



NEOPLASIA (I)

Tumor epidemiology, etiology

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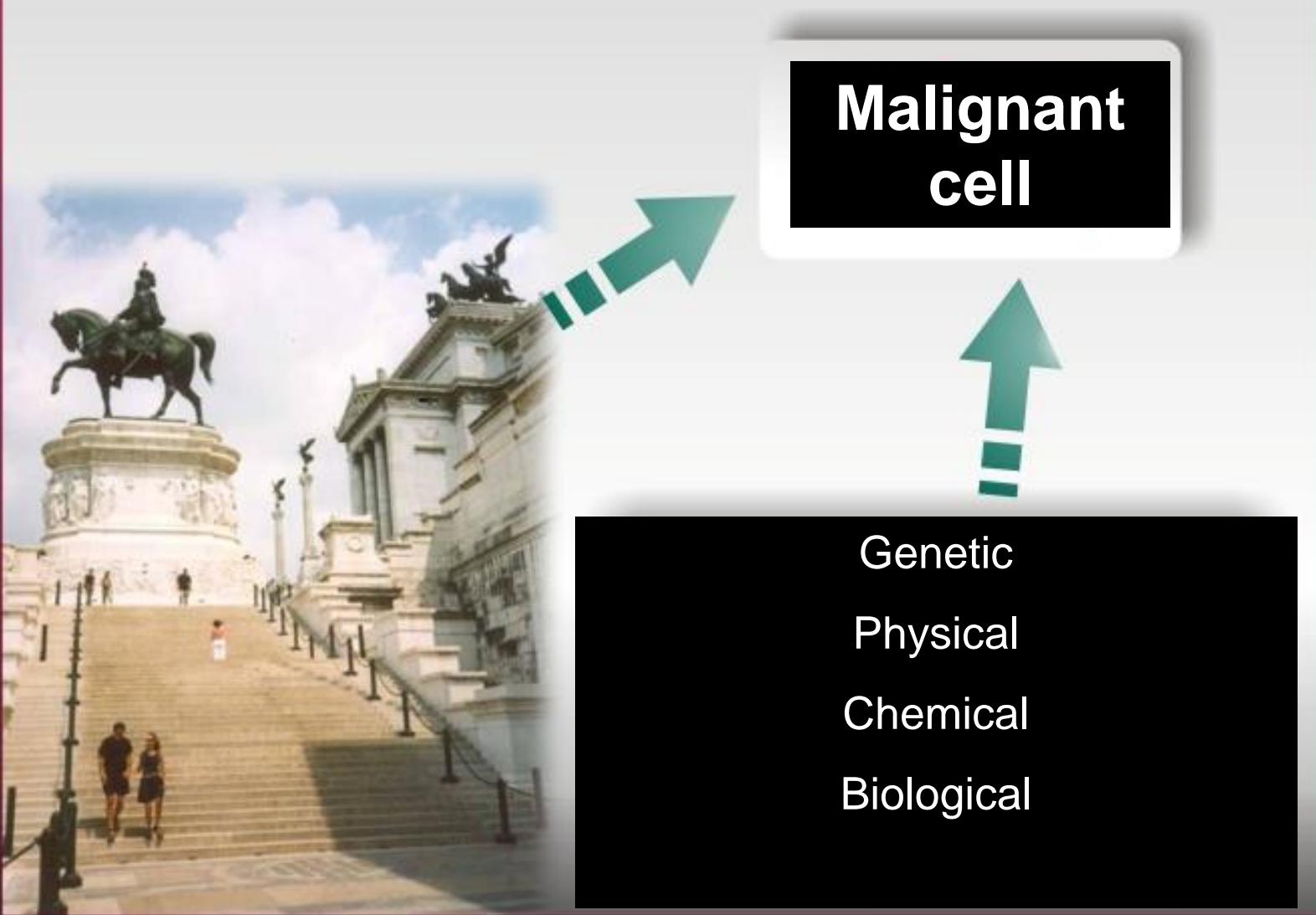
**Semmelweis University
2nd Department of Pathology
Budapest**

October 2020

„CANCER”



Carcinogenesis is a multifactorial and multistep process



Epidemiology

- **Cancer incidence** (number of new cases in a given period)
- **Mortality** (number of deaths in a given period),
 - mortality rate (age adjusted death rates): number of deaths per 100,000 population
- **Prevalence** (number of persons alive with the disease)
- **Significance of**
 - **Sex** (females: breast, lung, colorectal, uterus, ovary; males: lung, colorectal, prostate, pancreas)
 - **Age** (childhood cancers: Wilms tu, retinoblastoma, lymphomas/leukemias, neuroblastoma. Increased cancer mortality from 55-74 yr)
 - **geographic location/environmental factors** (UV, diet, smoking, drinking habits, mosquitos, aflatoxin etc)

Cancer epidemiology worldwide (2002)

- **Incidence:** 11 million new cases
- **Mortality:** 7 million death (12%) (total death: 56 million)
- **Prevalence:** 25 million alive diagnosed with cancer
- **Notes:**
 - Lung cancer is the most common cancer (12,4%)
 - Breast cancer is the most frequent cancer of women (23%), the most prevalent cancer
 - Mortality: lung (1,18 million), stomach (700 thousand), liver (600 thousand)
 - Cancers associated with viral etiology: appr.15%

Cancer epidemiology worldwide (2018)

(estimated by International Agency for Research on Cancer)

- **Incidence:** 18.1 million new cases
- **Mortality:** 9.6 million death (12%) (total death: 56 million)
- **Prevalence:** 43.8 million alive diagnosed with cancer
- **Notes:**
 - Lung cancer is the most common cancer (11.6%)
 - Breast cancer is the most frequent cancer of women (11.6%), the most prevalent cancer
 - Mortality: lung (18.4%), colorectal (9.2%), stomach (8.2%), liver (8.2%)
 - Cancers associated with viral etiology: appr.15%

Incidence and mortality worldwide



New Tumor cases in 2018: 18,1 million

Mortality 2018: 9,6 million

New Tumor cases in 2013: 14,9 million

Mortality in 2013: 8,2 millió

New tumor cases in 2008: 12,7 million

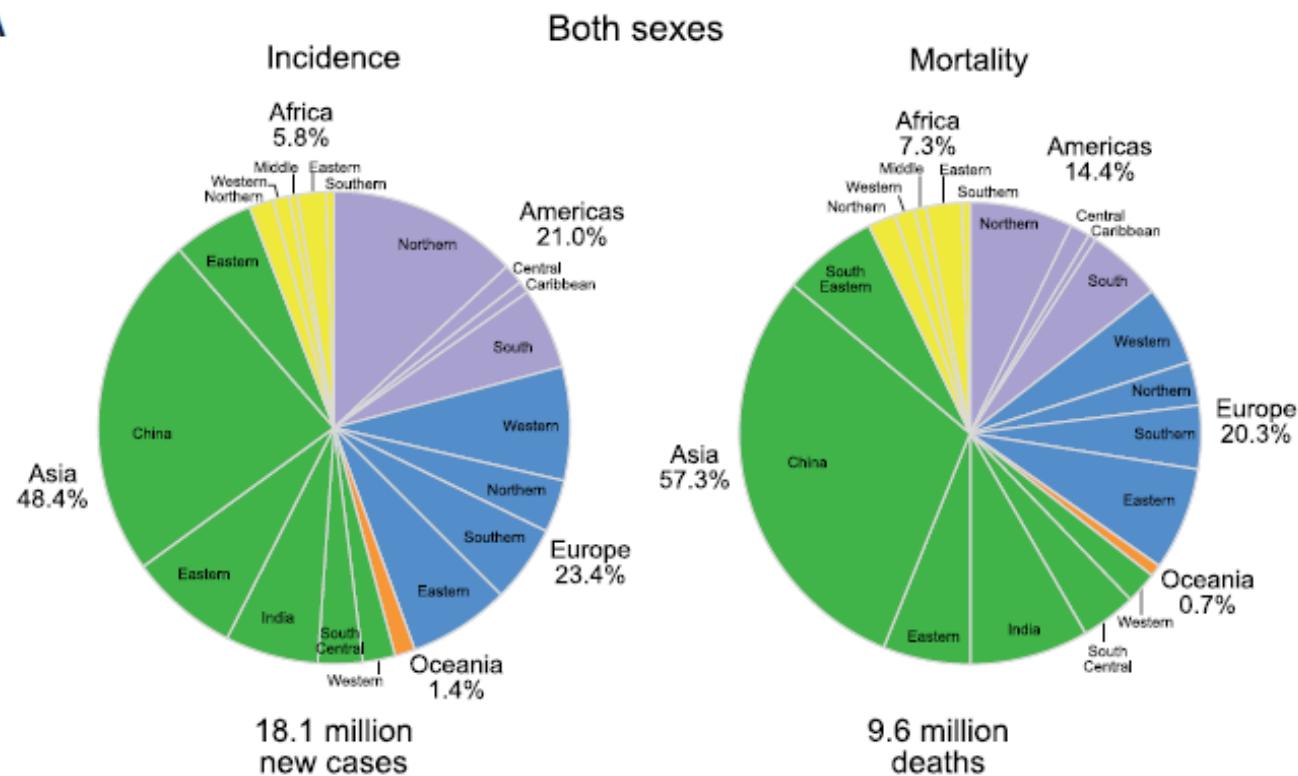
Mortality in 2008: 7,6 million

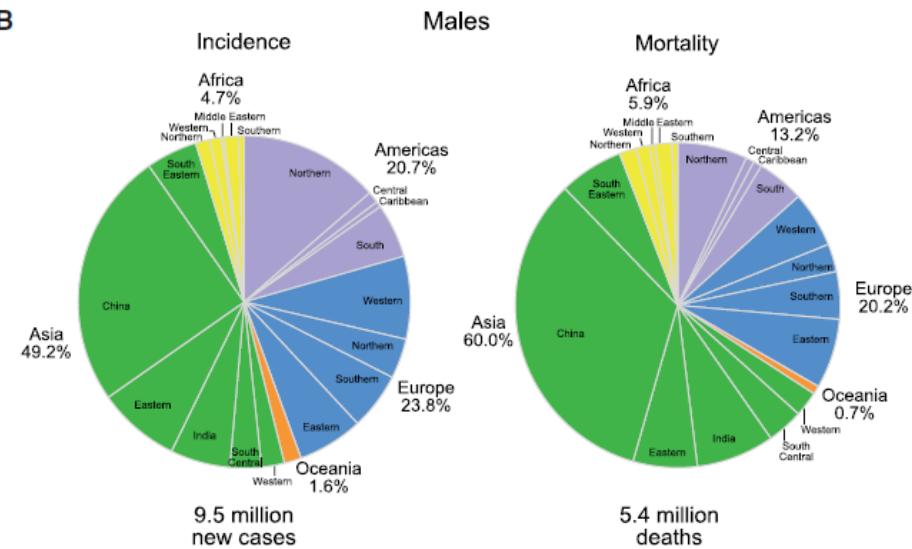
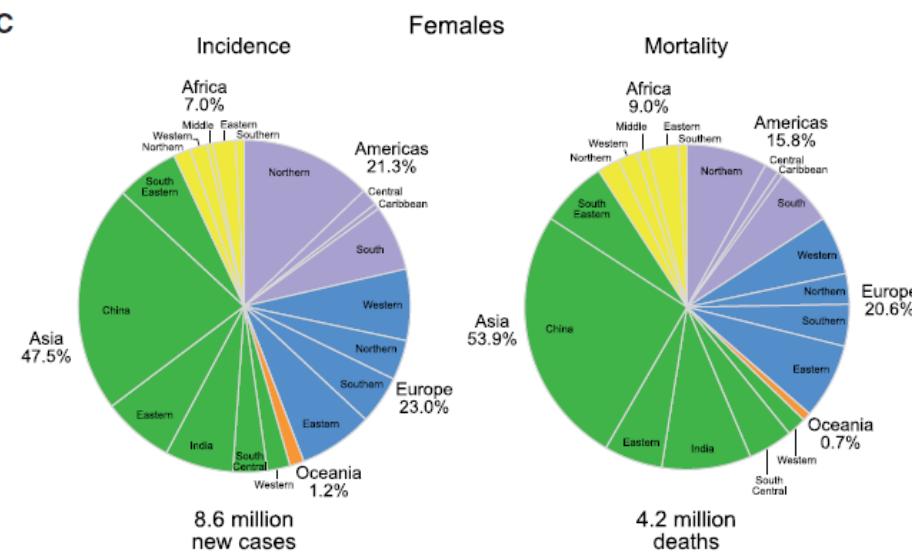
New tumor cases in 2002: 11 million

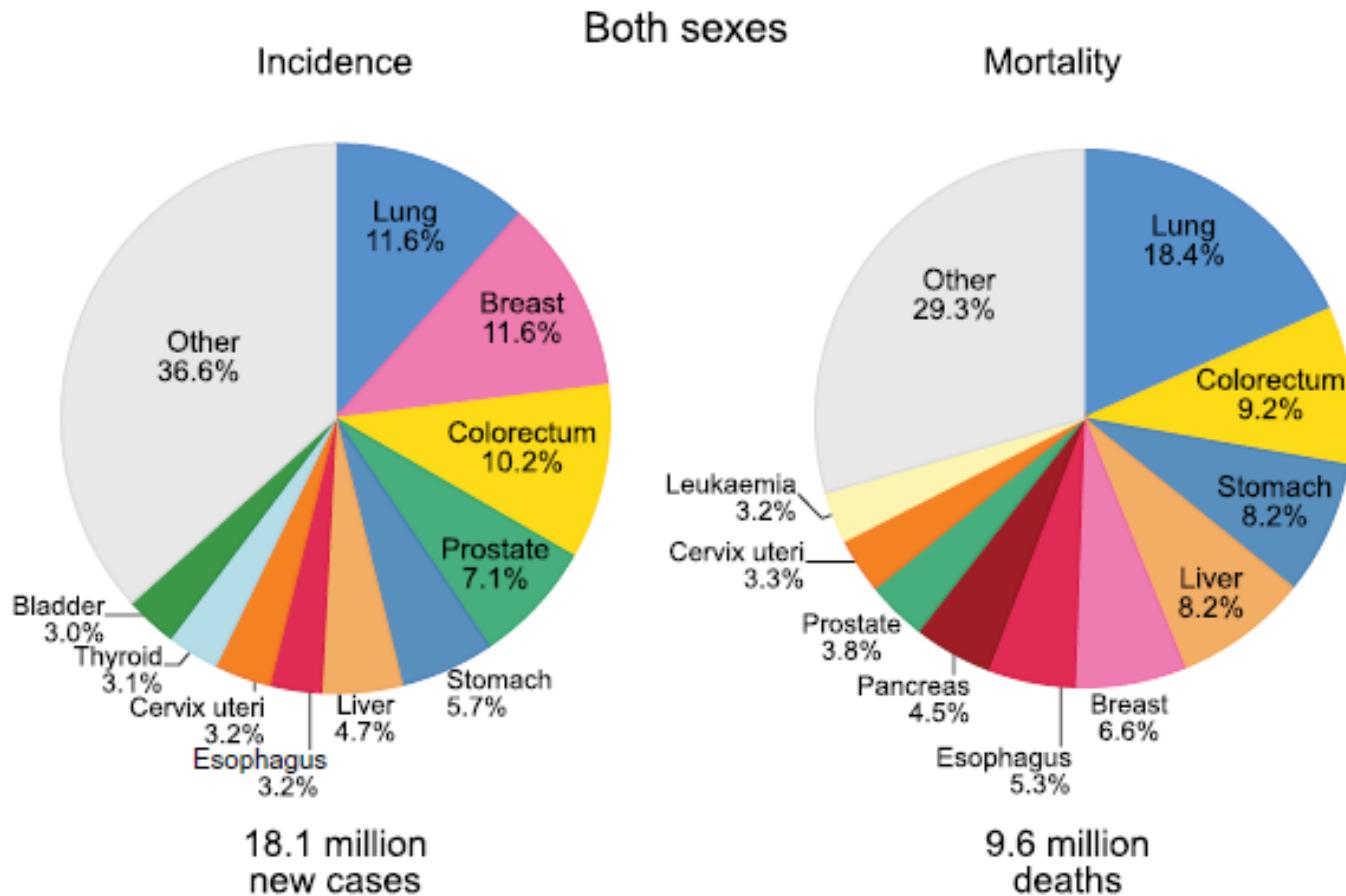
Mortality in 2002: 7 million

Ferlay J et al. Lyon, France: IARC Press; 2004.

