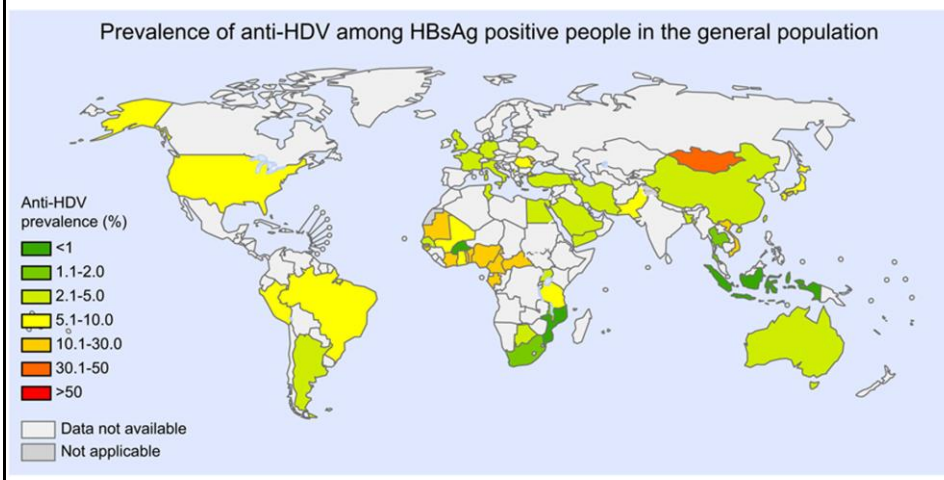
Hepatitis D Virus (HDV)



- ss RNA virus
- 36-43 nm
- HBV dependent virus (needs HBsAg)



Hepatitis D Virus (HDV) Geographic distribution

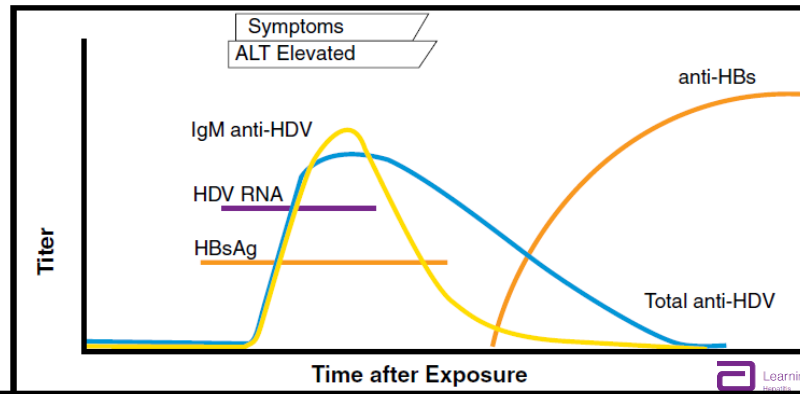


Journal of Hepatology 2020 73523-532DOI: (10.1016/j.jhep.2020.04.008)

EASL JOURNAL OF HEPATOLOGY

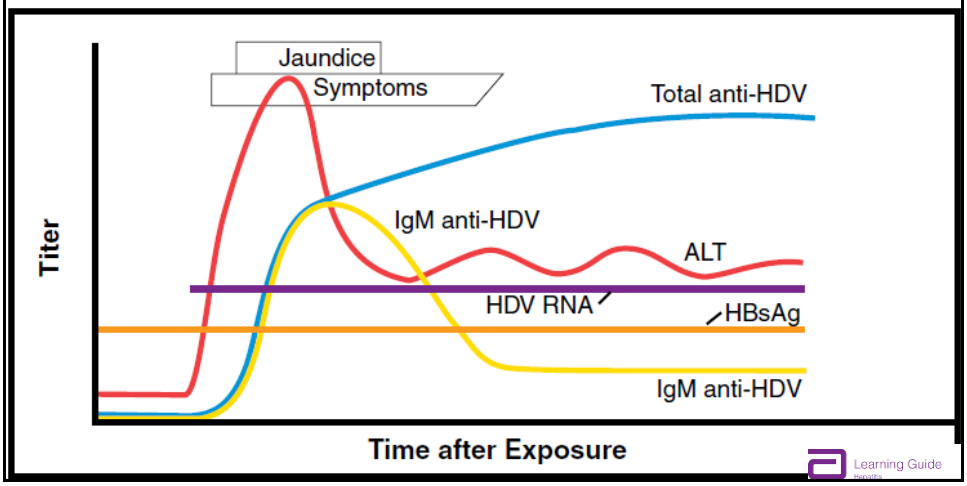
Hepatitis D Virus (HDV) Clinical symptoms

