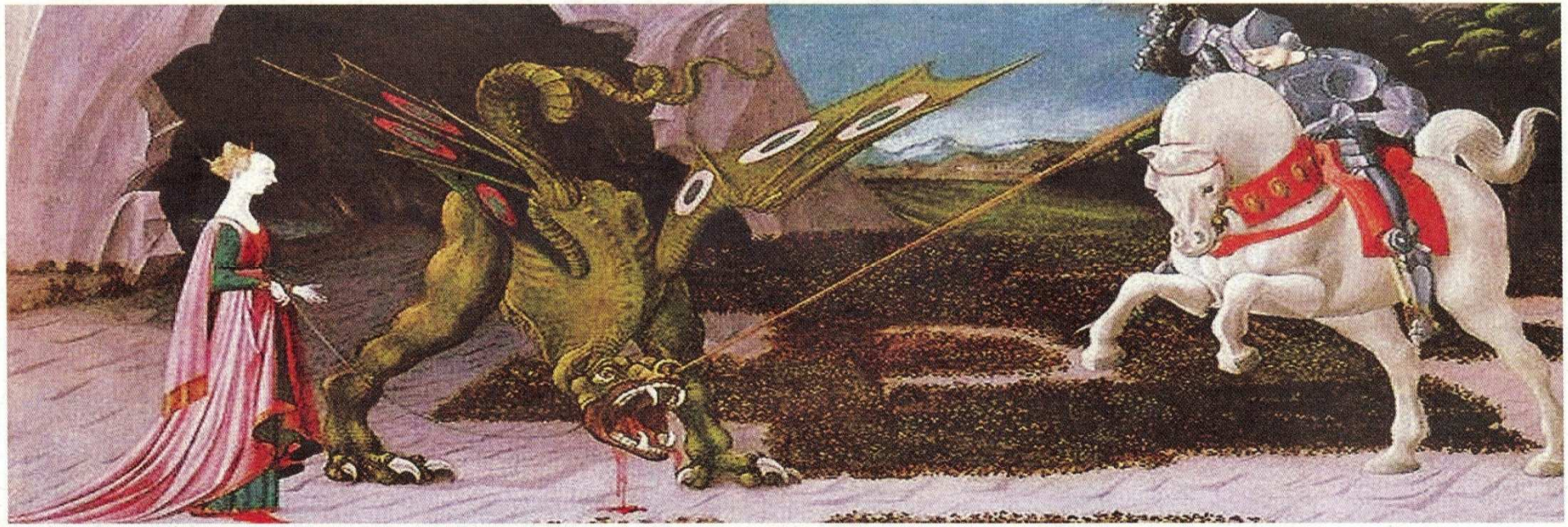
«IO MI VACCINO»

Incontro organizzato dal Rotary Club Teramo

Venerdì 28 settembre 2018



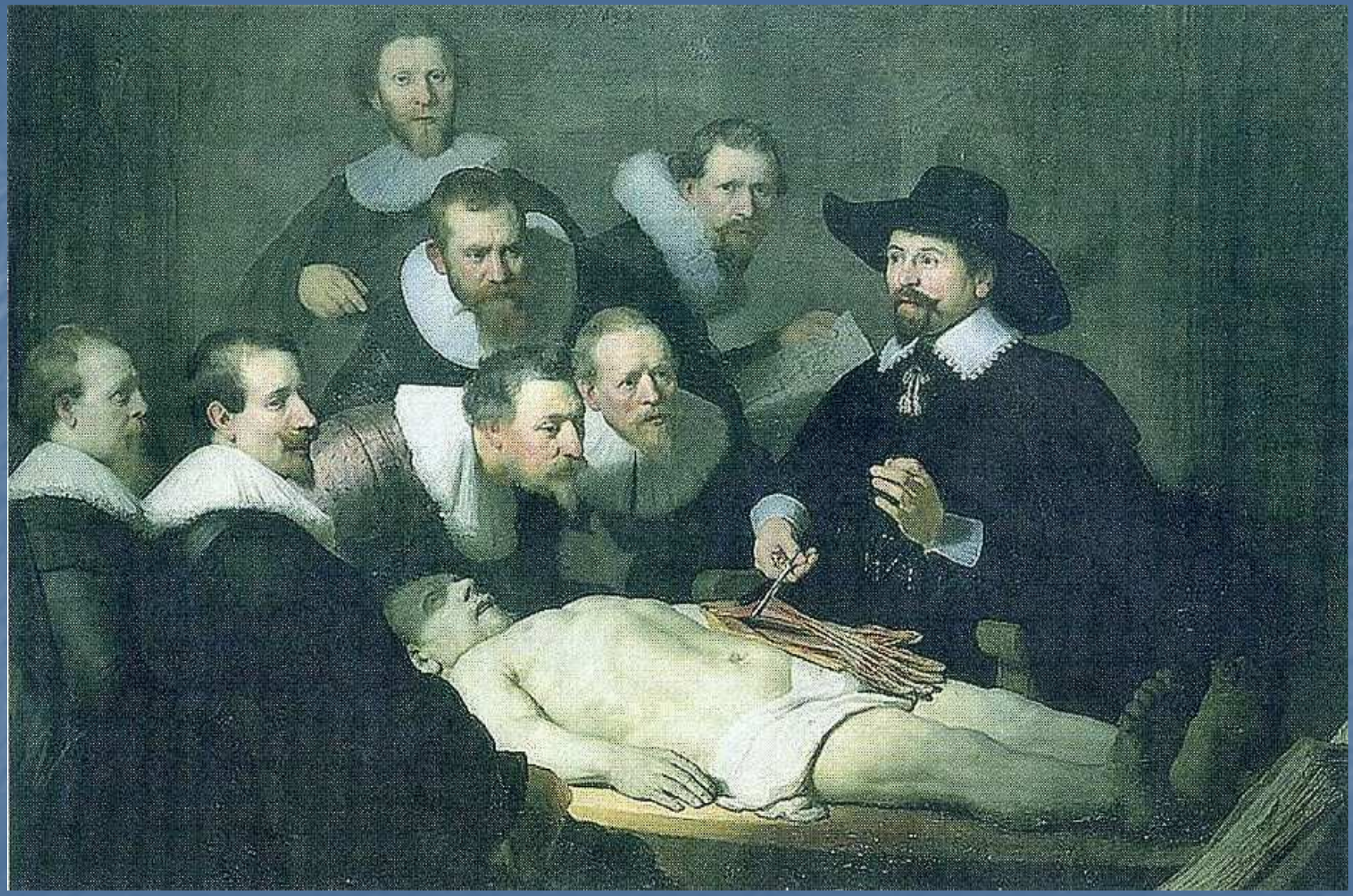
Prof. Giulio Tarro

Primario emerito dell' Azienda Ospedaliera "D. Cotugno", Napoli

Chairman della Commissione sulle Biotecnologie della Virosfera, WABT - UNESCO, Parigi

Magnifico Rettore dell'Università Tommaso Moro U.P.T.M., Roma

Presidente della Fondazione Teresa & Luigi de Beaumont Bonelli per le ricerche sul cancro



For Giulio Tarro – my scientific son – with great admiration and best wishes for a happy and successful life,
Albert B. Sabin June, 1968

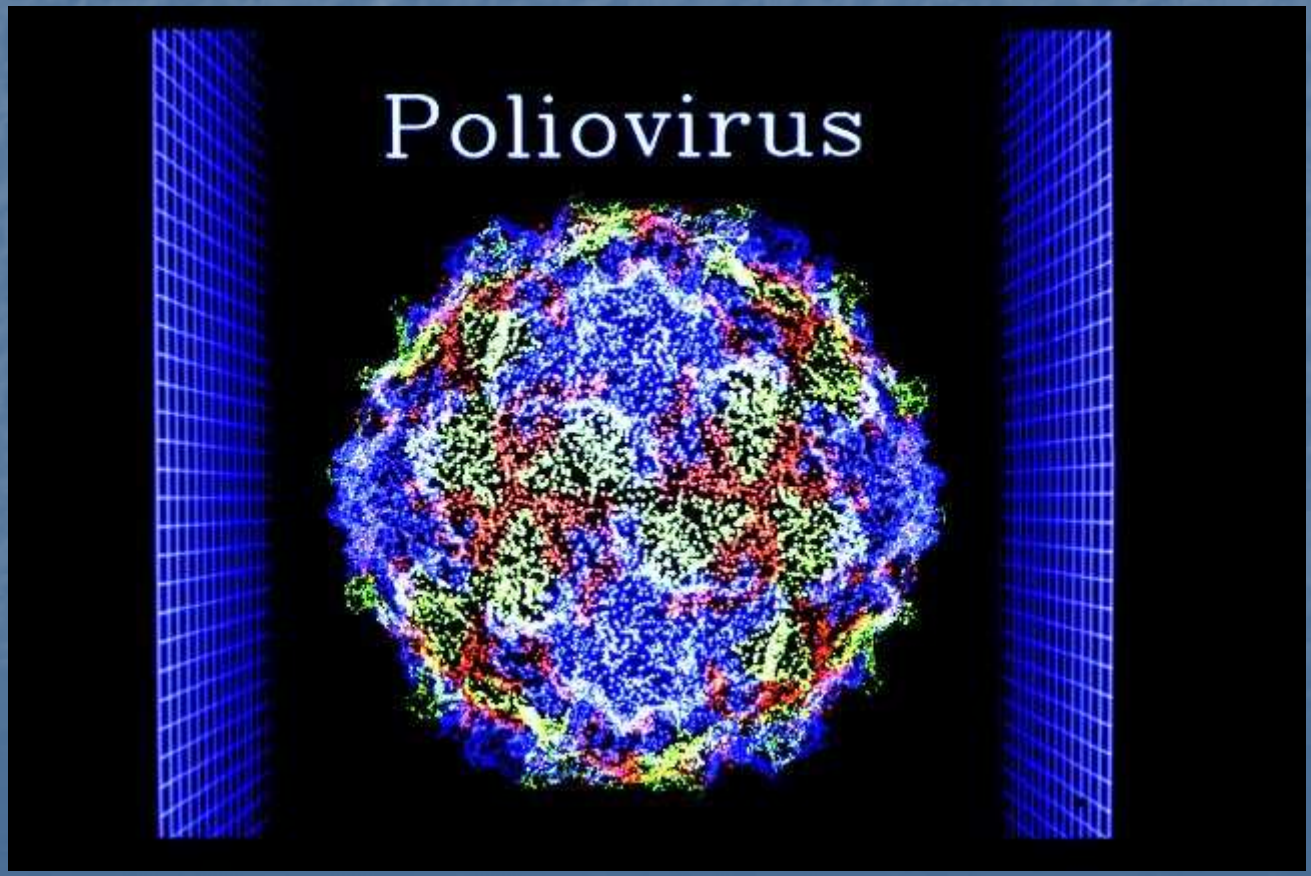
Theory Clin. Pract. Pediatr., 2017, 1 (1), 2-3
DOI: 10.25082/TCPP.2017.01.002

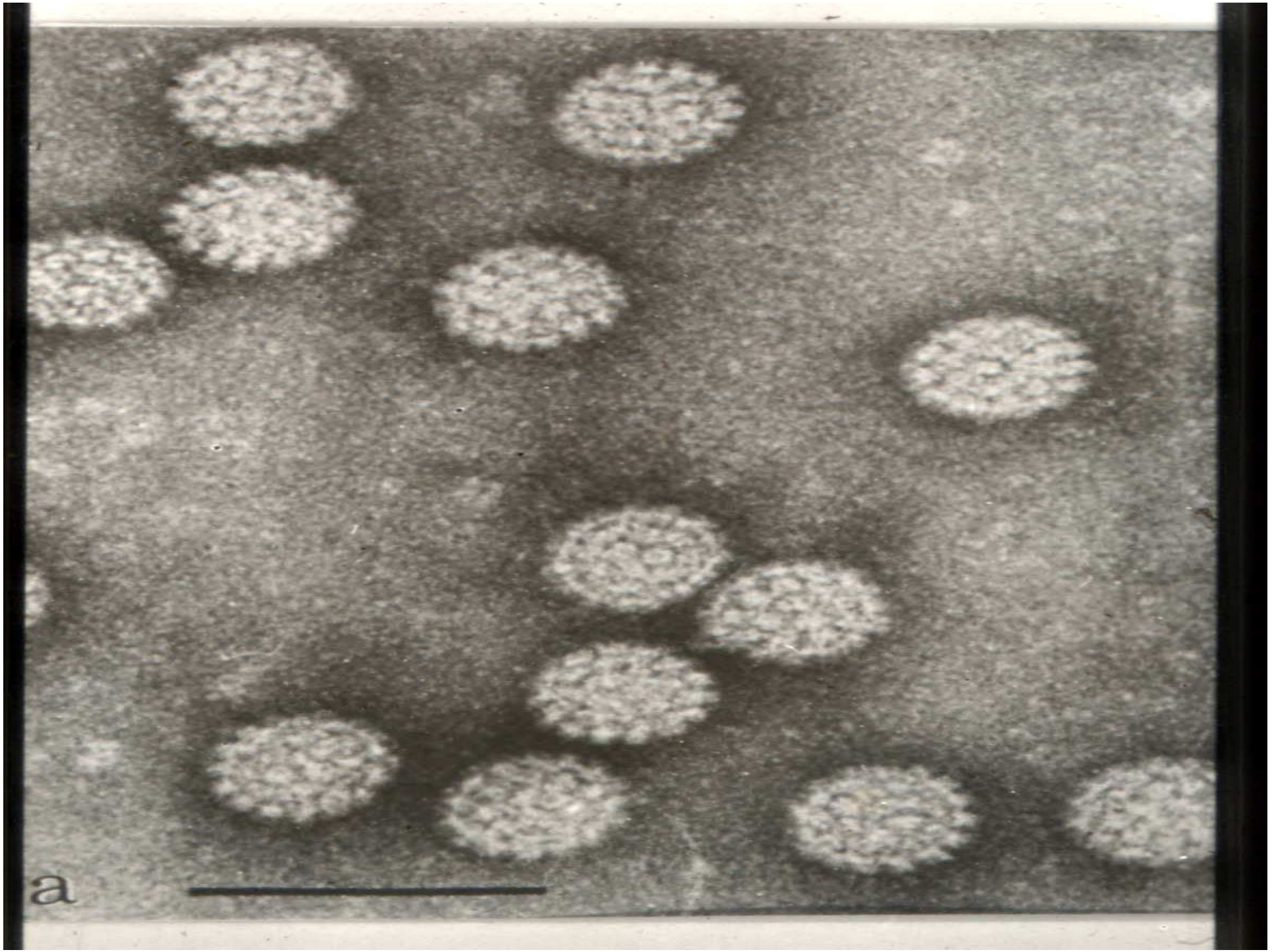
COMMENTARY

Exegesis of Sabin poliovaccine in terms of medical science

Giulio Filippo Tarro

Recently the Word Health Organization (WHO) declared that India and Southeast Asia are polio-free, really a great achivement since the vaccine for polio, an infectious desease that can cause paralisis, was certificated safe and useful only 60 years ago.