GLOBOCAN 2008 (IARC 2010), JAMA Oncol.2015, CA Cancer J.Clin. 2018 Sept

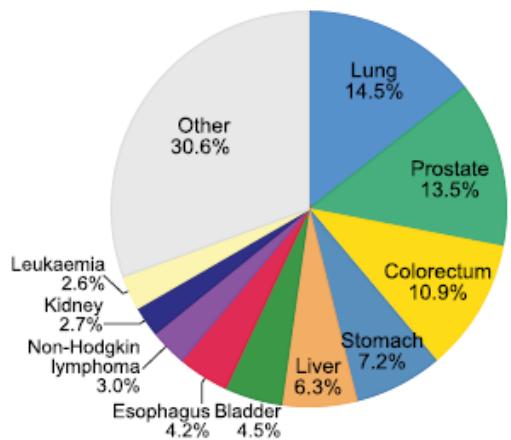
A

B**C**

A

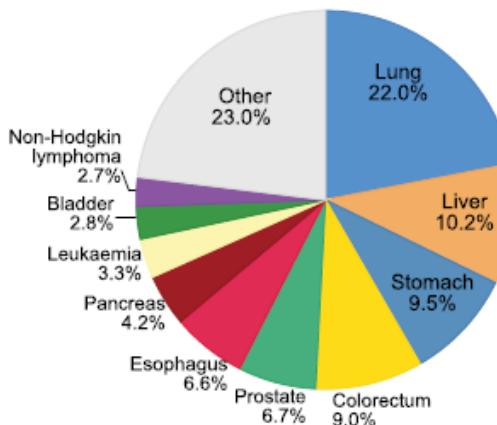
B

Incidence



Males

Mortality



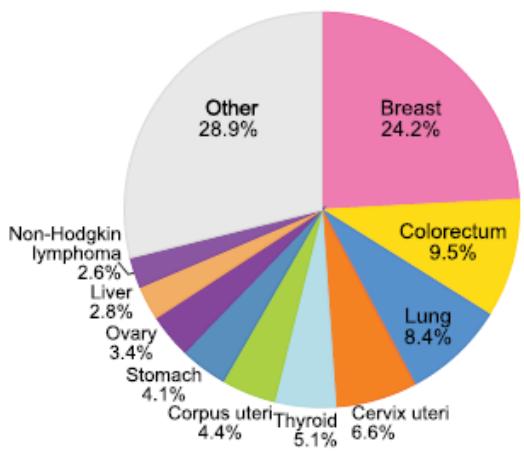
9.5 million new cases

5.4 million deaths

C

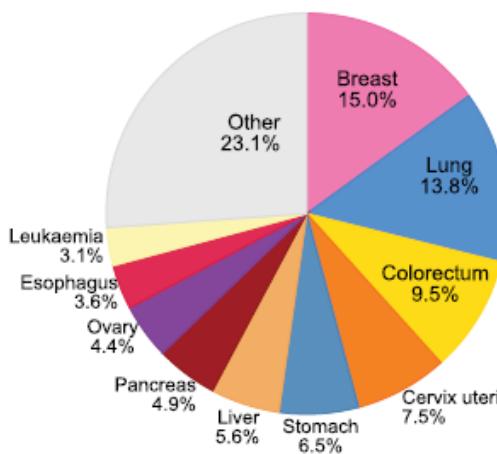
Females

Incidence



8.6 million new cases

Mortality

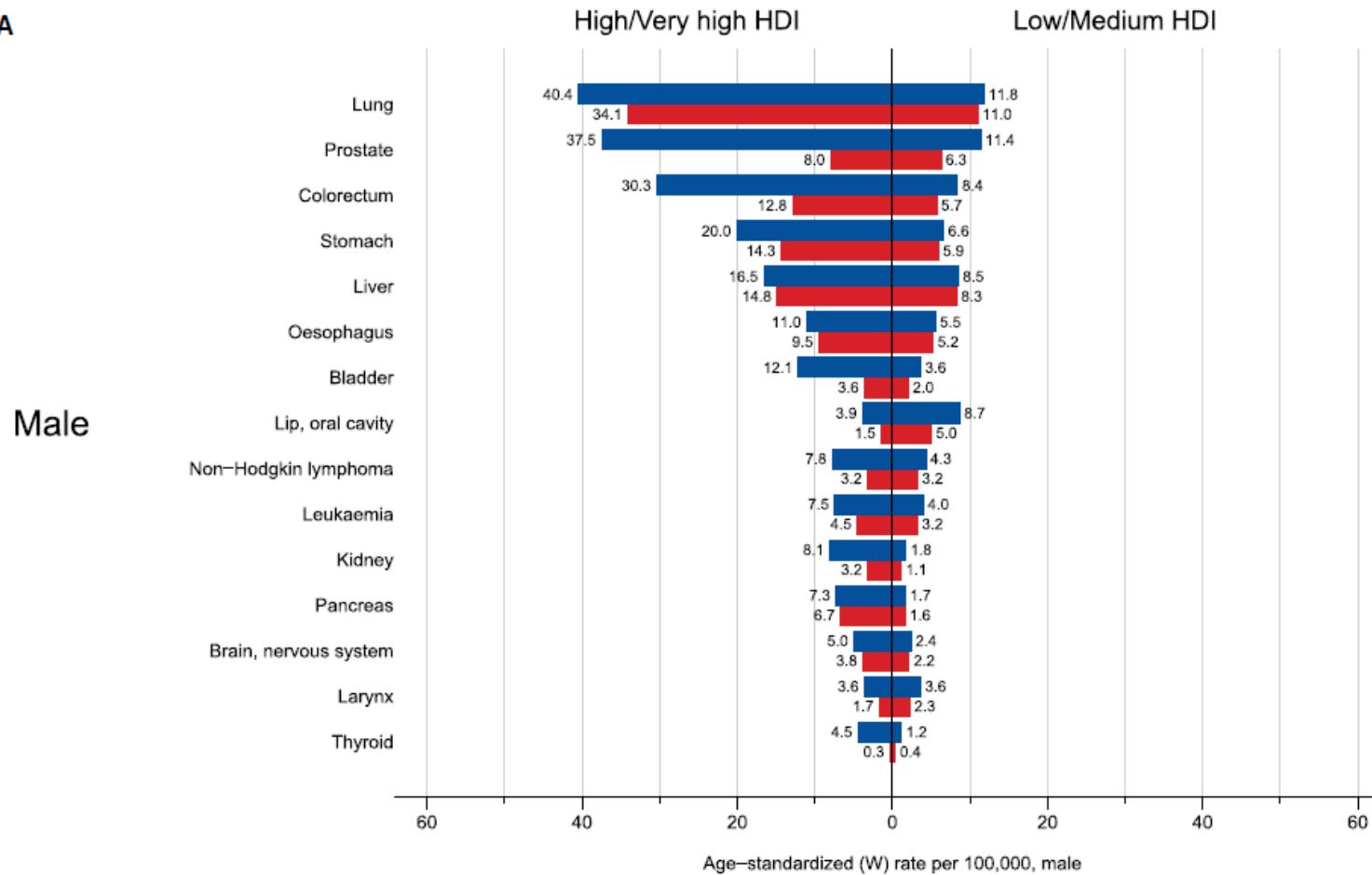


4.2 million deaths

Incidencia és mortalitás

CA CANCER J CLIN 2018;68:394–424

A



B

Female

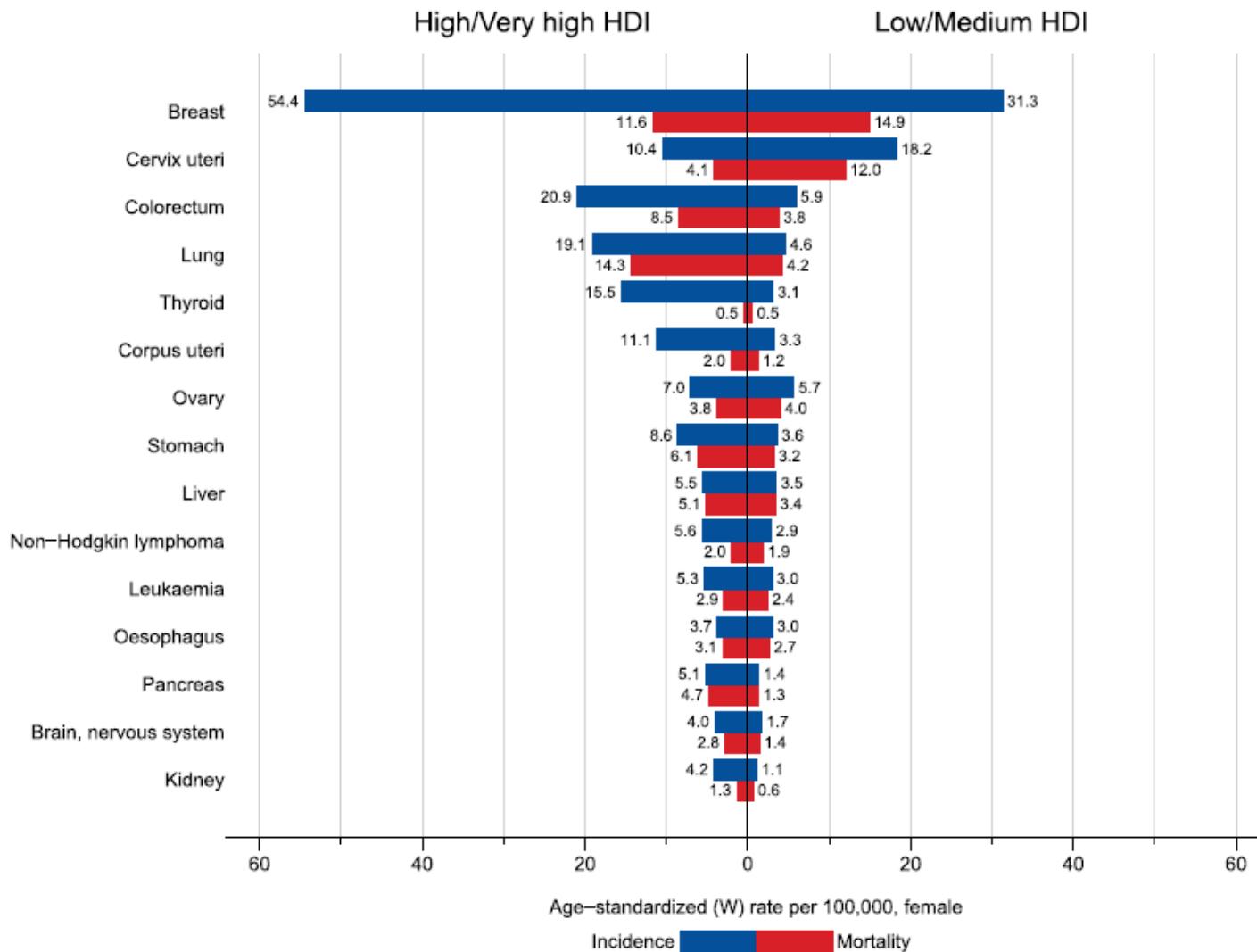


FIGURE 7. Bar Charts of Incidence and Mortality Age-Standardized Rates in High/Very-High Human Development Index (HDI) Regions Versus Low/Medium HDI Regions Among (A) Men and (B) Women in 2018. The 15 most common cancers world (W) in 2018 are shown in descending order of the overall age-standardized rate for both sexes combined. Source: GLOBOCAN 2018.

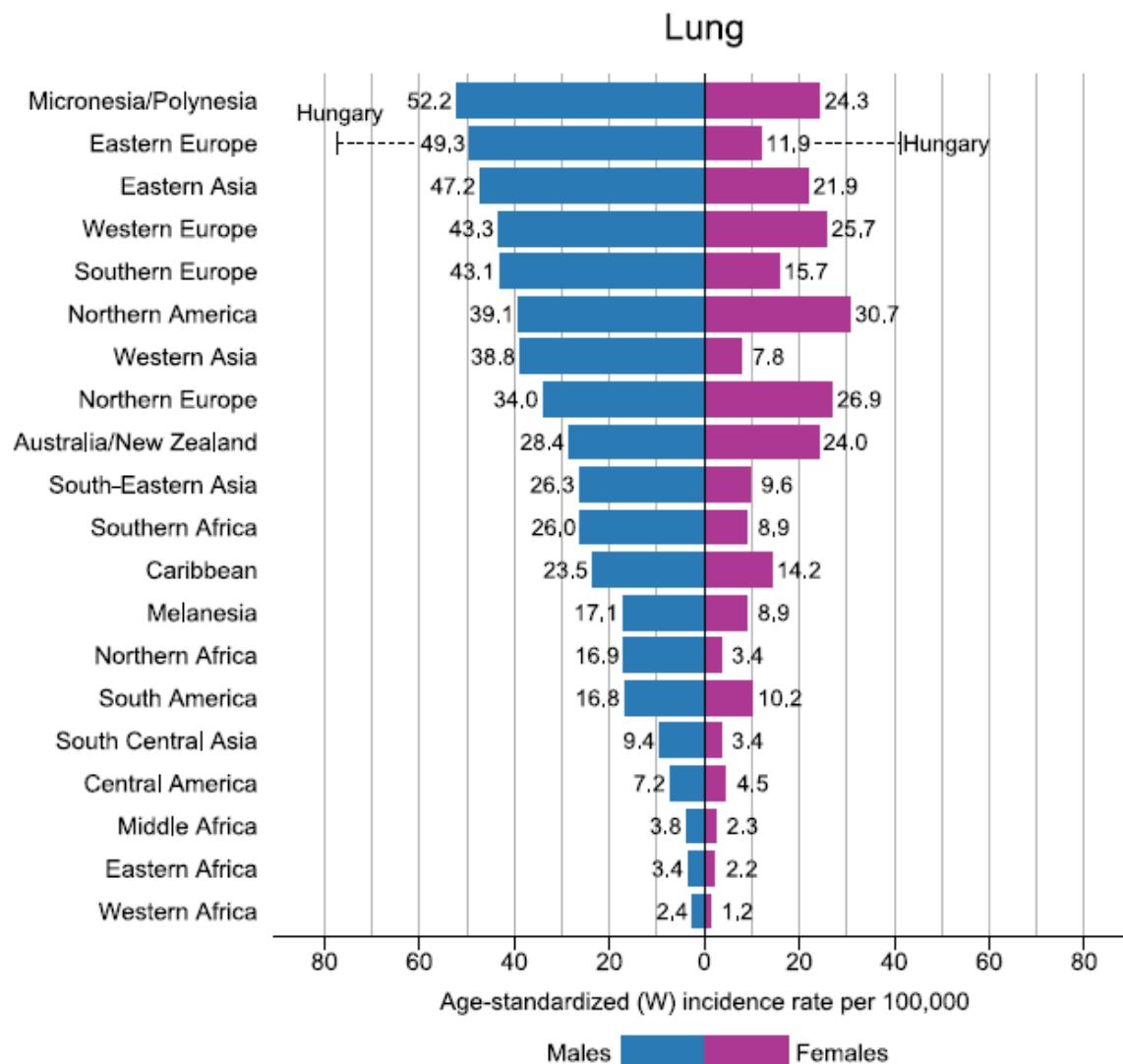
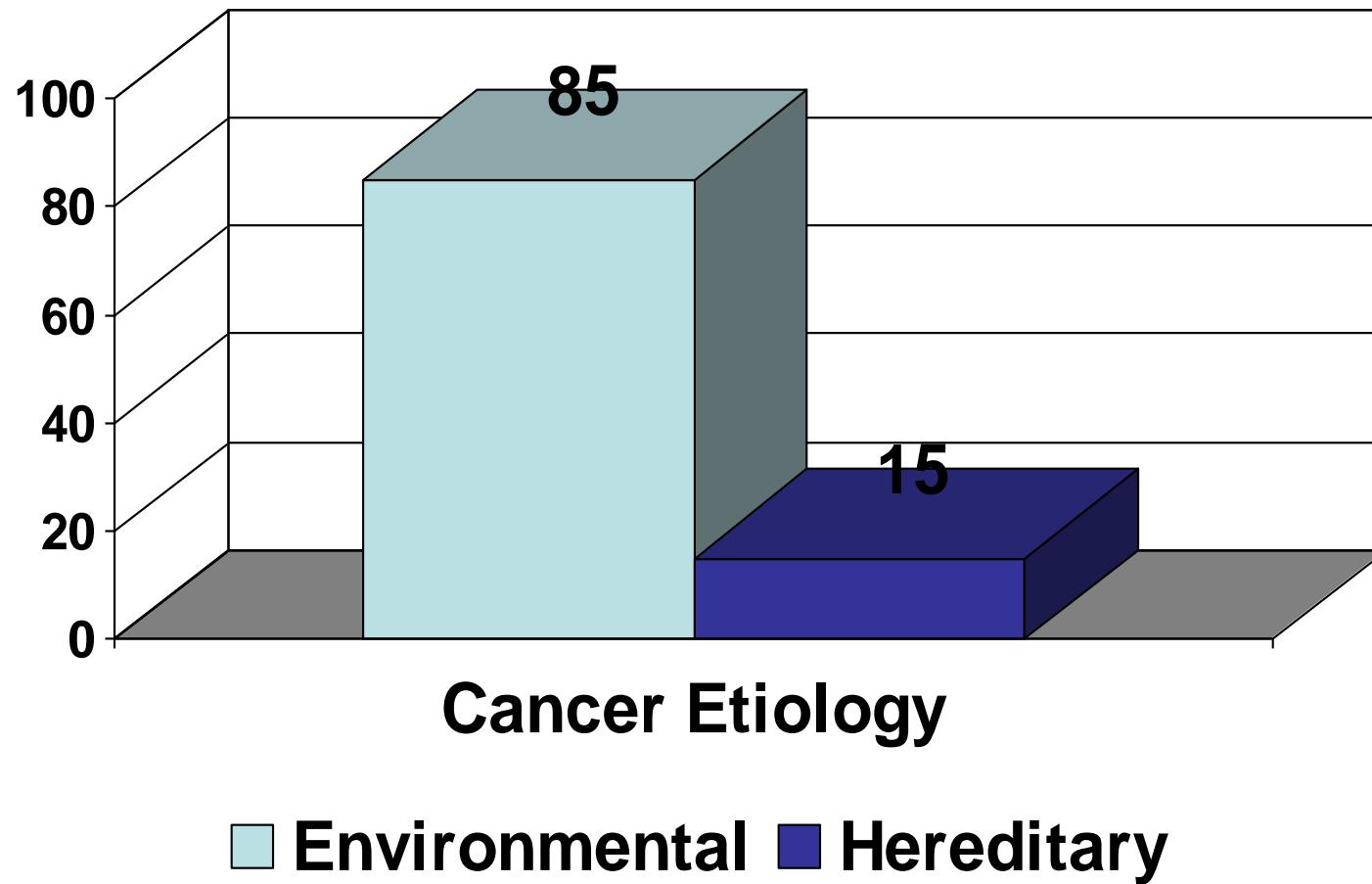
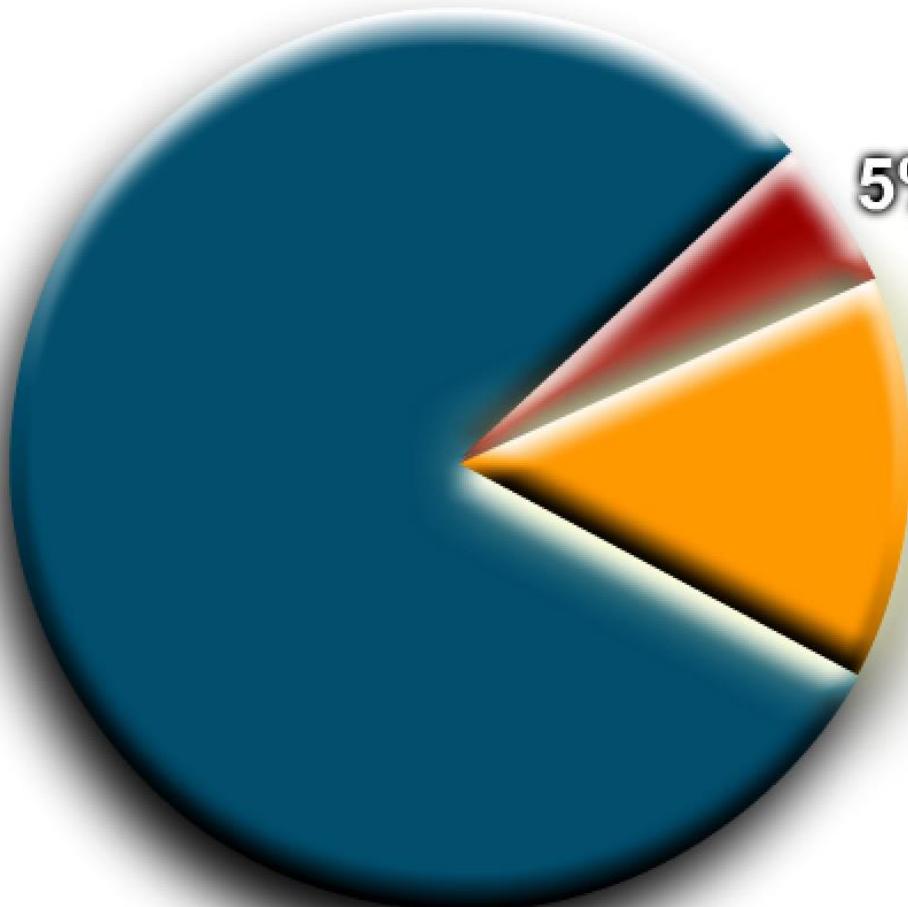


FIGURE 8. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Lung in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

Environmental vs. Hereditary Cancer



Etiology of tumors

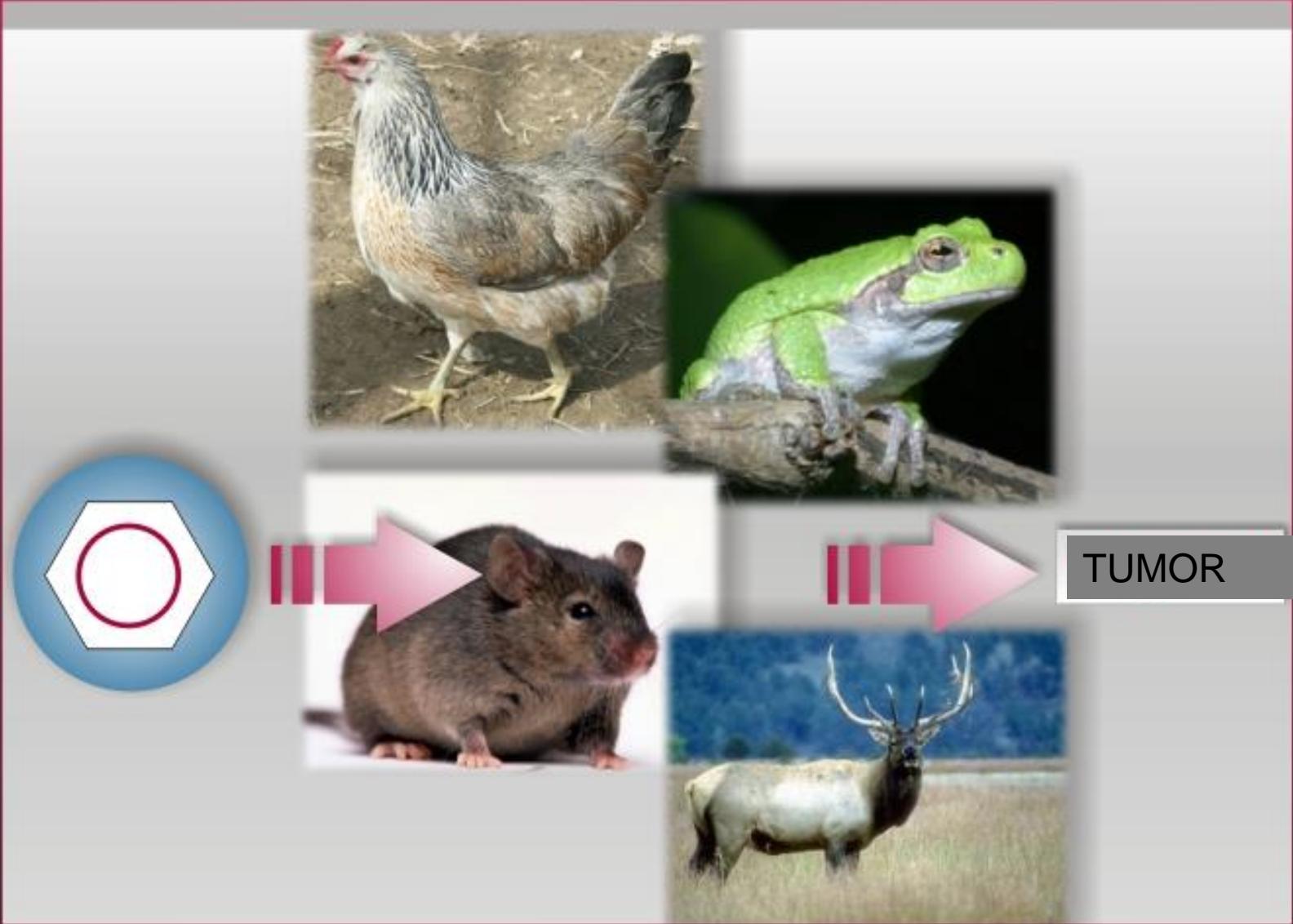


5% baktérium, parazita

15% vírus

GLOBOCAN 2008 (IARC 2010)

Experimental carcinogenesis



Cancer: General Etiology and Pathogenesis

- Etiologic agents:
 - Environmental (chemical, physical, and biological)
 - Hereditary (familial cancer syndromes)
- General mechanisms:
 - Acquired capabilities (self-maintained replication, longer survival, genetic instability, neoangiogenesis, invasion and metastasis)
 - Activation of oncogenes, inactivation of tumor suppressor genes, non-effective DNA repair
 - Caretaker and gatekeeper pathways

Environmental Carcinogens

- A cancer-causing agents
- Three main types:
 - Chemical
 - Physical
 - Biological

Chemical Carcinogenesis

- Firstly described by Sir Percival Pott in 1775
 - Chimney sweeps and scrotal cancer
 - Relationship between occupational exposure to chimney soot and scrotal carcinoma was established

Chemical Carcinogens

- Direct-acting
- Indirect-acting (must be metabolized to activated metabolic forms)

Direct-acting Carcinogens

- Nitrogen mustard
- Nitrosomethylurea
- Benzyl chloride etc.

Indirect-acting Carcinogens

- Polycyclic aromatic hydrocarbons (PAH)
- Produced by incomplete combustion of organic materials
- Present in chimney soot, charcoal-grilled meats, auto exhaust, cigarette smoke
- etc

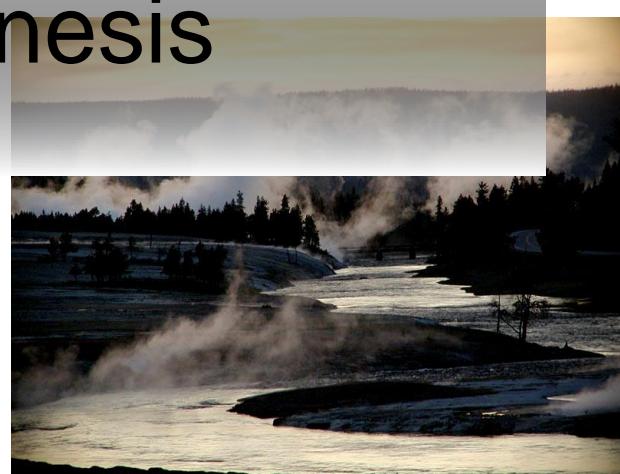
Human Carcinogens - Environmental

- Aflatoxins
- Asbestos
- Benzene
- Cadmium
- Coal tar
- Creosote
- DDT
- Polycyclic aromatic hydrocarbons
- Radon
- Solar radiation

Human Carcinogens - Drugs/therapeutic Agents

- Adriamycin
(doxorubicin)
- Androgenic steroids
- Chlorambucil
- Cisplatin
- Cyclophosphamide
- Cyclosporin A
- Diethylstilbestrol
- Ethylene oxide
- Melphalan
- Tamoxifen

Chemical carcinogenesis



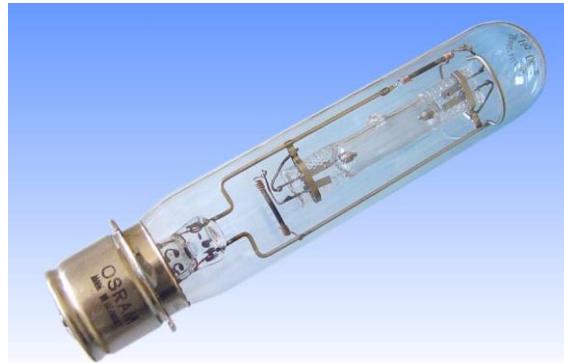
*Polycyclic CH - antracene, benzpyren, tarc, smog,
grilled meat, alcoholic drinks
Amins, anilin dyes
Nitrosamines*

From Prof.Tompa

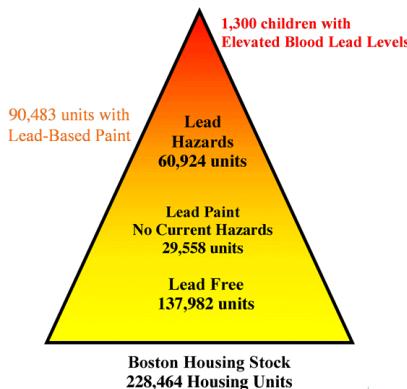


CHEMICAL CARCINOGENESIS

Carcinogenes
Berillium
Cadmium
Lead
Arsene
Asbest



Boston Housing Pyramid



Number of housing units were estimated using national data from Final Report, Volume I of the National Survey, "Analysis of Lead Hazards," Westat for HUD and NIEHS, Revision 6.0, April, 2001.