- **Co-infection** with HBV; transmission similar
- Incubation period 21-49 days; abrupt start
- More severe clinical course



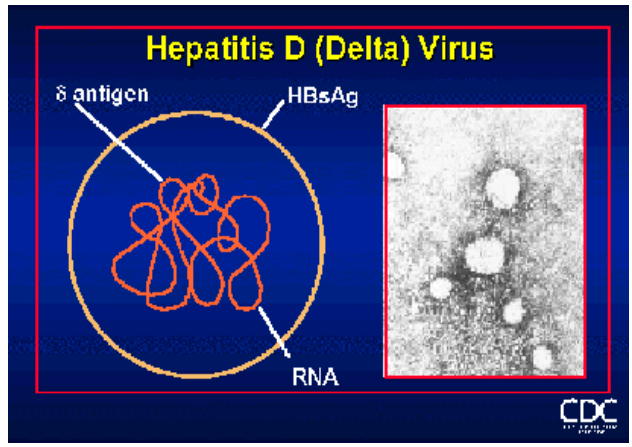
Hepatitis D Virus (HDV) Clinical symptoms

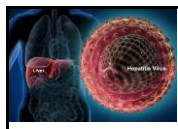
- Often chronic HBV **super-infection** (80%)



Hepatitis D Virus (HDV) Diagnostics

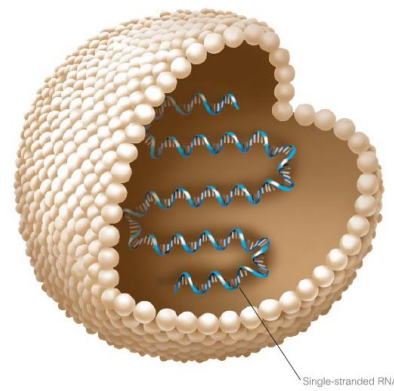
- RNA
- Antibody detection – IgM and IgG





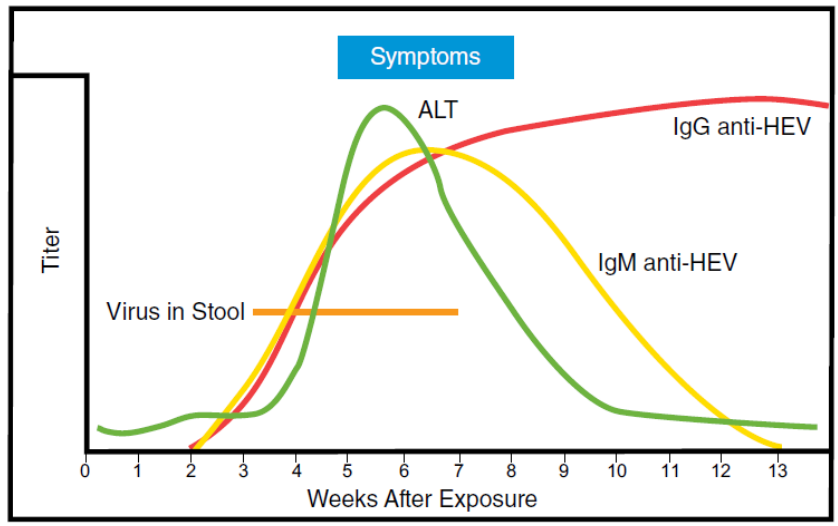
Hepatitis E Virus (HDV)

Virus Family	Hepeviridae
Route of Transmission	Fecal-oral (especially contaminated water)
Onset	Usually abrupt
Incubation	15 – 60 days, average 40 days
Chronicity	None reported
Mortality	About 1 – 3%, 15 – 25% in pregnant women