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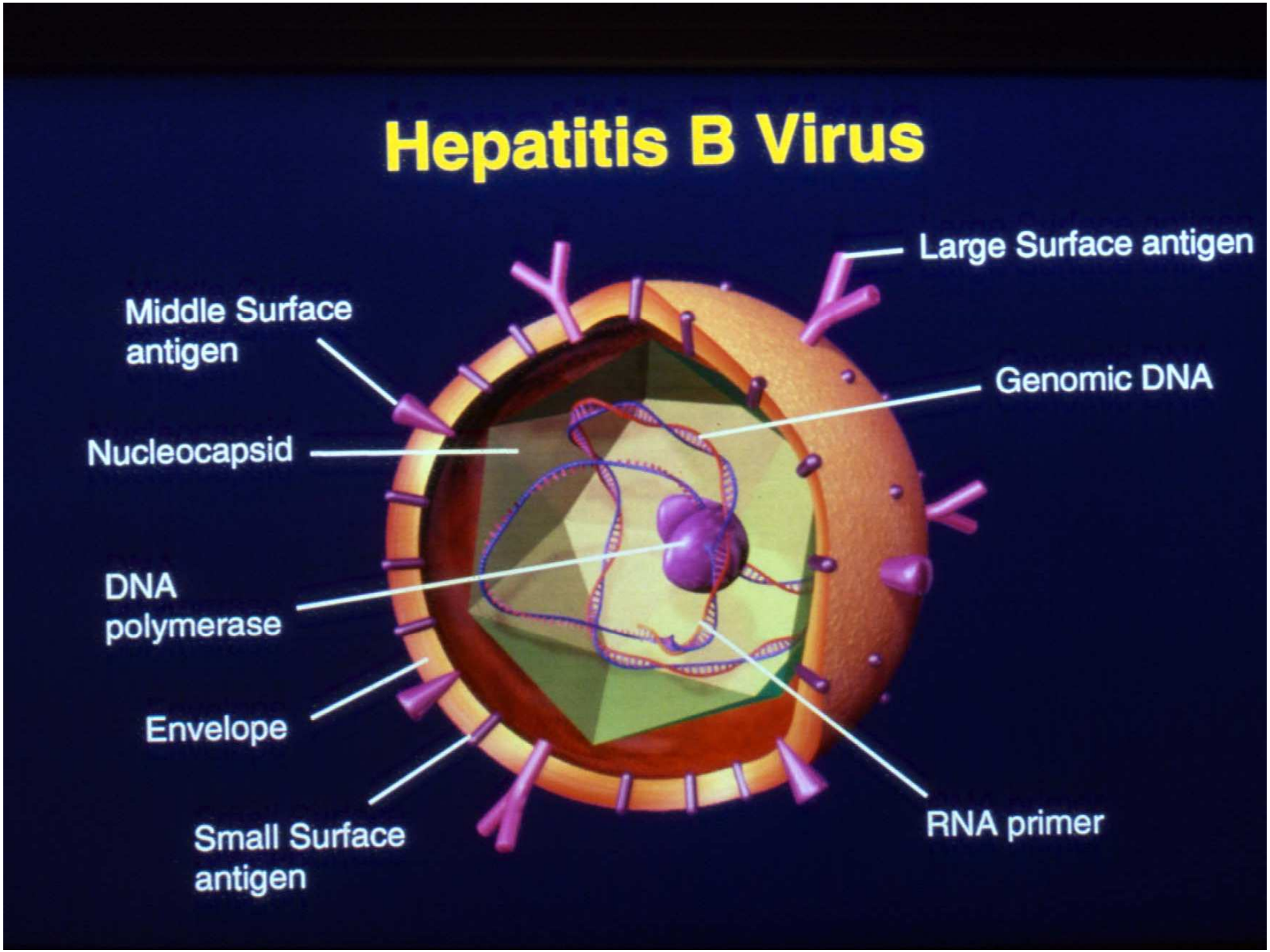
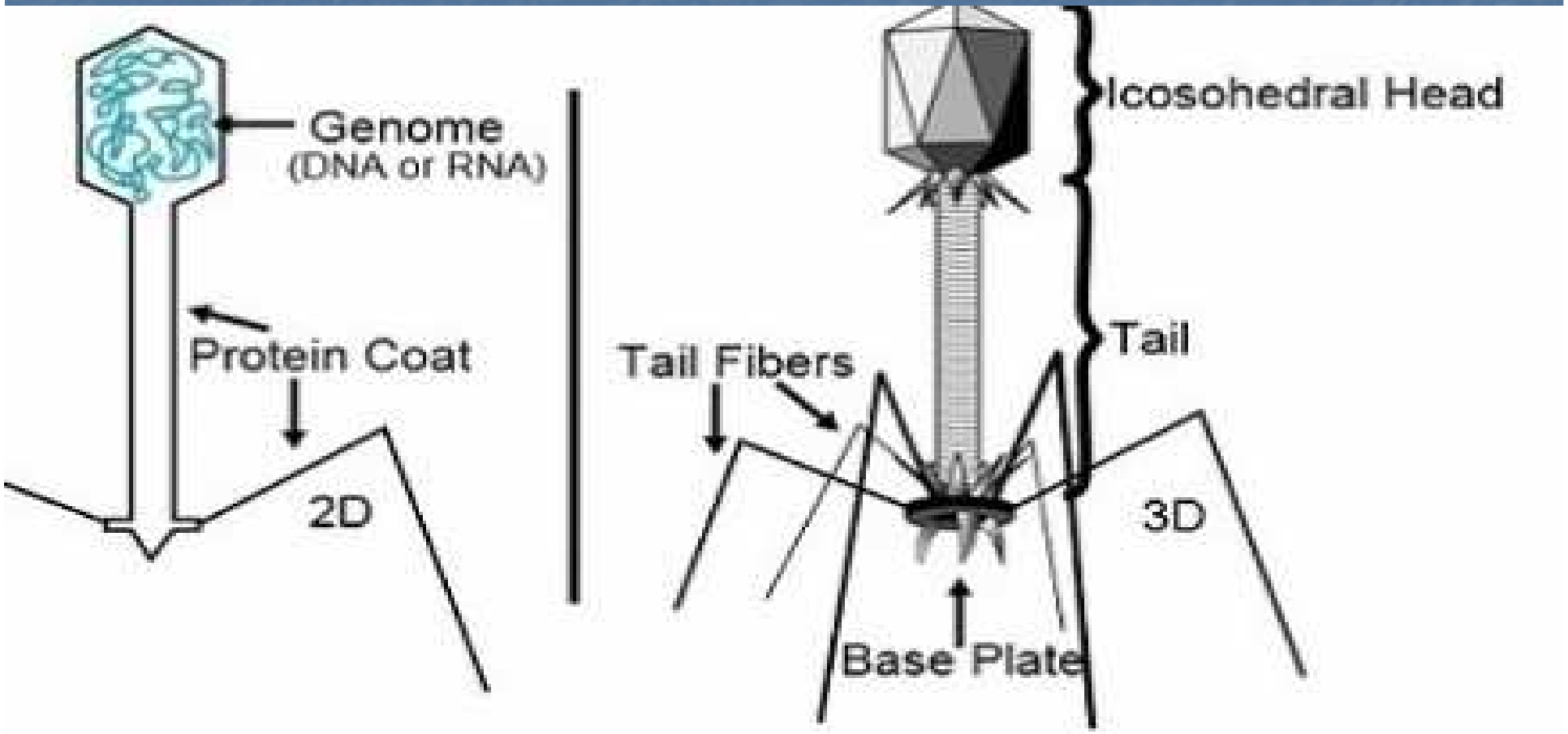
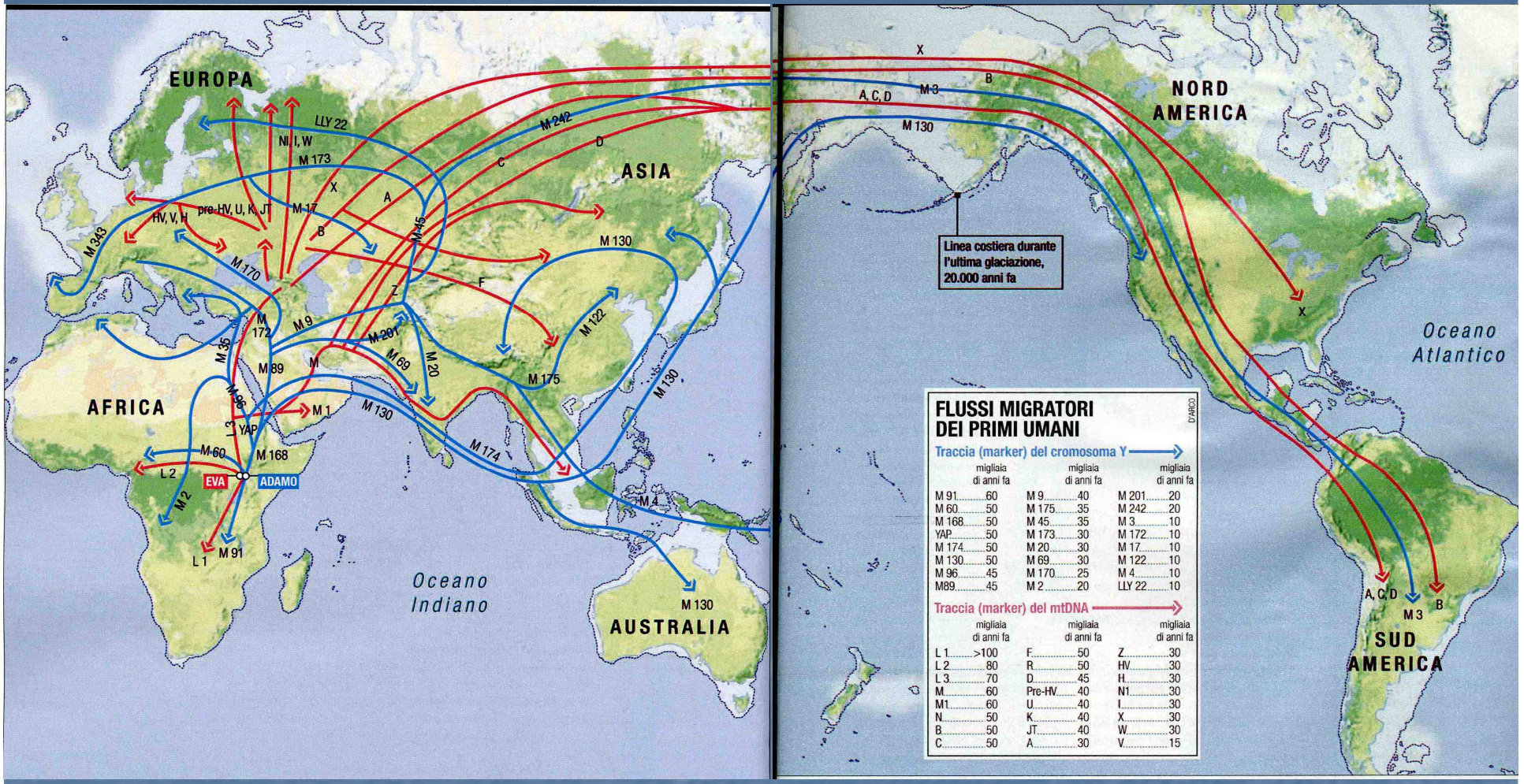

Hepatitis B Virus
Large Surface antigen
Middle Surface antigen
Genomic DNA
Nucleocapsid
DNA polymerase
Envelope
Small Surface antigen
RNA primer


Genome
(DNA or RNA)
Protein Coat
2D
Icosohedral Head
Tail
Tail Fibers
3D
Base Plate


Virosphere 2002
Invertebrates
Vertebrates
Bacteria
Plants
Invertebrates
Vertebrates
Bacteria
Fungi
dsDNA
ssDNA
dsDNA-RT
ssRNA-RT
dsRNA
ssRNA-
ssRNA+
Bacteria
Fungi
Plants
Invertebrates
Vertebrates
Plants
Invertebrates
Vertebrates
Bacteria
Fungi
Vertebrates
Invertebrates
Plants
DONALD DANFORTH
PLANT SCIENCE CENTER
copyright©2002 C.M.Fauquet
International Committee on Taxonomy of Viruses


EUROPA
ASIA
AFRICA
NORD AMERICA
SUD AMERICA
AUSTRALIA
Oceano Indiano
Oceano Atlantico
EVA
ADAMO
YAP
pre-HV, U, K, JT
HV, V, H
LLY 22
N, I, W
M 173
M 343
M 170
M 172
M 35
M 89
M 96
M 9
M 201
M 69
M 20
M 45
M 242
M 130
M 122
M 175
M 1
M 174
M 60
M 168
L 2
M 2
L 1
M 91
M 4
X
A
B
C
D
Z
F
A, C, D
M 3
Linea costiera durante l'ultima glaciazione, 20.000 anni fa
FLUSSI MIGRATORI DEI PRIMI UMANI
DARCO
Traccia (marker) del cromosoma Y
migliaia di anni fa
M 91 60
M 60 50
M 168 50
YAP 50
M 174 50
M 130 50
M 96 45
M89 45
M 9 40
M 175 35
M 45 35
M 173 30
M 20 30
M 69 30
M 170 25
M 2 20
M 201 20
M 242 20
M 3 10
M 172 10
M 17 10
M 122 10
M 4 10
LLY 22 10
Traccia (marker) del mtDNA
migliaia di anni fa
L 1 >100
L 2 80
L 3 70
M 60
M1 60
N 50
B 50
C 50
F 50
R 50
D 45
Pre-HV 40
U 40
K 40
JT 40
A 30
Z 30
HV 30
H 30
N1 30
I 30
X 30
W 30
V 15

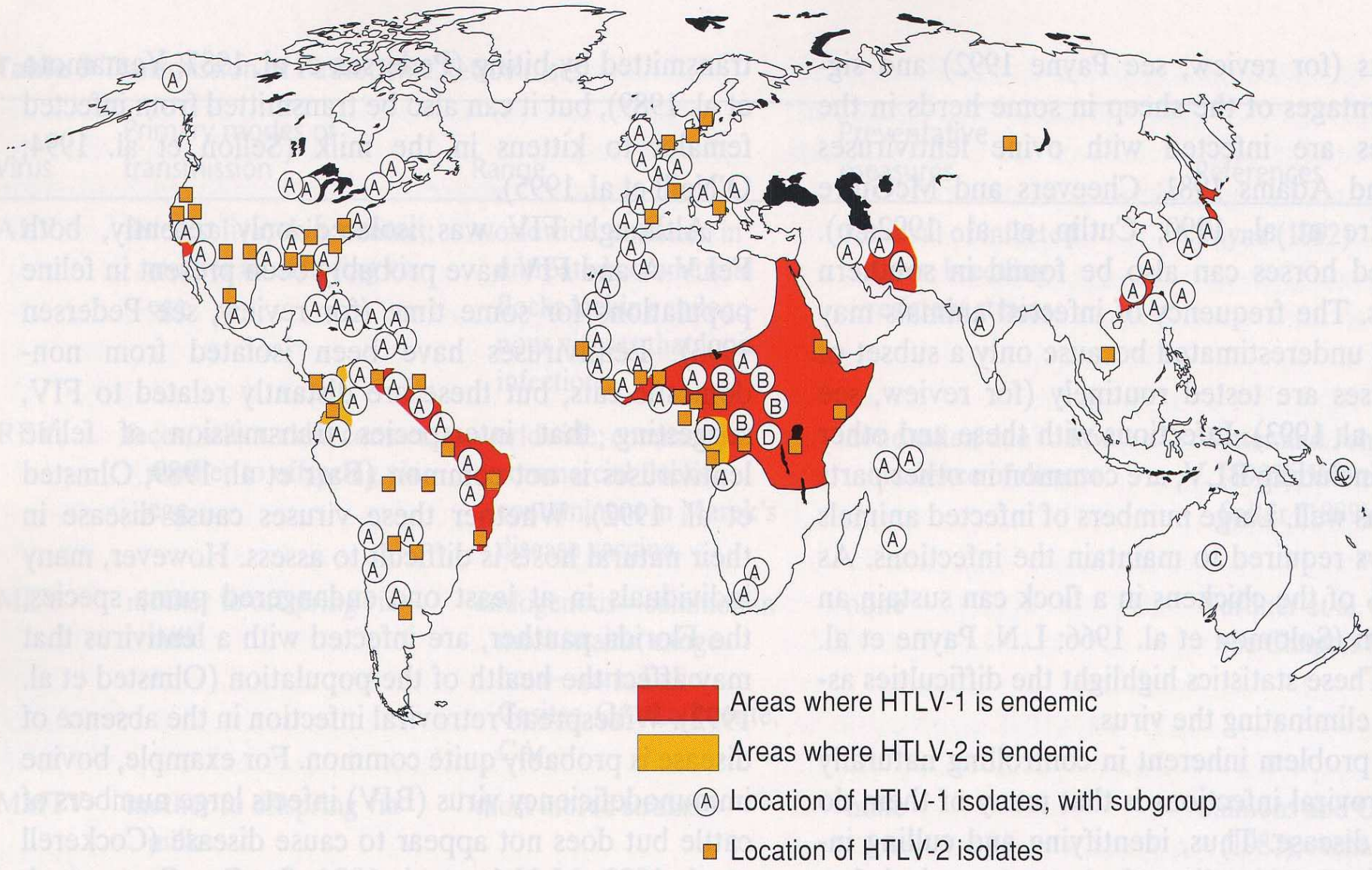
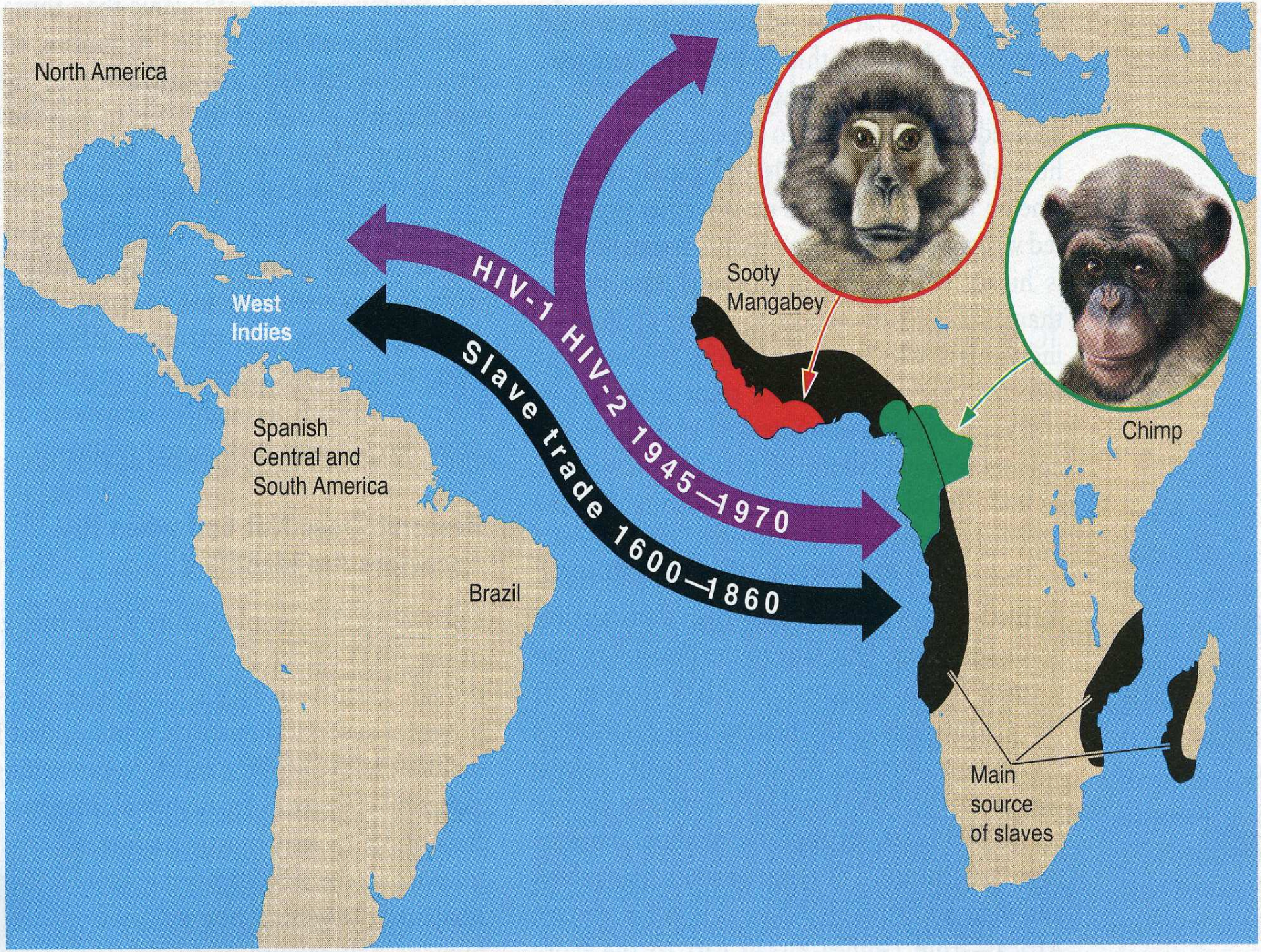
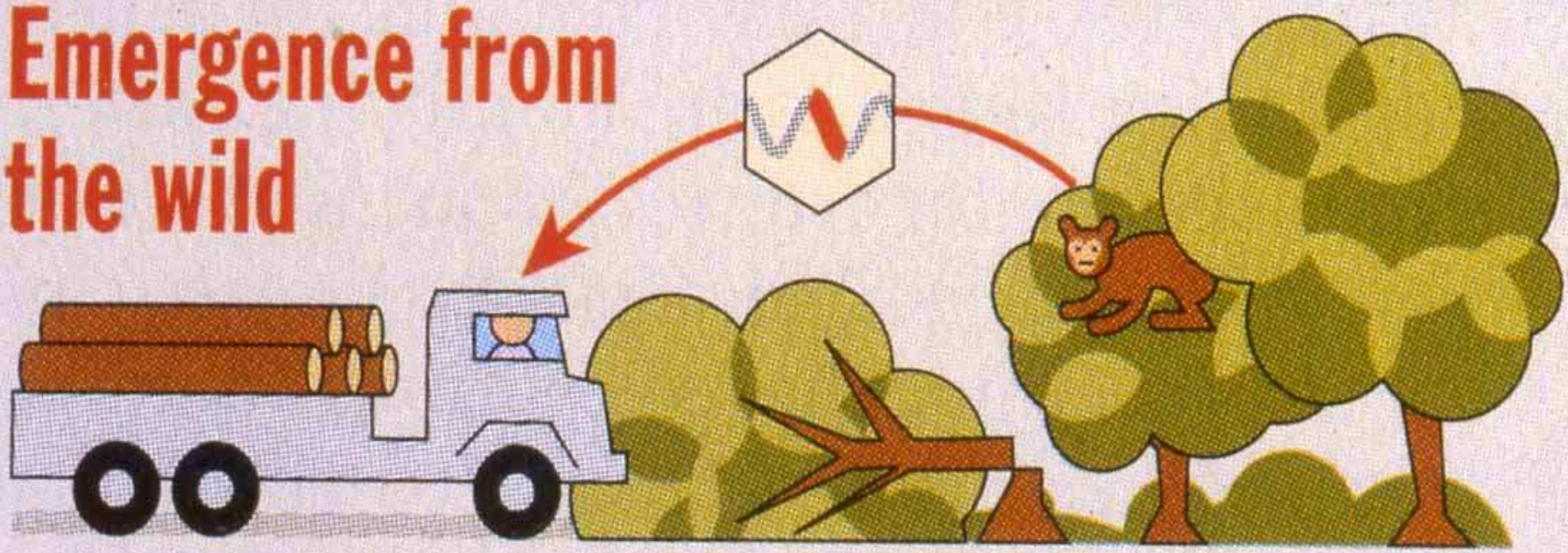


Figure 21 HTLV-1 and HTLV-2 distribution. The map illustrates the distribution of HTLV-infected individuals. (*A*) HTLV-1 cosmopolitan; (*B*) HTLV-1 Zaire (Central Africa); (*C*) HTLV-1 Melanesia; (*D*) HTLV-1 found in pygmies from Central Africa; (*gray boxes*) HTLV-2. (Modified from a figure provided by A. Gessain and G. Franchini.)