Chemical carcinogenesis

„Natural” carcinogens”

Aspergillus flavus -
aflatoxin



Safrol
Tee (senecio-pirrolizidin)

Pepper(capsain)

Tannic acide

Betelnuts



Physical Carcinogens

- Ultraviolet light
- Ionizing radiation (X-rays)
- Asbestos

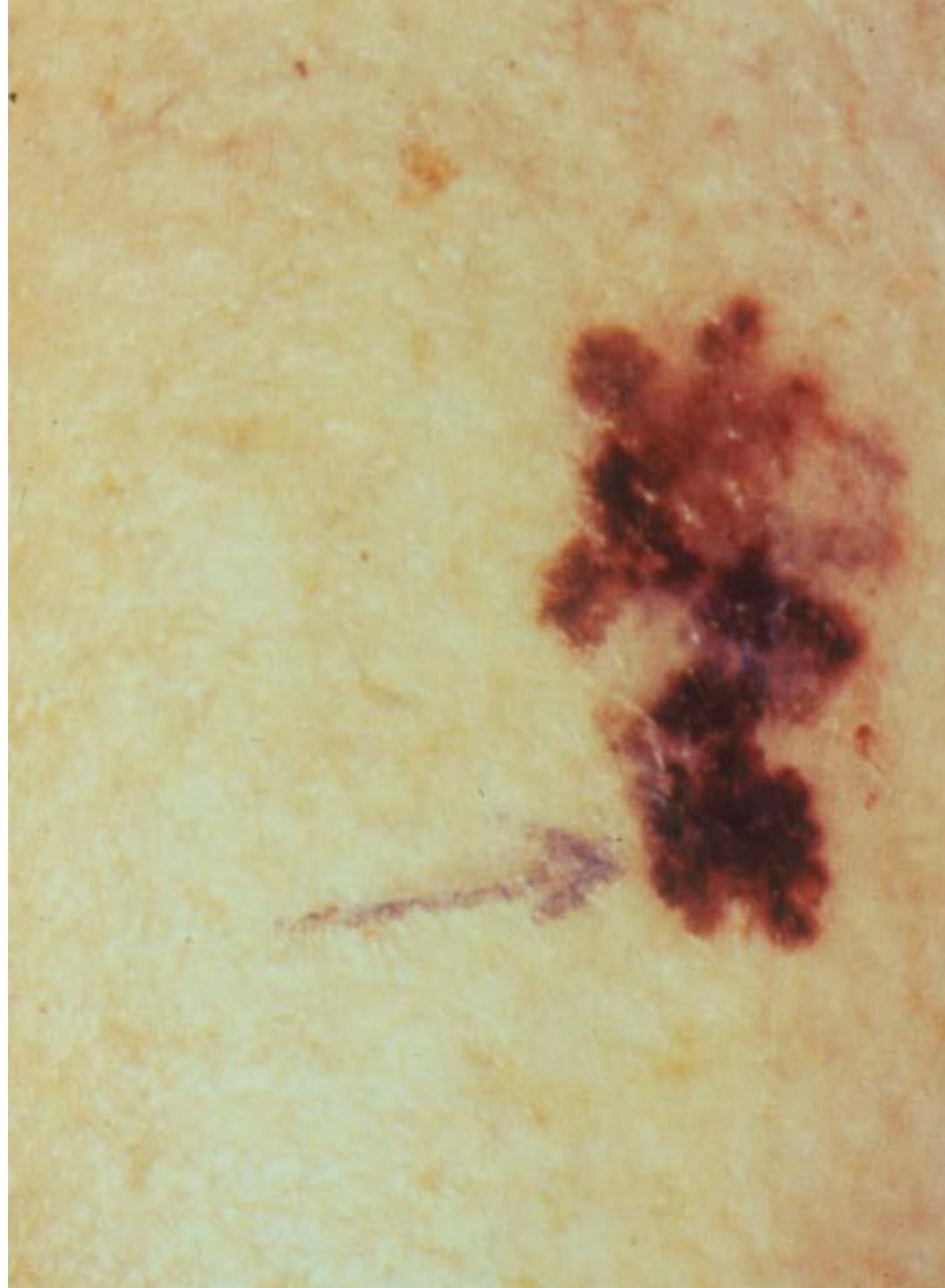
Ionizing Radiation

- Death of pioneer radiation researchers from neoplasms
- High incidence of leukemia among radiologists recognized in 1940s
- Osteosarcoma incidence in radium dial painters
- ...and Chernobyl...etc

Skin cancer is one of the most common human cancer and one of the most preventable

- ~ 10^6 cases of basal cell carcinoma and squamous cell carcinoma are diagnosed per year
- This is more than all other types of cancer combined
- Most of these will be caused by exposure to ultraviolet (UV) irradiation

Malignant melanoma in the skin



Asbestos fibers



Asbestos

- Widely used in construction, insulation, and manufacturing
- Family of related fibrous silicates

Malignant Mesothelioma

- Associated with asbestos exposition
- Mainly occurs in pleural and peritoneal cavities
- Rare in general population
- Latent period of ≥ 20 years

Biological agents

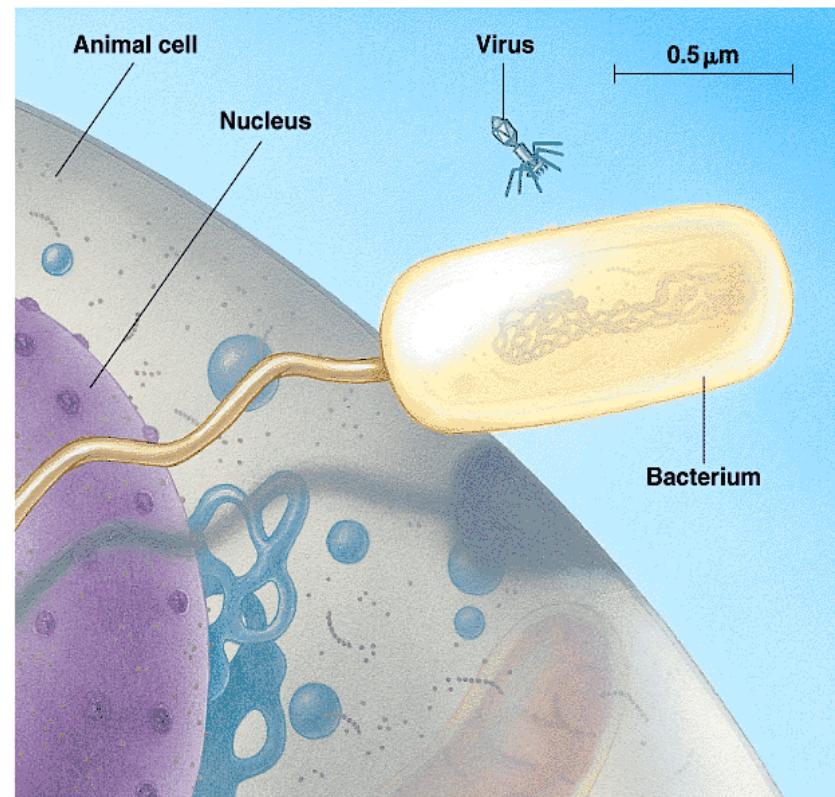
Bacteria

(*Helicobacter pylori*)

Parazites

(Schistosomiasis)

Viruses



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Human cancer-inducing agents

2 200 000 new cancer cases in 2012

- *Bacteria, paracytes*
 - *Helicobacter pylori* (770 million), *Schistosoma haem.*,
Clonorchis s.
- *Vírusok*
 - Hepatitis B virus (HBV) (257 million)
 - hepatocellular carcinoma (HCC)
 - Hepatitis C virus (HCV) (71 million)
 - hepatocellular carcinoma (HCC)
 - Human papillomaviruses (HPV) (640 million)
 - cervical, anogenital, head and neck cc, verruca stb.
 - Herpes viruses
 - Epstein-Barr virus (EBV) – Burkitt lymphoma (120 000)
 - Human herpes virus 8 (HHV8) – Kaposi sarcoma
 - Human T-cell leukemia
 - HIV (indirect?)
 - NHL, HL, KS

Plummer et al. Lancet 4:e609-616, 2016
WHO Global Hepatitis Report, 2017

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WHO Global Hepatitis Report, 2017

Helicobacter Pylori

- 1983. Campylobacter pylori
- Gram neg rods
- urease production- diagnostic testing!
- Associated with
 - chr. gastritis,
 - peptic ulcer disease,
 - **gastric carcinoma,**
 - **gastric MALT lymphoma**
- **Antibiotic therapy** and proton pump inhibitors

Human Oncogenic Viruses (DNA and RNA)

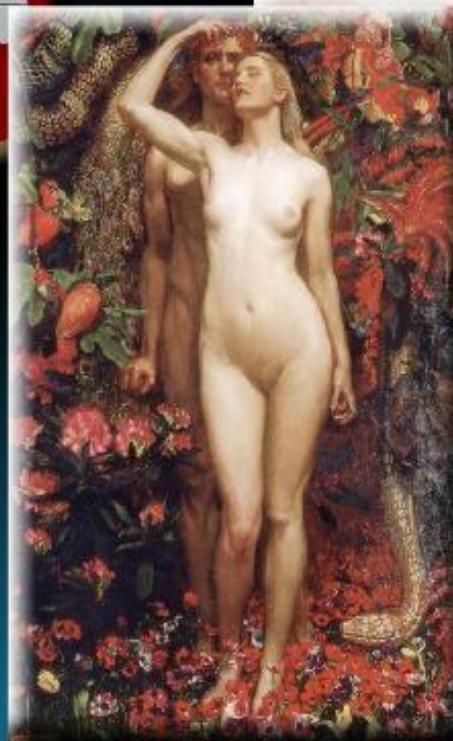
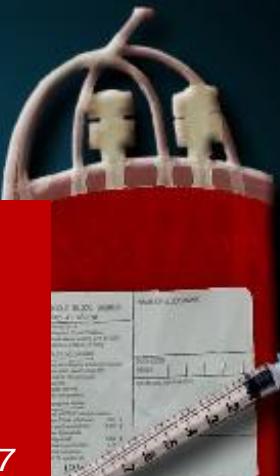
- Hepatitis B virus (HBV, DNA)
 - HCC
- Hepatitis C virus (HCV, RNA)
 - HCC
- Human papillomaviruses (HPV, DNA)
 - cervical, anogenital, head and neck cc, papillomas, condylomas
- Herpes viruses (DNA)
 - Epstein-Barr Virus (EBV) – Burkitt lymphoma
 - Human herpesvirus 8 (HHV8) – Kaposi sarcoma
- Retroviruses - HTLV-I - Human T cell leukaemia
- HIV (indirect?) – NHL, HL, KS



HBV

- **257** millio chronic HBV infected patients
- 3,5% of the world population

WHO Global Hepatitis Report 2017

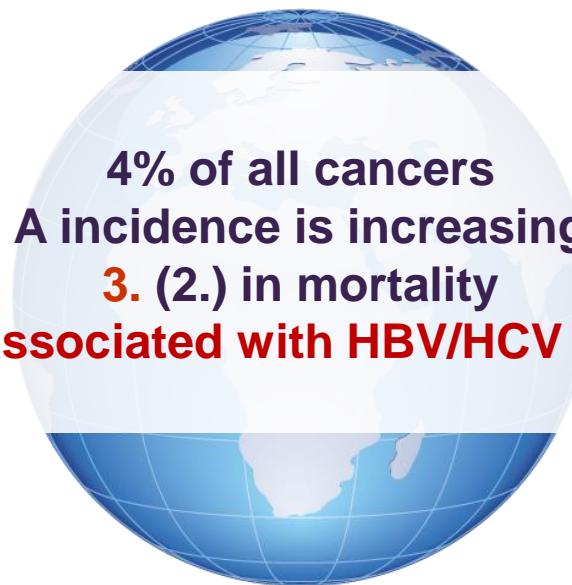
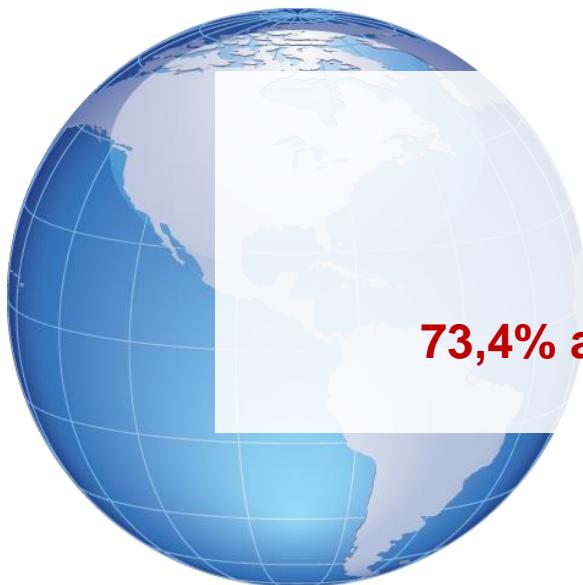


- **257** million chronic HBV infected
- 0,1%-6,2%
 - Far-East: 6,2%
 - Africa: 6,1%
 - East-Mediterraneum: 3,3%
 - South-East Asia: 2,0%
 - Europe: 1,6%
 - America: 0,7%

*WHO Global Hepatitis Report
2017*



Hepatocellular carcinoma, HCC



**4% of all cancers
A incidence is increasing
3. (2.) in mortality
73,4% associated with HBV/HCV infection**

Hepatocellular carcinoma, HCC



**2002: HCC incidence 626 162
mortality 598 321**
**2008: HCC incidence 750 000
mortality 695 000**
**2013: HCC incidence 818 000
mortality 792 000**
2018: HCC incidence 841 080



Hepatocarcinogenesis

Etiological factors

Metabolic diseases

HCC

ethanol

androgenes

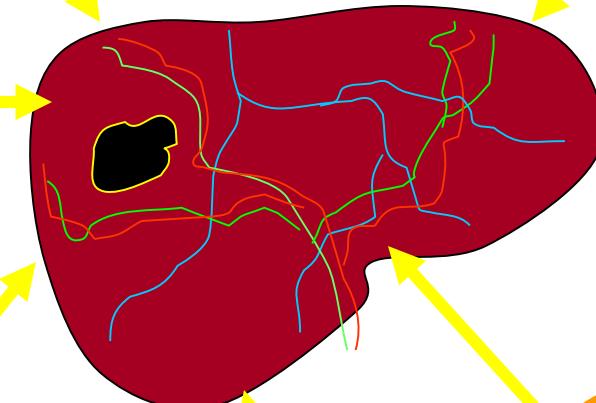
Mutagen agents

Cirrhosis !