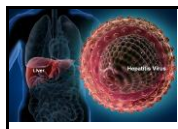


Learning Guide

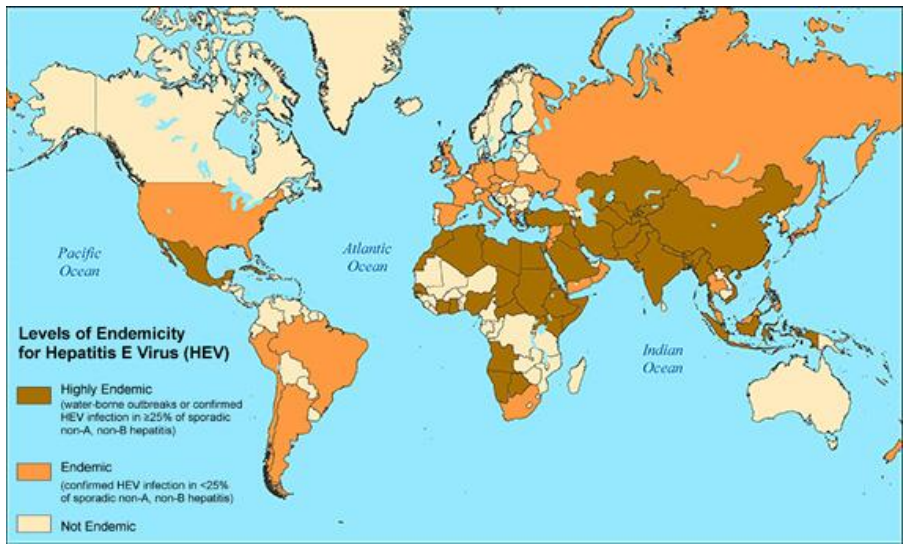
Hepatitis E Virus (HEV) Diagnostics



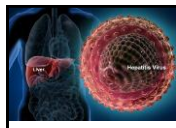
Learning Guide



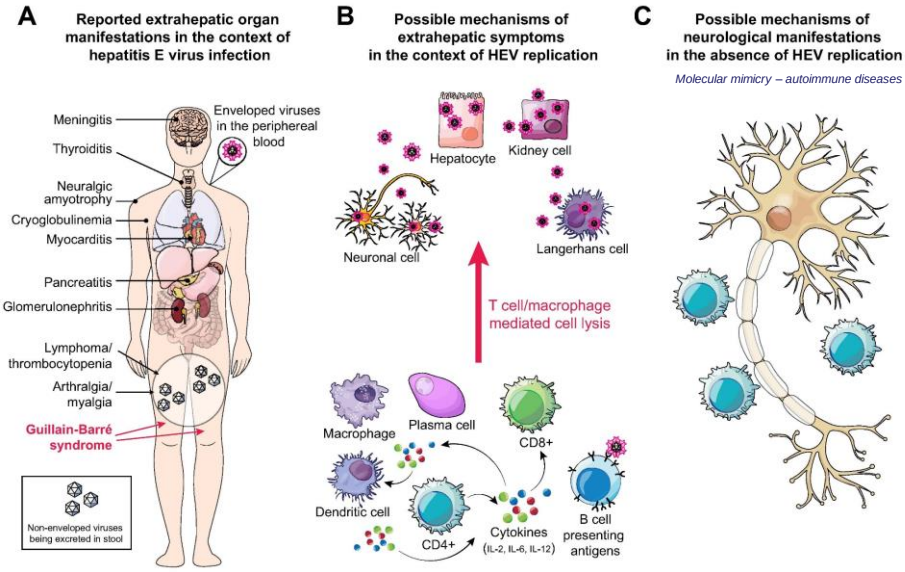
Hepatitis E Virus (HEV) Geographic distribution



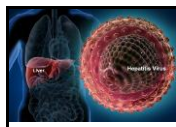
http://www.cdc.gov/hepatitis/HEV/images/Map5_4_HepatitisE_sml.jpg



HEV extrahepatic manifestation



Pischke et al. Hepatitis E virus: Infection beyond the liver? Journal of Hepatology 2017 vol. 66 j 1082–1095



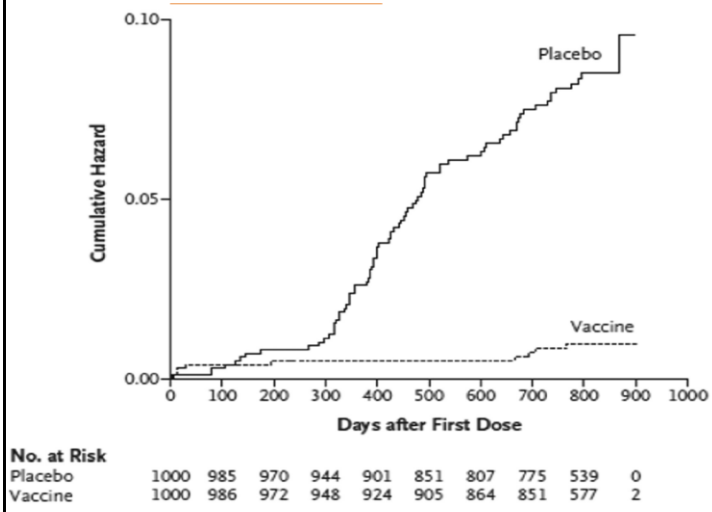
Hepatitis E Virus (HEV)

