Infectious *Agents*

Viruses

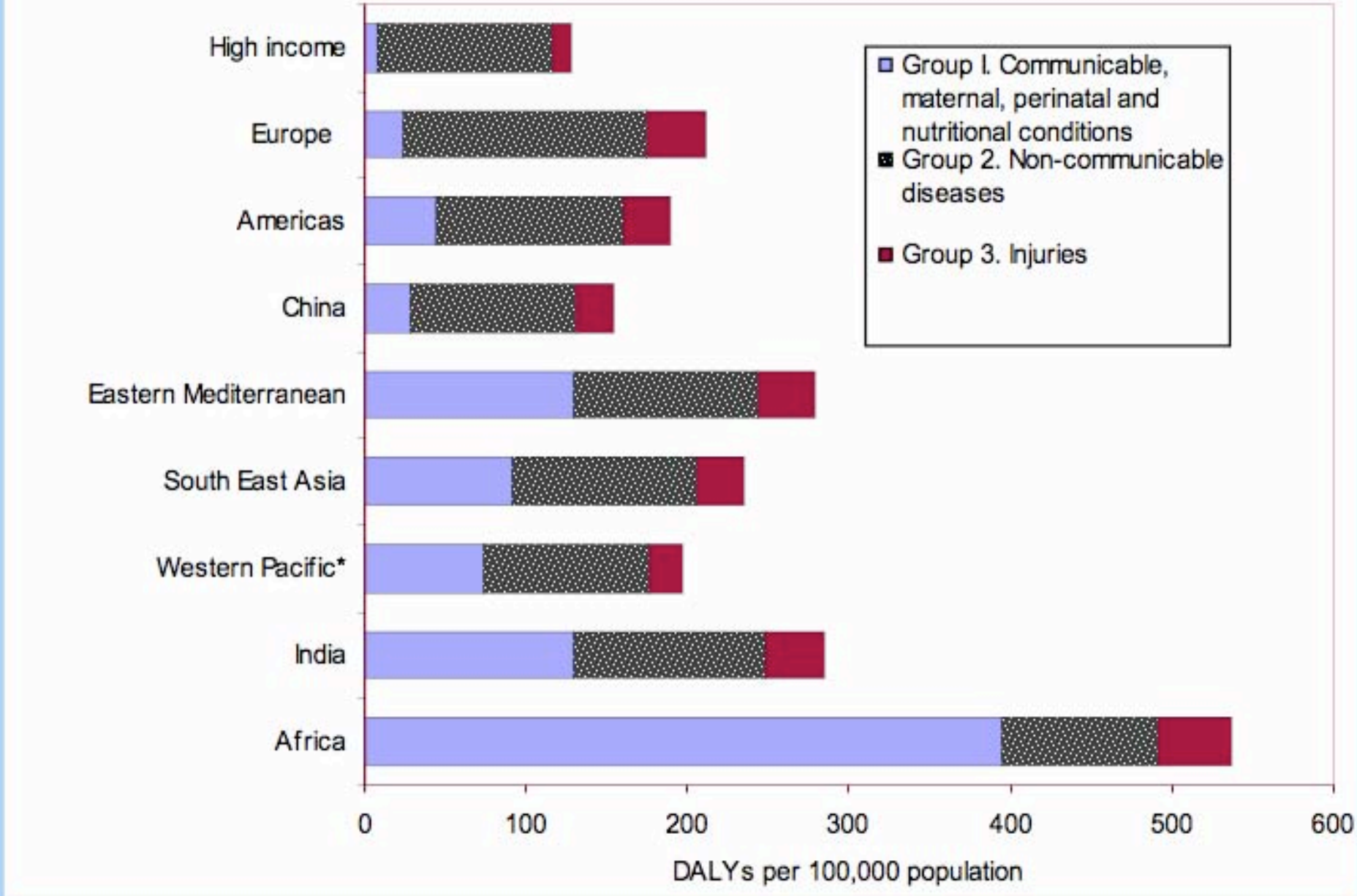
Bacteria

Worms

Protozoa

Fungi

Burden of disease by major cause groups and country groups, 2002



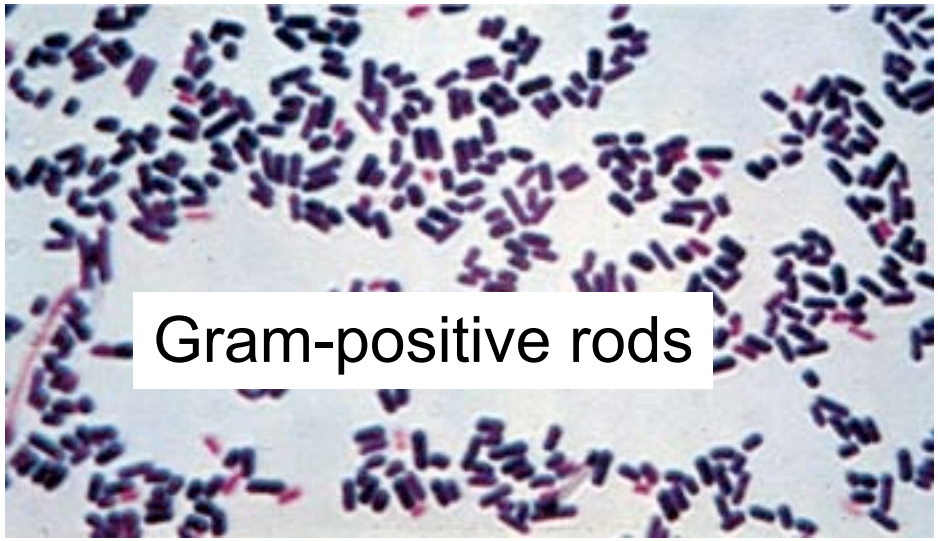
Leading causes of deaths, by country income level, 2002

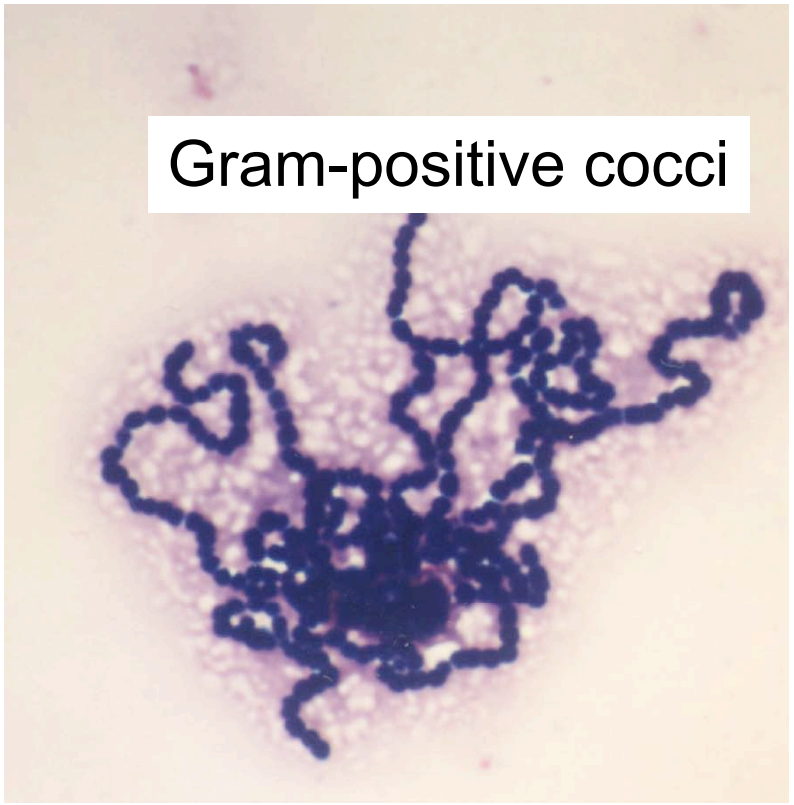
	High-income countries	% total deaths		Low- and middle-income countries	% total deaths
1	Cardiovascular diseases	38.1	1	Cardiovascular diseases	27.9
2	Malignant neoplasms	26.2	2	Malignant neoplasms	10.3
3	Neuropsychiatric disorders	5.0	3	Respiratory infections	7.4
4	Respiratory infections	4.3	4	Unintentional injuries	6.6
5	Unintentional injuries	4.1	5	HIV/AIDS	5.6
6	Diabetes mellitus	2.6	6	Perinatal conditions	4.9
7	Intentional injuries	1.9	7	Diarrhoeal diseases	3.6
8	Perinatal conditions	0.4	8	Tuberculosis	3.2
9	HIV/AIDS	0.3	9	Intentional injuries	3.0
10	Nutritional deficiencies	0.2	10	Malaria	2.6