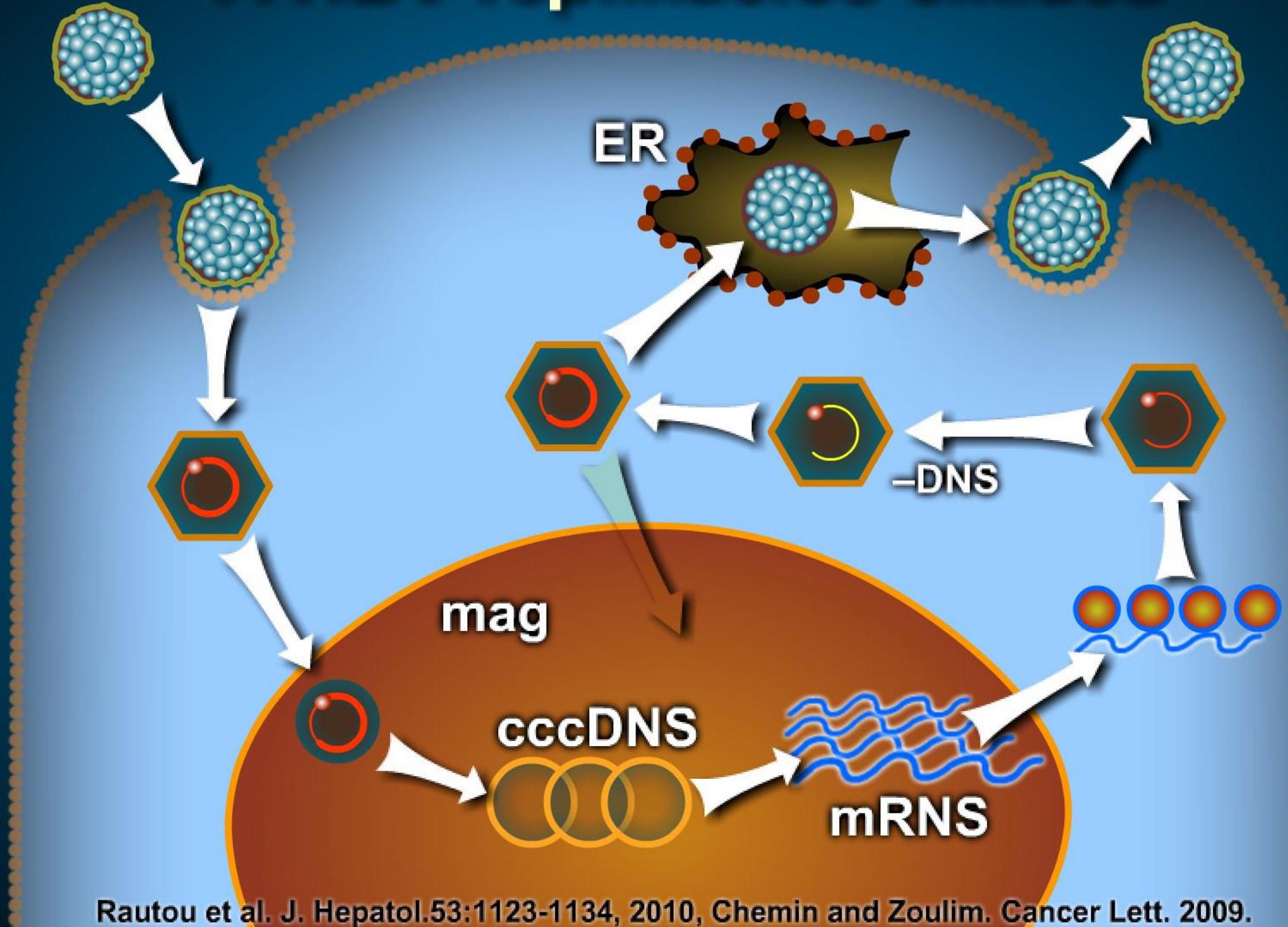
Schistosomiasis

HBV, HCV

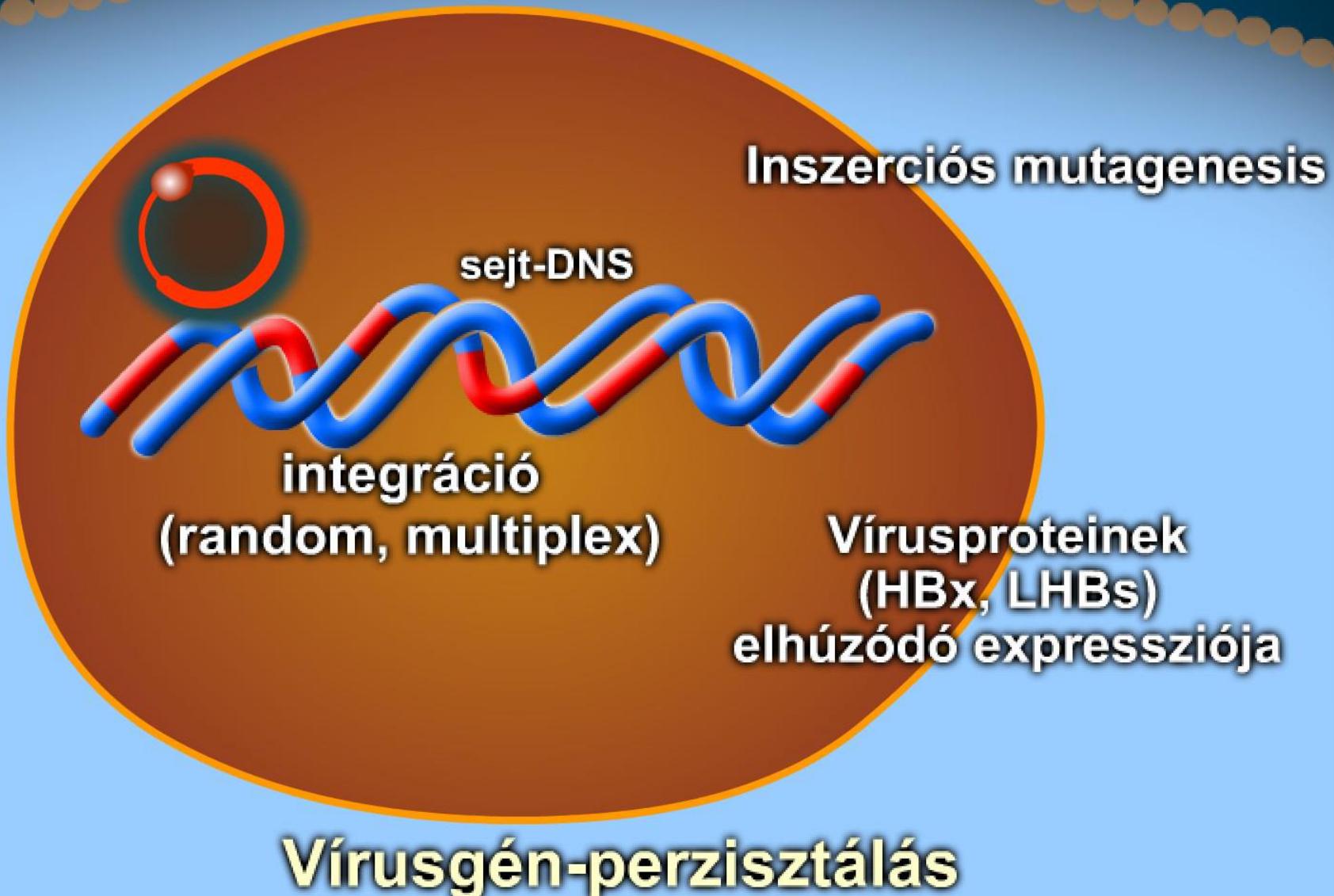
Aflatoxin

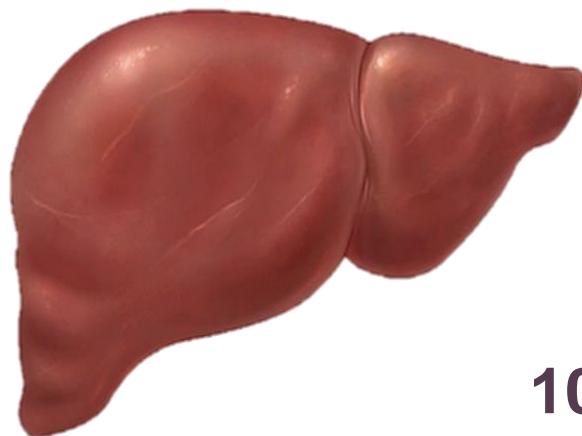


A HBV replikációs ciklusa

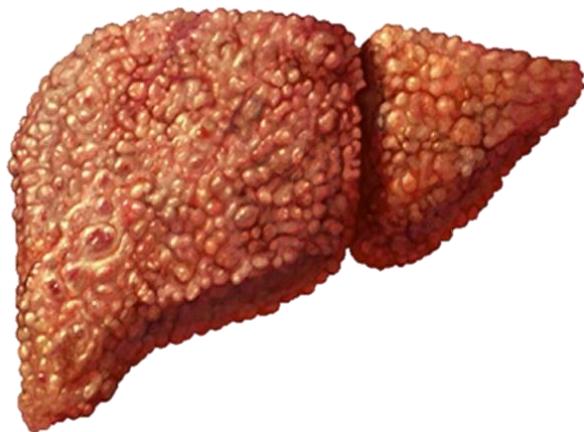


A HBV replikációs ciklusa





10-20 yrs

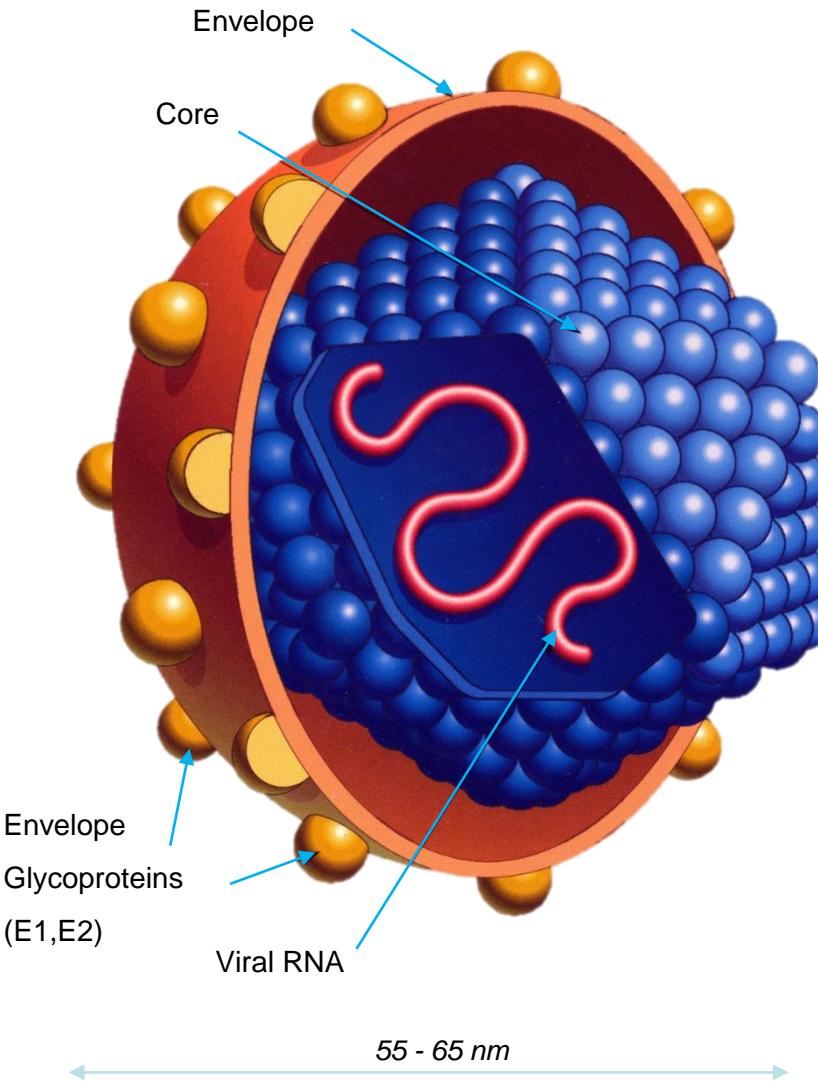


HBV

10%
Chronic hepatitis

Cirrhosis

HCC



Hepatitis C virus (HCV)

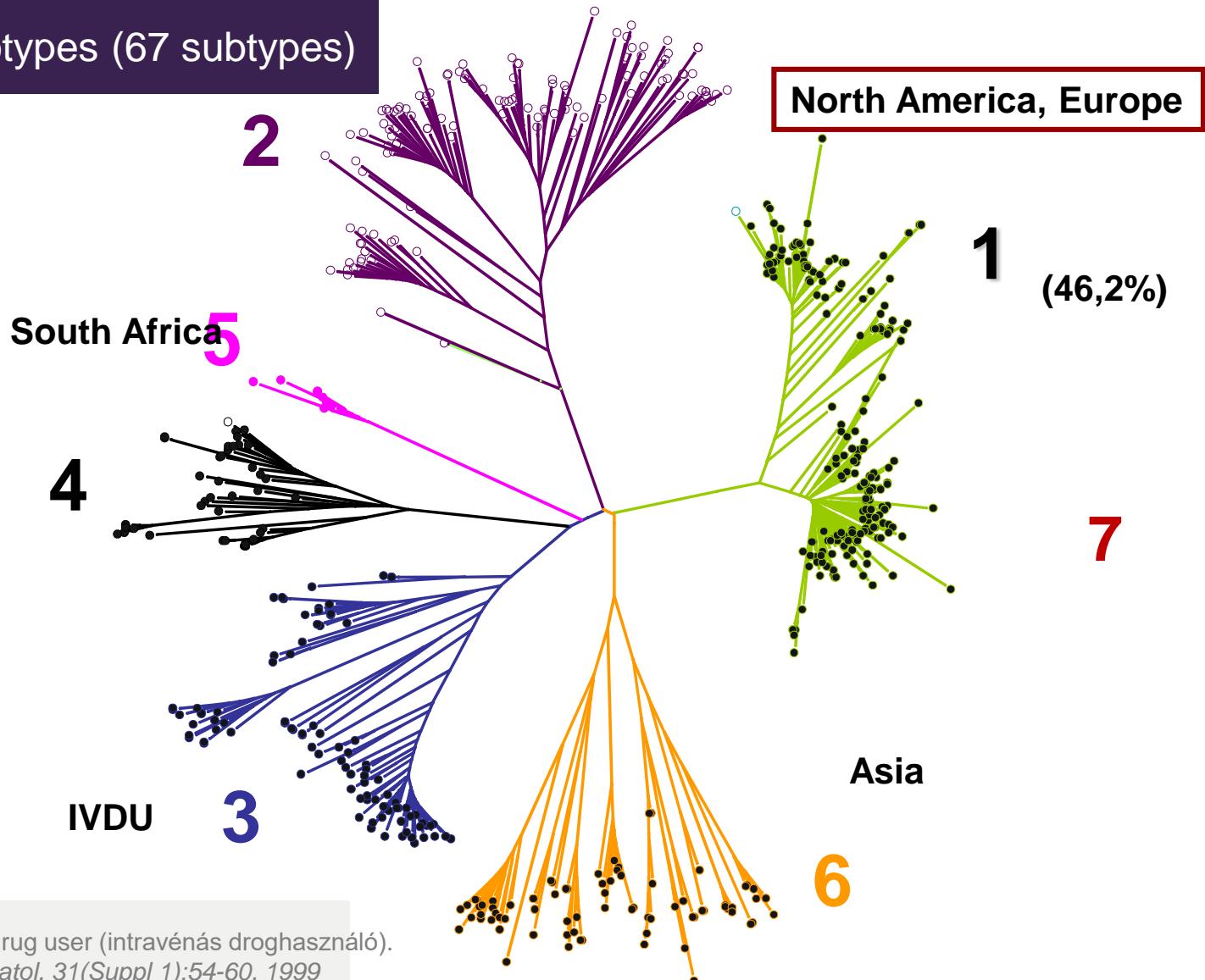
Hepacivirus

Flaviviridae

ssRNS

High genomic variability(7 genotípus, 67+20 szubtípus)

7 HCV genotypes (67 subtypes)

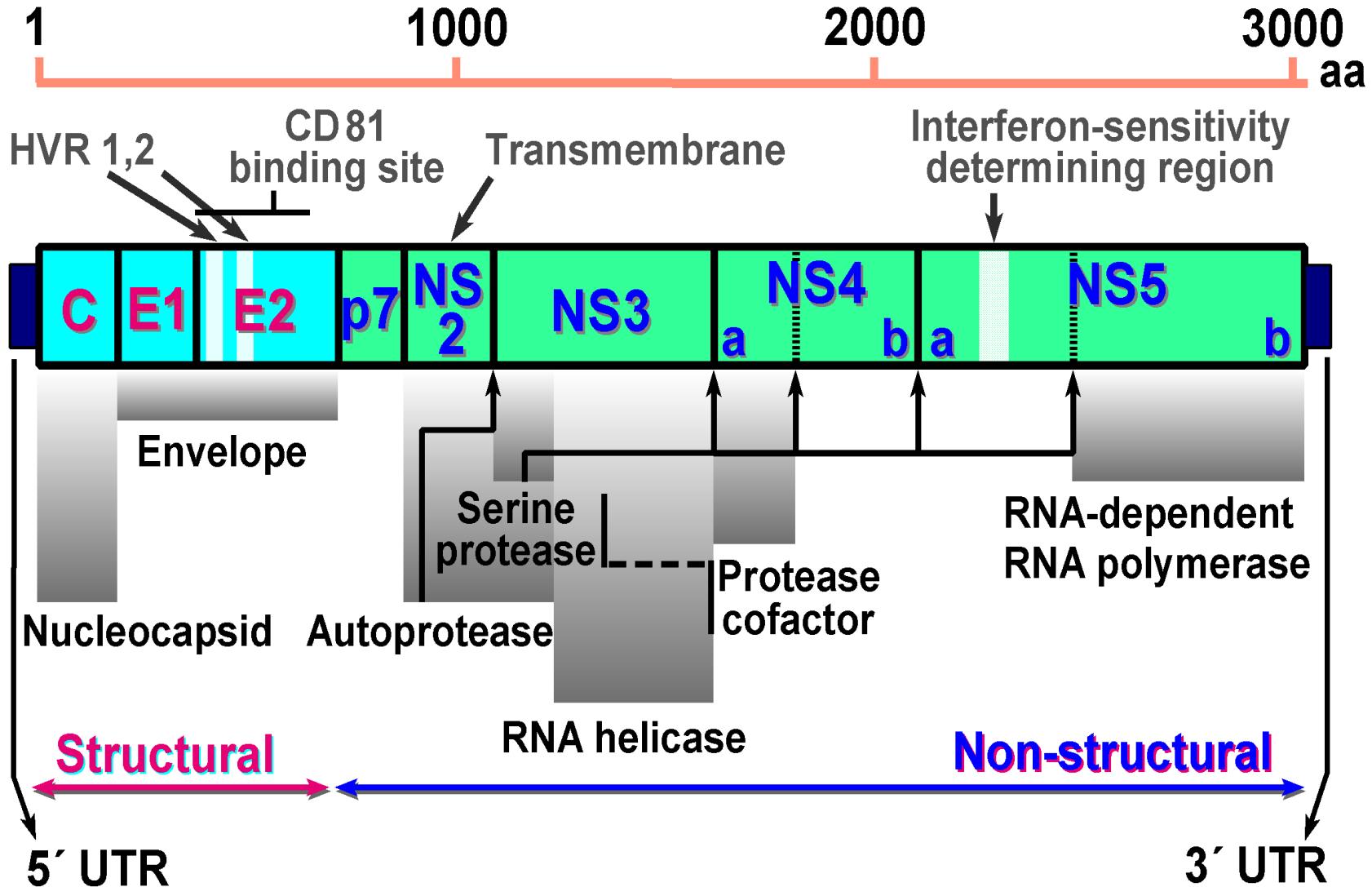


IVDU=intravenous drug user (intravénás droghasználó).

Simmonds P. *J Hepatol.* 31(Suppl 1):54-60, 1999

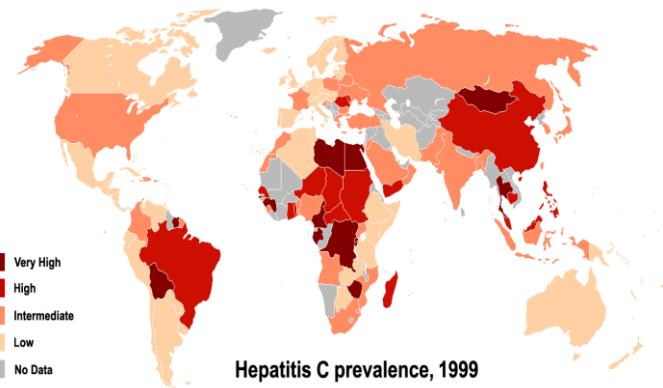
Murphy et al. *J.Clin.Microbiol.* 53:967-972, 2015

Structure of HCV genome



Epidemiology of HCV infection

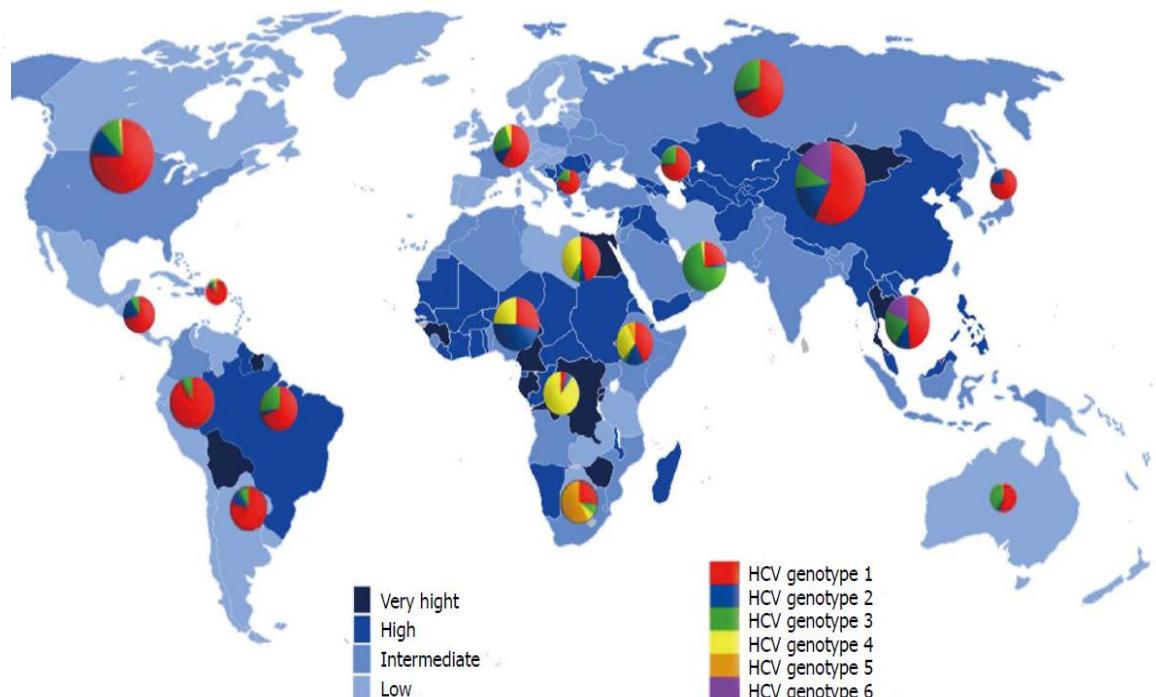
Chronic infection: 71 millió, 1% of world population



Highest: in Egypt e(14,7%)

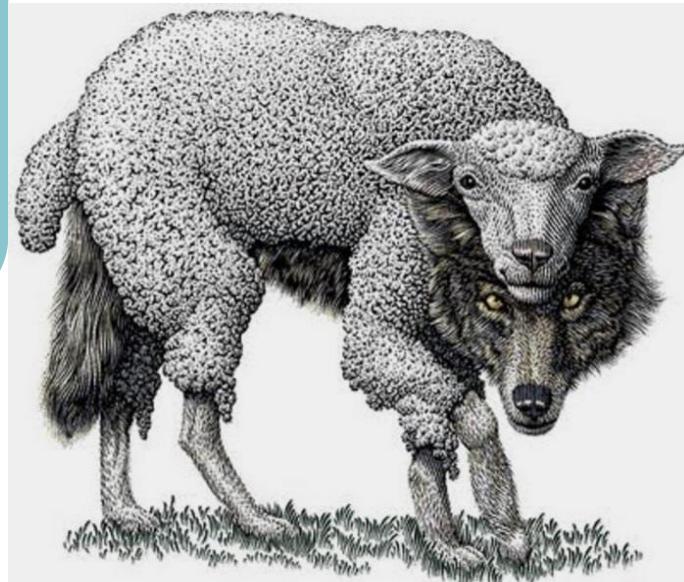
Middle-East-Europe

- **Low (0,2-1,0%):** Cseh, Alban, Croatia, **Hungary**
- **Middle (1,4%):** Poland, Bulgaria
- **High (2,3-3,3%):** Ukraina, **Romania**



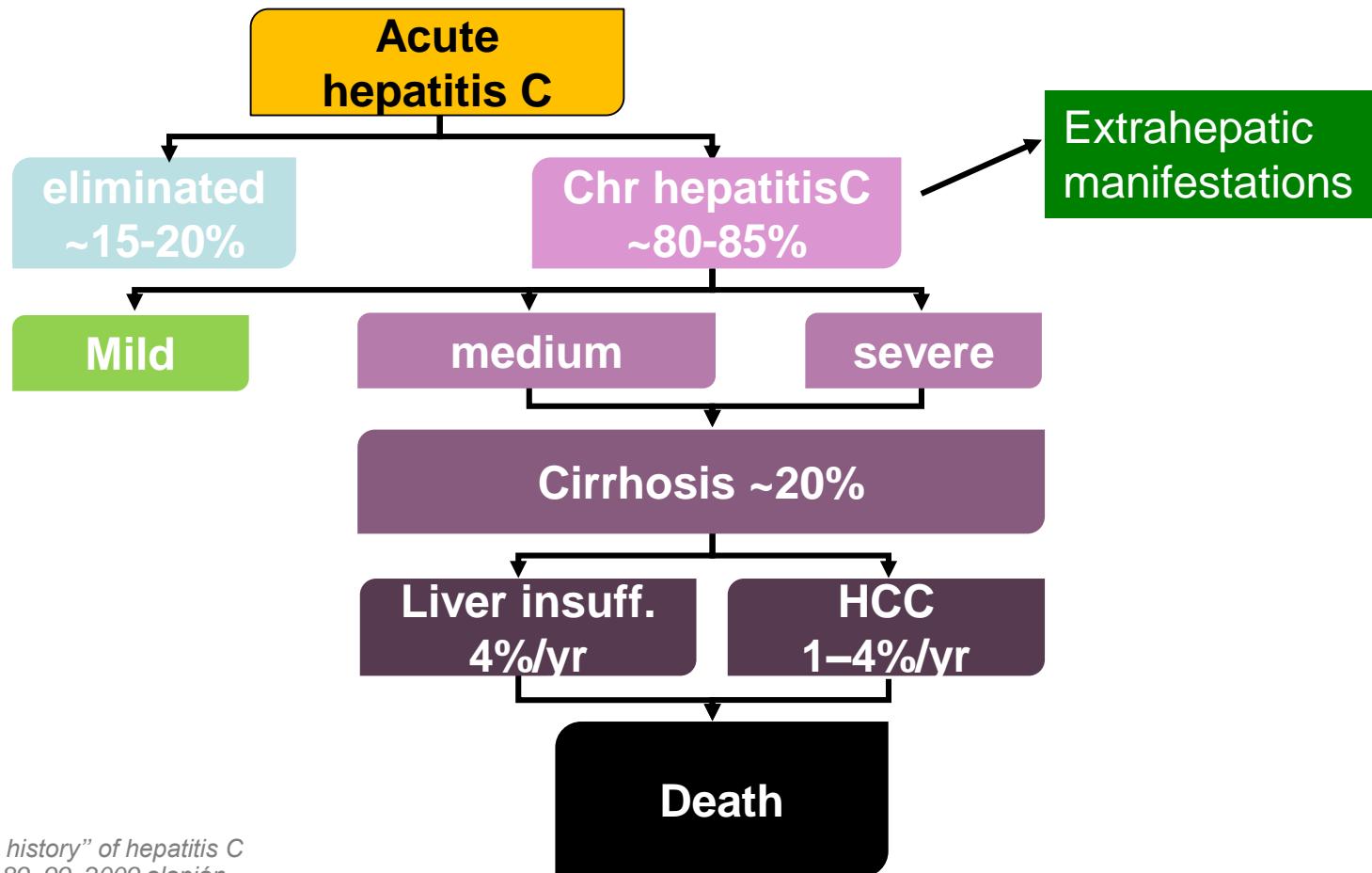
HCV: „wolf in lamb's clothing – wolf in sheep's clothing”

- Milder and more prolonged (15-30 év)
- Transmission: transfusion, sexual (rare), perinatal (rare)