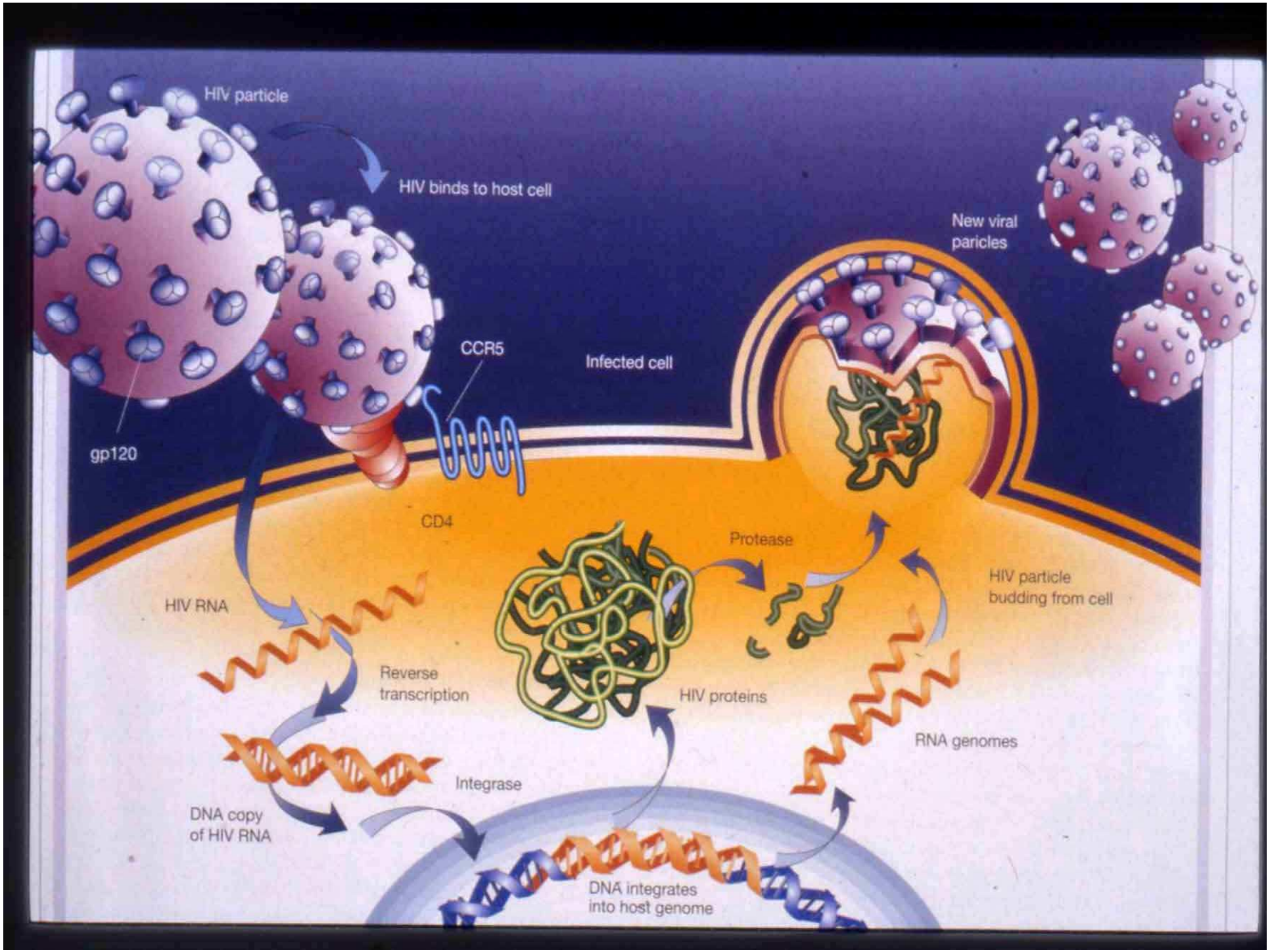

North America
West Indies
Spanish Central and South America
Brazil
HIV-1 HIV-2 1945—1970
Slave trade 1600—1860
Sooty Mangabey
Chimp
Main source of slaves

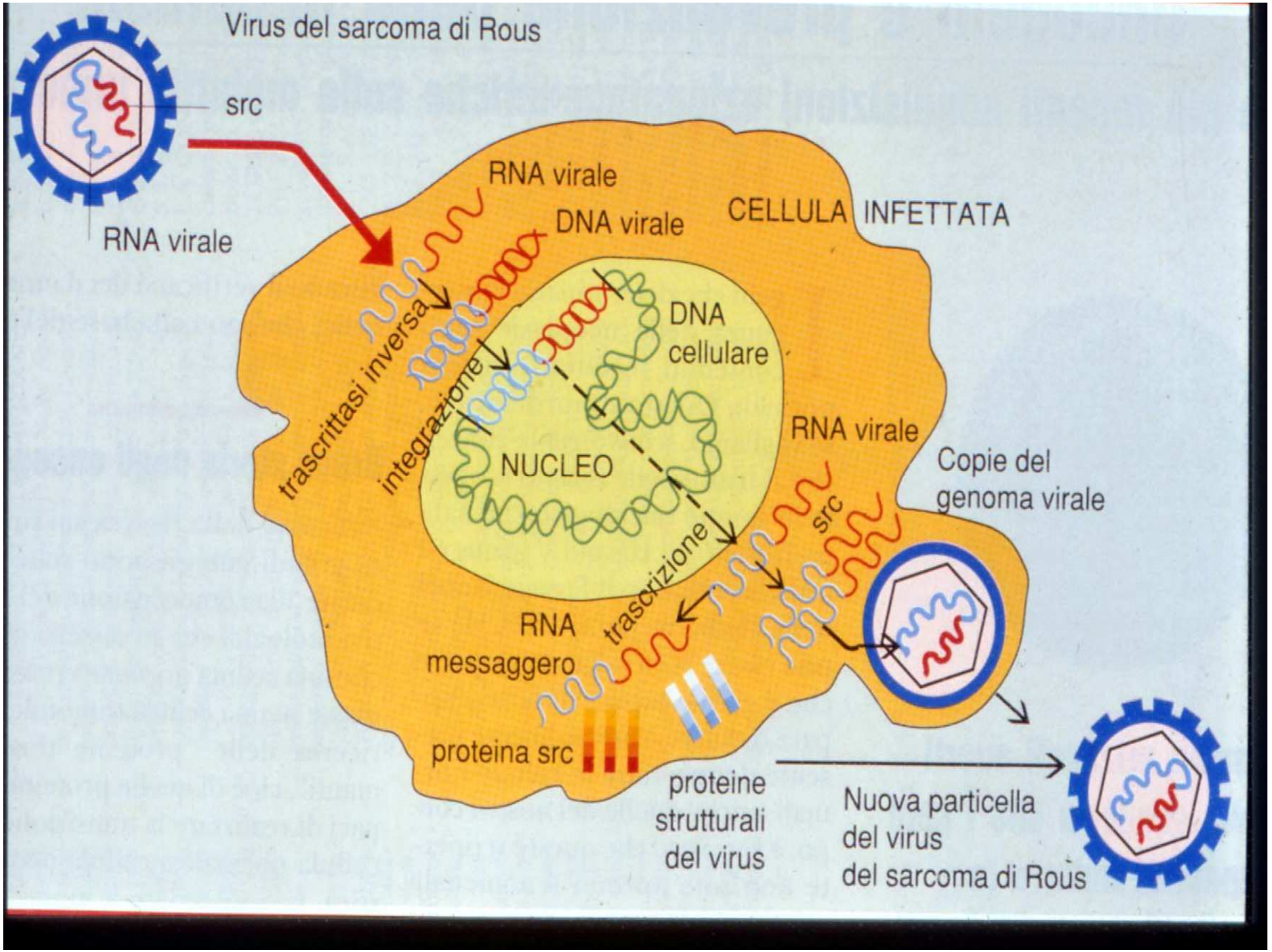
Emergence from the wild

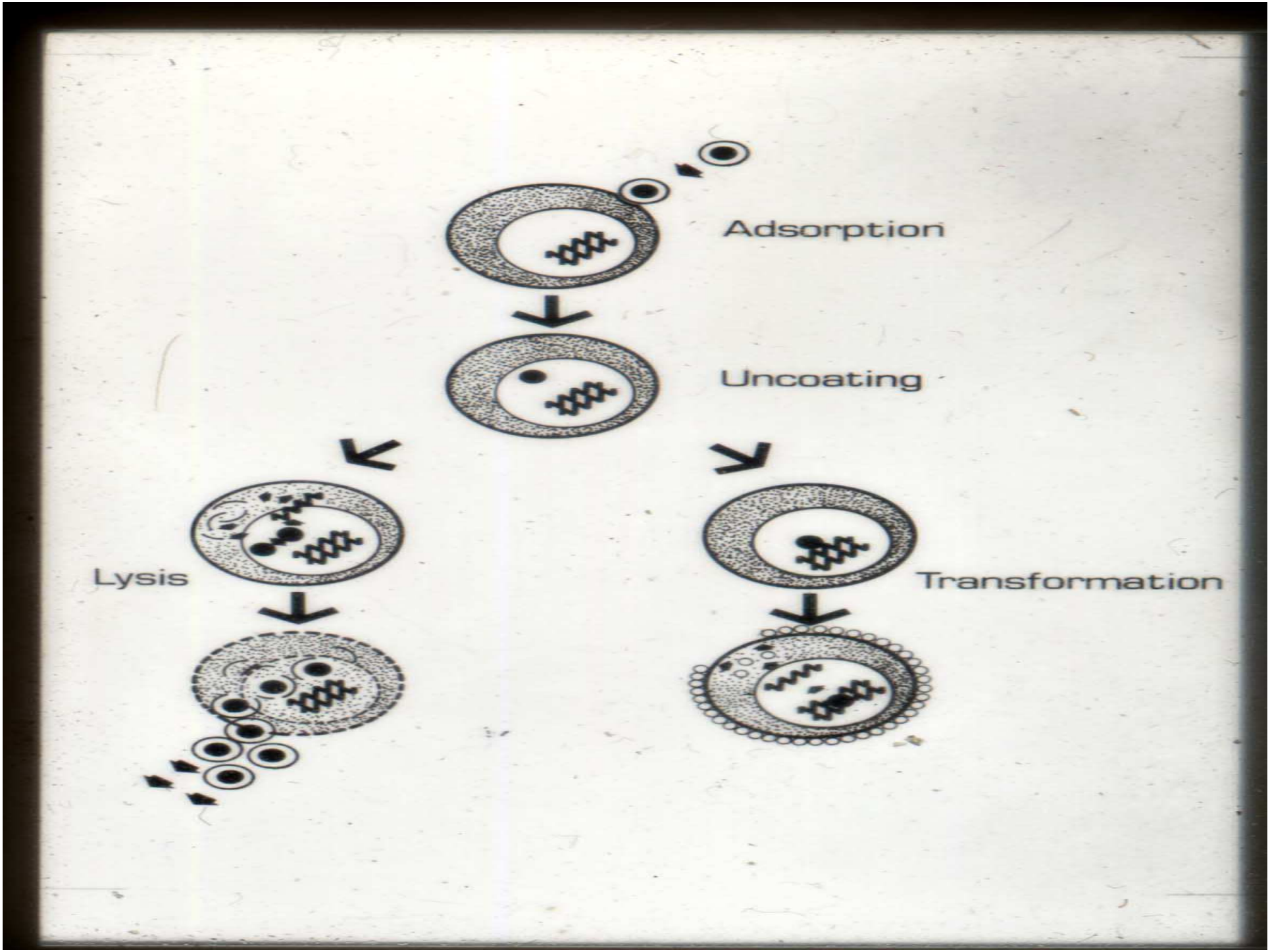


Some viruses lie hidden in environments that are isolated from humans. For example, when a forest is cleared, people may come into contact with animals carrying such viruses. If humans are infected, they can carry the disease back to populated areas. The AIDS virus may have entered the human population this way.

TIME Graphic by Joe Lertol


HIV particle
HIV binds to host cell
New viral
paricles
CCR5
Infected cell
gp120
CD4
Protease
HIV particle
budding from cell
HIV RNA
Reverse
transcription
HIV proteins
RNA genomes
Integrase
DNA copy
of HIV RNA
DNA integrates
into host genome


Virus del sarcoma di Rous
src
RNA virale
RNA virale
DNA virale
CELLULA INFETTATA
trascrittasi inversa
integrazione
DNA cellulare
NUCLEO
RNA virale
Copie del genoma virale
src
trascrizione
RNA messaggero
proteina src
proteine strutturali del virus
Nuova particella del virus del sarcoma di Rous


Adsorption
Uncoating
Lysis
Transformation

A PANDEMICS PRIMER

ENDEMICS

These diseases have a constant presence in a region. Colds and seasonal flus are endemic because they are expected, as is malaria in some tropical regions.

EPIDEMICS

These often sudden outbreaks occur when the tally of new cases exceeds what is expected for an infectious disease in a given region.

PANDEMICS

Like the H1N1 flu of 2009, pandemics not only exceed expected case levels but also spread over many countries—and often many continents too.

WHY THEY SPREAD

Despite advances in science, modern living still makes it easy for diseases to spread in a number of ways

URBANIZATION

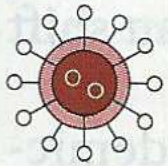
*Plagues once ravaged port cities that were overrun with vermin. Today viruses like **Zika** have hit slums especially hard.*

CONFLICT

*War in Syria has led to rises in **tuberculosis** and **polio** because of overburdened or destroyed hospitals and major population displacement.*

SLOW RESPONSE

*A known pathogen, **Ebola** still managed to spread widely in 2014 because of a slow response from the international community.*

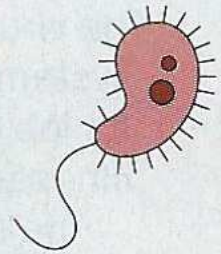


NATURAL DISASTERS

*Haiti's **cholera** outbreak following the 2010 earthquake stemmed from overwhelmed health services, displaced people and poor sanitation.*

AIR TRAVEL

*International flights are the fastest way for diseases to cross borders. In 2009, the **H1N1** virus spread to 48 countries in one month.*



OUTBREAKS ON THE RISE

The number of dangerous outbreaks has increased, but thanks to better modern disease control, the number of people infected per capita has fallen over time.