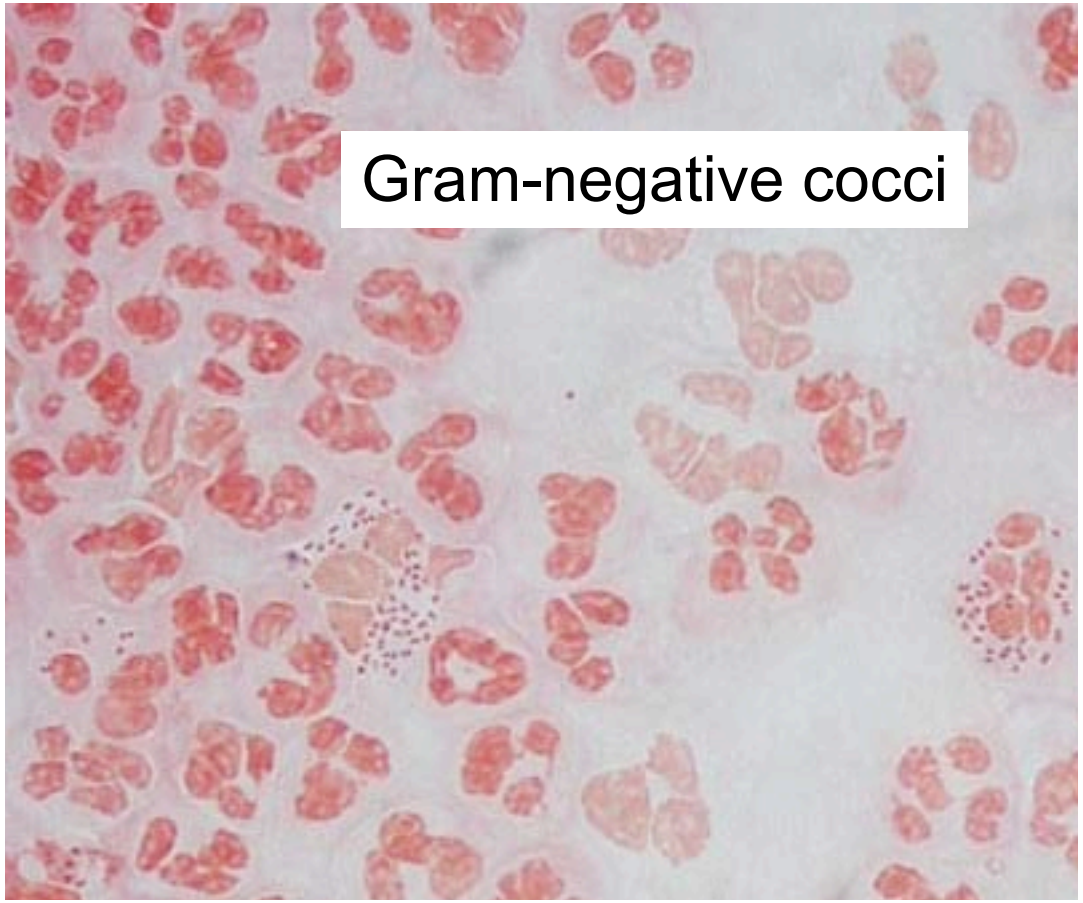
Some simple rules

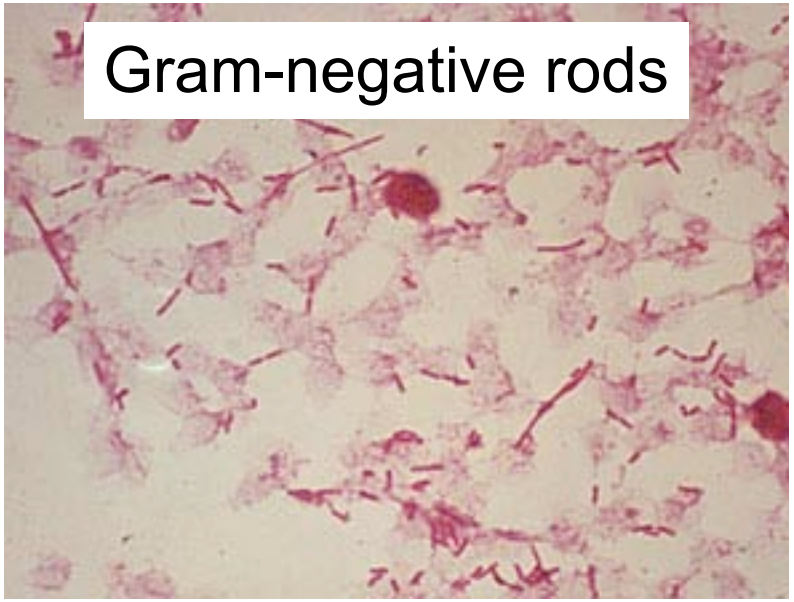
- Viral infections are most effectively controlled by vaccines (exceptions e.g. AIDS)
- All other types of infectious agents generally are most effectively controlled by therapy (antibiotics).
- Viral infections are primarily diagnosed by serologic tests (exception modern DNA and RNA detection)
- All other infections are primarily diagnosed by detection and/or culture of the agent.

Major infections caused by bacteria


Gram-positive rods


Gram-positive cocci


Gram-negative cocci

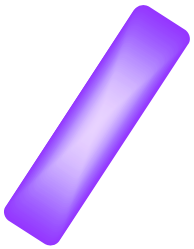

Gram-negative rods

Bacteria

Gram-positive cocci
Staphylococcus
Streptococcus

Gram-negative cocci
Neisseria

Gram-positive bacilli
Bacillus
Clostridium

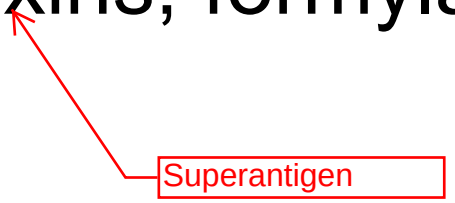


Gram-negative bacilli
E. Coli
Bordetella
Salmonella
Yersinia
Shigella
Vibrio

Staphylococcal infections

- Infectious agent: S. aureus
- Transmission: contact
- Pathogenesis:genome contains pathogenicity islands.

Adhesins, enzymes facilitate invasion, enterotoxins, formylated peptides attract PMNL.

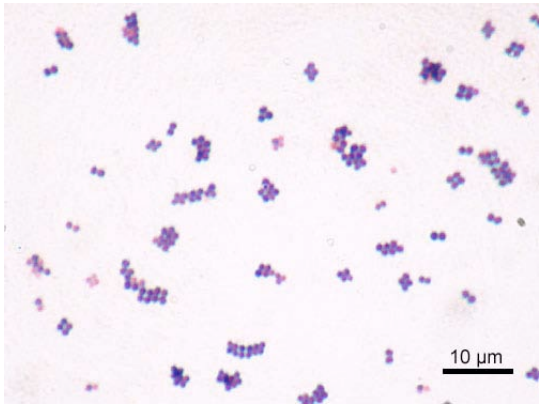


Staphylococcal infections

- Clinical manifestations: wound infections, skin infections. Nosokomial infections: MRSA.