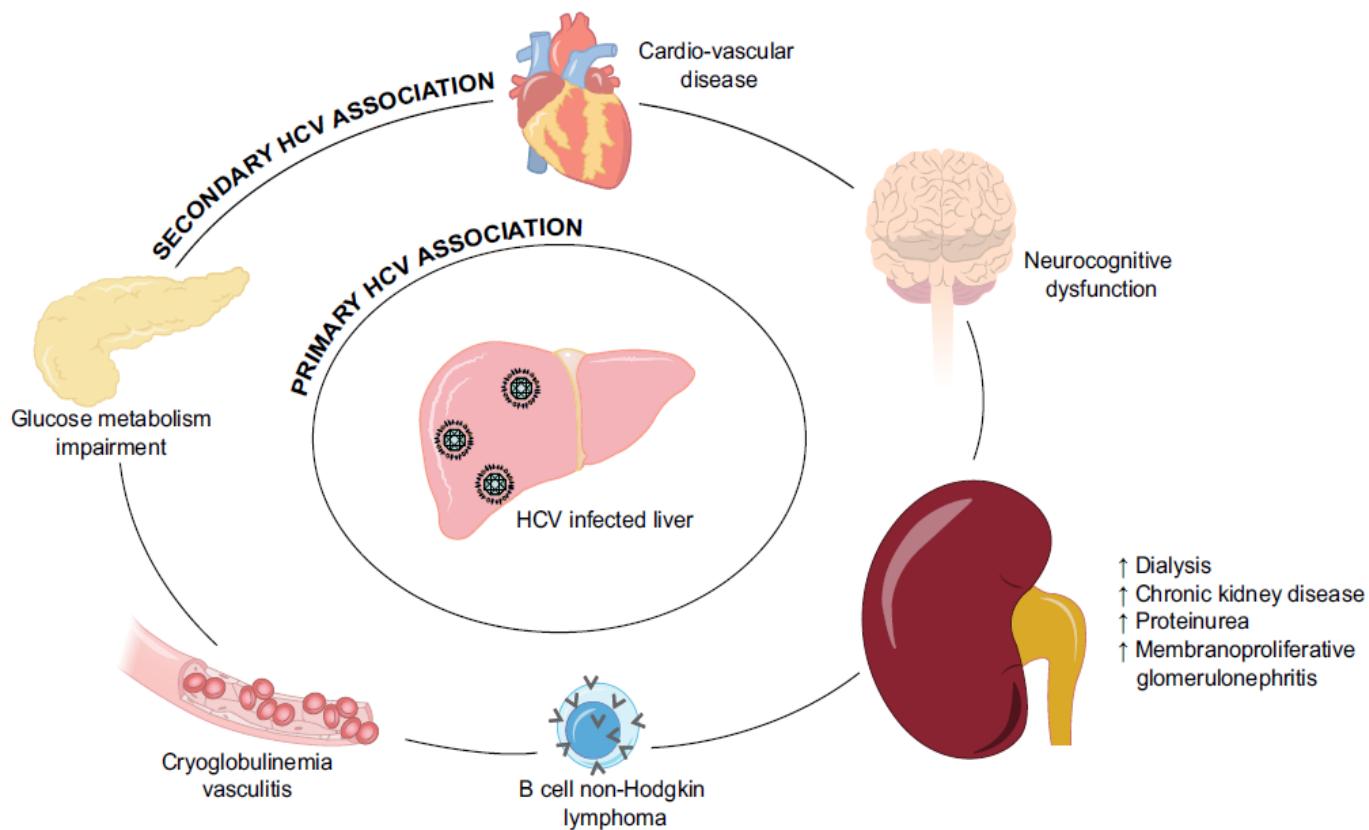
- 71 million infected
- 80% progression into chronicity
- No vaccine

HCV-infection: progression

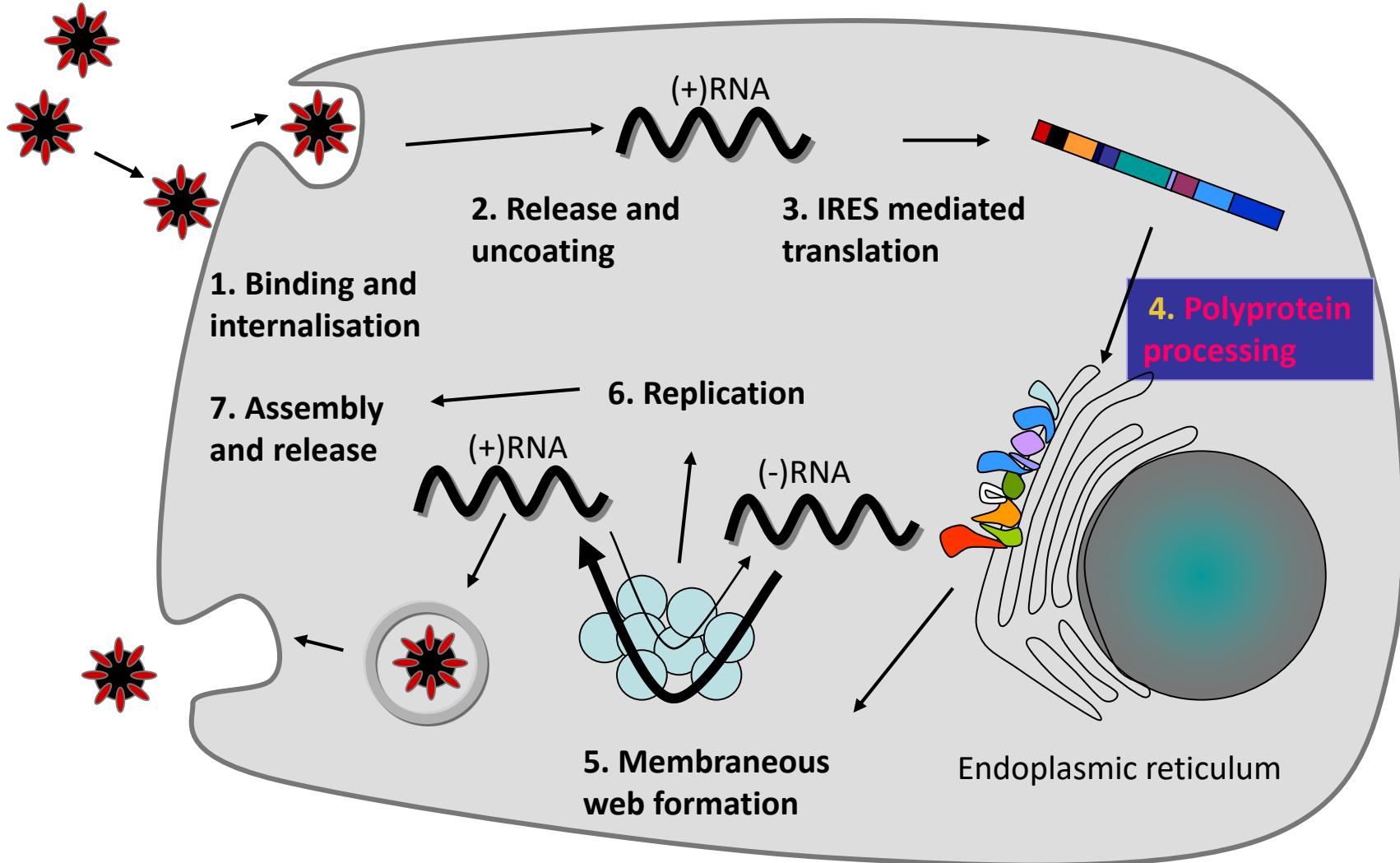


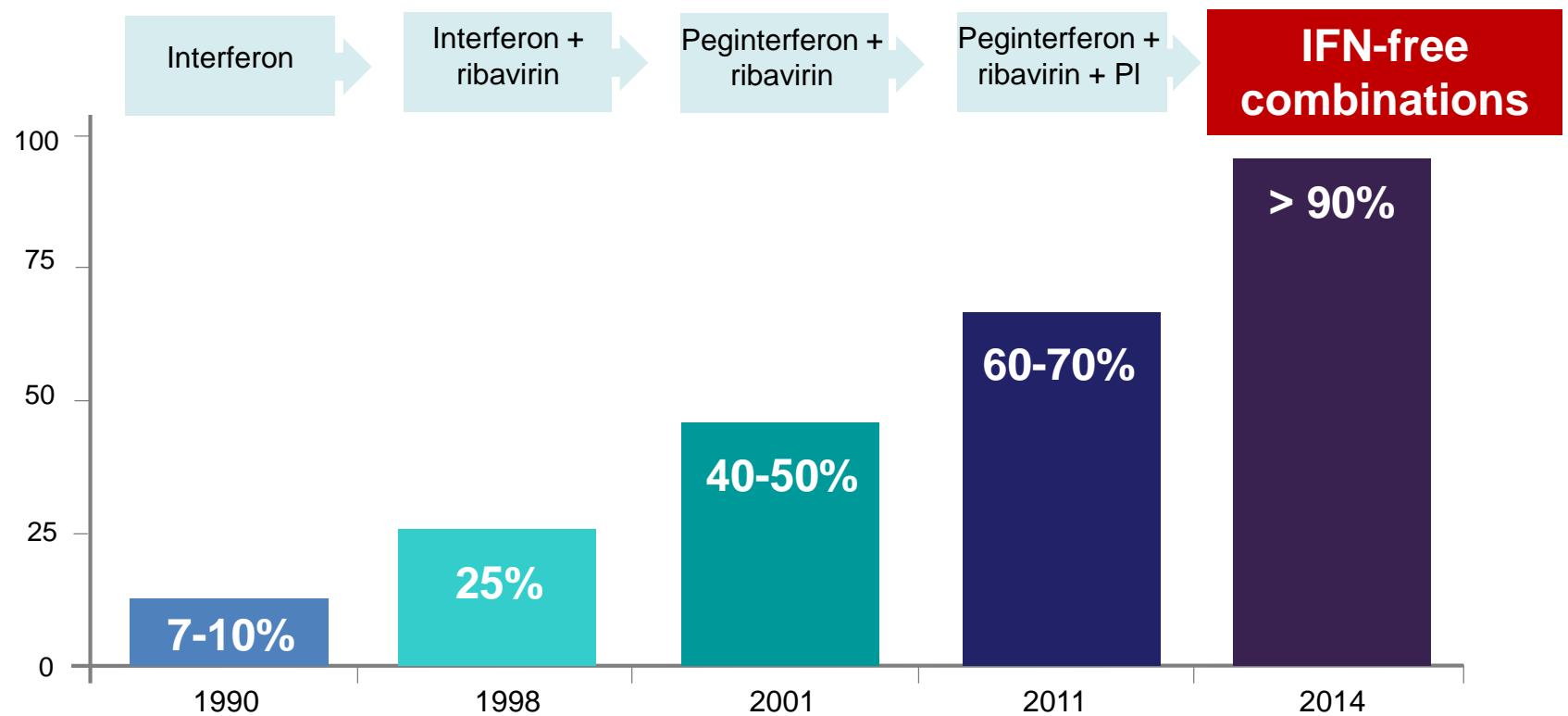
Seeff LB. The history of the “natural history” of hepatitis C (1968-2009). Liver Int. 29 (suppl 1): 89–99, 2009 alapján.

Extrahepatic manifestations



Life Cycle of HCV and Potential Direct Acting Antiviral (DAA) Targets





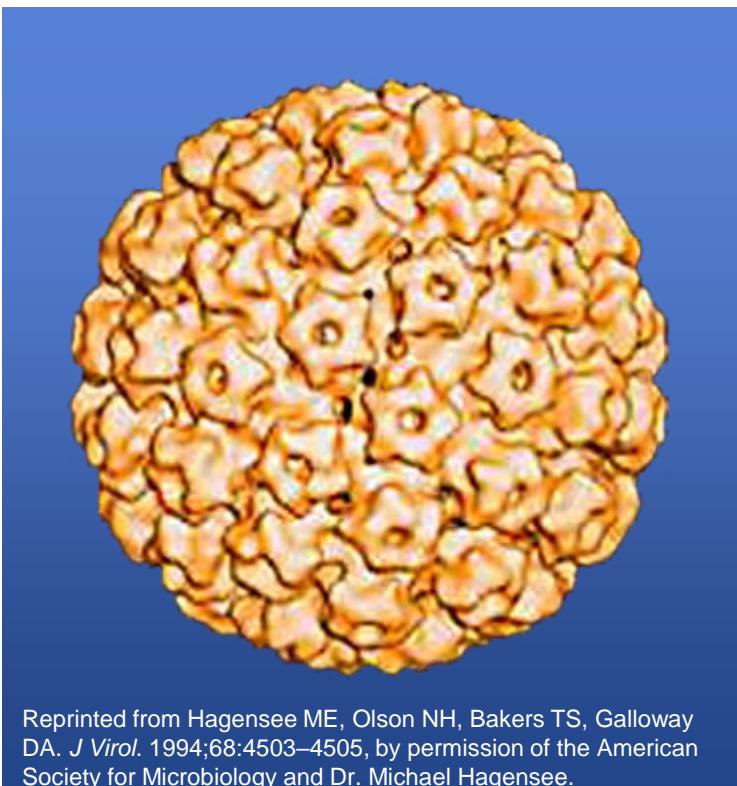
Webster et al. Lancet 385(9973):1124-1135, 2015 alapján

Human papilloma virus (HPV)

- Over 100 subtypes
- Small DNA virus with small double-stranded circular genome
- Subtypes possess varying degrees of
 - low
 - immediate
 - high risk

HPV

Nonenveloped double-stranded DNA virus¹



Reprinted from Hagensee ME, Olson NH, Bakers TS, Galloway DA. *J Virol.* 1994;68:4503–4505, by permission of the American Society for Microbiology and Dr. Michael Hagensee.

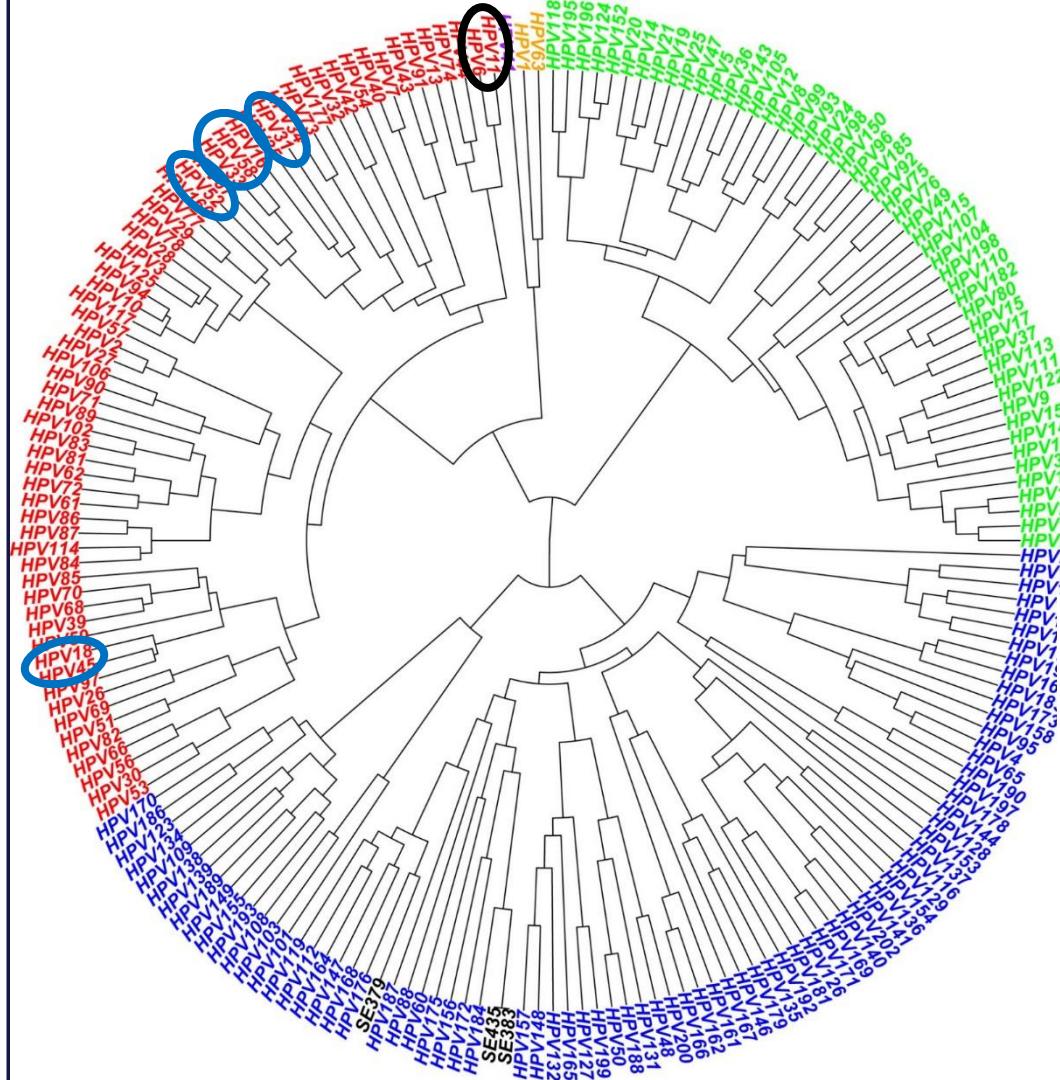
- >100 types identified²
- ~30–40 anogenital^{2,3}
 - ~15–20 high risk*,^{2,3}
 - **HPV 16 and HPV 18** types account for the majority of worldwide cervical cancers.⁴
 - Low risk
 - **HPV 6 and 11** are most often associated with external anogenital warts.³

*High risk; ** Low risk

1. Howley PM, Lowy DR. In: Knipe DM, Howley PM, eds. Philadelphia, Pa: Lippincott-Raven; 2001:2197–2229.
 2. Schiffman M, Castle PE. *Arch Pathol Lab Med.* 2003;127:930–934.
 3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis.* 2002;35(suppl 2):S210–S224.
 4. Muñoz N, Bosch FX, Castellsagué X, et al. *Int J Cancer.* 2004;111:278–285.
- Reprinted from *J Virol.* 1994;68:4503–4505 with permission from the American Society for Microbiology Journals Department.

HPV típusok

- 198 human papillomavirust azonosítottak
- kb. 40 típus okoz anogenitális fertőzést
- Onkogenitás alapján high risk (HR) és low-risk (LR) típusok ismertek
- 12 típus HR
- A természetes fertőzés nem hoz létre immunitást a reinfekcióval szemben



HPV types according to carcinogenecity

Species	Types							
α5	26	51	69	82				
α6	30	53	56	66				
α7	18	39	45	59	68	70	85	97
α9	16	31	33	35	52	58	67	
α11	34	73						

Adapted from IARC [1].

Group 1 carcinogens.

Group 2A carcinogens.

Group 2B carcinogens.

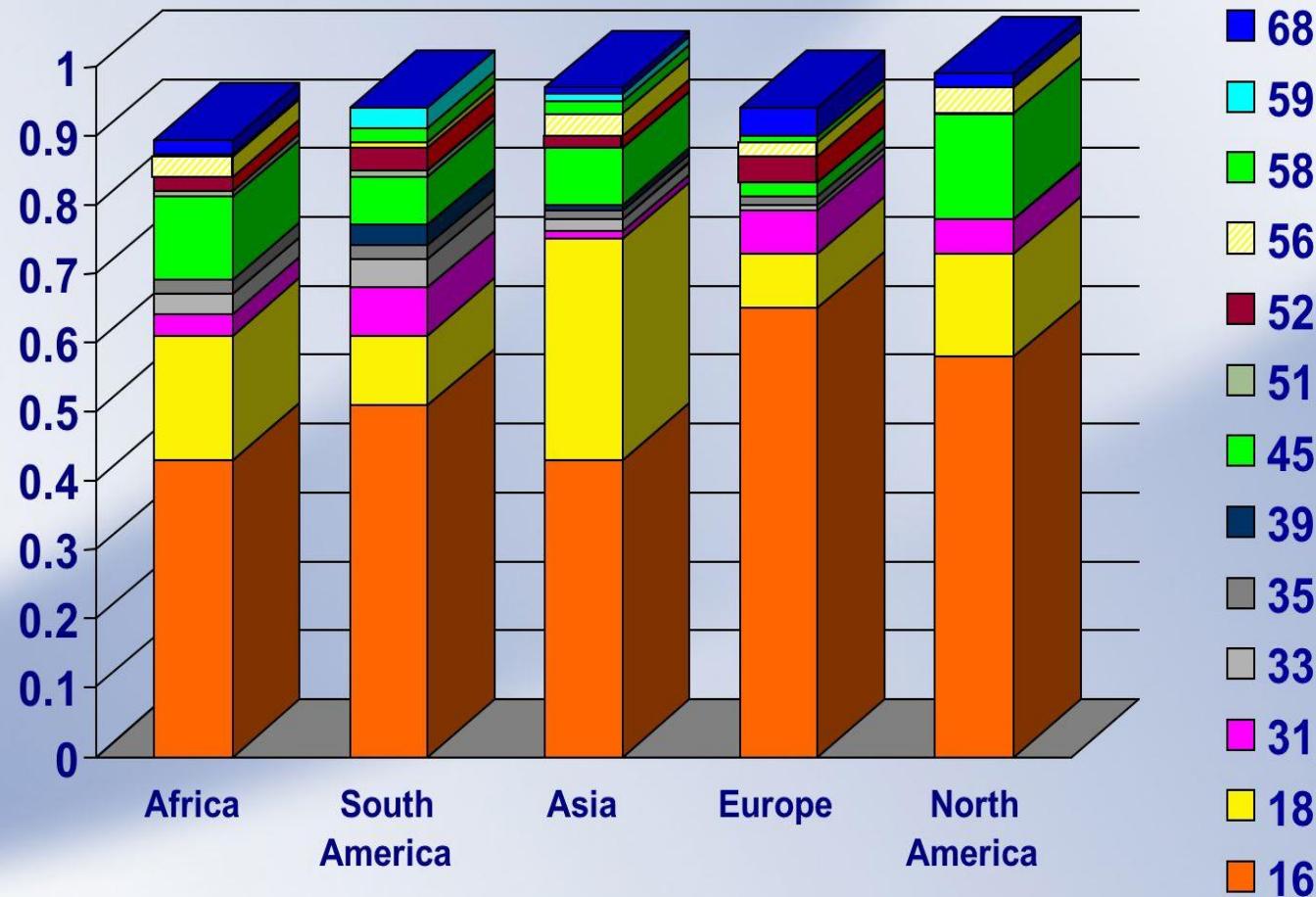
Phylogenetic analogy with carcinogenic types.