WHAT'S BEHIND THE MOST RECENT DISEASE OUTBREAKS

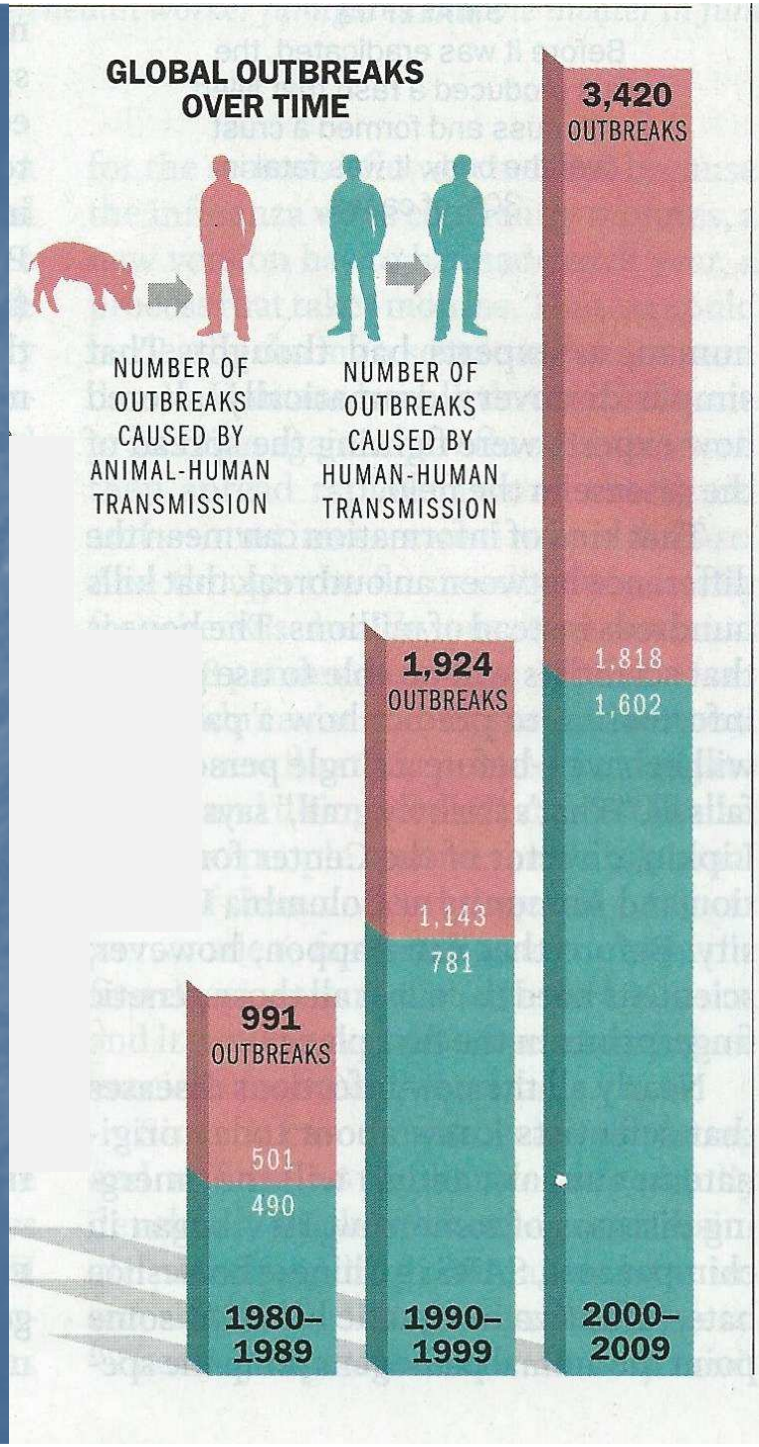
SALMONELLA	423
VIRAL GASTROENTERITIS	381
CHOLERA	251
MEASLES	246
E. COLI	239
INFLUENZA	209
HEPATITIS A	178
ENTEROVIRUS	175
ANTHRAX	169
DENGUE FEVER	150
SHIGELLOSIS	146
MENINGITIS	130
LEGIONNAIRES' DISEASE	117
TUBERCULOSIS	111
TYPHOID AND ENTERIC FEVER	106

__Measles__ is back in the U.S. and elsewhere because of lower childhood-vaccination rates

Most of the __influenza__ outbreaks between 2000 and 2010 stemmed from H1N1

Antibiotic-resistant strains of bacterial infections like __tuberculosis__ are on the rise

GRAPHIC SOURCES: CDC; KAISER FAMILY FOUNDATION; "GLOBAL RISE IN HUMAN INFECTIOUS DISEASE OUTBREAKS," JOURNAL OF THE ROYAL SOCIETY INTERFACE, 2014


GLOBAL OUTBREAKS OVER TIME
NUMBER OF OUTBREAKS CAUSED BY ANIMAL-HUMAN TRANSMISSION
NUMBER OF OUTBREAKS CAUSED BY HUMAN-HUMAN TRANSMISSION
991 OUTBREAKS
501
490
1980–1989
1,924 OUTBREAKS
1,143
781
1990–1999
3,420 OUTBREAKS
1,818
1,602
2000–2009

DISEASE HALL OF FAME

BUBONIC PLAGUE

It doesn't hit often anymore, but when it does, it causes swollen lymph nodes, fever and malaise. Without treatment, 50% of infected people die.

CHOLERA

It causes diarrhea and severe dehydration. If left untreated, it has a mortality rate of up to 50% and can kill within hours.

EBOLA

It causes fever, muscle pain, diarrhea, vomiting and bleeding. Recent outbreaks have had mortality rates of up to 90%. It has no cure.

HIV

The virus destroys the immune system so it can no longer do its job of fighting off common illnesses. Without treatment, life expectancy is about 10 years.

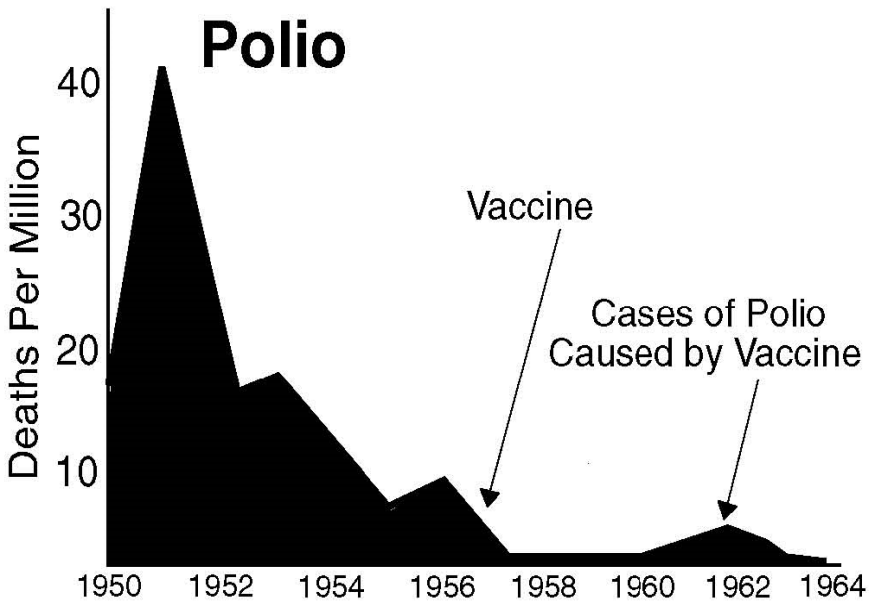
SMALLPOX

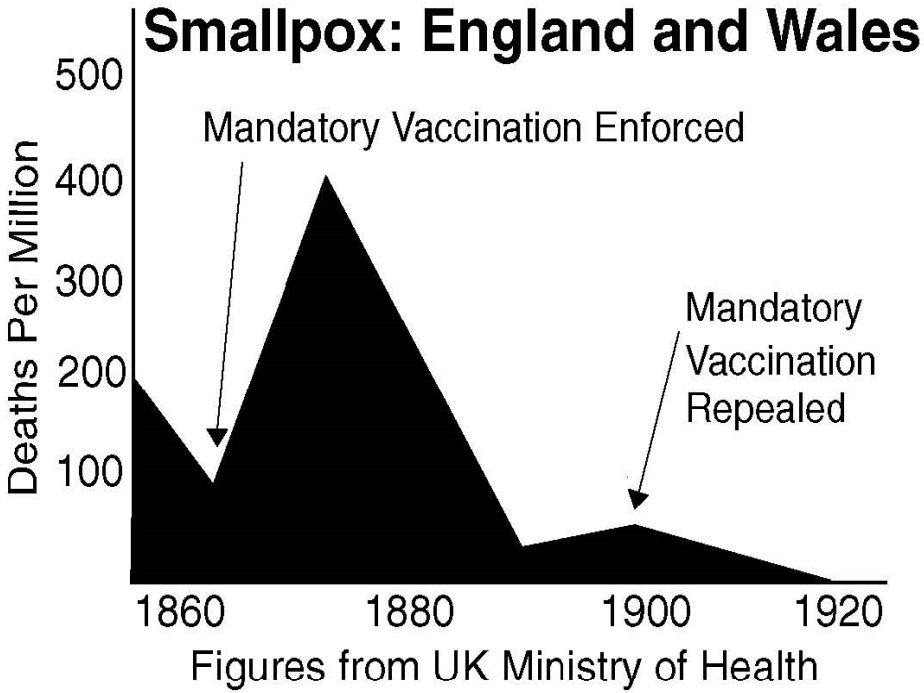
Before it was eradicated, the virus produced a rash that filled with puss and formed a crust over the body. It was fatal in 30% of cases.

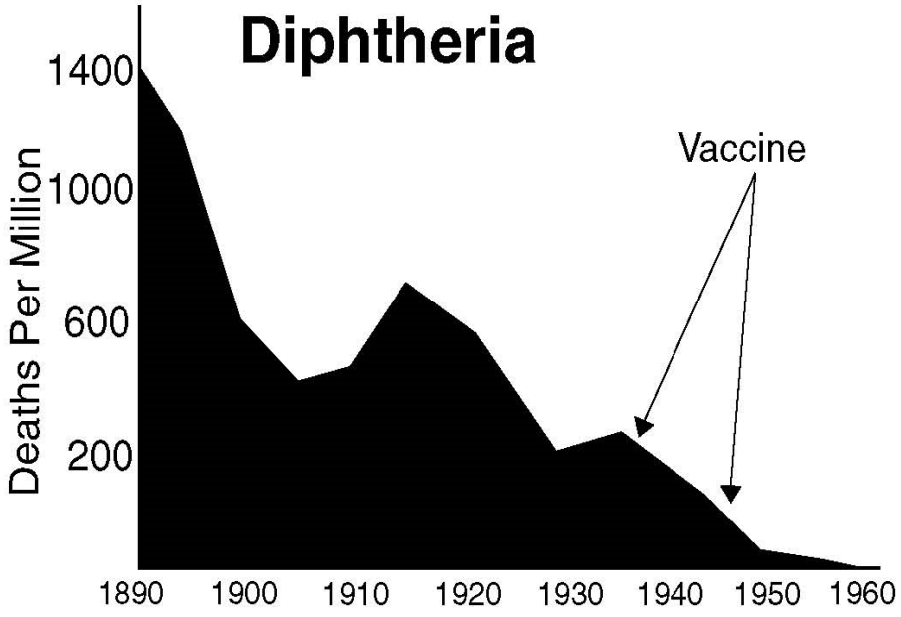
VIRUS BUSTERS *A South Korean health worker fumigates a movie theater in June 2015 after MERS cases were reported*

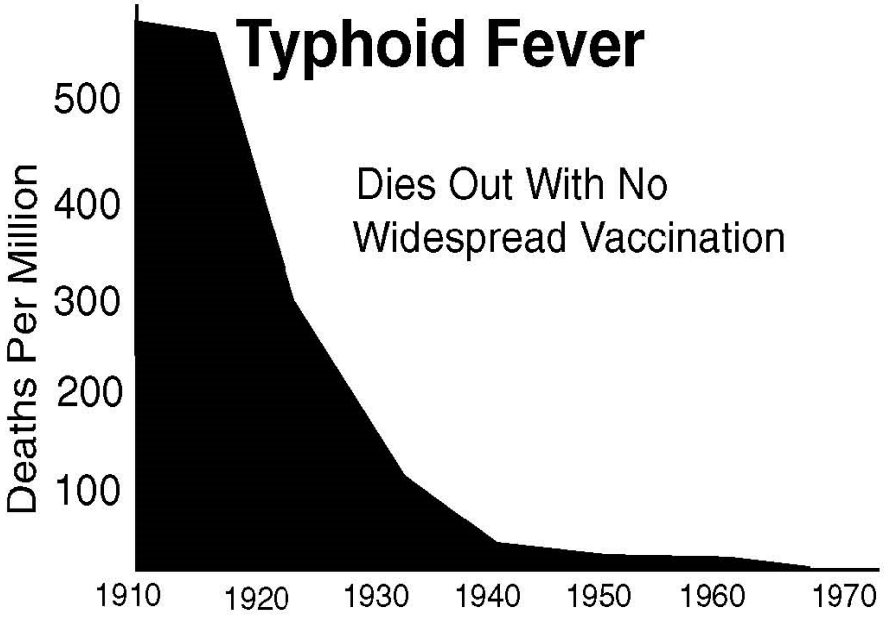
CRISIS PREP *A dummy body is transported during an Ebola drill in Lyon, France, in 2015*

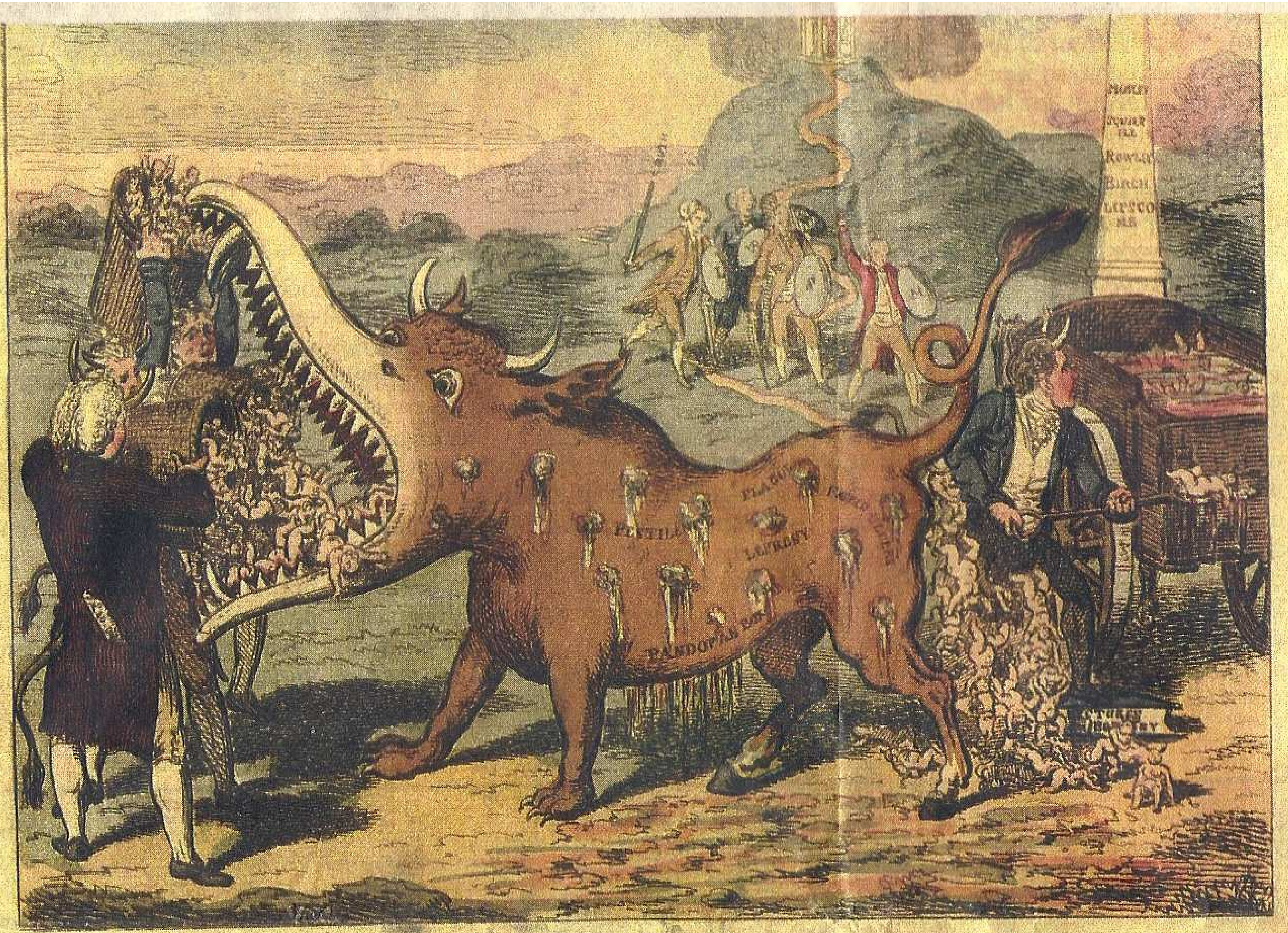
Across China, the virus that could spark the next pandemic is already circulating. It's a bird flu called H7N9, and true to its name, it mostly infects poultry. Lately, however, it's started jumping from chickens to humans more readily – bad news, because the virus is a killer. During a recent spike, 88% of people infected got pneumonia, three-quarters ended up in intensive care with severe respiratory problems, and 41% died.


Polio
Deaths Per Million
40
30
20
10
Vaccine
Cases of Polio
Caused by Vaccine
1950
1952
1954
1956
1958
1960
1962
1964


Smallpox: England and Wales
Deaths Per Million
500
400
300
200
100
Mandatory Vaccination Enforced
Mandatory
Vaccination
Repealed
1860
1880
1900
1920
Figures from UK Ministry of Health


Diphtheria
Deaths Per Million
1400
1000
600
200
Vaccine
1890
1900
1910
1920
1930
1940
1950
1960


Typhoid Fever
Deaths Per Million
500
400
300
200
100
Dies Out With No
Widespread Vaccination
1910
1920
1930
1940
1950
1960
1970



VACCINATION.