Staphylococcal infections

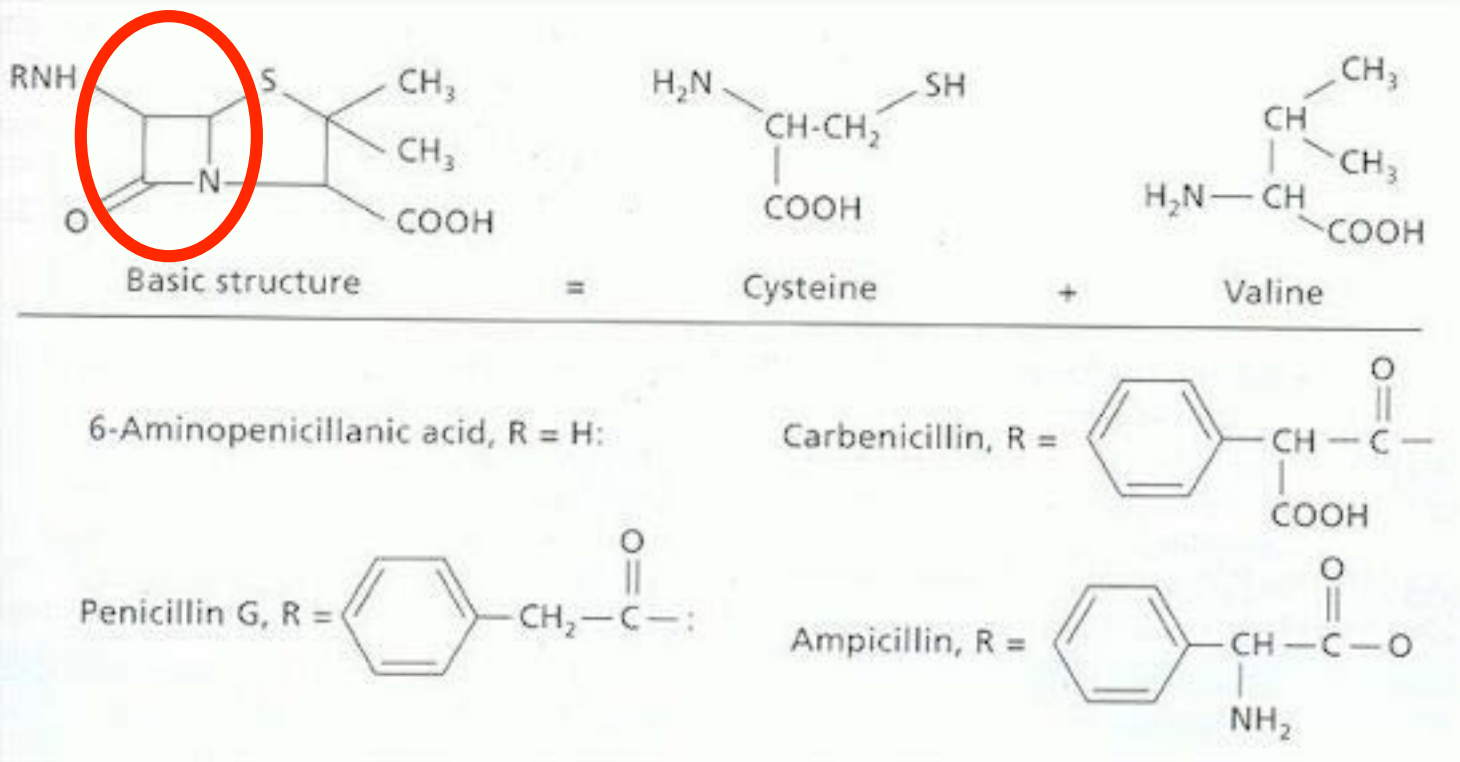
- Diganosis:



- Treatment: Beta-lactamase resistant penicillins (methicillin)

  MRSA: vancomycin
- Prevention: Hygiene

Beta lactam antibiotics



- β-lactam antibiotics include penicillin derivatives, cephalosporins, monobactams, carbapenems and β-lactamase inhibitors
- contains a β-lactam nucleus in its molecular structure.
- the most widely used group of antibiotics available
- β-Lactam antibiotics are bactericidal
- act by inhibiting the synthesis of the peptidoglycan layer of bacterial cell walls.

Bacteria

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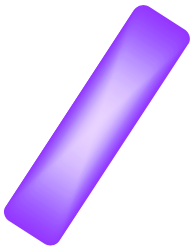
Staphylococcus
Streptococcus

Gram-negative cocci
Neisseria

Gram-positive bacilli
Bacillus
Clostridium



Gram-negative bacilli
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Pneumococcal infections

Infectious agent: Streptococcus pneumoniae, 23 common serovars

=

A **serovar** or **serotype** is a grouping of microorganisms or viruses based on their cell surface antigens. Serovars allow organisms to be classified at the sub-species level; an issue of particular importance in epidemiology

Pneumococcal infections

Infectious agent: Streptococcus pneumoniae, 23 common serovars

Transmission: droplet, in nasopharynx of 5-10% of healthy individuals

Pathogenesis:

Attaches to Epithelia by specific adhesins

Causes disease at sites other than nasopharynx

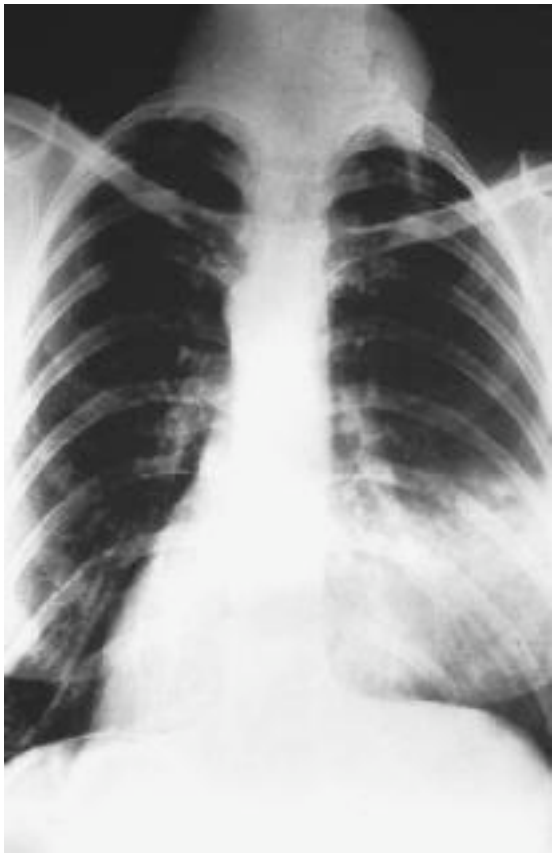
Evades immune system by polysaccharide capsule

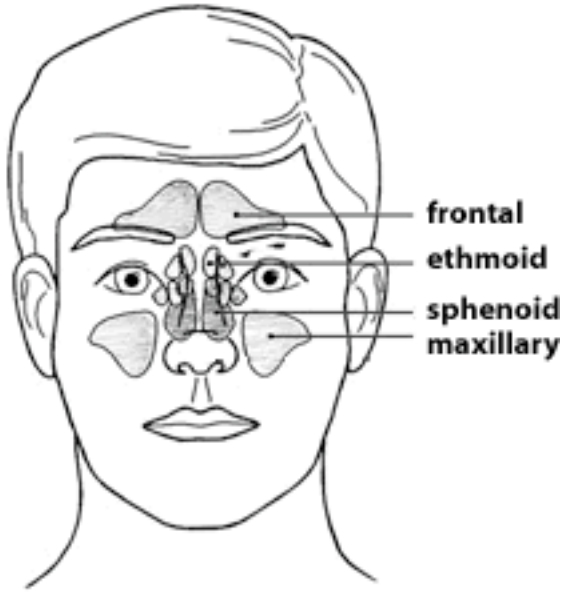
Expresses IgA1 protease that destroys IgA

Risk increased in patients with impaired Ig or phagocytosis, after spleenectomy

Pneumococcal infections

Clinical manifestations:
Lobar pneumonia, acute sinusitis, otitis media, meningitis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess





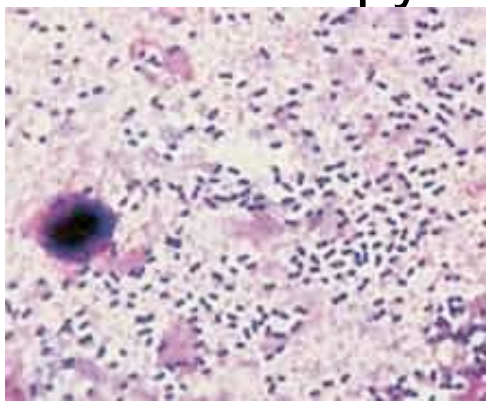
Pneumococcal infections

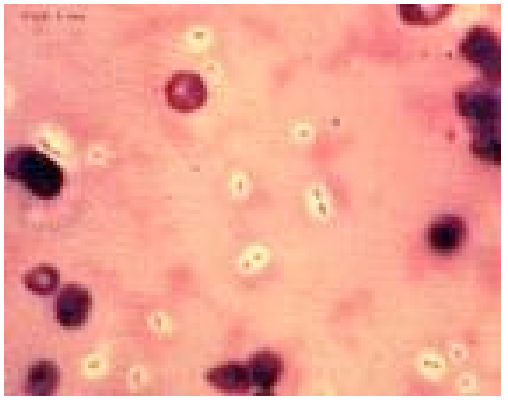
Clinical manifestations:
Lobar pneumonia, acute sinusitis, otitis media, meningitis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess

Cellulitis is an inflammation of the connective tissue underlying the skin, that can be caused by a bacterial infection.