Study site	Patients (n)	Seroprevalence of HEV infection (%)	Prevalence of fulminant liver failure (%)	Mortality rate (%)	References
North India	127	58	58	45	(Jaiswal, Jain, Naik, Soni, & Chitnis, 2001)
North India	60	37	64	64	(Singh et al., 2003)
North India	76	86	69	55	(Khuroo & Kamili, 2003)
North India	97	47.4	75	39.1	(Beniwal, Kumar, Kar, Jilani, & Sharma, 2003)
Ethiopia	32	59	–	42	(Tsega, Krawczynski, Hansson, & Nordenfelt, 1993)
North India	65	45	32	73	(Kumar, Beniwal, Kar, Sharma, & Murthy, 2004)
North India	220	60	55	41	(Patra, Kumar, Trivedi, Puri, Sarin, 2007)
North India	61	58	50	57	(Saravanabalaji et al., 2009)
Egypt	2428	84.3	0	0	(Stoszek et al., 2006)
South India	115	75	3.4	3.4	(Rasheeda, Navaneethan, Jayanthi, 2008)

Shata et al. Viral hepatitis in pregnancy J Viral Hepat. 2022;29:844–861.

Hepatitis E Virus (HEV)

FIGURE 2 HEV vaccine

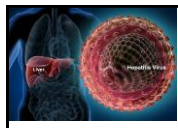


Shata et al. Viral hepatitis in pregnancy J Viral Hepat. 2022;29:844–861.

Hepatitis E Virus (HEV)

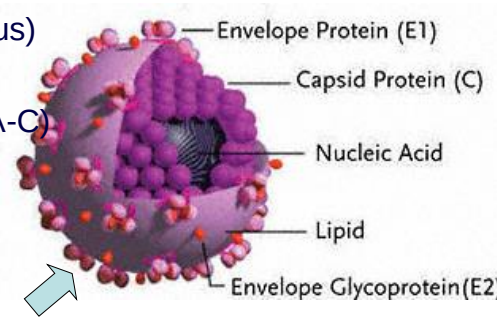
Character	Hepatitis A (HAV)	Hepatitis B (HBV)	Hepatitis C (HCV)	Hepatitis E (HEV)	Hepatitis D (HDV)
Classification	*Picornaviridae*	*Hepadnaviridae*	*Flaviviridae*	*Hepeviridae*	*Deltaviridae*
Genome	RNA (+)	DNA	RNA (+)	RNA (+)	RNA (−)
Envelop	No	Lipid envelop	Lipid envelop	No	Lipid envelop from HBV
Spread	Feco-oral/sexual	Parenteral/sexual	Parenteral/sexual	Feco-oral/zoonotic	Parenteral/sexual
Course in pregnancy	Benign/self- limiting	acute/chronic	acute/chronic	Acute/fulminant 20% mortality	coinfection with HBV
Maternal to child transmission (MTCT)	(++)	(+++)	(+)	(+++)	(−)
Caesarian section recommendation	No	No	No	May be	No
Breastfeeding	Yes	Yes	Yes	No	Yes
Vertical transmission	Rare	30%	5%	50%	Rare
Complications	Rare preterm/foetal liver injury	Preterm delivery/chronic HBV	Rare	Preterm delivery/stillbirth/infant mortality	Require HBV coinfection
Treatment	Post-exposure prophylaxis IgG	Monitor/assesses for anti-viral treatment	Anti-viral therapy after delivery	Supportive care	Monitor/assesses for anti-viral treatment
Prevention	HAV vaccine	HBV vaccine	No vaccine available	Vaccine is available but not FDA approved yet	HBV vaccine

Shata et al. Viral hepatitis in pregnancy J Viral Hepat. 2022;29:844–861.



Hepatitis G Virus (HGV)

- RNA viry similar to HCV (Flavivirus- genus Pegivirus)
- several types
- different HGV and GBV (A-C)
- Blood transmission
- Also in health population
- Patogenic likely **GBV-C**



http://www.prn.org/images/uploads/gbv-c_3d_high.jpg

- **Diagnostics mainly PCR**
  (Antibody non reliable)