Low and High Risk HPV

- HPV subtypes classified as low risk or high risk based on whether the genital tract lesions with which these HPVs are associated are at significant risk for malignant progression
 - High risk: 16, 18, 31, 33, 35 (15 types)
 - Intermediate: 26, 53, 66
 - Low risk: 6, 11, 40, 42

HPV Types in Cervical Cancer by Region

15 types are associated with cervical cancer

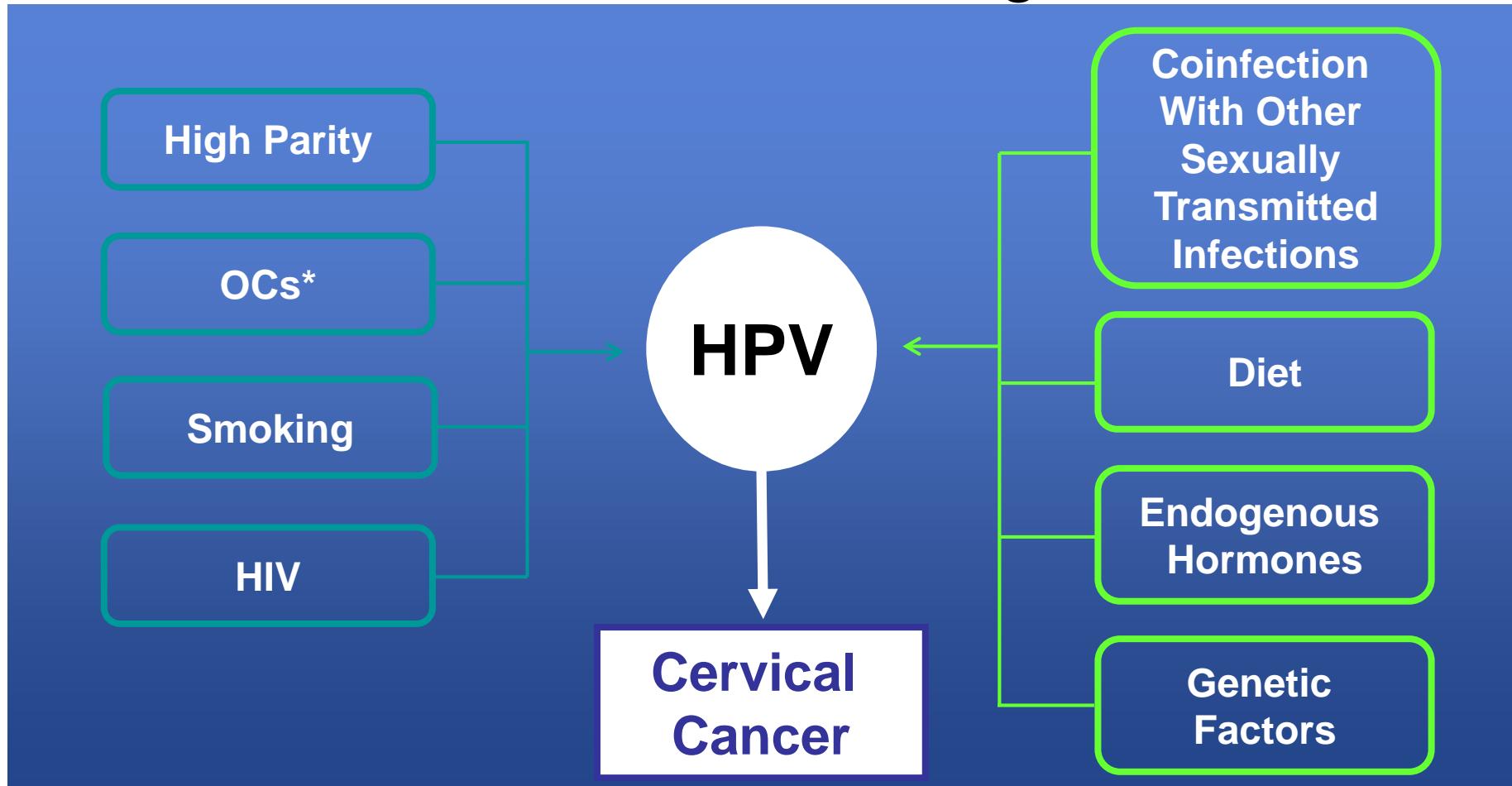


Cervical cancer incidence and mortality (2002)



- Incidence (worldwide) = 481,480
- Mortality (WW) = 267,752

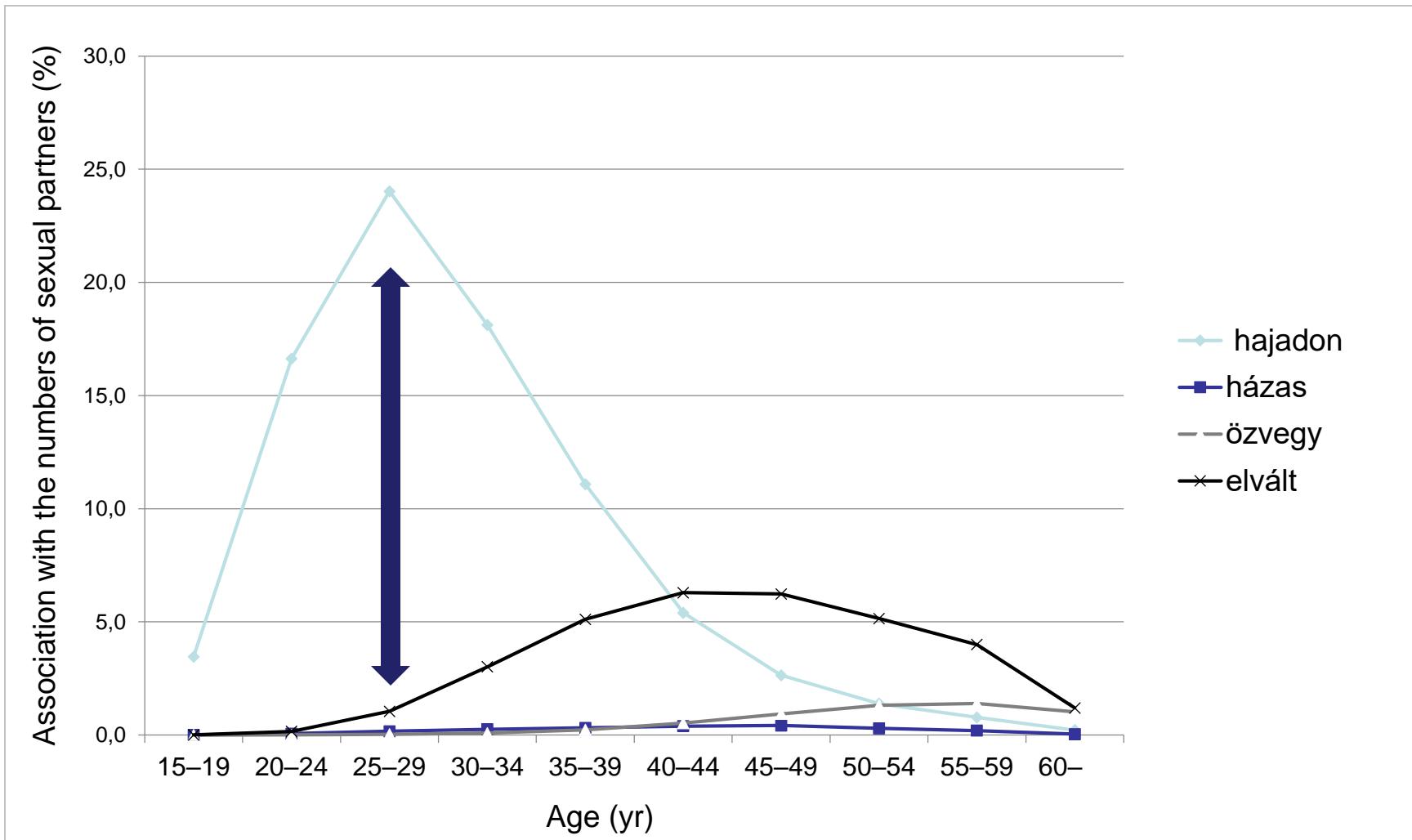
Established and Potential Cofactors Involved in HPV Carcinogenesis¹



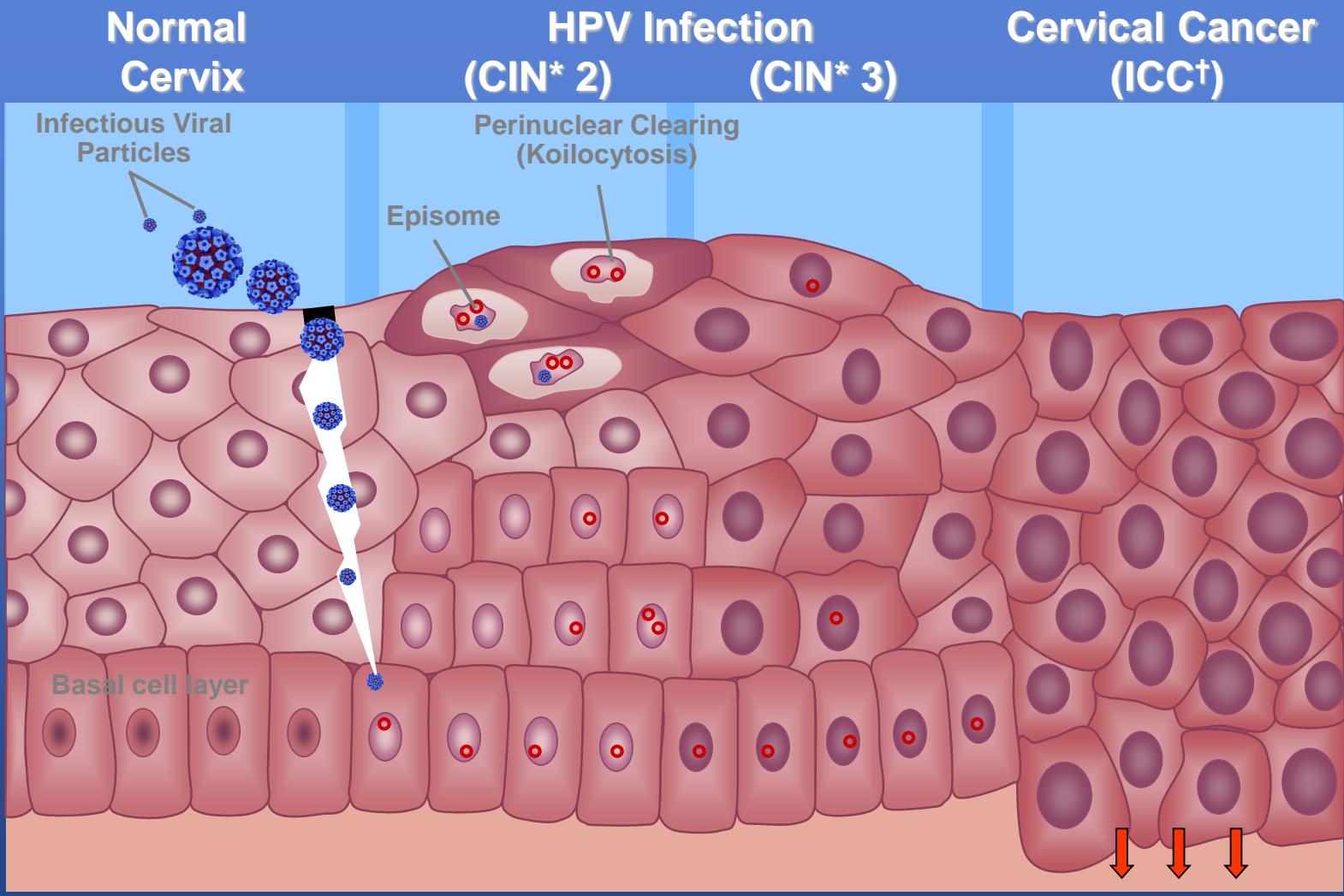
*OCs = oral contraceptives

1. Castellsagué X, Muñoz N. *J Natl Cancer Inst Monogr*. 2003;31:20–28.

HPV infection in adult females



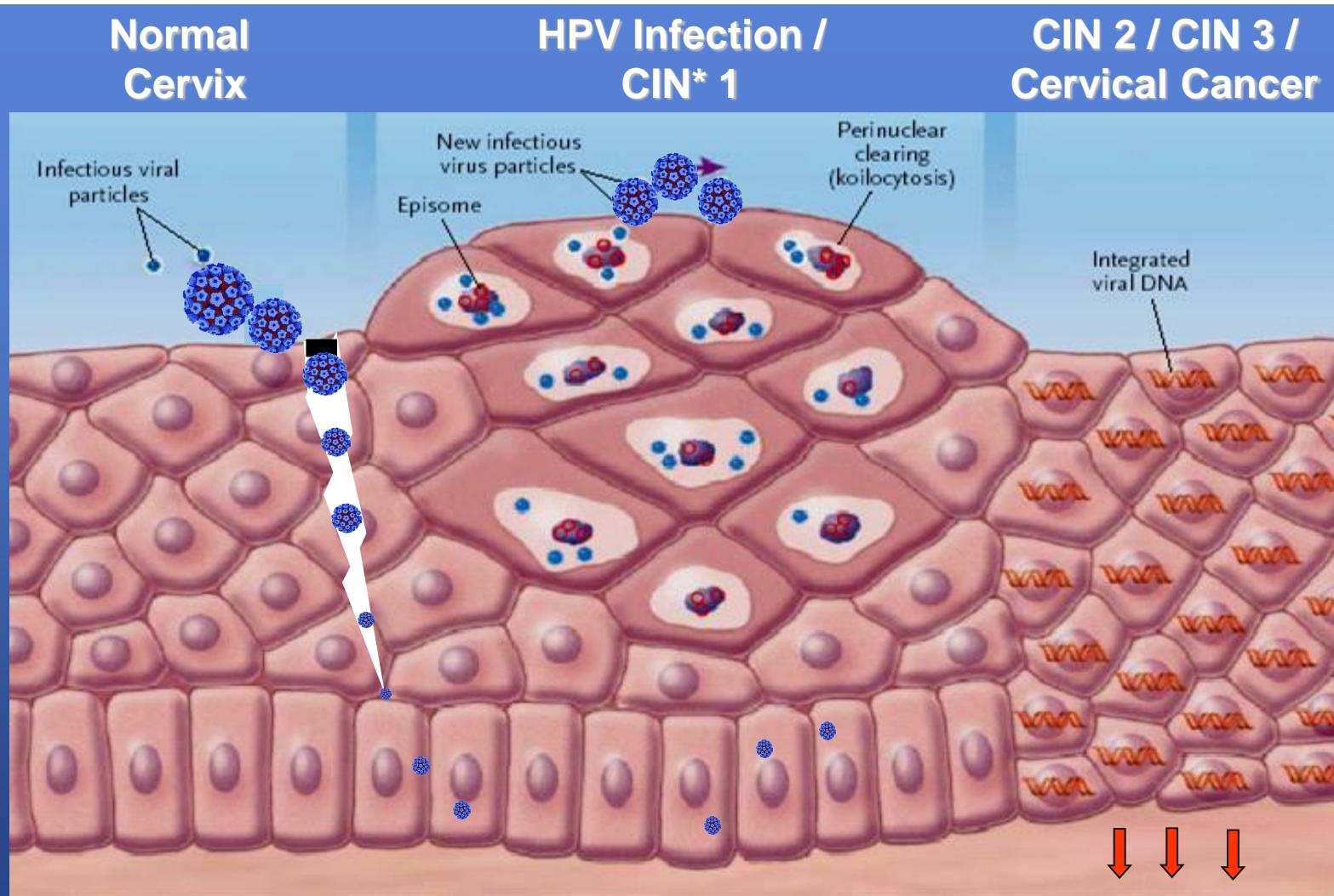
HPV Infection: „High-Grade Lasions”^{1–3}



*CIN = cervical intraepithelial neoplasia; †ICC = invasive cervical cancer

1. Goodman A, Wilbur DC. *N Engl J Med.* 2003;349:1555–1564. Adapted with permission from the Massachusetts Medical Society.
2. Doorbar J. *J Clin Virol.* 2005;32(suppl):S7–S15.
3. Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. *Clinical Virology*. 2nd ed. Washington, DC: American Society for Microbiology Press; 2002:557–596.

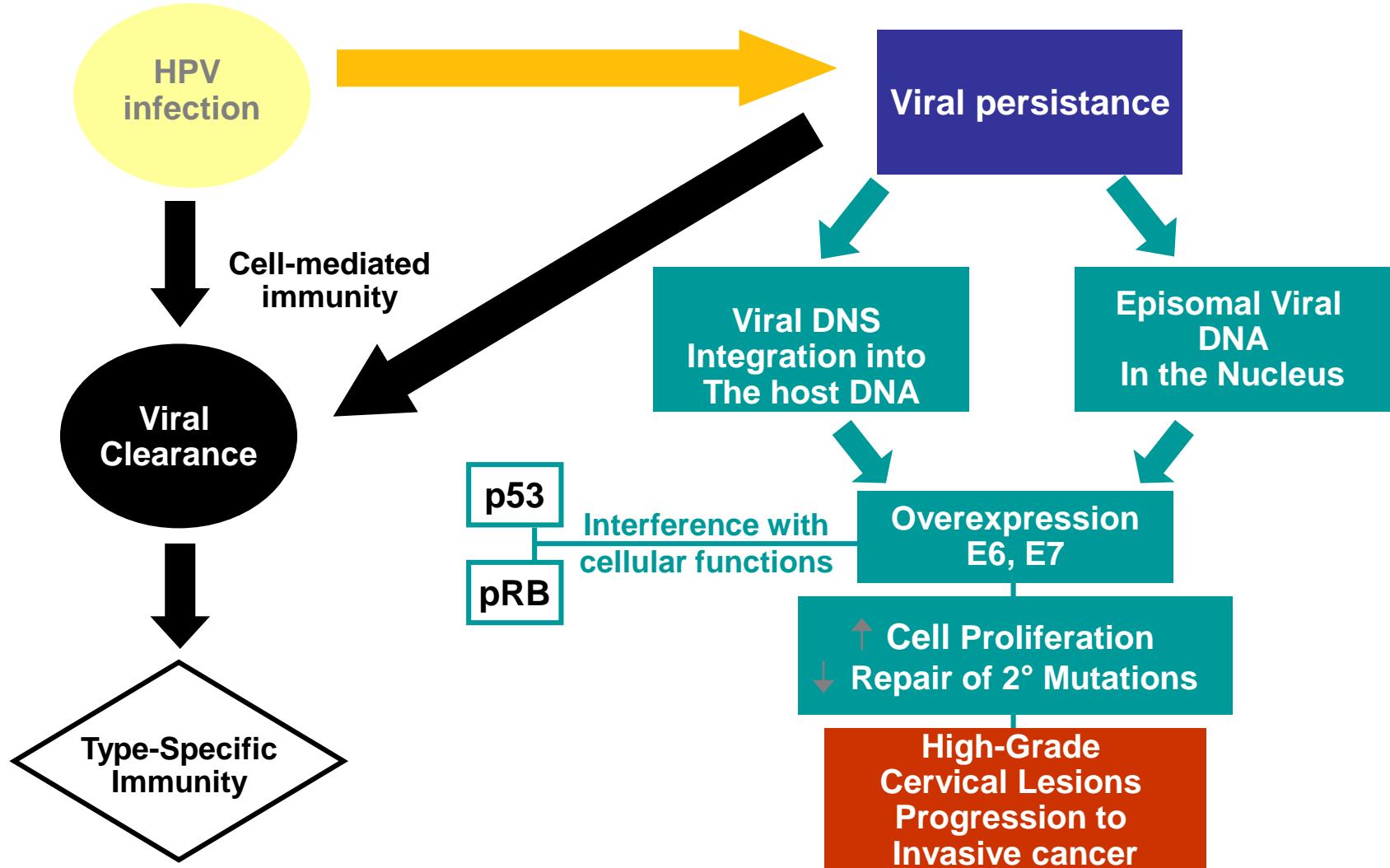
Spectrum of HPV induced cervical alterations



*CIN = cervical intraepithelial neoplasia

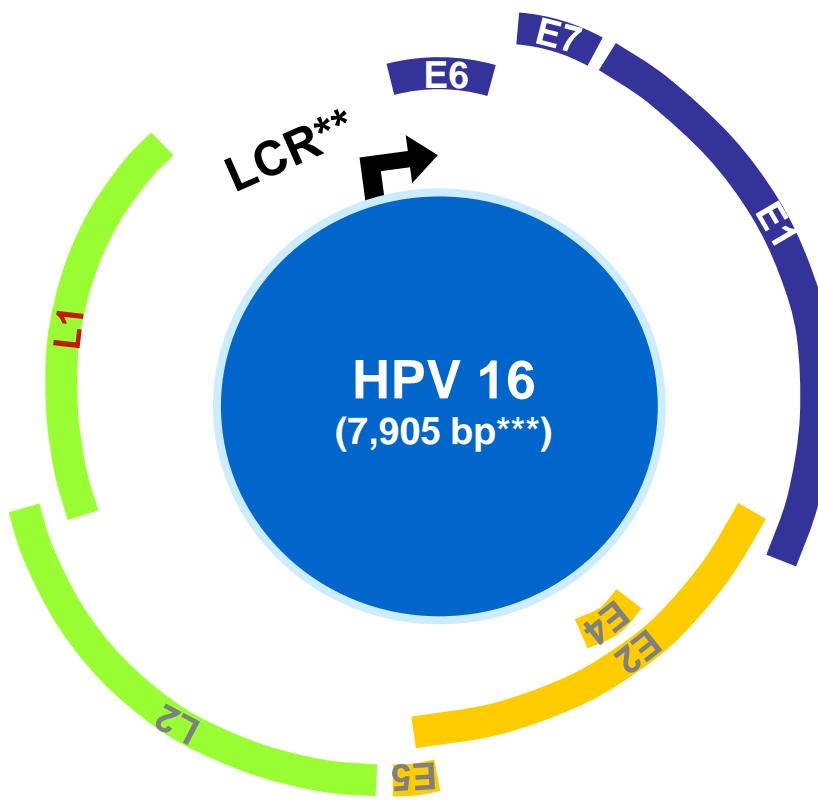
1. Adapted from Goodman A, Wilbur DC. *N Engl J Med.* 2003;349:1555–1564. Copyright © 2003 Massachusetts Medical Society. All rights reserved. Adapted with permission.

Mechanism of HPV carcinogenesis



1. Castle PE. *J Low Genital Tract Dis.* 2004;8:224–230.
2. Frazer IH. *Nature Rev Immunol.* 2004;4:46–54.
3. Doorbar J. *J Clin Virol.* 2005;32(suppl):S7–S15.
4. Münger K, Basile JR, Duensing S, et al. *Oncogene.* 2001;20:7888–7898.
5. Furumoto H, Irahara M. *J Med Invest.* 2002;49:124–133.