Pneumococcal infections

Diagnosis: Direct microscopy and culture





Treatment:
Penicillin, if resistant (frequency increasing)
erythromycin, macrolides, clindamycin, quinolones. Vancomycin

Prevention: Polysaccharide vaccine
(US all children, Germany >65)

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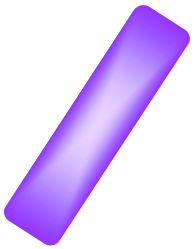
Staphylococcus
Streptococcus

Gram-negative cocci
Neisseria

Gram-positive bacilli
Bacillus
Clostridium



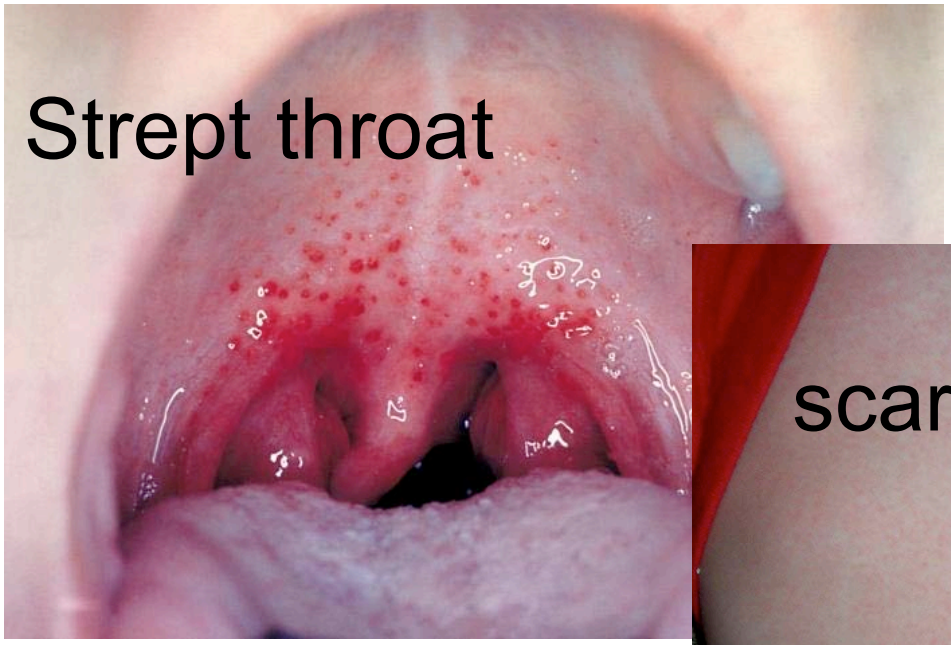
Gram-negative bacilli
E. Coli
Bordetella
Salmonella
Yersinia
Shigella
Vibrio

Streptococcal infections

- Infectious agent: stryptococcus pyogenes = group A streptococcus (GAS)
- Transmission: droplet
- Pathogenesis: M surface protein protects from phagocytosis (protective immunogen), polysaccharide capsule binds CD44 in pharynx, streptolysins, pyrogenic exotoxins cause rash,

Streptococcal infections

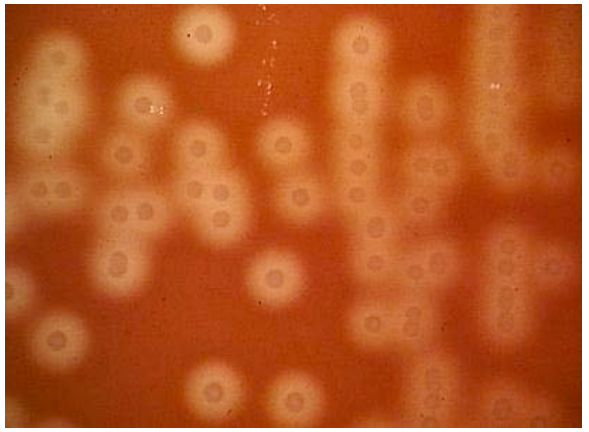
- Clinical manifestations:



Acute rheumatic fever,
poststreptococcal glomerulonephritis

Streptococcal infections

- Diagnosis:
  Typical beta hemolysis
  on blood agar plates



- Treatment: Penicillin, erythromycin
- Prevention: hygiene

DD Pharynigitis

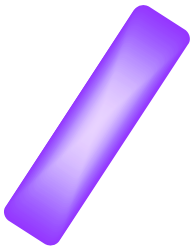
- Viruses: Rhinovirus (cc), Coronavirus (CC), Adenovirus (pharyngoconjunctivis), Influenza, Parainfluenza (croup), coxsackievirus (herpangina, herpes simplex virus, EBV (Mononucleosis)
- Bacteria: GAS, other streptococci, mixed anaerobes, arcanobacterium hemolyticum

Bacteria

Gram-positive cocci
Staphylococcus
Streptococcus

Gram-negative cocci
Neisseria

Gram-positive bacilli
Bacillus
Clostridium



Gram-negative bacilli
Bordetella
E. Coli
Salmonella
Yersinia
Shigella
Vibrio

Bacterial Diarrhea

- Infectious agents: Enterpathogenic E. coli, Salmonella enterica, Campylobacter, Yersinia enterocolitica, Shigella, vibrio cholerae
- Transmission: fecal.....oral
- Pathogenesis: via toxins:

enterotoxin->destruction of epithel

shiga toxin-> blocks protein synthesis in cells

Cholera toxin->activates adenylate cyclase ->massive fluid and electrolyte efflux. CT is encoded by phage, infection is dependent on toxin coregulated pilus encoded on V. cholerae pathogenicity island.

Bacterial Diarrhea

Clinic:

Enterpathogenic E. coli: travelers' diarrhea

Salmonella enterica:limited diarrhea, problem chronic carrier

Shigella: dysentery

Vibrio cholerae: Cholera

Bacterial Diarrhea

Diagnosis: culture, serovar (O, H1,H2 for salmonella)

Therapy: fluoroquinolones such as ciprofloxacin

Prevention: hygiene

DD Diarrhea

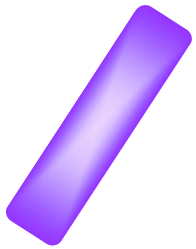
- Cryptosporidien, Giardia lamblia, Entamoeba histolytica
- Rotavirus
- Food poisoning
- Celiac disease, lactose intolerance, IBD

Bacteria

Gram-positive cocci
Staphylococcus
Streptococcus

Gram-negative cocci
Neisseria meningitidis
->meningitis
N. Gonorrhoeae
->gonorrhea

Gram-positive bacilli
Bacillus
Clostridium



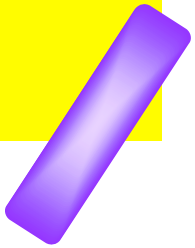
Gram-negative bacilli
E. Coli
Bordetella
Salmonella
Yersinia
Shigella
Vibrio