Virus	Estimated number of infections worldwide	Mode of transmission	Typical clinical signs/symptoms	Natural history	Diagnosis	Treatment	Prevention
Hepatitis A	1.4 million annually	Fecal-oral route	Many asymptomatic. Most with non-specific symptoms of fatigue, nausea, vomiting, anorexia, jaundice	Asymptomatic, self-limited illness, prolonged cholestasis, relapsing, fulminant hepatitis (very rare)	Hepatitis A IgM	Supportive care, post-exposure vaccination and HAV immuno-globulin	Sanitation efforts, vaccination
Hepatitis B	257million chronic HBV infections (WHO 2017 Global Hepatitis Report)	Vertical transmission (common for chonic HBV); IVDU, blood product transfusions, sexual contact (common for acute HBV)	Acute: non-specific symptoms (fatigue, nausea, vomiting, anorexia, jaundice); chronic: often asymptomatic, can progress to cirrhosis and HCC	Infection at birth: chronic HBV infection (immune tolerance, immune clearance, inactive carrier, reactivation). Eventual progression to cirrhosis and HCC; infection in adulthood: > 95% clearance	Past infection- HBsAg negative, HBsAb positive, HBcAb positive, HBeAb +/-; current infection- HBsAg positive, HBsAb negative, HBcAb positive, HBeAb +/-	Nucleot(s)ide reverse transcriptase inhibitors (entecavir, tenofovir); interferon	HBV vaccine (universal vaccination recommended at birth); HBIG in select cases
Hepatitis C	71 million (WHO 2017 Global Hepatitis Report)	Direct blood stream inoculation (IVDU; unregulated tattoos/piercings, blood transfusion and organ transplants)	Typically asymptomatic until cirrhosis develops	Spontaneous clearance: 10%-25%; chronic infection: 75%-90%, can progress to cirrhosis and HCC	HCV antibody, HCV RNA viral load	Direct acting antivirals	Widespread screening efforts
Hepatitis D	12 million cases annually, 4.5% of HBV-infected individuals	Similar to Hepatitis B (IVDU, blood product transfusions, sexual contact)	Non-specific symptoms of fatigue, nausea, vomiting, anorexia, jaundice	Simultaneous coinfection of HDV and HBV: rare fulminant hepatitis, usually complete recovery; superinfection on chronic HBV: accelerated progression of chronic HBV	HDV IgM (acute), HDV IgG (chronic)	Hepatitis B treatment	Hepatitis B vaccination
Hepatitis E	20 million acute infections (The Global Burden of Hepatitis E Virus Genotypes 1 and 2 in 2005)	Genotypes 1 and 2: Fecal-oral route; genotypes 3 and 4: Zoonotic, contaminated meat	Commonly asymptomatic; prodromal flu-like symptoms, nausea, vomiting, anorexia, fatigue followed by jaundice	Acute self-limited in majority of cases, severe in pregnant women; chronic hepatitis in immunocompromised hosts	HEV IgM (acute), HEV IgG (chronic)	Chronic infection: decrease immunosup-pression, ribavirin	Genotypes 1 and 2: Sanitation efforts, vaccine available in China
Hepatitis G	4.8% worldwide	Direct blood stream inoculation (IVDU, unregulated tattoos/piercings, blood transfusion and organ transplants)	Not well-described, likely asymptomatic	Not well-described. Unlikely to cause clinically significant hepatitis in humans.	Hepatitis G RNA; not currently used clinically	None	None

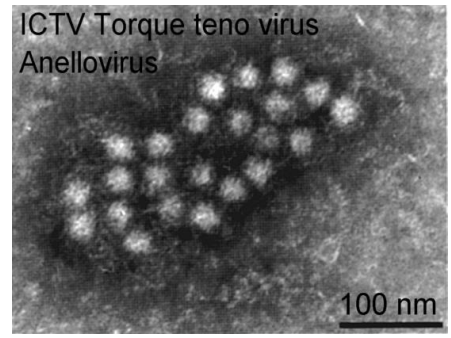
Hepatitis overview

Odenwald MA et al. The ABCs of Viral Hepatitis World J Gastroenterol 2022 April 14; 28(14): 1405-1429

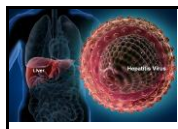
Torque Teno Virus (TTV)

- DNA virus
- Uncertain pathogenity
- Blood transmission
- Also in health population

- **Diagnostics only PCR**

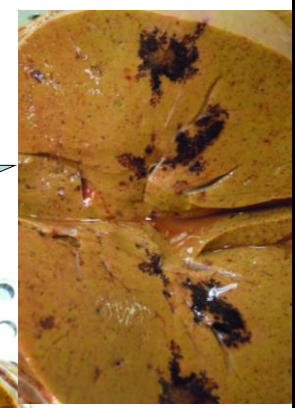


http://ictvdb.bio-mirror.cn/WIntkey/Images/em_anell_ICTV.jpg



Other viruses associated with hepatitis/hepatopathy

- **CMV**
- **EBV** (hepatopathy)
- **HSV**
- **adenovirus**
- **enterovirus**
- **Influenza**



- **From exotic viruses – yellow fever virus, dengue fever virus and more…**


Thank you for your attention