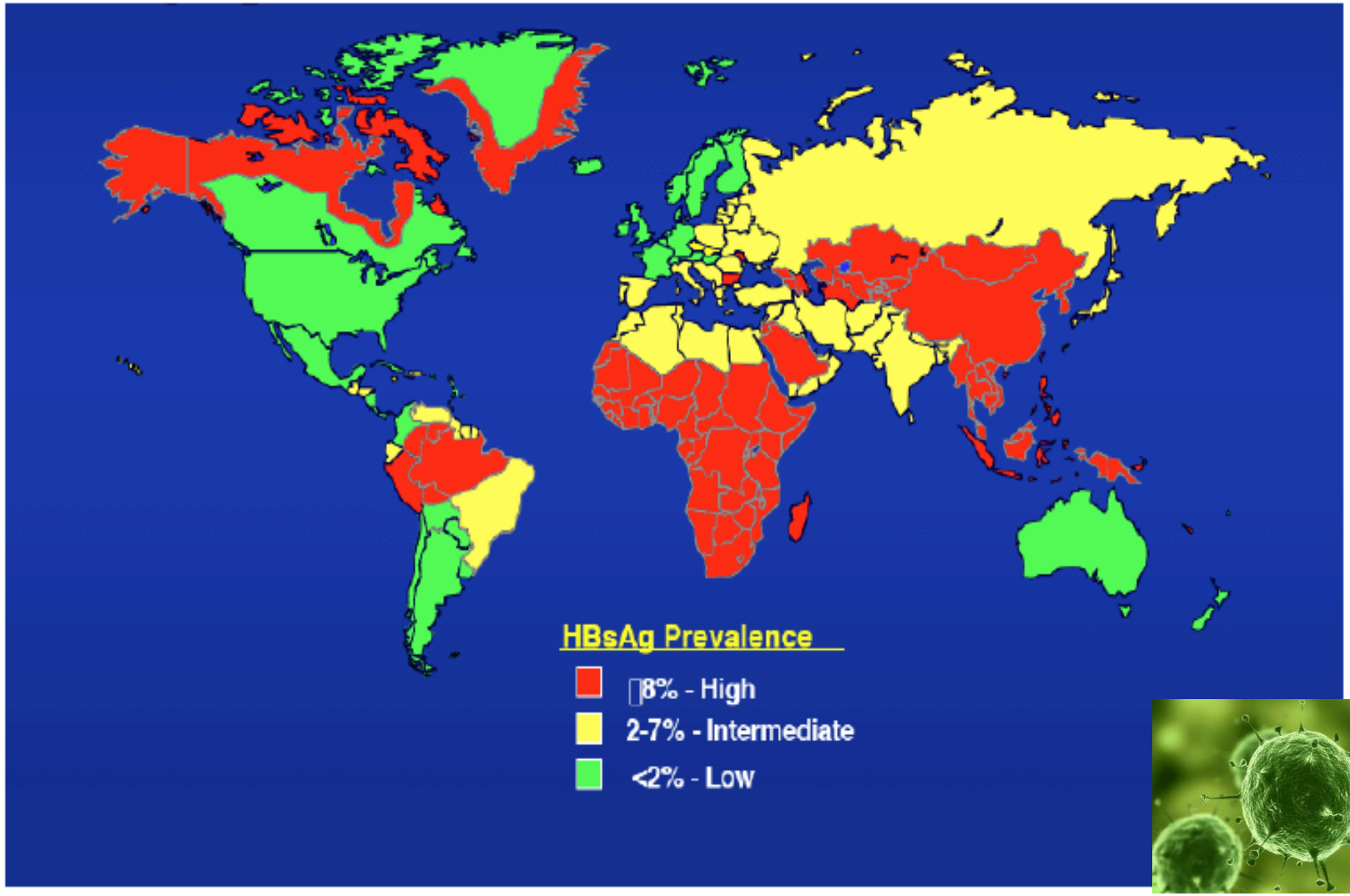
I VACCINI OBBLIGATORI

	dal 3° mese	dal 13° mese	copertura attuale (dati 2016)
Difterite	■		93,5%
Tetano	■		93,7%
Epatite B	■		93,0%
Poliomielite	■		93,3%
Pertosse	■		93,6%
Haemophilus influenzae	■		93,0%
Morbillo		■	87,3%
Parotite		■	87,2%
Rosolia		■	87,2%
Varicella		■	46,1%

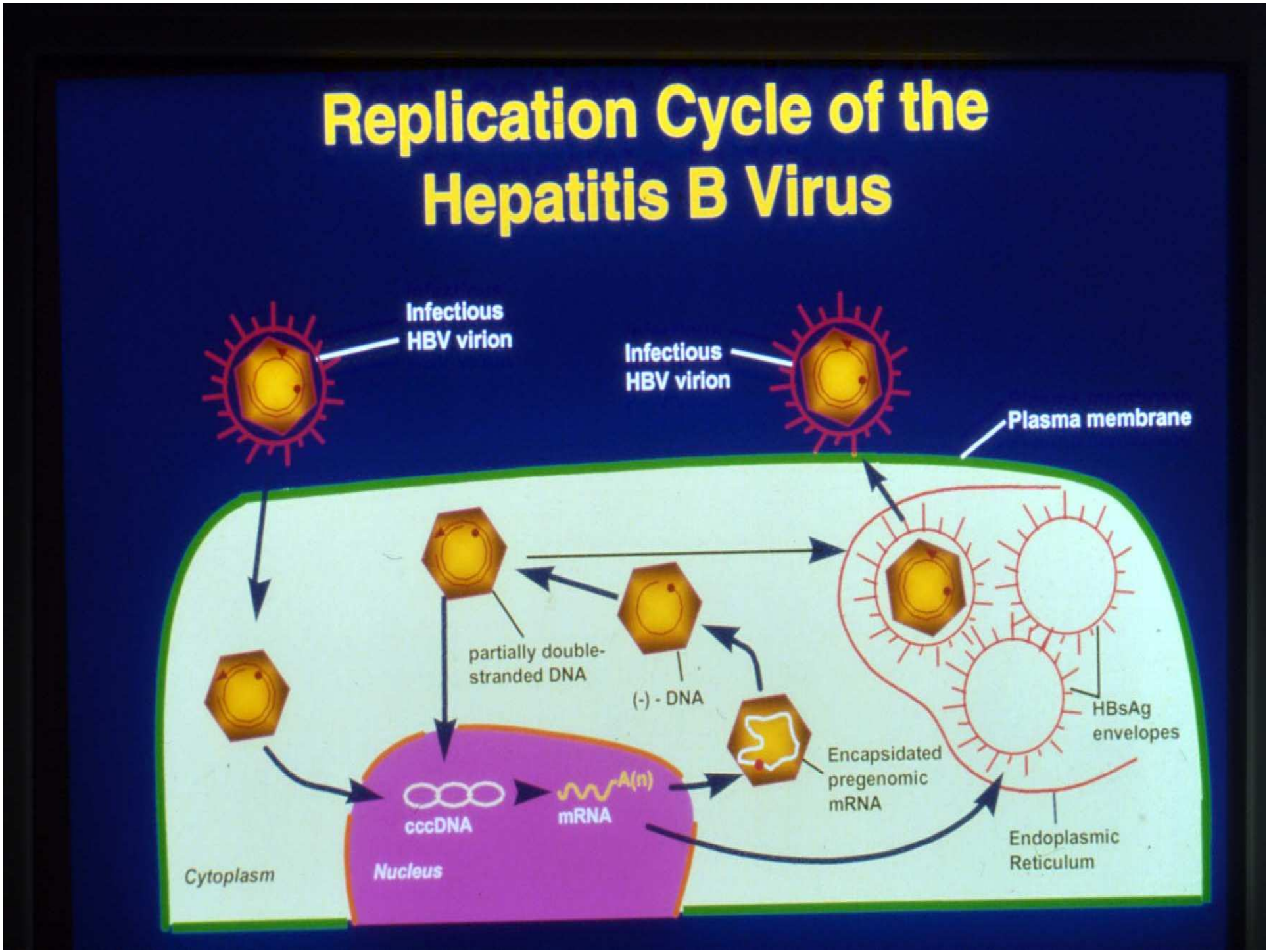
Fonte: ministero della Salute

P&G Infograph

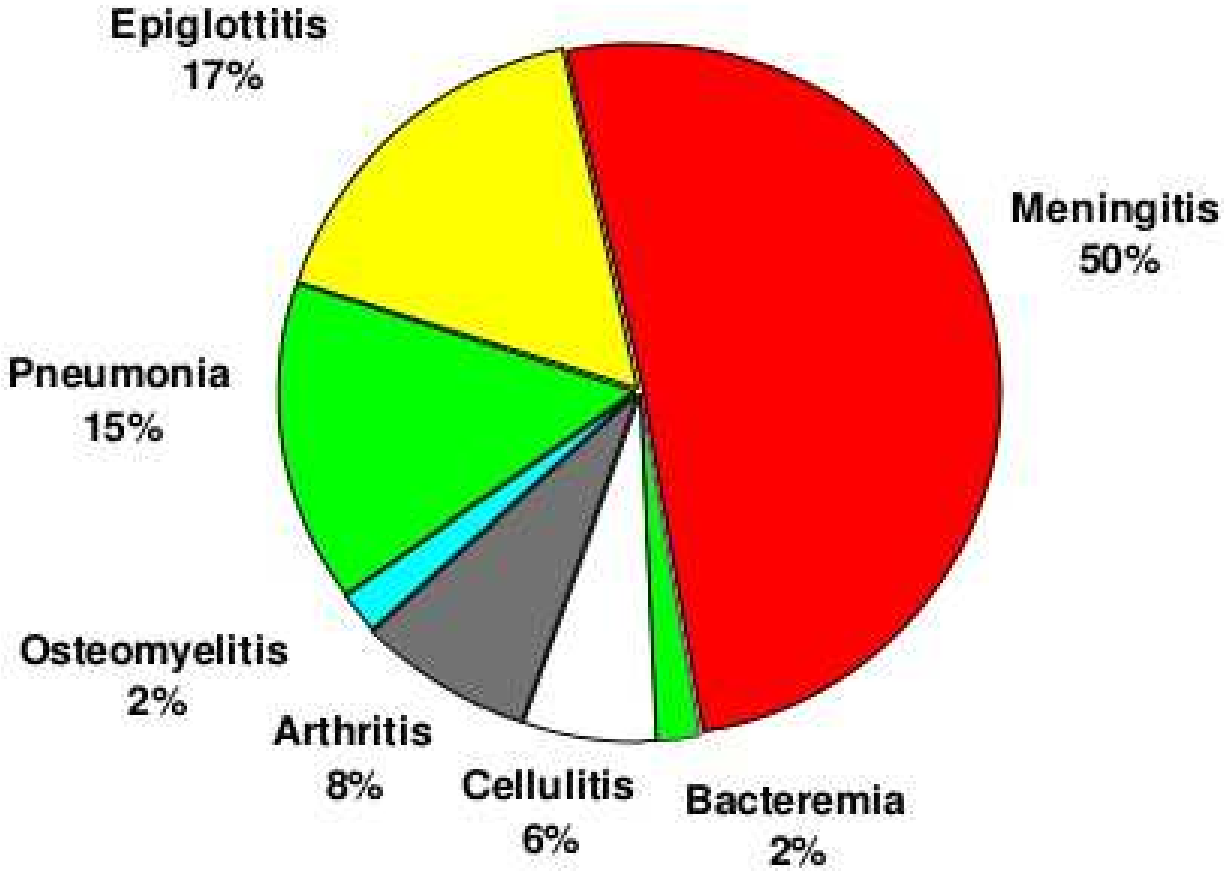
HBV infection worldwide



Replication Cycle of the Hepatitis B Virus

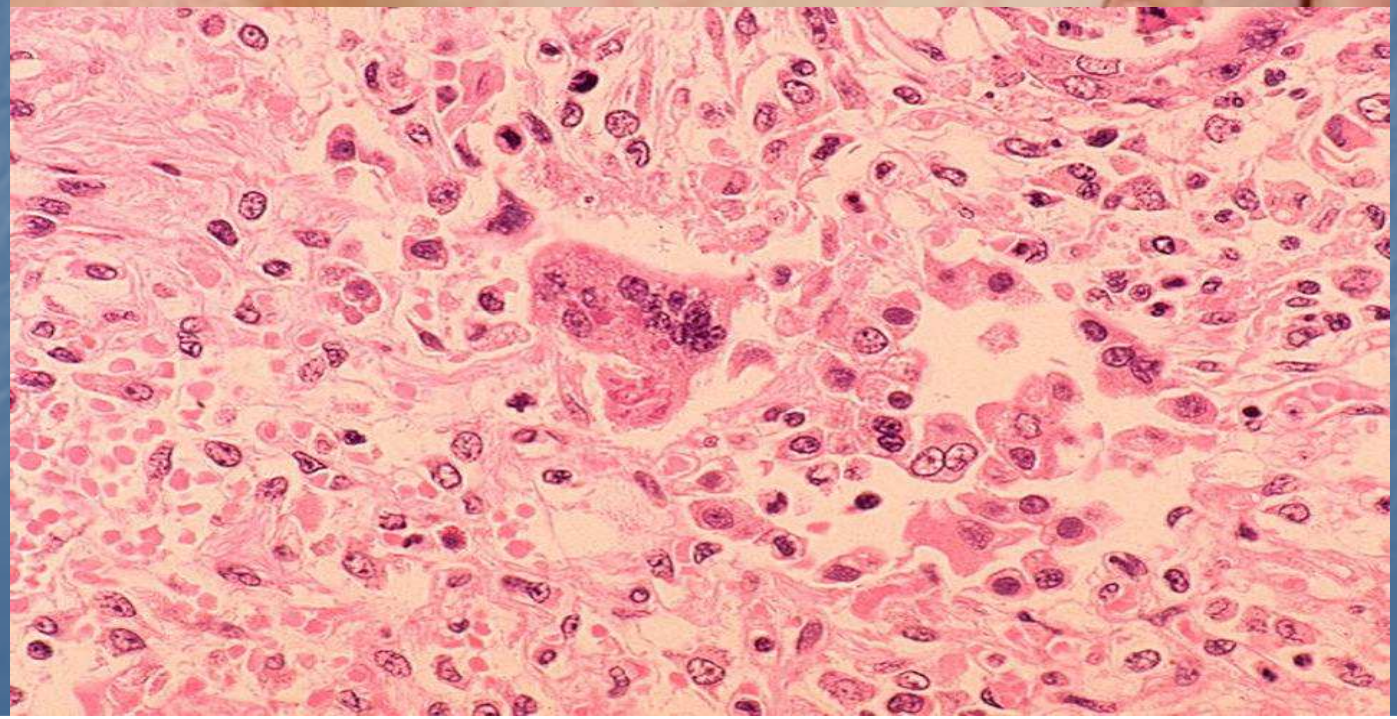


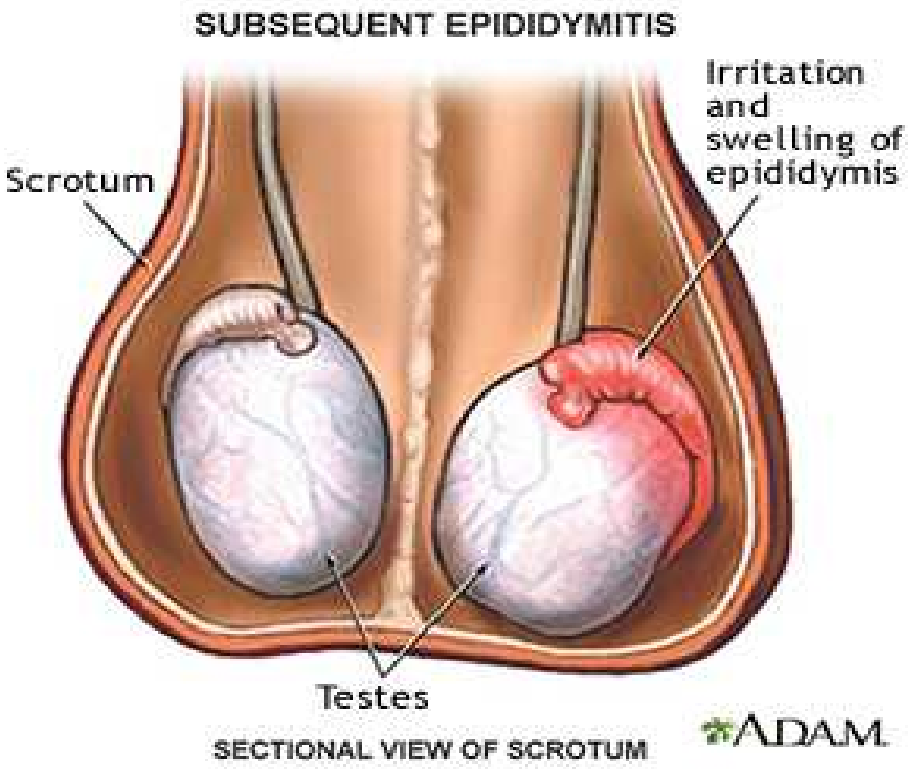
Haemophilus influenzae type b
Clinical Features*



Dr.T.V.Rao MD


photo by: jennyandshannon




SUBSEQUENT EPIDIDYMITIS
Irritation and swelling of epididymis
Scrotum
Testes
SECTIONAL VIEW OF SCROTUM
ADAM.

Le vaccinazioni previste dalla Legge 119 del 28 luglio 2017:

1) anti-poliomelitica: ciclo di base 3 dosi nel primo anno di vita e richiamo a 6 anni

2) anti-difterica: ciclo di base 3 dosi nel primo anno di vita e richiamo a 6 anni

3) anti-tetanica: ciclo di base 3 dosi nel primo anno di vita e richiamo a 6 anni

4) anti-epatite B: 3 dosi nel primo anno di vita

5) anti-pertosse: ciclo di base 3 dosi nel primo anno di vita e richiamo a 6 anni

6) anti Haemophilusinfluenzae tipo B: 3 dosi nel primo anno di vita

7) anti-morbillo: 1° dose nel secondo anno di vita e 2° dose a 6 anni

8) anti-rosolia: 1° dose nel secondo anno di vita e 2° dose a 6 anni

9) anti-parotite: 1° dose nel secondo anno di vita e 2° dose a 6 anni

10) anti-varicella: 1° dose nel secondo anno di vita e 2° dose a 6 anni

I soggetti danneggiati da complicanze di tipo irreversibile a causa di vaccinazioni obbligatorie, possono - come previsto dalla Legge 210/92 e dalla Legge 29 ottobre 2005 n. 229 - fare richiesta di riconoscimento economico. Il riconoscimento dell'indennizzo, come previsto dalla Legge 210/92, non preclude la possibilità di rivolgersi all'Autorità Giudiziaria per ottenere il risarcimento del danno in caso di comportamenti colposi di terzi (ai sensi dell'art. 2043 del Codice Civile). L'esistenza della Legge 210/92 è legata alla obbligatorietà delle vaccinazioni e non alla loro "pericolosità".

ON THE COVER

Vaccines are our best defenses against many infectious diseases, having saved millions of lives and prevented immeasurable suffering. Yet today, in many developed countries, these defenses are fraying as parents, swayed by persistent untruths about the risks, hesitate to vaccinate their children. This special package sizes up the actual, rare risks of vaccines and what is known about how to overcome groundless fears. See page 364. *Illustration: Ben Wiseman*

FEATURES

THE VACCINE WARS

Debunking myths, owning real risks, and courting doubters

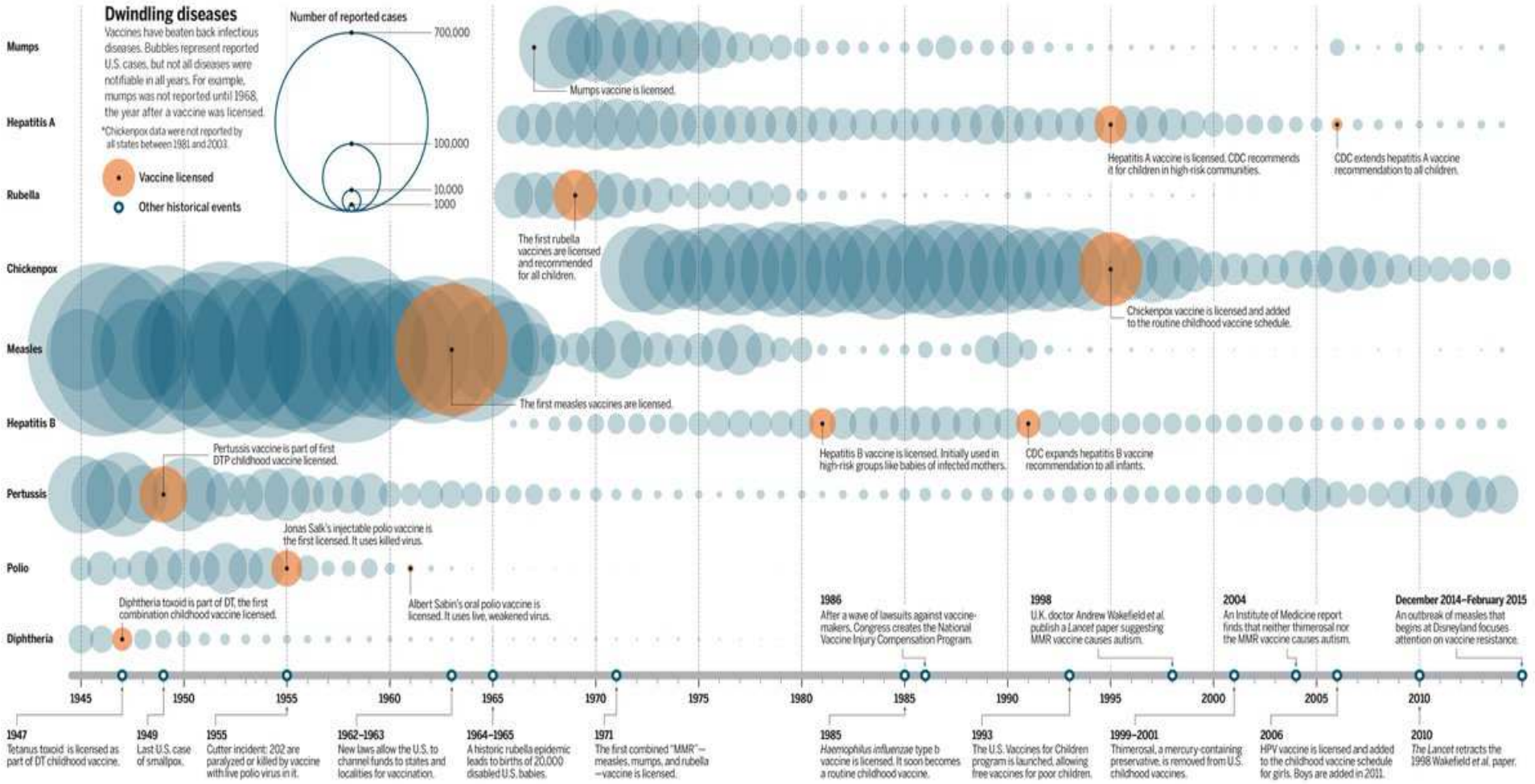
By **Meredith Wadman** *and* **Jia You**

LAST WEEK, PUBLIC HEALTH AUTHORITIES in Minnesota asked more than 200 people to quarantine themselves after 12 cases of measles were diagnosed in less than 2 weeks—all of them in unvaccinated children younger than 6 years. Across the ocean, an unvaccinated 17-year-old Portuguese girl died of measles after the virus invaded her lungs, in the midst of an outbreak there that mirrors surges in cases in Germany, Italy, and Romania.