Bacteria

Gram-positive cocci
Staphylococcus
Streptococcus

Gram-negative cocci
Neisseria

Gram-positive bacilli
Bacillus
->anthrax
Clostridium tetani
->tetanus



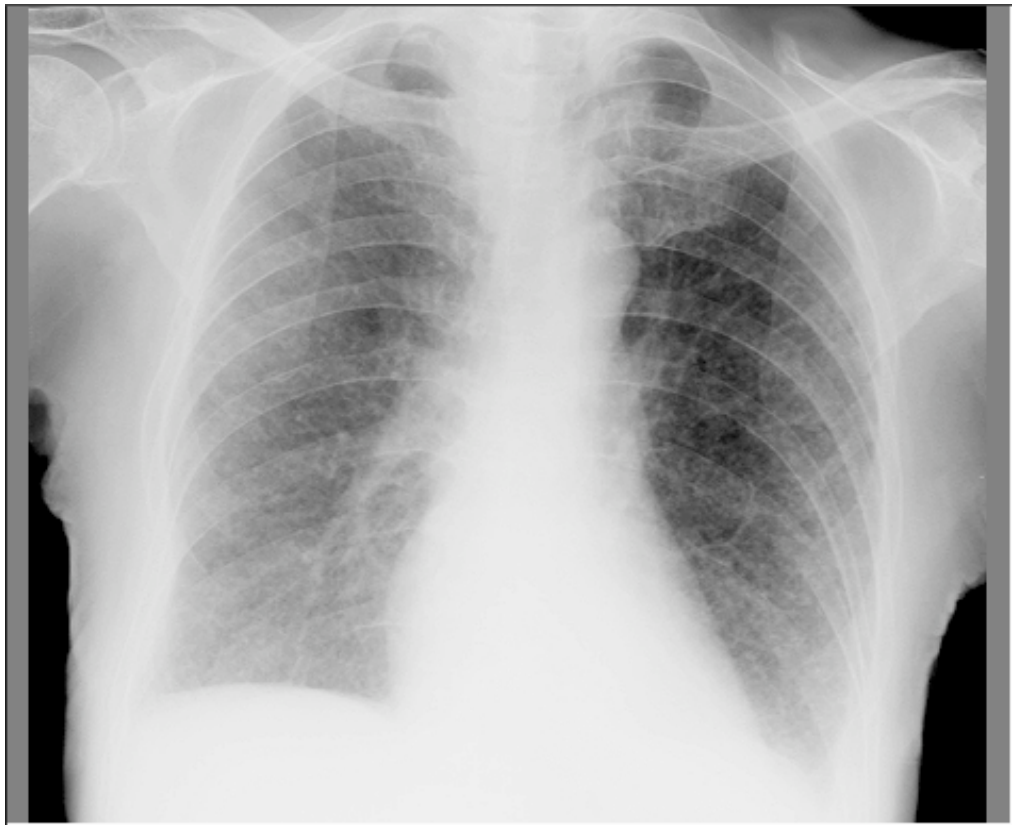
Gram-negative bacilli
E. Coli
Bordetella
Salmonella
Yersinia
Shigella
Vibrio

Tuberculosis

Infectious agent: Mycobacterium tuberculosis
Transmission: droplet, prevalence 14 Mio,
incidence 9 Mio pa, mortality 2 mio
Pathogenesis:
90 % asymptomatic, 10% lifetime chance to progress,
infects alveolar macrophages, transported with DC to local lymph nodes. Attracts macrophages, T lymphocytes, B lymphocytes and fibroblasts to form granuloma. Can form caseous necrosis. Remain in granuloma in a dormant state. If macrophages cannot contain replication of M.tub. infection disseminates.

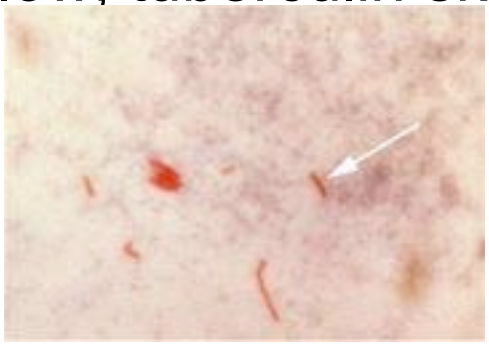
Tuberculosis

- Clinic: pulmonary TB, meningitis, lymphatic system, Miliary tuberculosis, genitourinary system, bones and joints.



Tuberculosis

- Diagnosis: Direct microscopy: acid fast, Ziehl-Neelsen stain, grows slow, tuberculin skin test



- Treatment: isoniazid, rifampicin, pyrazinamide and ethambutol for two months, then isoniazid and rifampicin alone for a further four months. Multiresistance a problem.
- Prevention: identify and isolate infectious individuals
- BCG (Bacillus Calmette-Guérin) of limited value. Only for highly exposed tuberculin skin test negative individuals.