General Organization of a Papillomavirus Genome^{*,1}



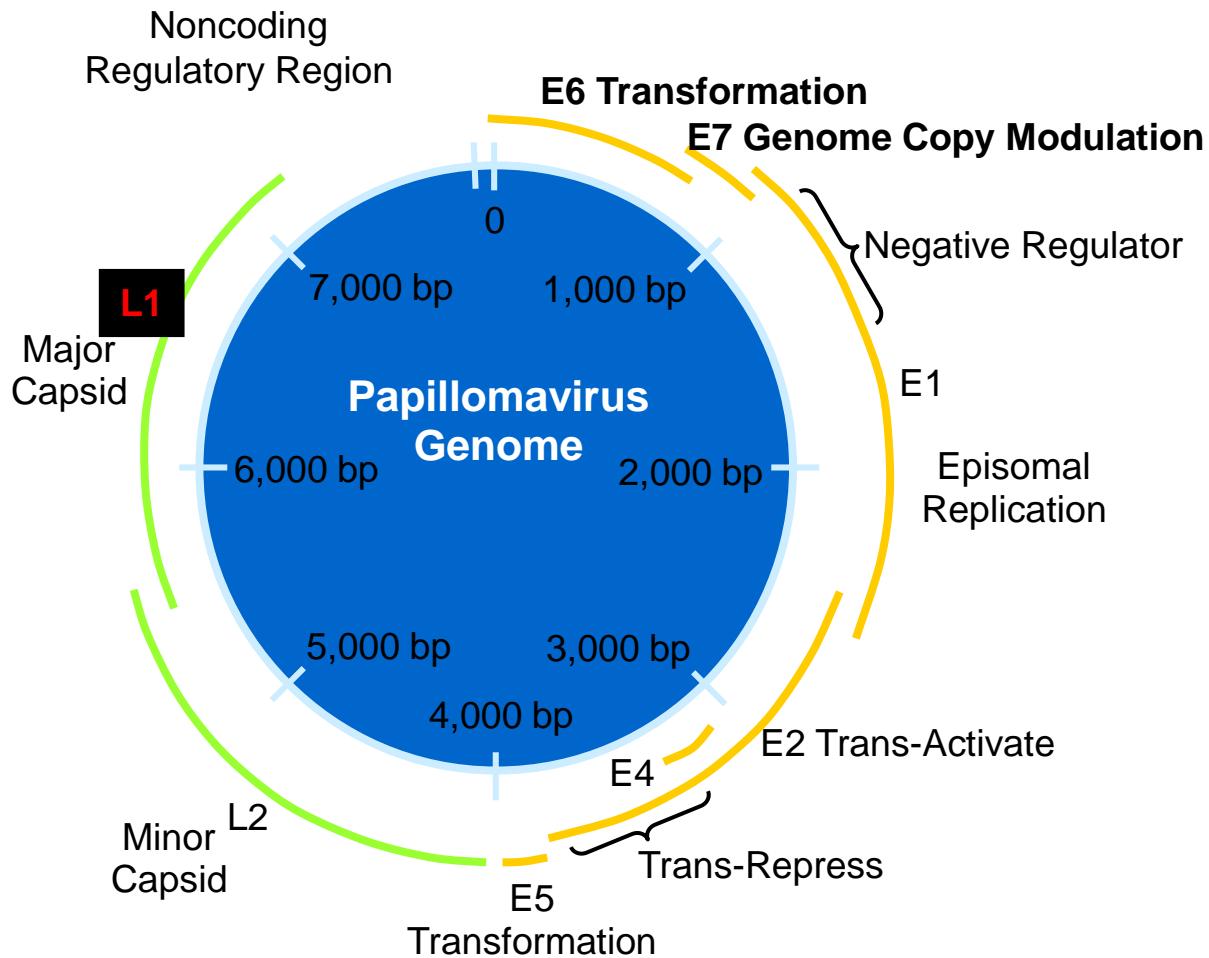
*Bars represent open reading frames.

**LCR = long control region

***bp = base pair

1. Münger K, Baldwin A, Edwards KM, et al. *J Virol*. 2004;78:11451–11460. Adapted with permission from the American Society for Microbiology Journals Department.

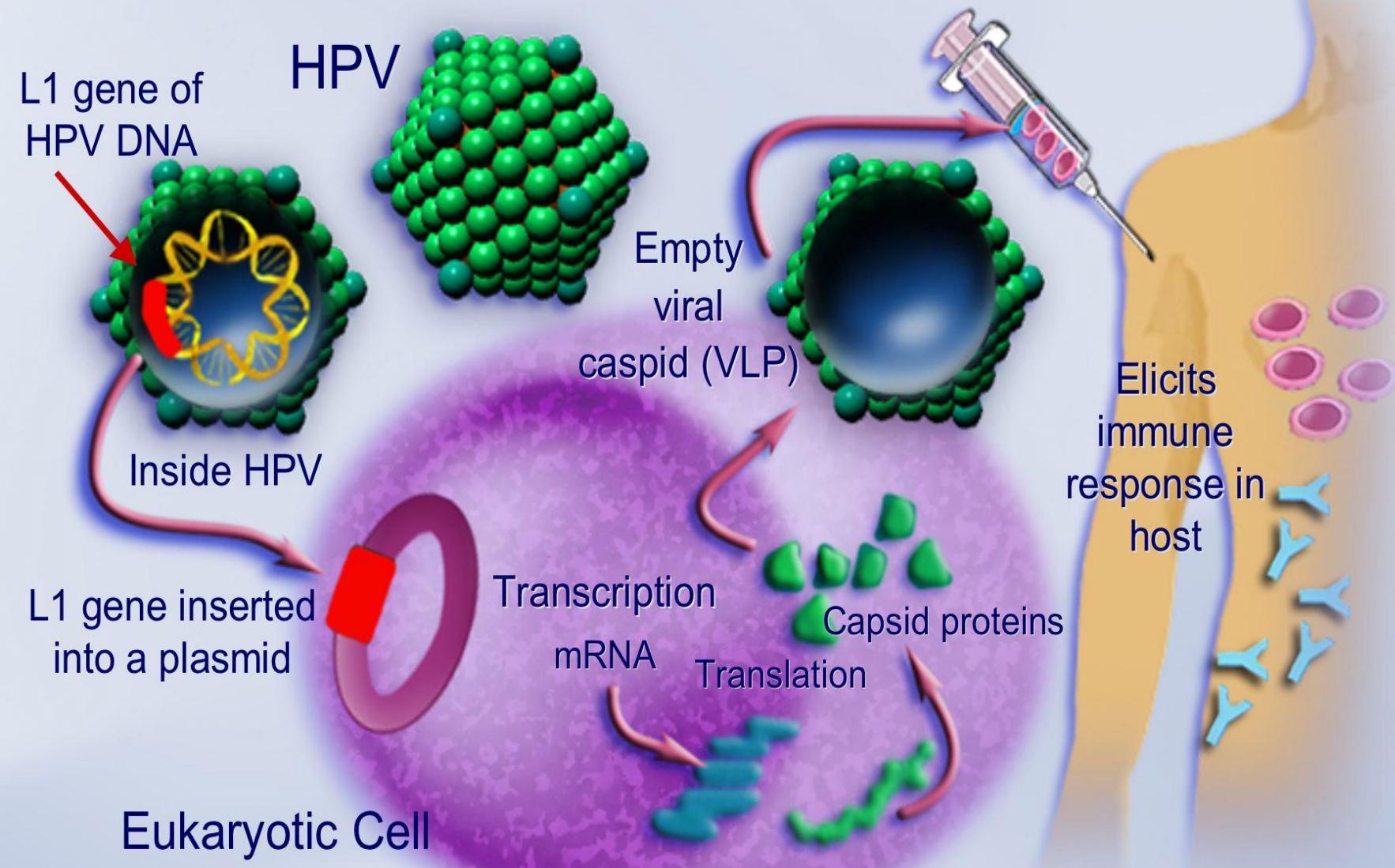
Papilloma Virus Genome



*Bars represent open reading frames. E = early region; L = late region; bp = base pair

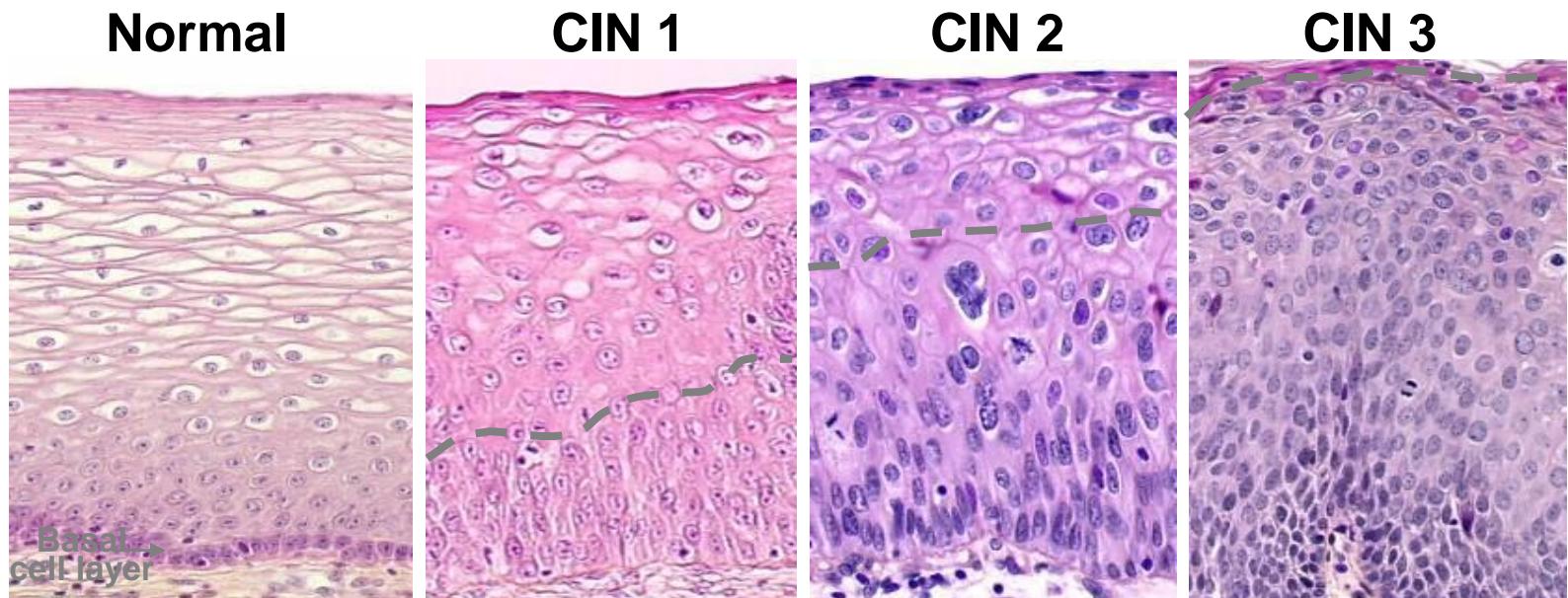
1. Koutsy LA, Galloway DA, Holmes KK. *Epidemiol Rev*. 1988;10:122–163. Reprinted by permission of Oxford University Press.

HPV L1 Virus-Like-Particle (VLP) Vaccine Synthesis



Histopathology: CIN¹

- CIN 1: Mild dysplasia; includes condyloma (anogenital warts)
- CIN 2: Moderate dysplasia
- CIN 3: Severe dysplasia; CIS; FIGO stage 02,3



All figures reprinted with permission from Frappart, et al. Histopathology and Cytopathology of the Uterine Cervix. Digital Atlas, Lyon, France: IARC Press, 2004.

Cytology findings confirmed by histology⁴

1. Frappart L, Fontaniere B, Lucas E, Sankaranarayanan R, eds. Lyon, France: International Agency for Research on Cancer; 2004. Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. Washington, DC: American Society for Microbiology Press; 2002:557–596. 3. Canadian Cancer Society. Cervical Cancer: What you need to know. Available at: http://www.cancer.ca/vgn/images/portal/cit_8675114/63/40/151140772cw_library_wyntk_cervical_en.pdf. Accessed March 13, 2006. 4. Wright TC Jr, Cox JT, Massad LS, et al, for the ASCCP-Sponsored Consensus Congress. JAMA. 2002;287:2120–2129.

Vulvar Intraepithelial Neoplasia (VIN)

- Incidence of VIN is increasing in the United States and worldwide.¹
- Mean age of women with VIN is decreasing^{2–4}
- Symptoms occur and may be present for a long time prior to diagnosis (median of 1 year)⁴
- HPV 16 appears to be the dominant HPV type associated with high-grade VIN⁵
 - Majority of VIN 1 cases are associated with HPV types 6 and 11⁶
 - HPV 6, 11, 16, or 18 can be found in VIN 2 or 3⁷



Photo courtesy of Dr. J. Monsonego



Photos courtesy of Dr. E.J. Mayeaux



1. Joura EA. *Curr Opin Obstet Gynecol*. 2002;14:39–43.
2. Sturgeon SR, Brinton LA, Devesa SS, Kurman RJ. *Am J Obstet Gynecol*. 1992;166:1482–1485.
3. Jones RW, Rowan DM, Stewart AW. *Obstet Gynecol*. 2005;106:1319–1326.
4. Herod JJ, Shafi MI, Rollason TP, et al. *Br J Obstet Gynaecol*. May 1996;103:446–452.
5. Buscema J, Naghashfar Z, Sawada E, et al. *Obstet Gynecol*. 1988;71:601–606.
6. Koutsky L. *Am J Med*. 1997;102:3–8.
7. Liaw KL, Kurman RJ, Ronnett B, et al. EUROGIN, April 2006. Paris, France.

HPV and Anogenital Warts

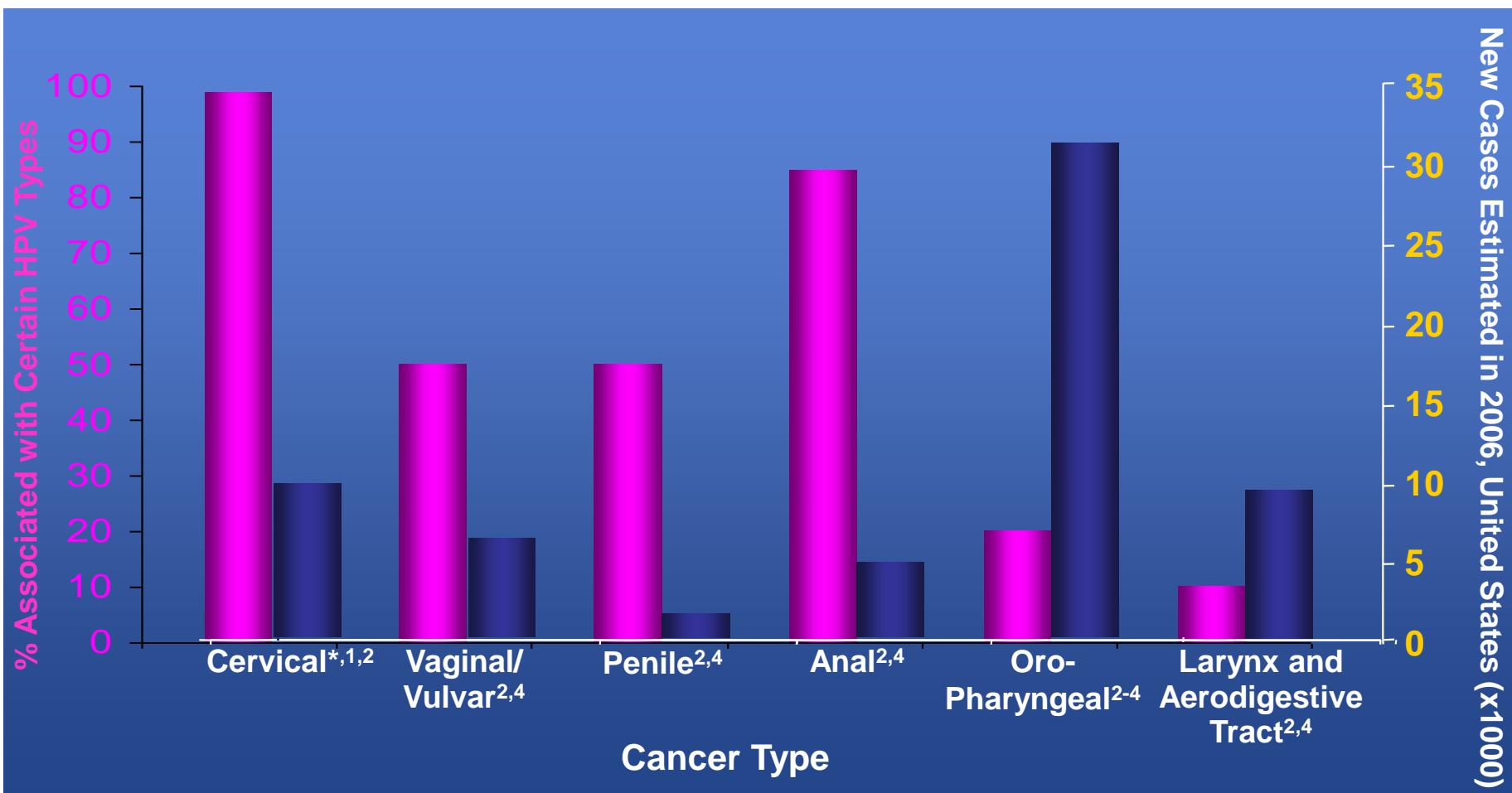


- HPV 6 and 11 responsible for >90% of anogenital warts¹
- Clinically apparent in ~1% of sexually active US adult population²
- Estimated lifetime risk of developing genital warts ~10%^{3,4}

Images top left and top right: Reprinted with permission from NZ DermNet (www.dermnetnz.org)

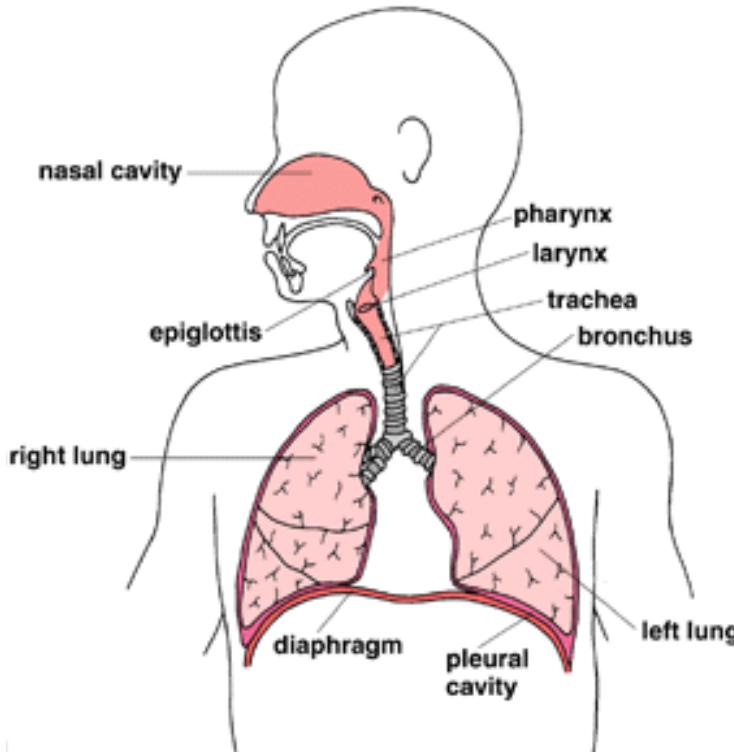
1. Jansen KU, Shaw AR. *Annu Rev Med*. 2004;55:319–331. 2. Koutsky L. *Am J Med*. 1997;102:3–8. 3. Franco EL, Villa LL, Richardson H, Rohan TE, Ferenczy A. In: Franco EL, Monsonego J, eds. Oxford, UK: Blackwell Science; 1997:14–22. 4. Tortolero-Luna G. *Hematol Oncol Clin North Am*. 1999;13:245–257, x.

HPV and Cancer: A Broader Picture

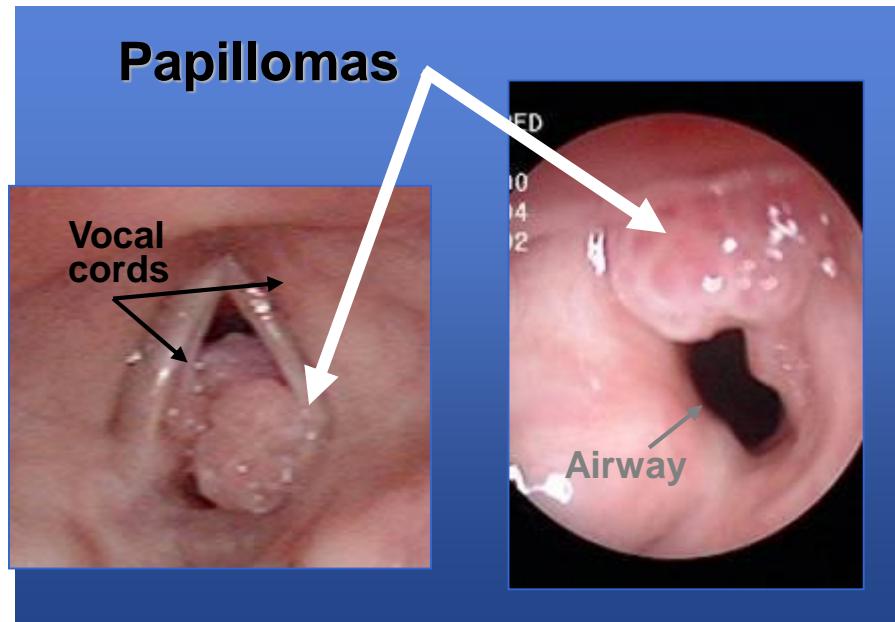


Walboomers JM, Jacobs MV, Manos MM, et al. *J Pathol*. 1999;189:12–19. 2. American Cancer Society. Available at: <http://www.cancer.org>. Accessed March 30, 2006. 3. Herrero R, Castellsagué X, Pawlita M, et al. *J Natl Cancer Inst*. 2003;95:1772–1783. 4. World Health Organization. Geneva, Switzerland: World Health Organization; 1999:1–22.