In 2015, the most recent year for which data are available, just 72% of U.S. toddlers had received seven key vaccines recommended by the Centers for Disease Control and Prevention (CDC), which together protect against 11 potentially deadly diseases. That is actually an improvement from 2011, when the number was 69%; but it also indicates that much work remains to be done, particularly in an environment in which vaccine skeptics have been emboldened, not least by the current occupant of the Oval Office.

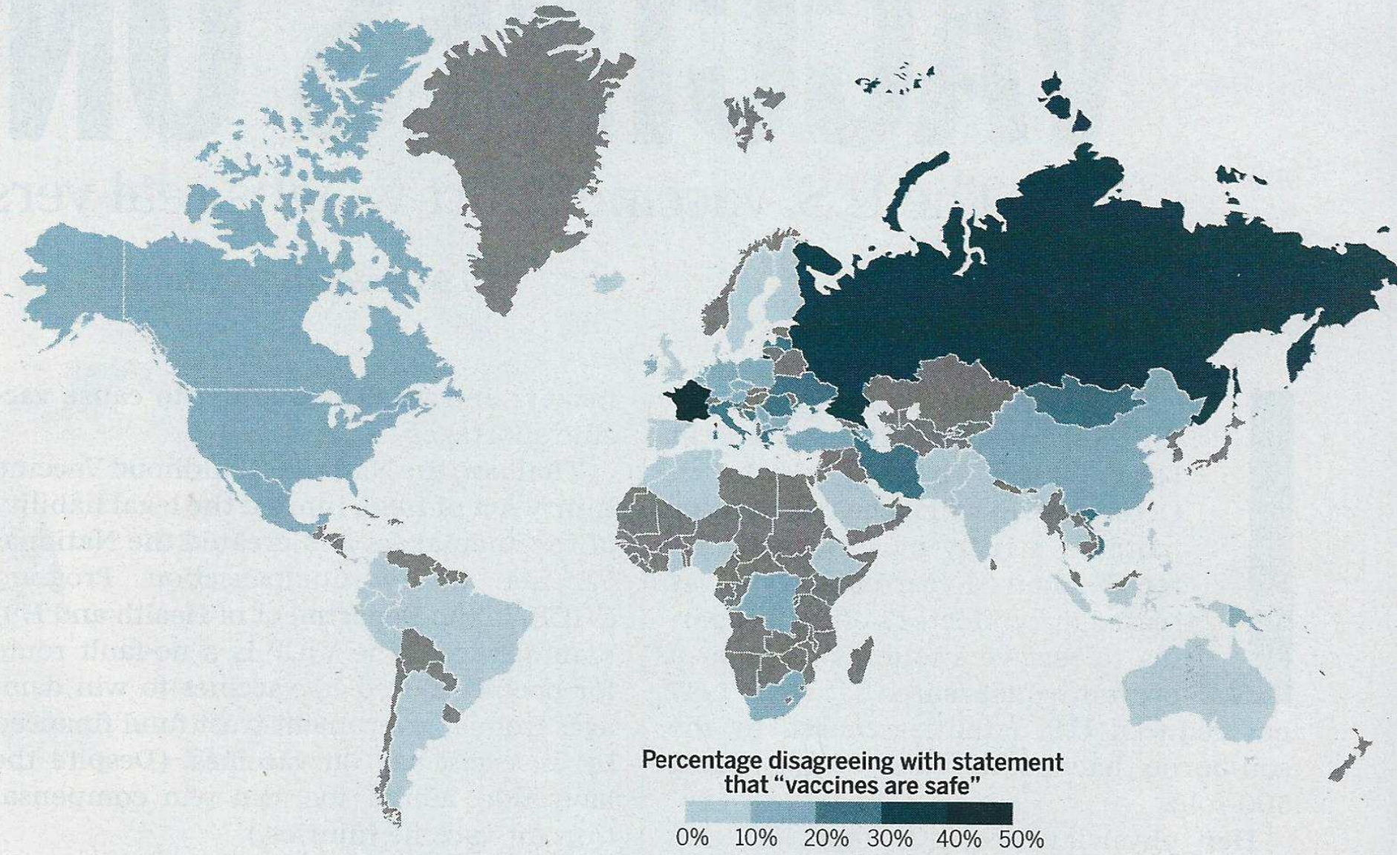
As once common diseases of childhood fade from public view, it is understandable that parents' attention would shift from the fear of disease to concerns about risks of the vaccines themselves. The articles in this issue debunk myths old and new about these risks, while acknowledging the real, rare vaccine injuries that do occur. The data on these pages make clear the power of vaccines to vanquish disease—an impact that far eclipses their minute risks. Identifying the best ways to convince hesitant parents of this calculus in an age of internet-fed misinformation is an ongoing challenge for researchers. ■

DATA: CDC



A matter of trust

A 2016 survey in 67 countries found that trust in vaccines is high overall but varies by country. Safety concerns were highest in Europe and Russia; in France, 41% disagreed with the statement that vaccines are safe.



FEATURES

Jama: 21 aprile 2015 – 313 (815) 153-40. il vaccino MMR non è associato ad un maggior rischio di disturbi dello spettro autistico.

Dal momento che l'individuo non è una macchina biologica senza altre distinzioni e l'infezione non è una guerra da cui proteggerci fortificando soltanto le nostre difese immunitarie: basterebbe un vaccino contro tutte le malattie da somministrare alla nascita per neutralizzare qualsiasi microorganismo e garantirsi una vita sana e lunga come possiamo leggere in qualche libro di fantascienza o in servizi giornalistici sostenuti da qualche sospetta inserzione pubblicitaria.

Le vaccinazioni sono uguali per ogni soggetto che si sottopone ad esse e rappresentano quindi una nuova interazione tra microrganismo e soggetto umano. Secondo Louis Pasteur, padre della immunologia e della moderna medicina «Il microbo è nulla, il terreno è tutto». Pertanto spetta al medico di vivificare questo organismo prima ancora di qualsiasi vaccino.

Some Proved or Putative Cancer Viruses of Man

- **Established**

Hepatitis B (Hepadnaviridae)
Epstein-Barr (Herpesviridae)
HTLV-I and –II (Retroviridae)
HIV-1 and -2 (Retroviridae)
Papillomavirus (Papovaviridae)
Human Herpes Virus-8 (Herpesviridae)
Merkel cell polyomavirus (MCV)

- **Suspect**

Herpes simplex (cofactor) (Herpesviridae)
Hepatitis c (Flaviridae)
Papovavirus (BK, JC) (Papovaviridae)

- **Possible**

Adenovirus (Adenoviridae)

Source: Modified from Annals N.Y. Academy of Science

Examples of Licensed and Experimental Vaccines against Established or Putative Virus Cancers of Man

- **Licensed**

Hepatitis B (plasma-derived and recombinant)

Adenovirus (live and killed)

Papillomavirus

- **Experimental-Investigative**

Retrovirus

HIV-1 and -2	**AIDS**
HTLV-1 and HTLV-2	**Leukemia**

Epstein-Barr virus

Hepatitis C

Source: Modified from annals N.Y. Academy of Science

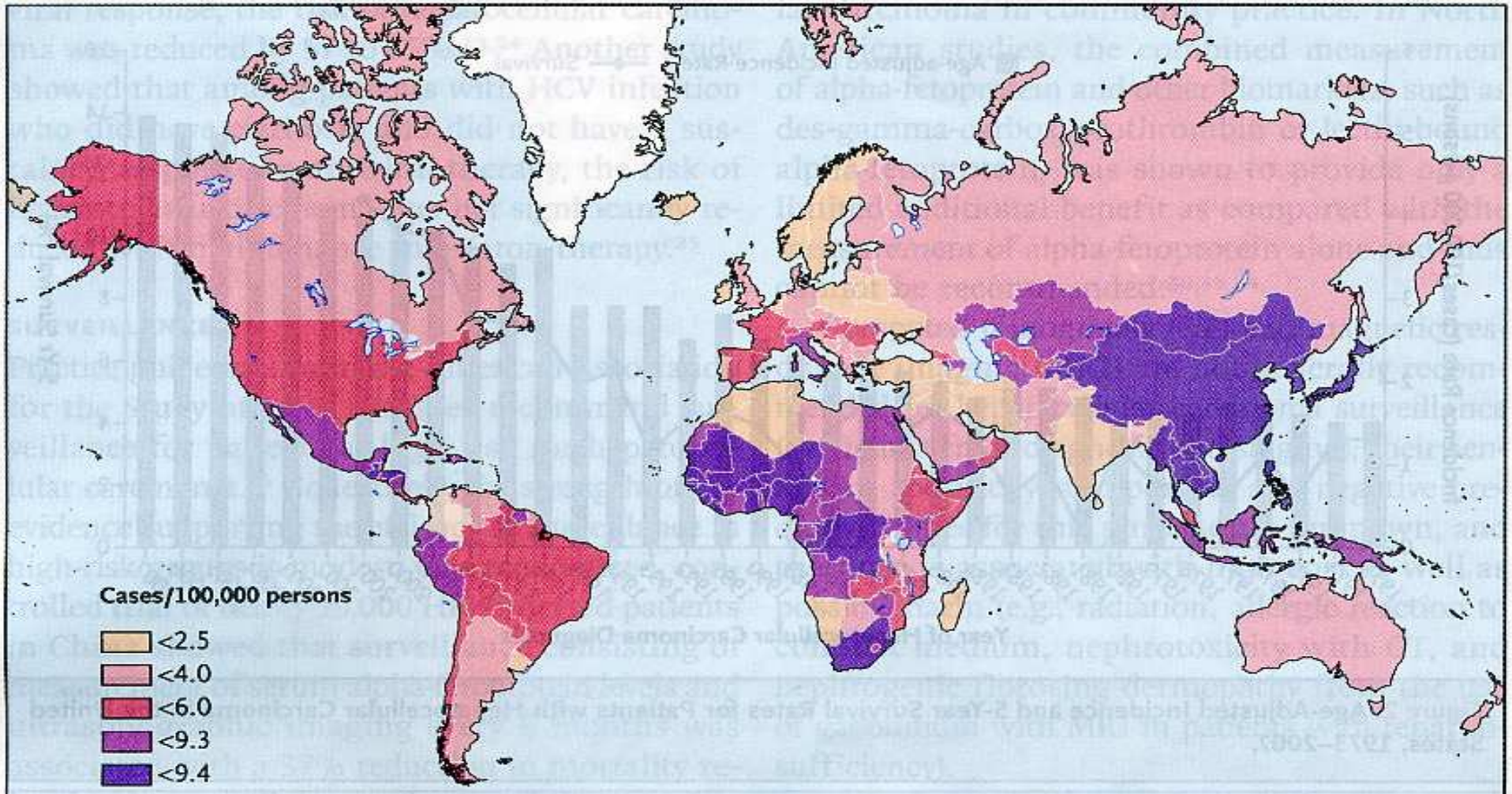
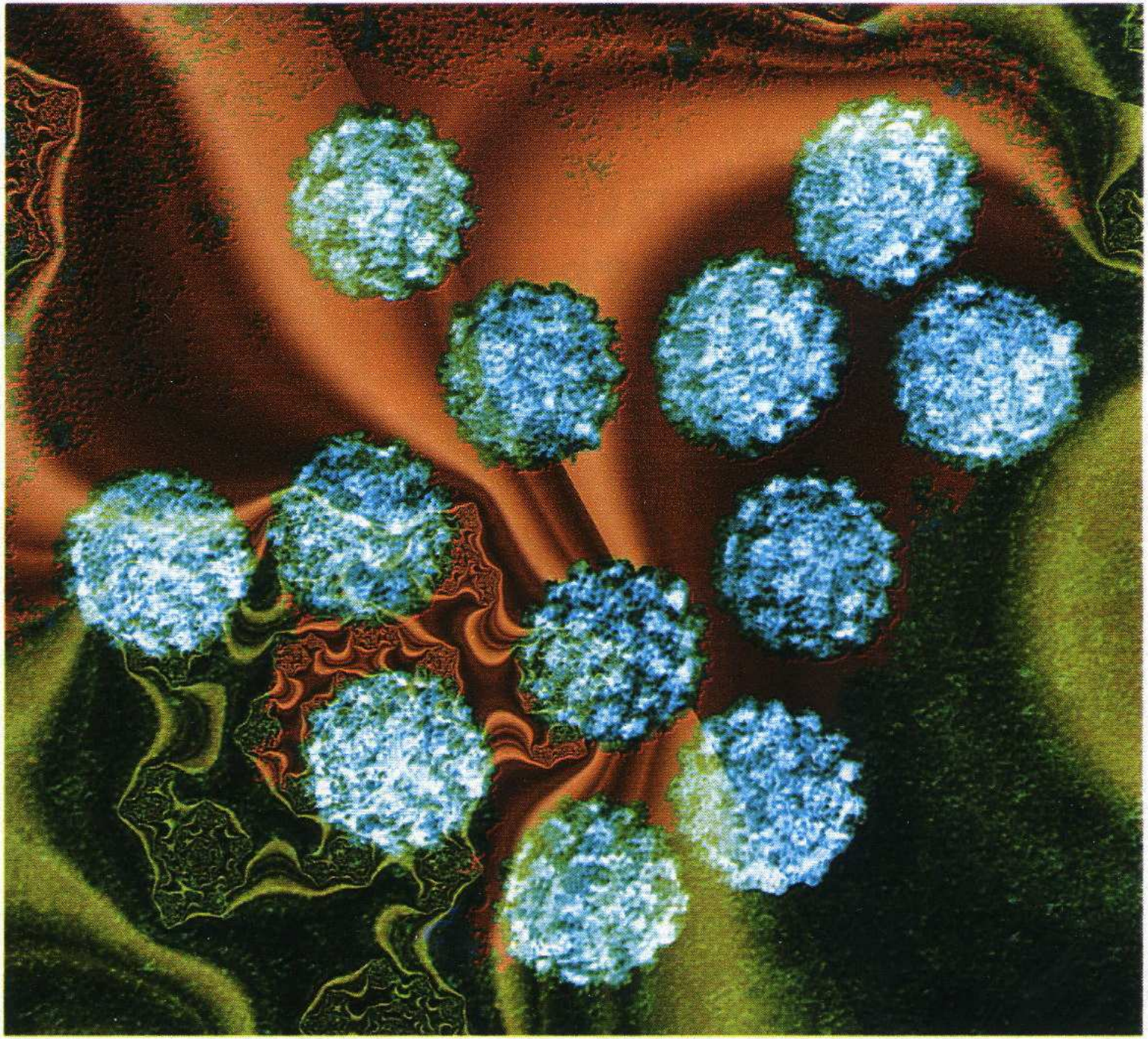
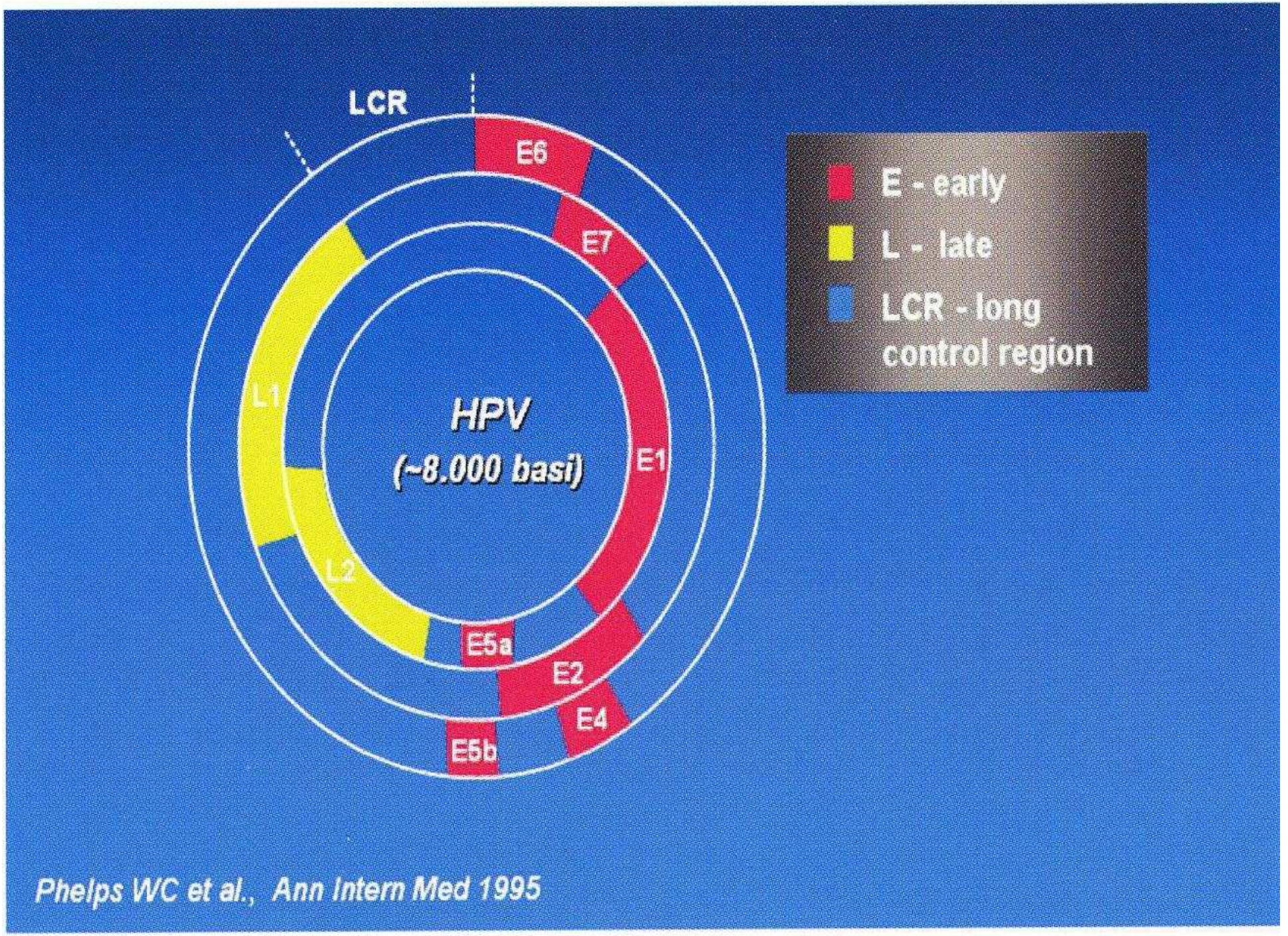
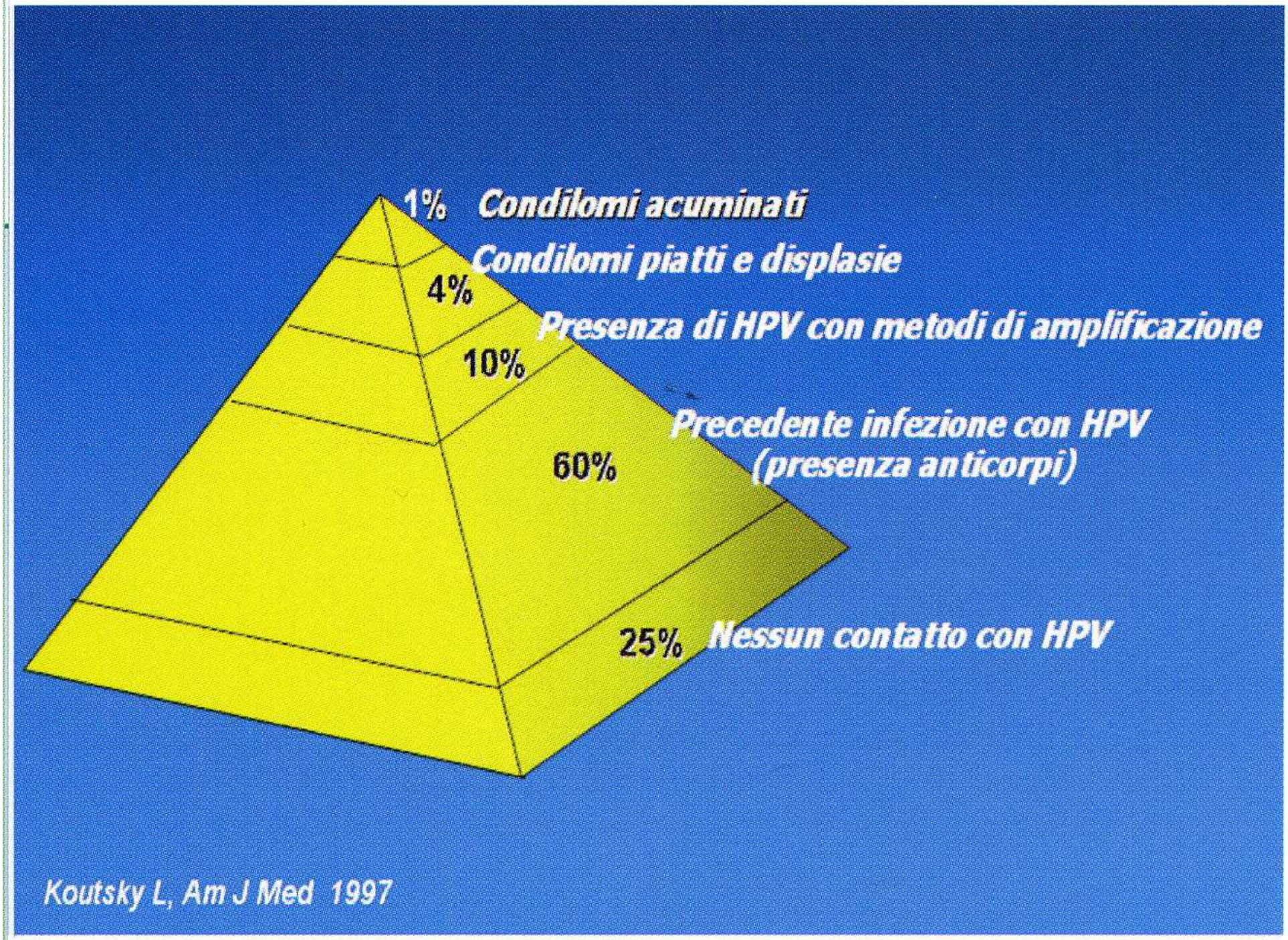