Viral Infections

Luc Montagnier Françoise Barré-Sinoussi Harald zur Hausen

Luc Montagnier

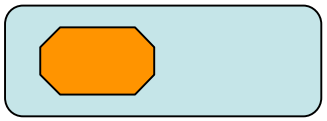
HIV-1
Pasteur, Paris

Françoise Barré-Sinoussi

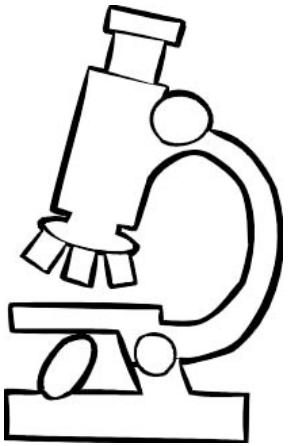
Harald zur Hausen

HPV
DKFZ, Heidelberg

Viruses are submicroscopic

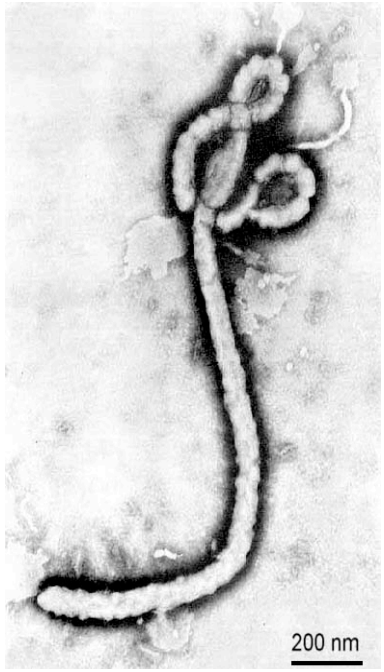


Cell: ca 20 µm =0,02 mm



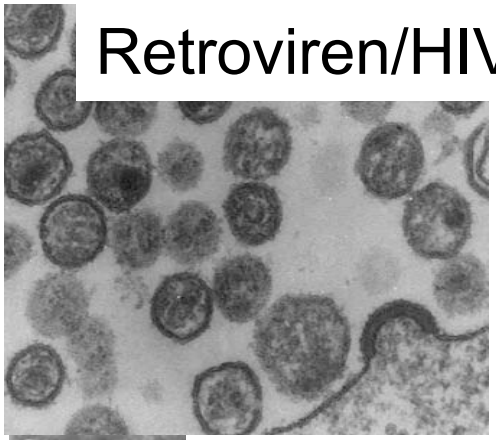
Bacteria: ca. 1 µm

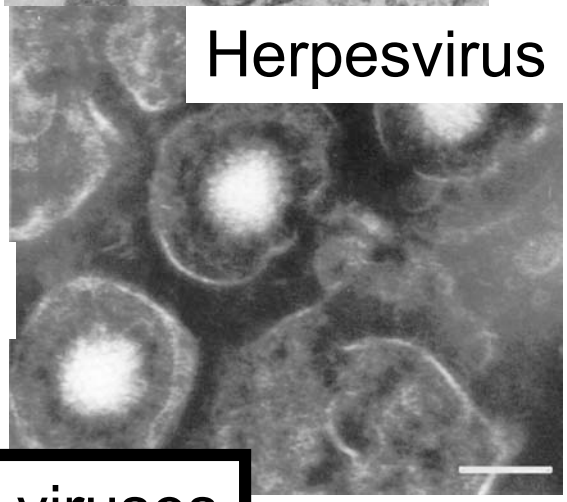
Virus: ca. 100 nm



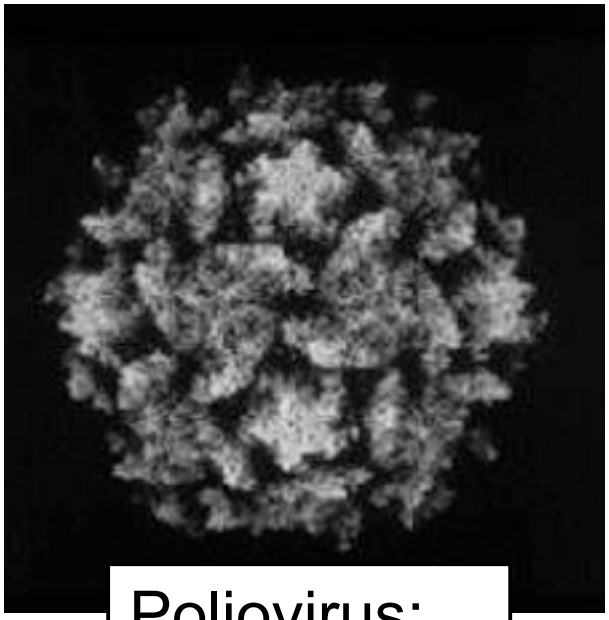
Filoviren/EBOLA

Retroviren/HIV



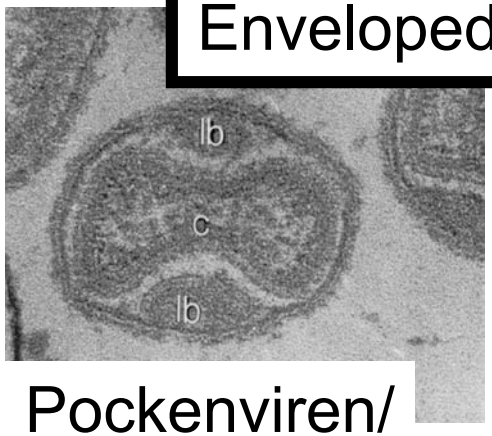


Herpesvirus



Poliovirus:
No envelope

Enveloped viruses



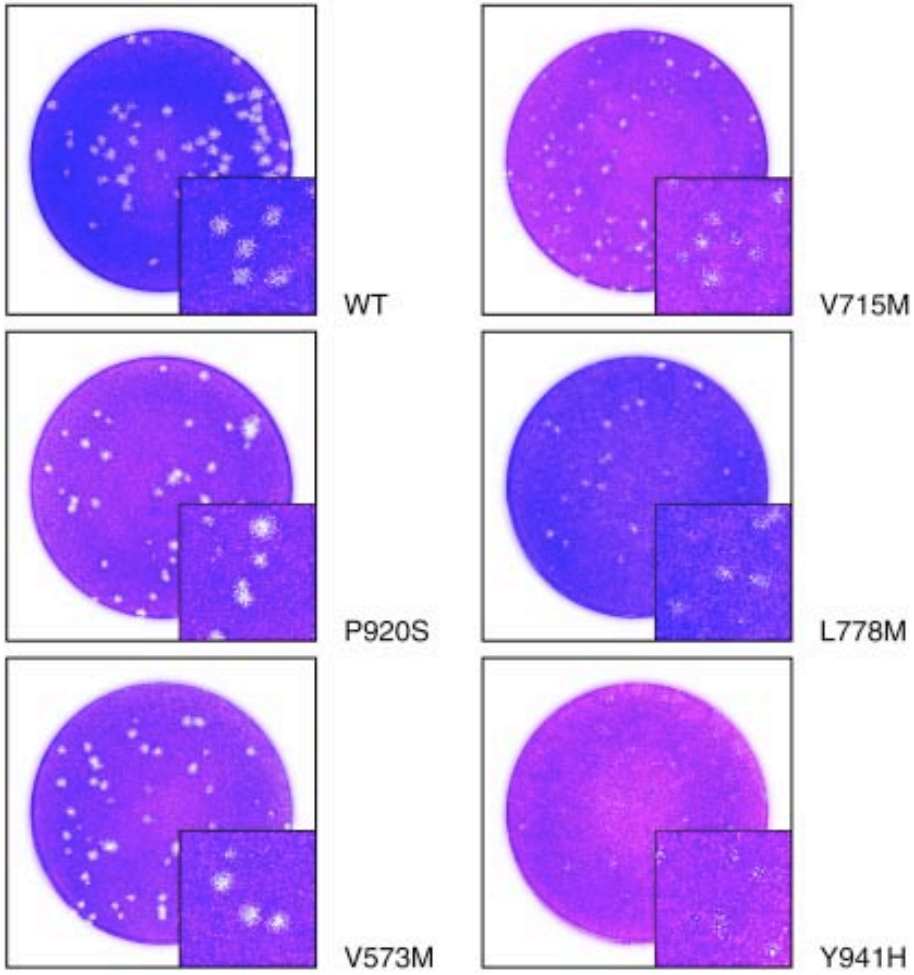
Pockenviren/
Vaccinia

Rhabdoviren/Rabiesvirus

Orthomyxo/FLuA

Viruses grow on cell layers under semisolid medium and form characteristic plaques

Different polymerase mutants of HSV



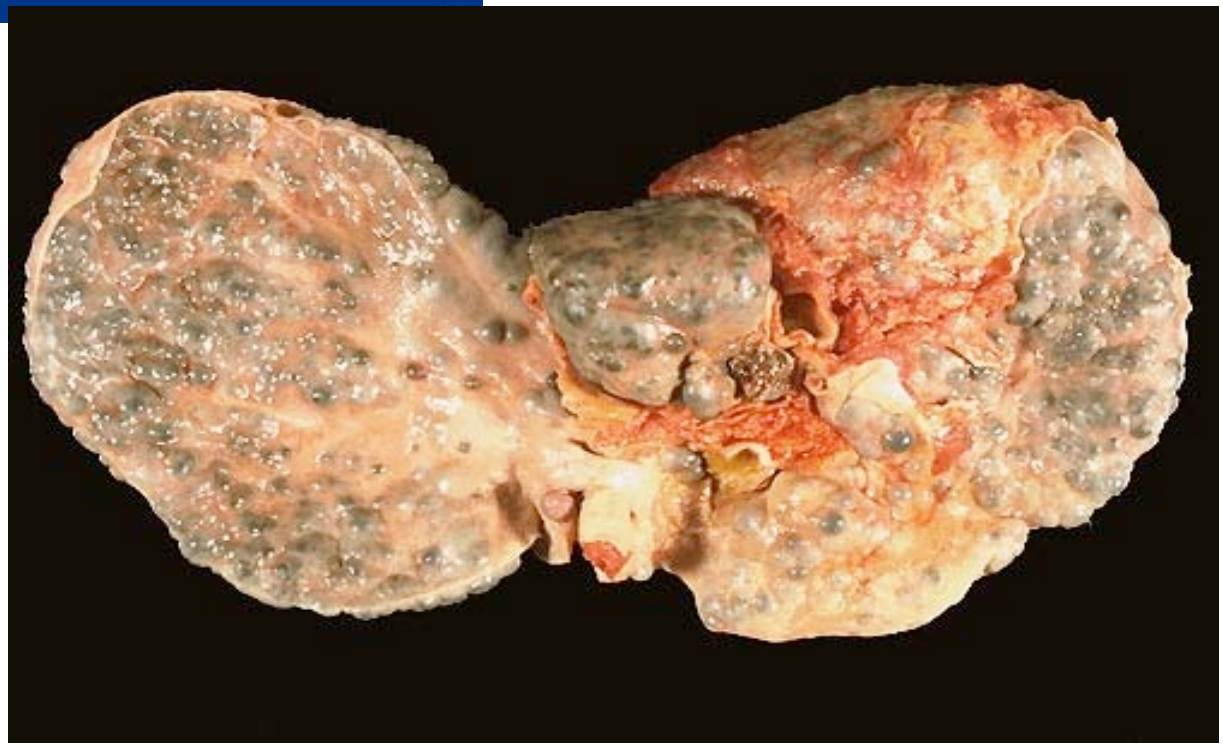
	No Envelope	Envelope
DNA	Adenovirus Parvovirus/Parvo B19 Papillomavirus /HPV	Herpesviruses: CMV/HSV/ EBV/VZV Poxviren/Pockenvirus Hepadnavirus: Hepatitis B virus
RNA	Picornavirus/Poliovirus /Hepatitis A virus	Orthomyxovirus/Influenzavirus Rhabdovirus/Rabiesvirus Arenavirus/ Lassavirus/LCMV Coronavirus/SARS-Virus Retrovirus/ HIV-1/MLV Flavivirus: Hepatitis C

Viral Hepatitis

- Inflammation of the liver
- Acute symptoms: nausea, vomiting, jaundice, abdominal pain, fever, fatigue
- Causes are diverse:
  - Viruses (Hep A, B, C, D, G, Epstein Barr, etc)
  - Toxins (Including alcohol, drugs)
- Chronic hepatitis *can* lead to scarring (fibrosis→cirrhosis) and liver cancer