Locations of Papillomas in RRP



Reprinted with permission of the University of Maryland Medical Center (www.ummc.edu)¹



Photos courtesy of Craig S. Derkay, MD
Eastern Virginia Medical School

1. University of Maryland Medicine. Available at: <http://www.marylandthoracic.com>. Accessed March 29, 2006.

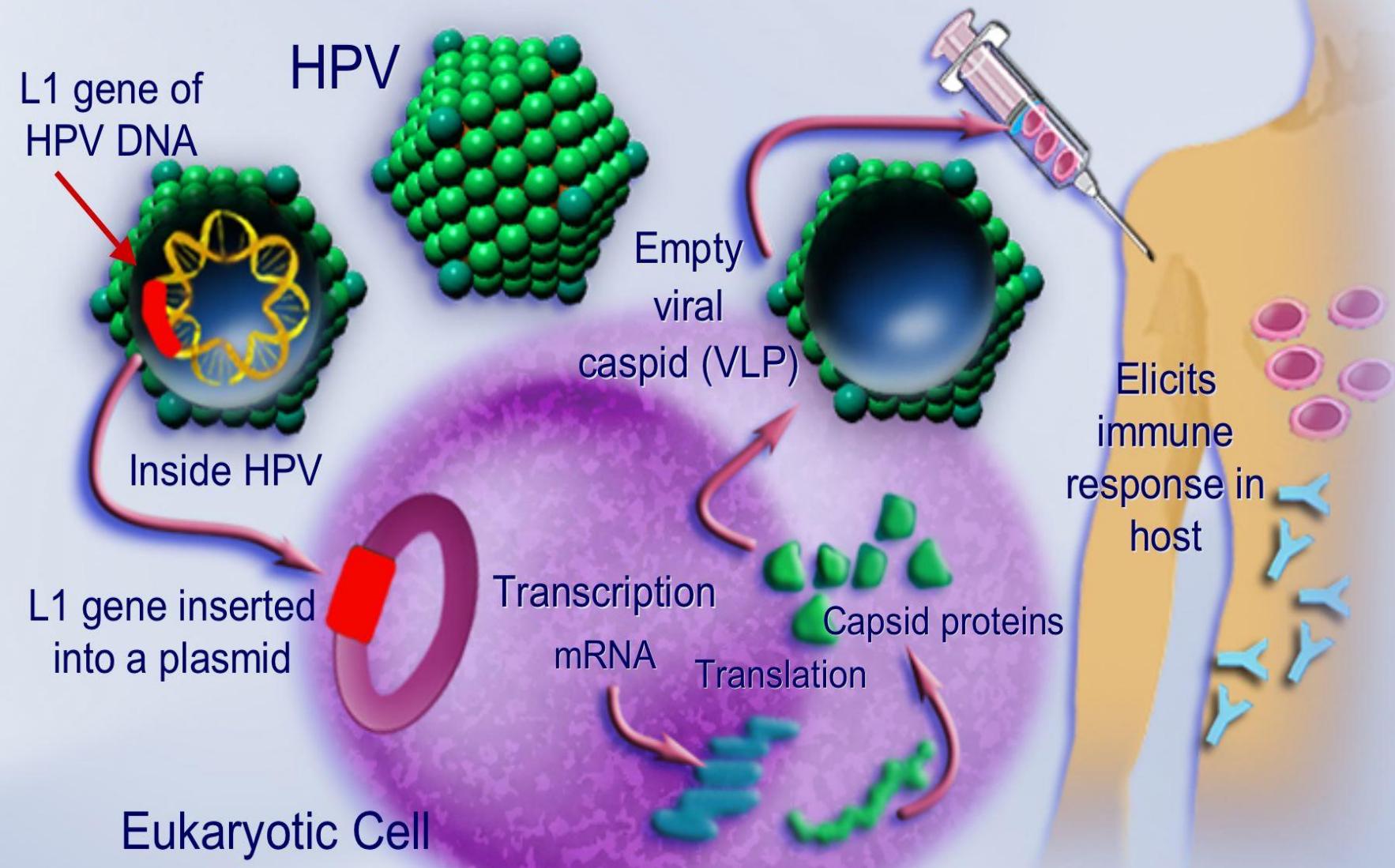
A HPV-fertőzés gyakorisága férfiakban

egyetemi hallgatóknál

- finn: 16,5%
- amerikai: 33%



HPV L1 Virus-Like-Particle (VLP) Vaccine Synthesis



Safety of HPV vaccines



- Local reaction.
- All vaccines (2, 4 and 9-v) safe.
- After 19 million vaccination by 9vHPV in the USA the vaccine safety is as it is described in the instruction

EMA, EMA/714950/2015

Cervarix, alkalmazási előírás, 2017; Silgard, alkalmazási előírás, 2017; Gardasil9, alkalmazási előírás, 2017

CDC. Gee J et al. Post-licensure monitoring 9-valent human papillomavirus vaccine safety. Scientific lecture in EUROGIN, 2017:

www.eurogin.com/2017

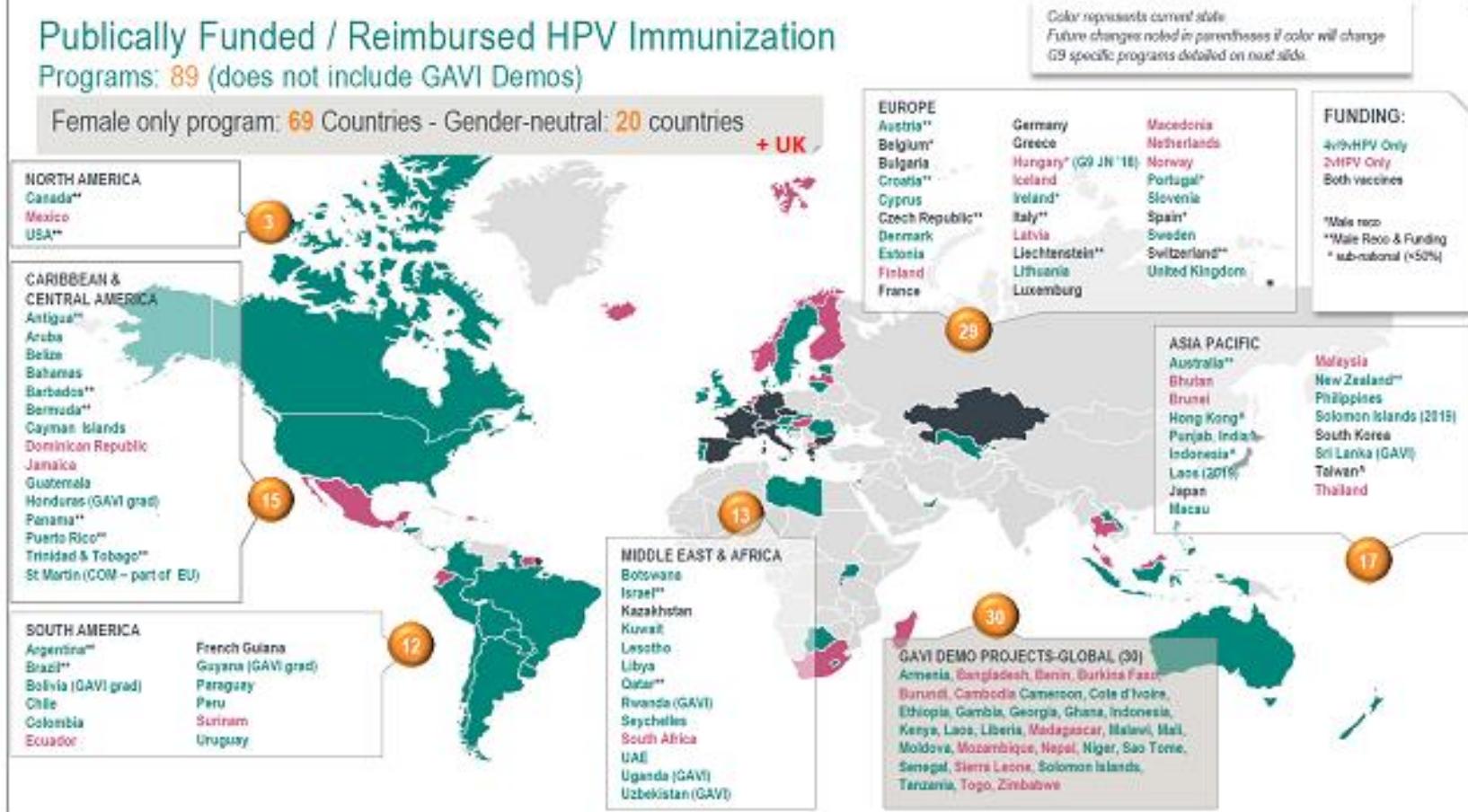
Costa APF et al. Safety of Human Papillomavirus 9-Valent Vaccine: A Meta-Analysis of Randomized Trials. J Immunol Res. 2017;2017:3736201.

Már 89 állam olt a HPV ellen – ebből 21 a fiúkat is

2018. július

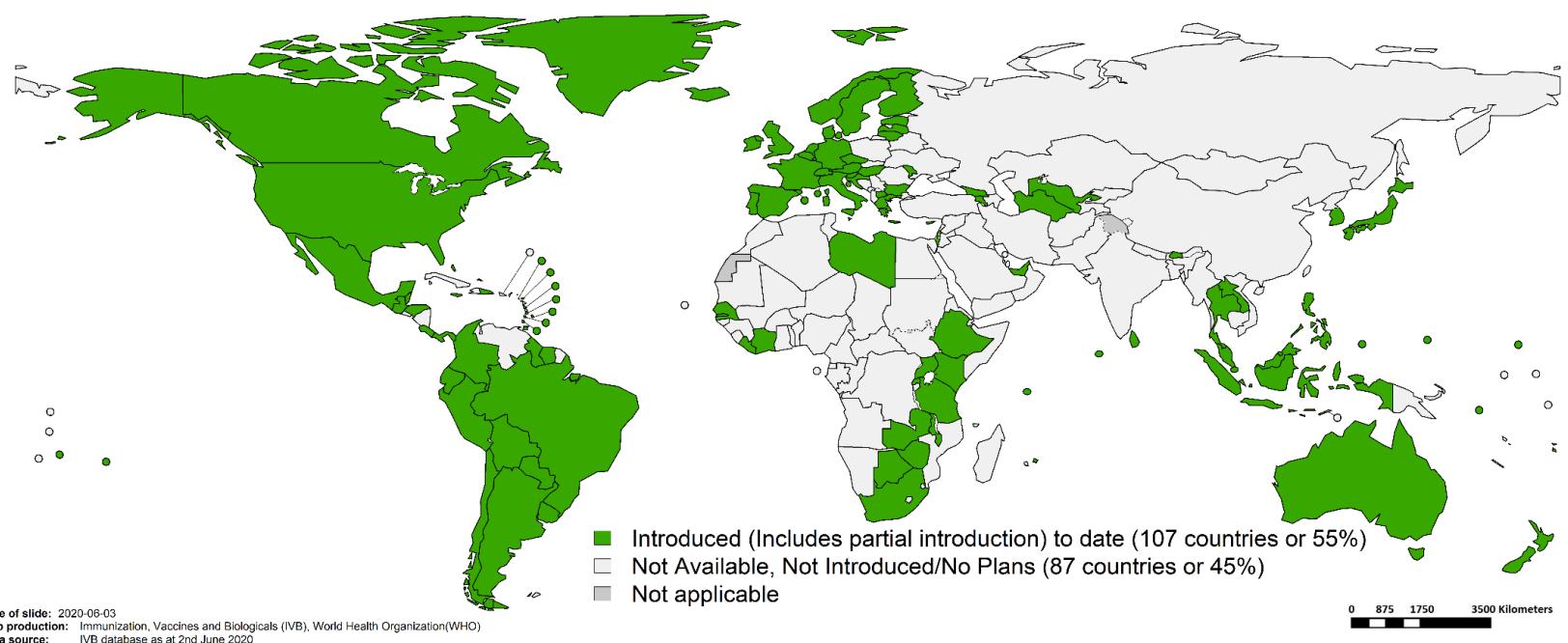
Publically Funded / Reimbursed HPV Immunization Programs: 89 (does not include GAVI Demos)

Female only program: 69 Countries - Gender-neutral: 20 countries



2018. júliusában UK Kormánya döntött - a HPV vakcinációs programot kiterjesztik a 12-13 éves fiúkra is

2020 June - 107 country introduced population based HPV vaccination, 39 vaccinate boys too

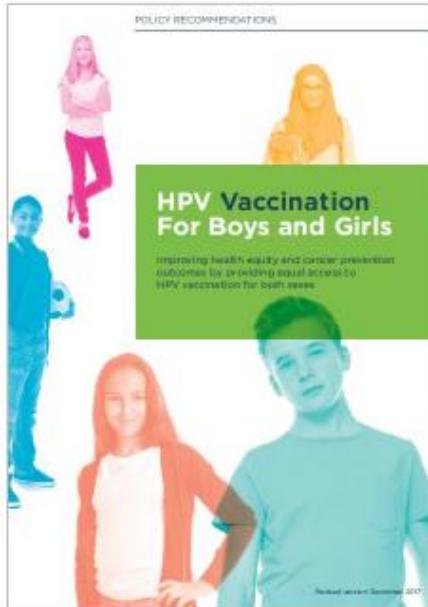


GNV – 39 ország (2019. október) : USA, Kanada, Amerikai Virgin-szigetek, Ausztrália, Guam, Amerikai Szamoa, Északi Mariana-szigetek, Új-Zéland, Brazília, Argentína, Chile, Ausztria, Belgium, Németország, Cseh Köztársaság, Dánia, Horvátország, Gibraltár, Man-sziget, Írország, Olaszország, Jersey-sziget, Liechtenstein, Luxemburg, Svájc, Norvégia, UK, Szlovákia, Izrael, Türkmenisztán, Antiqua, Bahamák, Panama, Puerto Rico, St Lucia, Barbados, Bermuda, Guyana, Trinidad



European Parliament, 2017

Policy recommendation on HPV Vaccination for boys and girls



Considering the high impact of HPV on young generations, it is critical to take actions to stop the transmission of the virus and work towards disease elimination, in order to protect the future generations of European citizens.

Yet, prevention currently represents only 3% of healthcare budgets in Europe¹²⁸ and vaccination only 0.5%¹²⁹. In constrained environments, delivering sustainable and cost-effective healthcare interventions is a top priority. Disease prevention expenditure must not and cannot be seen as a cost, but rather as an investment into healthier and active populations:

Because promoting good health outcomes via prevention is a cornerstone of the Europe 2020 strategy, HPV vaccination programmes would contribute to Europe 2020's objectives for a smart and inclusive growth:

- By protecting against infectious diseases and their life-span consequences, as this contributes to improve prospects for EU citizens and the economy
- By keeping people healthy and active for longer, in particular young adults at fertile age, with a positive impact on productivity and competitiveness
- By reducing the burden of costly diseases, such as cancers or genital warts, contributing to healthcare systems' sustainability
- By tackling health inequalities and their economic impact

HPV vaccination is one of the cheapest and most efficient primary interventions for HPV-related cancers, as compared to treatments, and given the sustainability of the protection it offers, it is an example of efficient spending on health, promoting growth which is consistent with European objectives.

The European Parliament event, hosted by MEP Nessa Childers on the occasion of European Immunisation Week. Improving health equity and cancer prevention outcomes: HPV vaccination for boys and girls.<https://www.vaccinestoday.eu/stories/hpv-vaccines-boys/>



The Nobel Prize in Physiology or Medicine 2008

"for his discovery of human papilloma viruses causing cervical cancer"

"for their discovery of human immunodeficiency virus"



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Springer Medizin Verlag

Harald zur Hausen

1/2 of the prize

Germany

German Cancer Research Centre
Heidelberg, Germany



Photo: Sakutin/SCANPIX

Françoise Barré-Sinoussi

1/4 of the prize

France

Regulation of Retroviral Infections Unit, Virology Department, Institut Pasteur
Paris, France



Photo: Magunia/SCANPIX

Luc Montagnier

1/4 of the prize

France

World Foundation for AIDS Research and Prevention
Paris, France

EBV (HHV-4)

- African Burkitt lymphoma (1956-58)
- Epstein-Barr (1964) – virus identification
- EBV associated diseases:
 - Infectious Mononucleosis
 - Burkitt lymphoma (B cells, high mal. NHL)
 - Nasopharyngeal cc
 - HL (?)

Virus induced human cancers

Malaria infection induced
immunosuppression



African Burkitt
lymphoma



Epstein-Barr virus caused
infectious mononucleosis

Human herpesvirus 8 (HHV-8) and Kaposi sarcoma

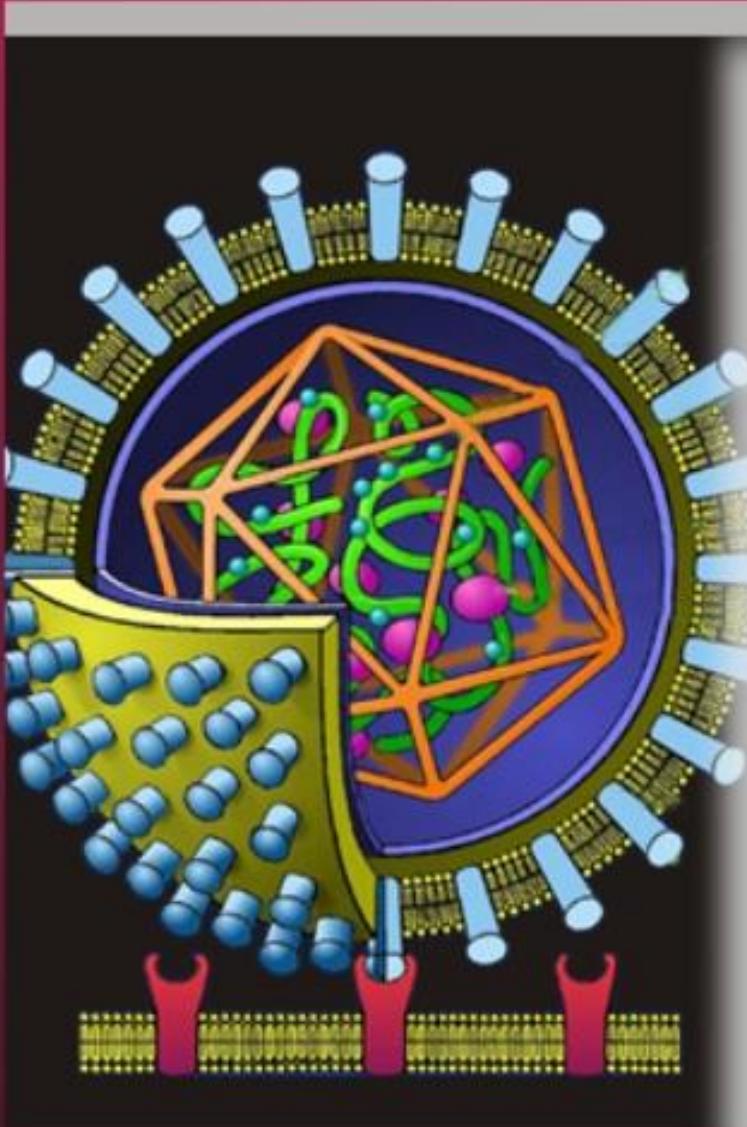
- **Kohn to Moritz Kaposi (1837-1902)** (born in Kaposvár, worked in Vienna, „classic” Kaposi sarcoma: sarcomatous skin lesions on the legs and arms of elderly men – predominantly in men of Mediterranean, Eastern European or Jewish heritage.
- Aggressive form of KS in HIV-1-infected individuals (mainly in gay men)
- The „newest” discovered human oncogenic virus (1994)

A HHV-8 és a Kaposi-szarkóma

- Kaposi Mór, 1872**
- leggyakoribb
AIDS-zel kapcso-
latos daganat**
- átvitel**



Human retroviruses (HTLV-1)



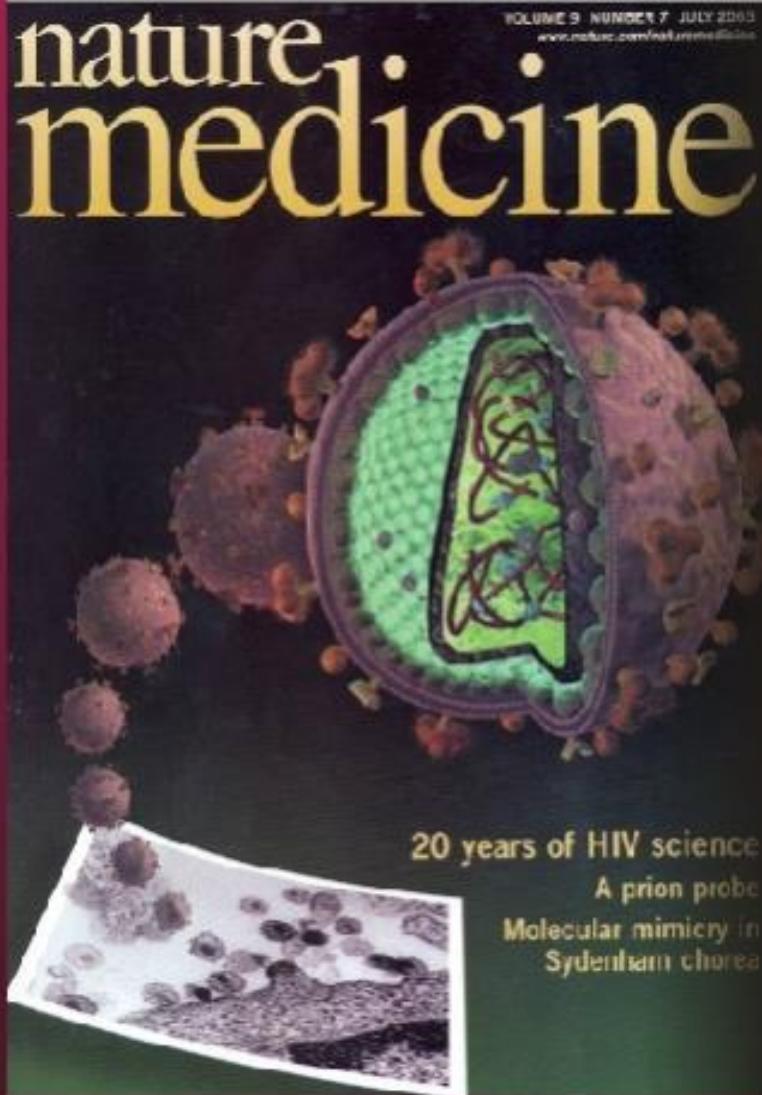
Human
T-cell leukaemia

Forms:
epidemic and sporadic

Transmission:
by body fluid,
sexually

Clinic: aggressive,
bad prognosis

Human retroviruses HIV



Associated tumors

Kaposi sarcoma
Non-Hodgkin lymphoma

Pathomechanism
mainly indirect
direct?