Figure 1. Regional Variation in the Estimated Age-Standardized Incidence Rates of Liver Cancer.

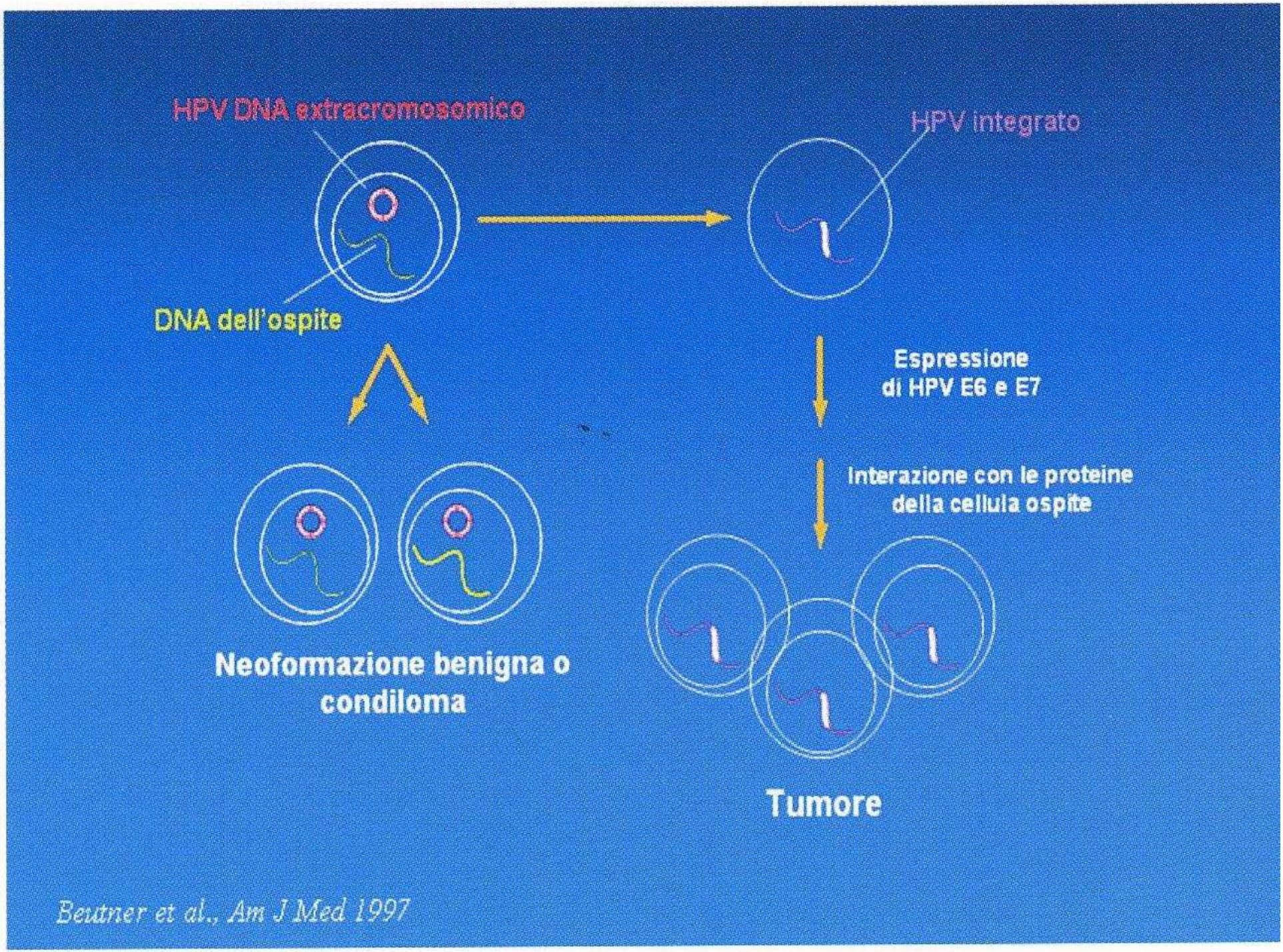
The incidence rates shown (numbers of cases per 100,000 persons) pertain to both sexes and all ages. Adapted from the World Health Organization.[3]

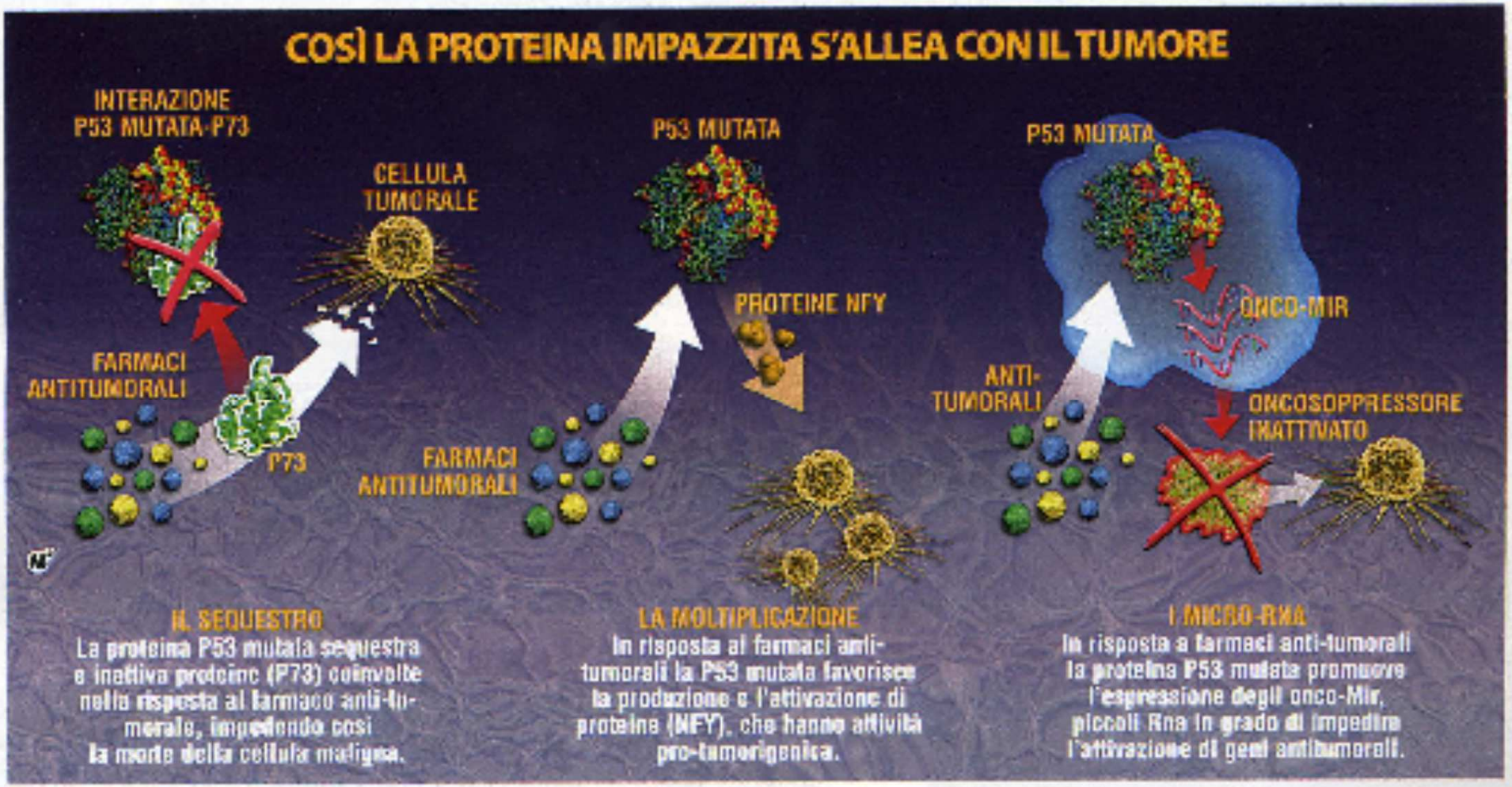



LCR
E6
E7
E1
E2
E4
E5b
E5a
L2
L1
HPV
(~8.000 basi)
E - early
L - late
LCR - long control region
Phelps WC et al., Ann Intern Med 1995



Koutsky L, Am J Med 1997


HPV DNA extracromosomico
HPV integrato
DNA dell'ospite
Espressione
di HPV E6 e E7
Interazione con le proteine
della cellula ospite
Neoformazione benigna o
condiloma
Tumore
Beutner et al., Am J Med 1997


COSÌ LA PROTEINA IMPAZZITA S'ALLEA CON IL TUMORE
INTERAZIONE P53 MUTATA-P73
CELLULA TUMORALE
FARMACI ANTITUMORALI
P73
IL SEQUESTRO
La proteina P53 mutata sequestra e inattiva proteine (P73) coinvolte nella risposta al farmaco anti-tumorale, impedendo così la morte della cellula maligna.
P53 MUTATA
PROTEINE NFY
FARMACI ANTITUMORALI
LA MOLTIPLICAZIONE
In risposta ai farmaci anti-tumorali la P53 mutata favorisce la produzione e l'attivazione di proteine (NFY), che hanno attività pro-tumorigenica.
P53 MUTATA
ONCO-MIR
ANTI-TUMORALI
ONCOSOPPRESSORE INATTIVATO
I MICRO-RNA
In risposta a farmaci anti-tumorali la proteina P53 mutata promuove l'espressione degli onco-Mir, piccoli Rna in grado di impedire l'attivazione di geni antitumorali.