Healthy Liver

Cirrhotic Liver



End Stage Liver Disease: Liver Cancer

Source: Beri Hull, National HIV/HCV Co-infection Coalition

Different Forms of Hepatitis

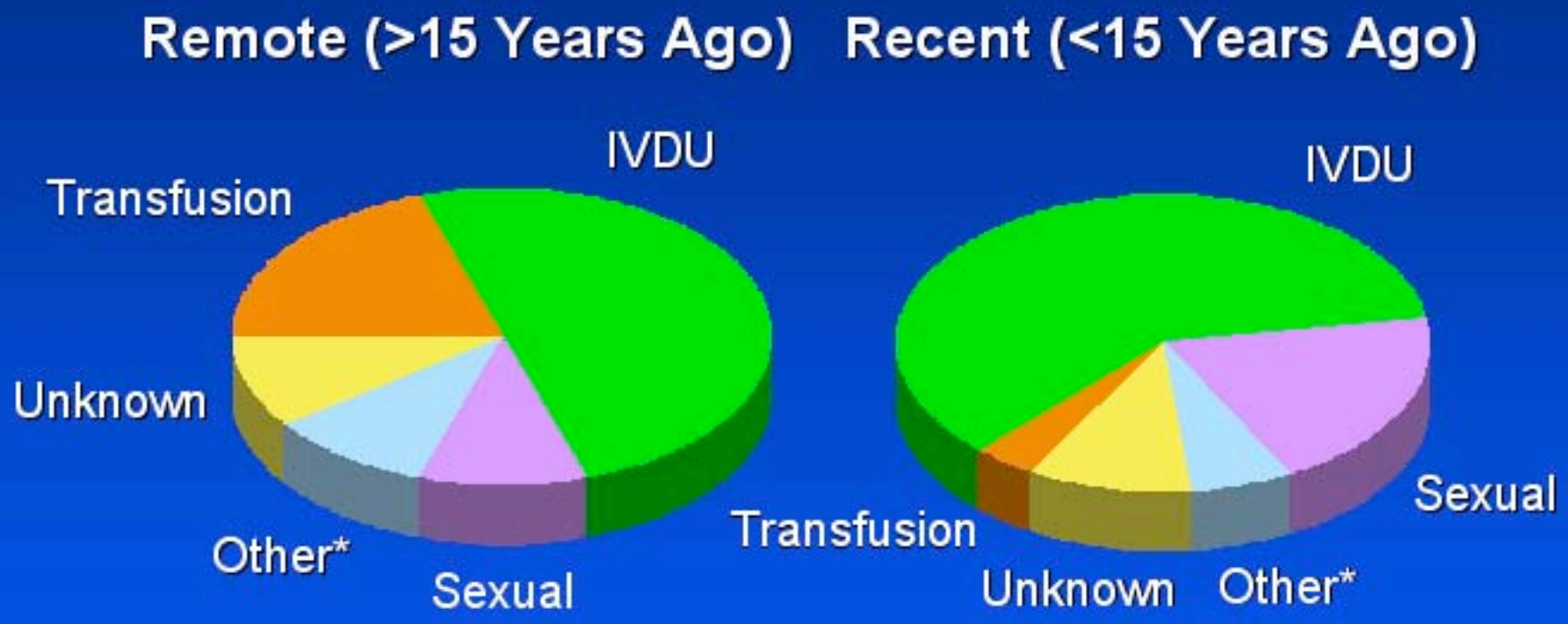
	HAV	HBV	HCV
How is this virus transmitted?	Through fecal-oral contact (changing diapers, rimming, eating contaminated food)	Through sexual contact, blood, breast milk, or perinatal. Endemic in Asia. MSM at high risk	By blood-to-blood contact. Sexual transmission is uncommon and mother-to-child possible
What are the symptoms of acute infection?	Fever, loss of appetite, fatigue, dark urine, nausea, vomiting, jaundice; 1 wk - 2 mo	Similar to HAV; no symptoms common; 30%-50% develop acute symptoms within 4 wk to 6 mo	Similar to HAV though most people with HCV (75%) have no symptoms
Is it a life-long infection?	No. Never chronic	Yes, for some. Most adults clear virus; <5% chronically infected; 15%-20% will die of cirrhosis	Yes, for most; 15%-25% clear virus; 75%-85% become chronically infected; 5%-20% cirrhosis

Adapted from CommonHealth Alcohol and Drug Addiction Counseling for HCV Patients

Hepatitis C: The Basics

- 4 million have been infected in the US
  - Leading cause of liver transplant
- Four genotypes (1-4)
  - Genotype 1 most common among IDUs in US
  - Genotype 1 and 4 least likely to respond to treatment

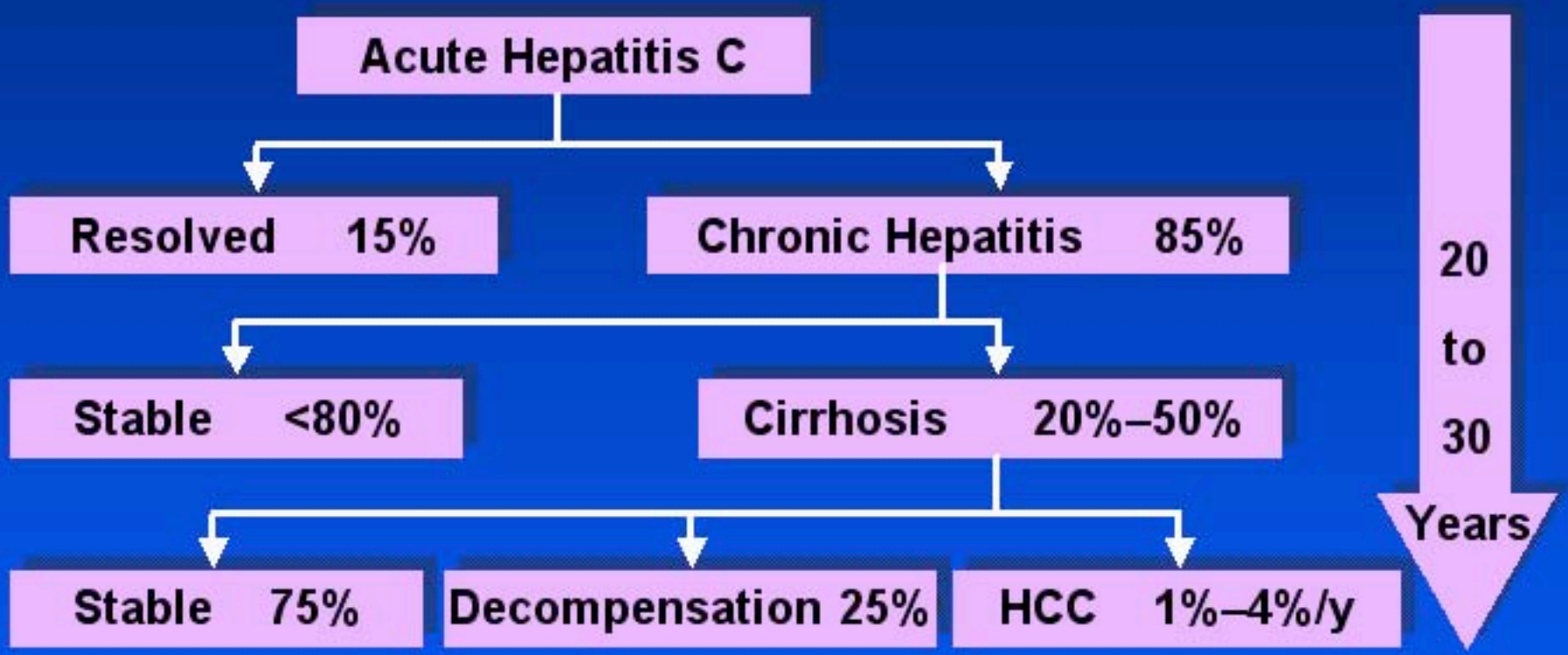
Relative Importance of Risk Factors for Remote and Recent HCV Infection



*Nosocomial, occupational, perinatal

Alter MJ, et al. *N Engl J Med*. 1999;341;556. CDC. *MMWR*. 1998;47:1.