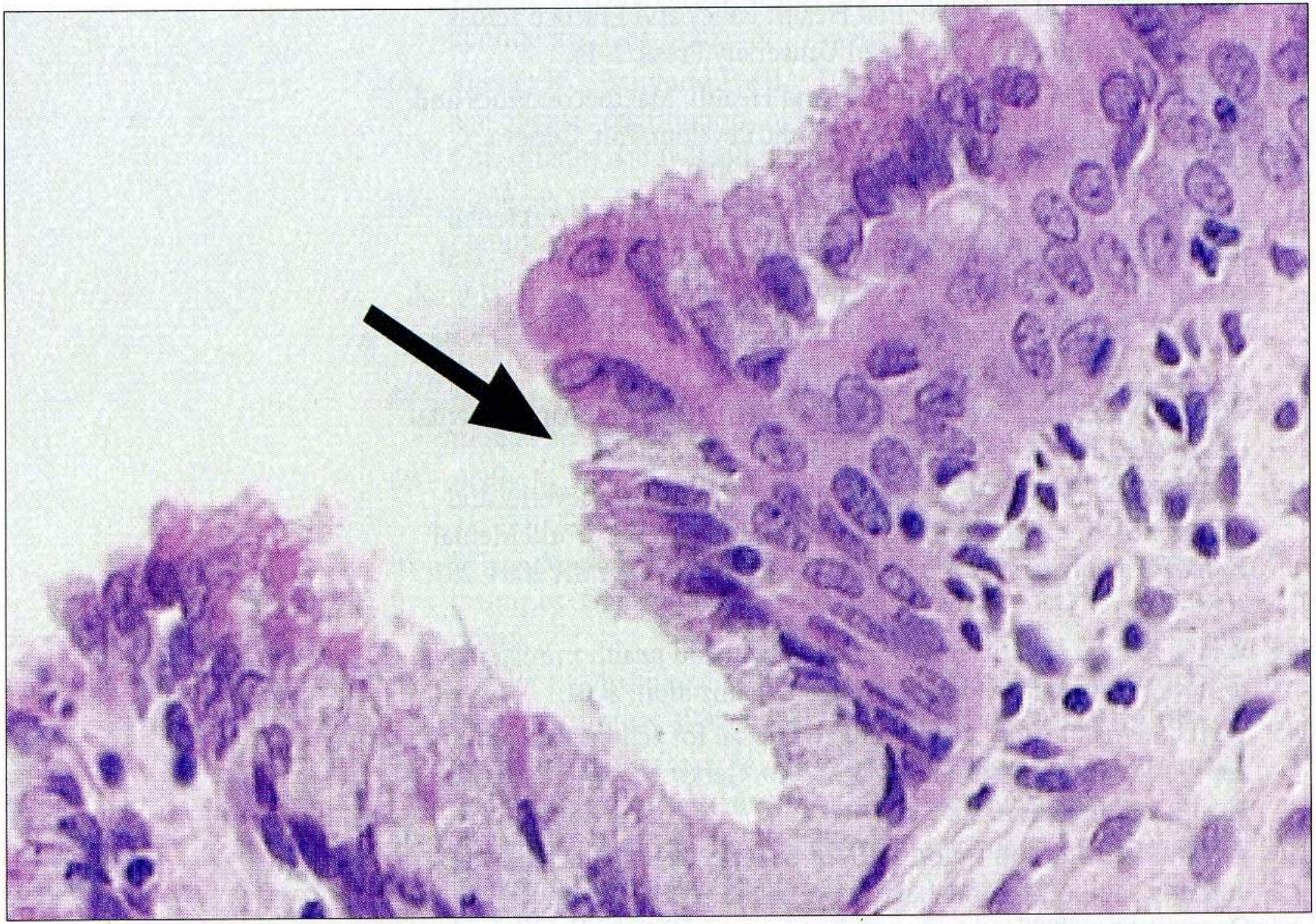


Figure 1: The cervical transformation zone

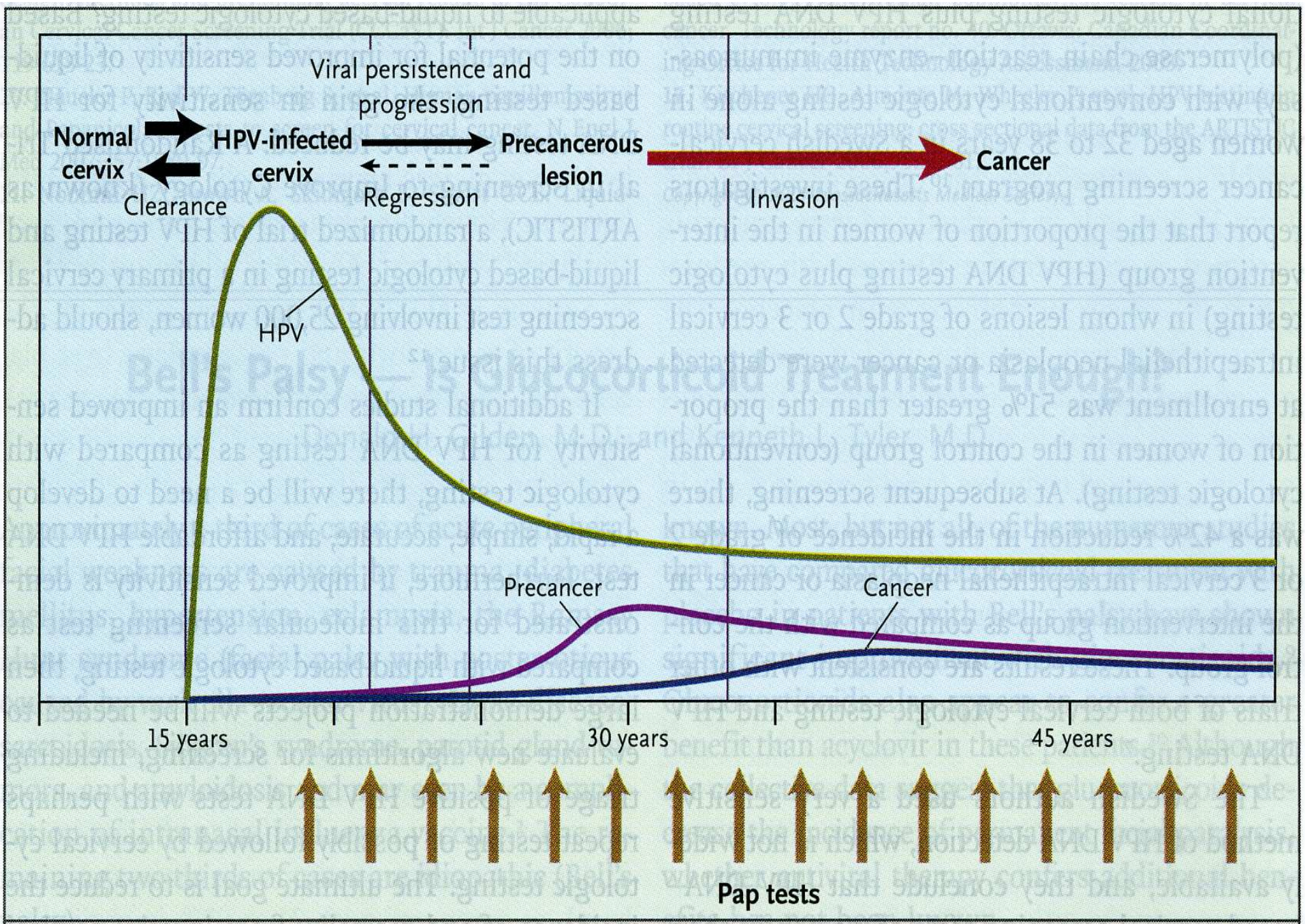
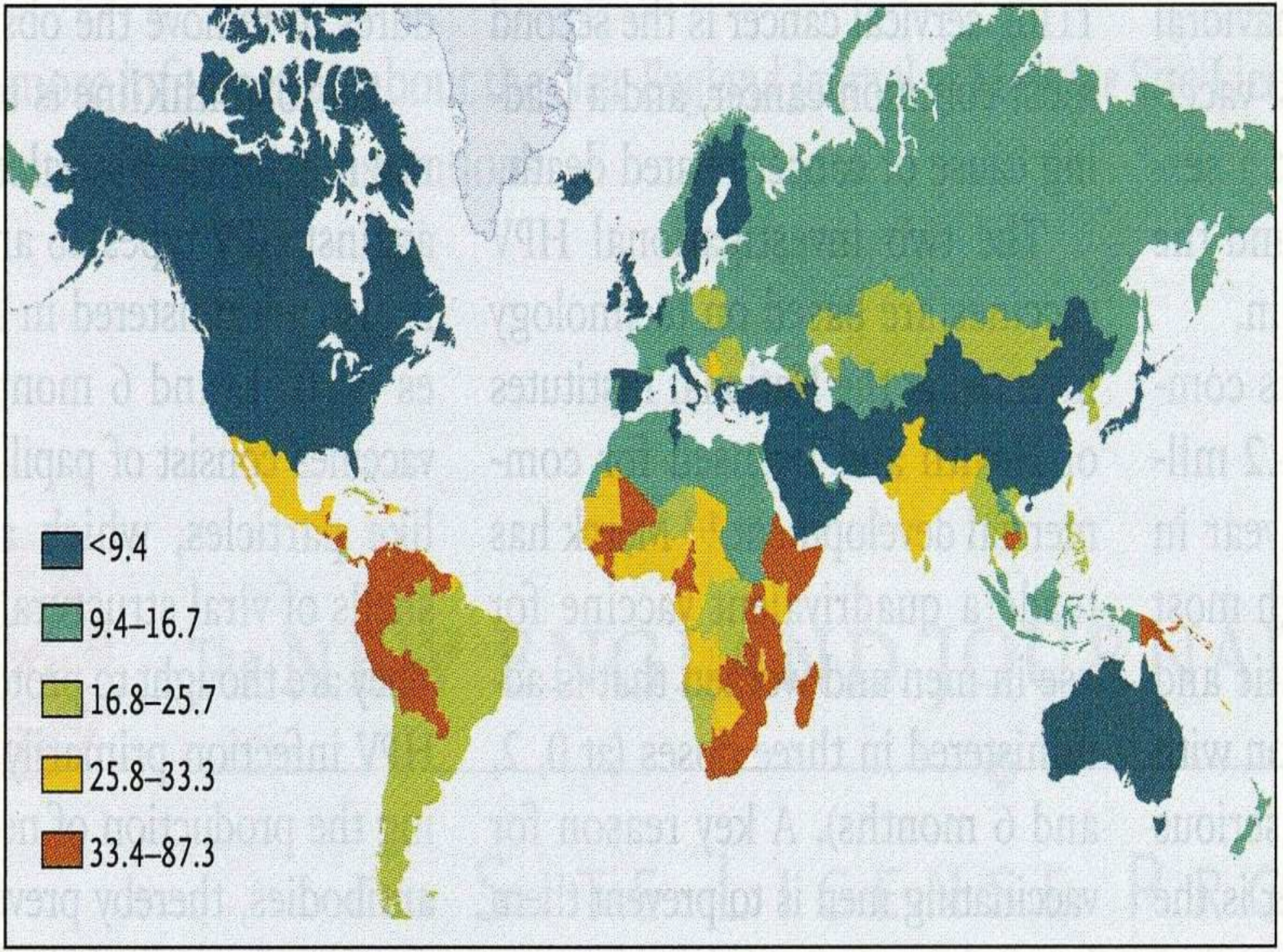


Figure 1. Natural History of HPV Infection and Cervical Cancer.

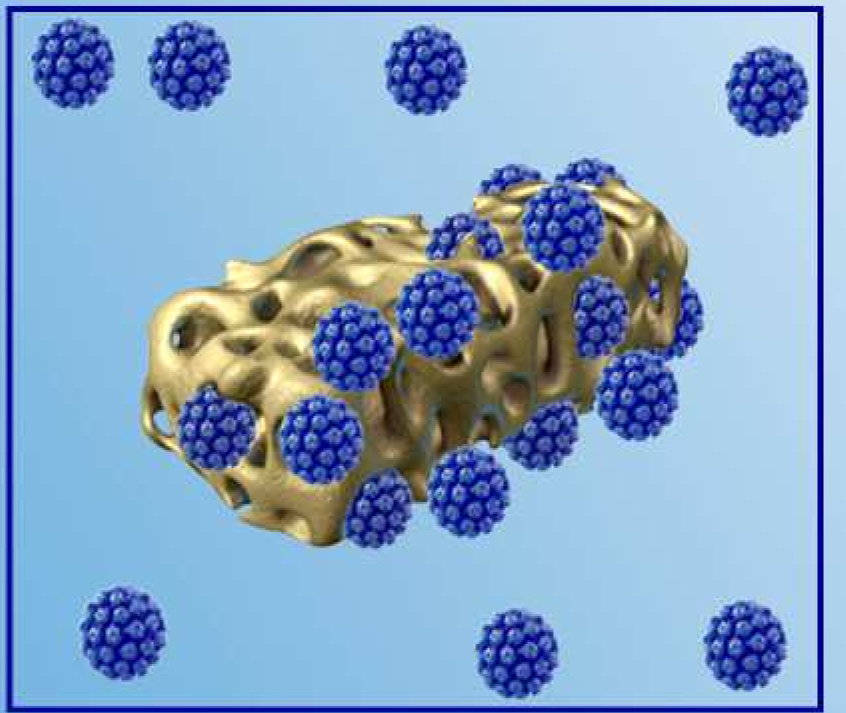
	Proportion of cervical cancers caused	Cumulative total
HPV16	54·6%	54·6%
HPV18	15·8%	70·4%
HPV33	4·4%	74·8%
HPV45	3·7%	78·5%
HPV31	3·5%	82·0%
HPV58	3·4%	85·4%
HPV52	2·5%	87·9%
HPV35	1·8%	89·7%
HPV59	1·1%	90·8%
HPV56	0·8%	92·2%
HPV51	0·7%	92·9%
HPV39	0·7%	93·6%
HPV73	0·5%	94·1%
HPV68	0·5%	94·6%
HPV82	0·2%	94·8%
No type identified	5·2%	**100%**

Data adapted from reference 18.

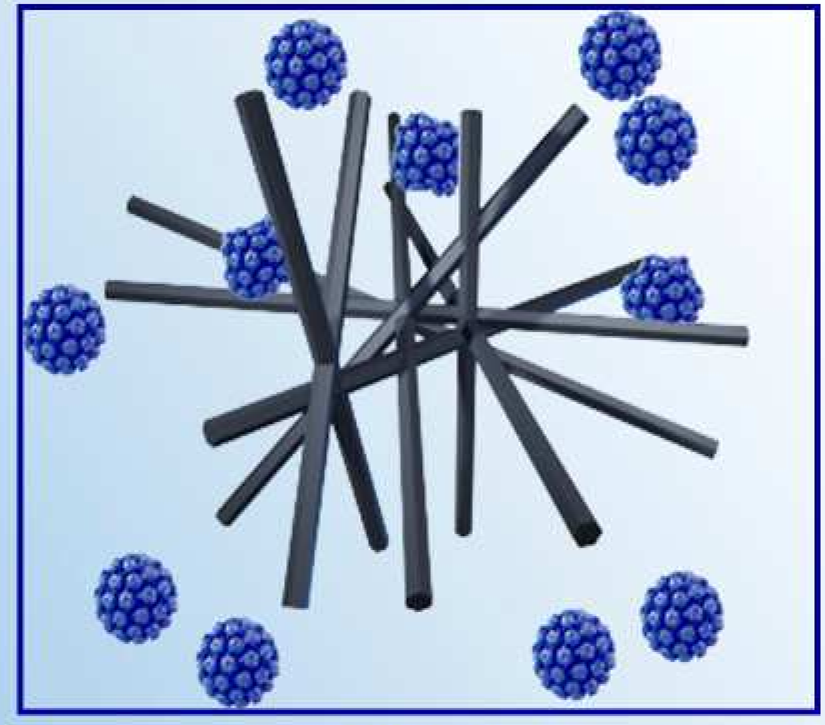
Table 2: **Proportion of cervical cancer caused by the carcinogenic HPV types**


<9.4
9.4–16.7
16.8–25.7
25.8–33.3
33.4–87.3

AAHS* e legame con le VLP



AAHS*



$Al(OH)_3$**

La capacità di legare le particelle del vaccino in modo stabile è importante.

AAHS*è in grado di stabilizzare il legame delle particelle virali in modo più stabile rispetto all'idrossido di alluminio.

*Alluminio Idrossifosfato Solfato Amorfo

** Idrossido di Alluminio

| *Caulfield MJ, Shi L, Wang S et al. Vaccine 2007*

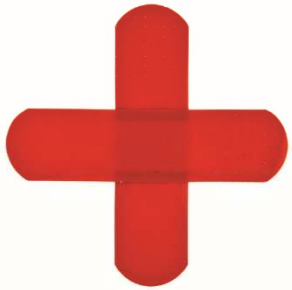
VACCINI PER L'HPV

FARMACO*	TIPI HPV	FORMULAZIONI	DOSE/SCHEDULA	COSTO (EURO)[1]
Cervarix-GlaxoSmithKline	16 e 18	siringhe monodose da 0,5 ml[2]	0,5 ml IM/3 dosi (0, 1 e 6 mesi)	470,37
Gardasil-Sanofi	6, 11, 16 e 18	siringhe monodose da 0,5 ml[3]	0,5 ml IM/3 dosi (0, 2 e 6 mesi)	514,92
Gardasil 9[4] (Sanofi)	6, 11, 16, 18, 31, 33, 45, 52 e 58		0,5 ml IM/3 dosi (o, 2 e 6 mesi)	n.d.

*Possono essere disponibili altri medicinali contenenti gli stessi principi attivi.

1. Farmaco ospedaliero esitabile. Costo all'ospedale per un ciclo vaccinale (3 dosi).
2. Venduto in confezioni da 1 o 10 siringhe monodose preriempite.
3. Venduto in confezioni da 1 siringa monodose preriempita.
4. Il farmaco ha ricevuto il parere positivo del CHMP in data 26 marzo 2015; non disponibile in commercio in Italia.

10 COSE DA SAPERE SUI VACCINI

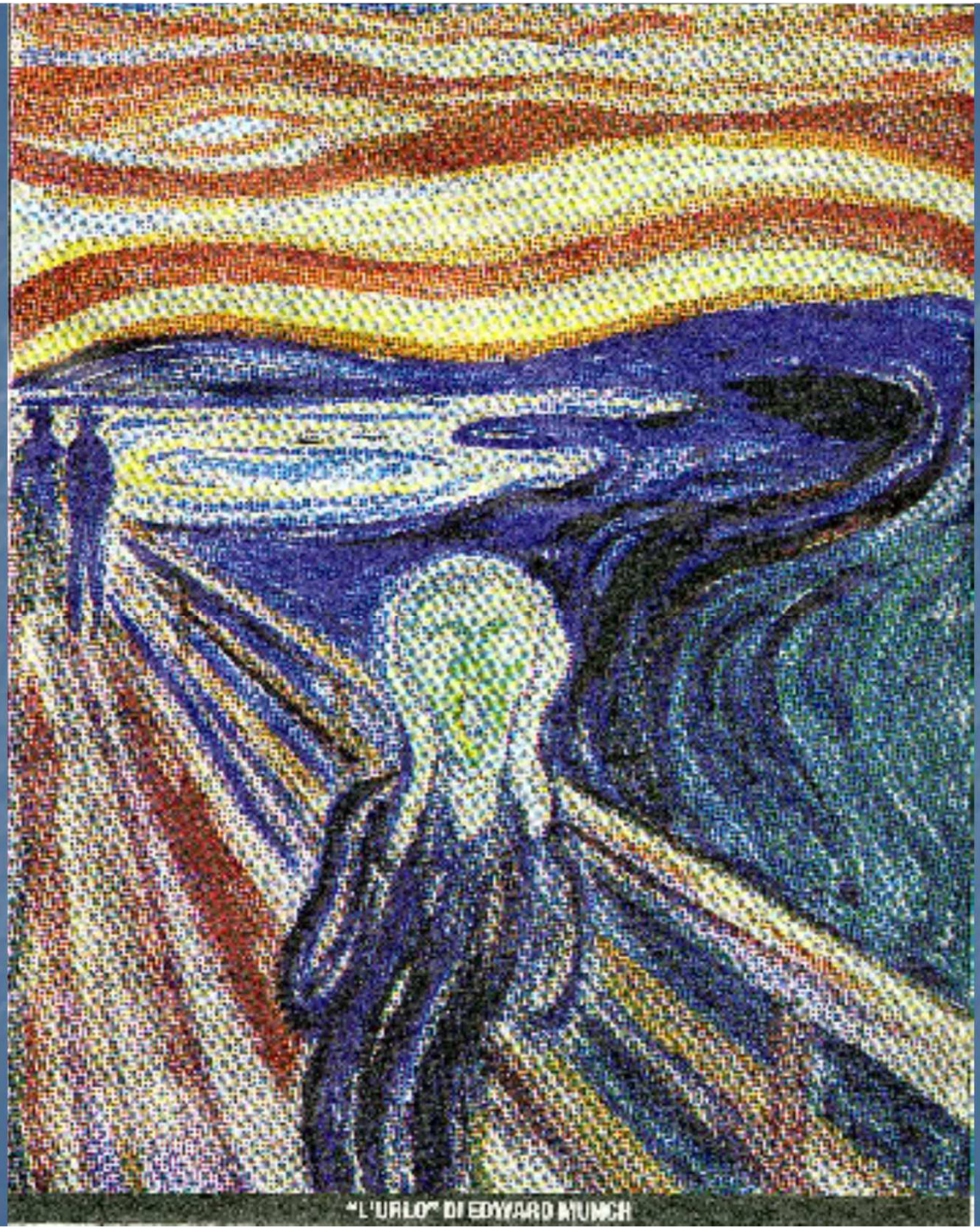


GIULIO TARRO

LA VERITÀ CHE L'INDUSTRIA, LA POLITICA E I MEZZI DI COMUNICAZIONE TENGONO NASCOSTA

NEWTON COMPTON EDITORI

Indice



"L'URLO" DI EDVVARD MUNCH