Progression of HCV Is Variable



HCV Treatment

- Standard of care is Pegylated interferon (inject every week) and Ribavirin (daily pill) for 6-12 months
- Most centers do liver biopsies to assess fibrosis prior to treatment
- Treatment response is low (app 50 %)
  - Especially for Genotype 1, 4
  - Response rates lower in African Americans
- Treatment has many side effects

	No Envelope	Envelope
DNA	Adenovirus Parvovirus/Parvo B19 Papillomavirus /HPV	Herpesviruses: CMV/HSV/ EBV/VZV Poxviren/Pockenvirus Hepadnavirus: Hepatitis B virus
RNA	Picornavirus/Poliovirus /HAV	Orthomyxovirus/Influenzavirus Rhabdovirus/Rabiesvirus Arenavirus/ Lassavirus/LCMV Coronavirus/SARS-Virus Retrovirus/ HIV-1/MLV Flavivirus: Hepatitis C

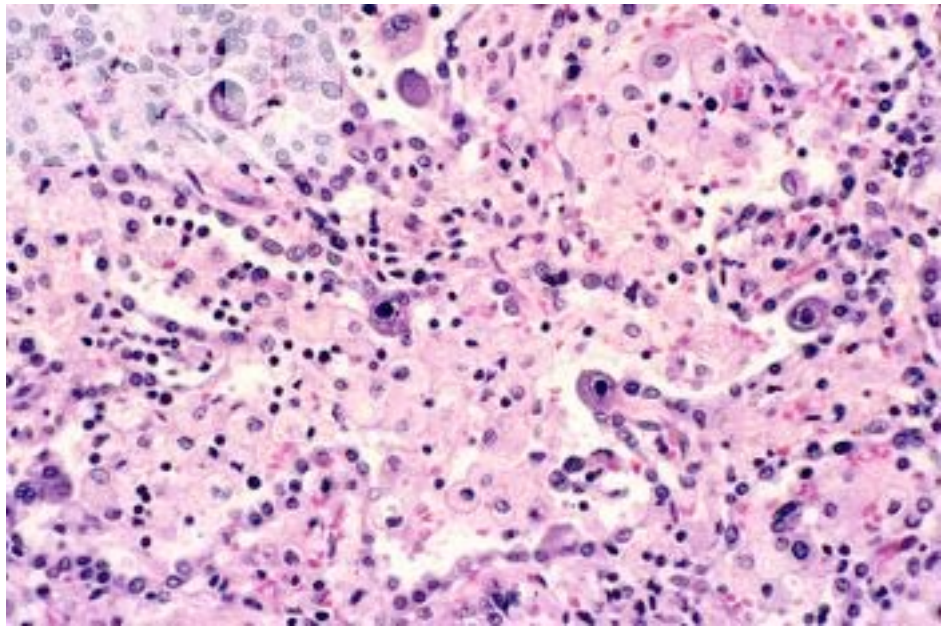
CMV infections

Infectious agent: cytomegalovirus, beta Herpesviridae (HHV-5)
Transmission: close contact, transplantation, app 50% adults carrier
Pathogenesis:
Virus persists in latent state after primary infection.
Severe disease manifests in fetus after primary infection or in immunodeficient patient after reinfection or infection via transplant. AIDS, post tx
Kidney transplant: + to -
BMT: - to +

CMV replicates in vivo in a broad range of cells, HPC, leukocytes.
Normally controlled by CTL.

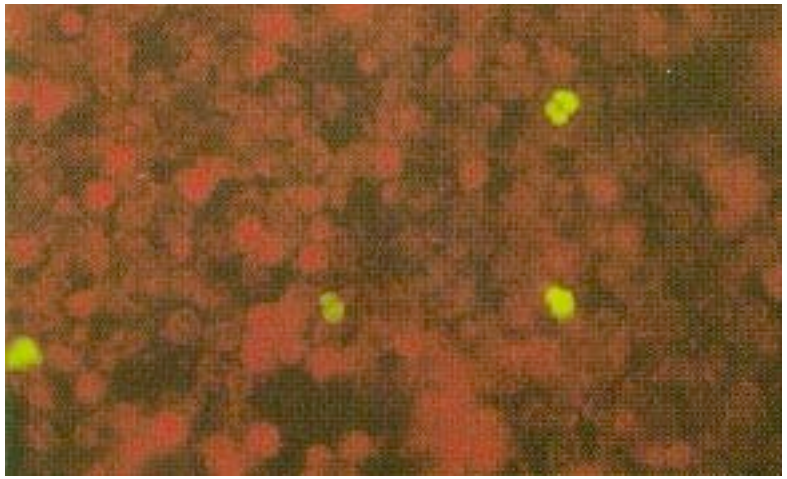
CMV

Clinic: fetal infection-> hepatosplenomegalie, death or survival, healthy or with hearing loss, vision impairment, and varying degrees of mental retardation.
Immunocompromised-> retinitis (AIDS), pneumonitis (BMT), colitis, hepatitis.



CMV

Diagnosis: DNA and pp65 antigen in blood.
Serology only useful if seroconversion



Treatment: ganciclovir, foscavir
Prophylaxis: screening in tx, prevention of exposure

EBV

Infectious agent: Epstein-Barr virus, HHV-4

Transmission: close contact, >90% adults are carriers

Pathogenesis: lytic cycle, latency programme

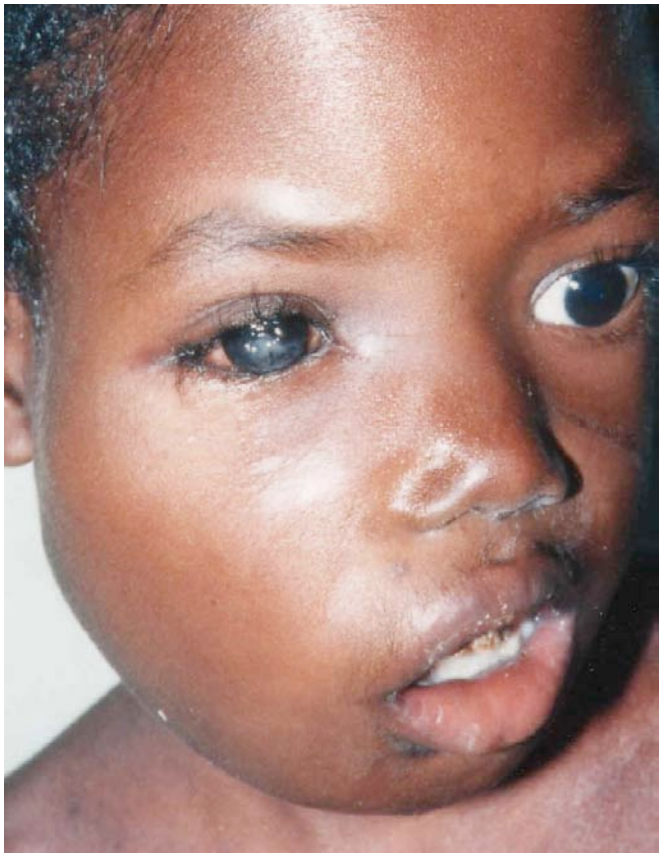
Transform B cells via EBNA-2, EBNA-3C and LMP-1 in vitro

Persistence in bone marrow?

BMT-> neg to pos, recipient becomes negative

EBV

Clinic: infectious mononucleosis, Burkitt's lymphoma



Nasopharynx ca,
chronic fatigue syndrome

EBV

Diagnosis:
IgG+IgM antibody to early antigen, capsid antigen+EBNA

No treatment or prevention

Burkitt's lymphoma responds to chemotherapy,
cyclophosphamide

HSV

Infectious agent: HSV-1/-2 = HHV-1/2, alphaherpesvirus
Transmission: close contact, 50% carriers, latency in neuron

Pathogenesis: replicates lytically in epithelial cells and then travels along the axons to establish latency in neuron. LAT keep latent state. Reactivation vice versa.

HSV

Clinic: orofacial infections: gingivostomatitis (primary infection); recurrent: cold sore (HSV-1),
genital infections (HSV-2),
Herpes encephalitis (letality 70% w/o treatment)
Neonatal herpes if mother has genital herpes at birth ->skin, CNS, visceral (mortality 70%)

HSV

Diagnose: Clinic, PCR of CSF, culture

Treatment: thymidine analoga:acyclovir (Zovirax),
valacyclovir (Valtrex),
famcyclovir (Famvir), and pencyclovir.

	No Envelope	Envelope
DNA	Adenovirus Parvovirus/Parvo B19 Papillomavirus /HPV	Herpesviren/HSV/EBV VZV: chickenpox,herpes zoster Poxviren/Pockenvirus
RNA	Picornavirus/Poliovirus /HAV	Orthomyxovirus/Influenzavirus Rhabdovirus/Rabiesvirus Arenavirus/ Lassavirus/LCMV Coronavirus/SARS-Virus Retrovirus/ HIV-1/MLV

	No Envelope	Envelope
DNA	Adenovirus Parvovirus/Parvo B19 Papillomavirus /HPV	Herpesviren/HSV/EBV VZV: chickenpox,herpes zoster Poxviren/Pockenvirus
RNA	Picornavirus/Poliovirus /HAV	Orthomyxovirus/Influenzavirus Paramyxoviruses: Measles v., parainfluenza v. Mumps v.,RSV Rhabdovirus/Rabiesvirus Arenavirus/ Lassavirus/LCMV Coronavirus/SARS-Virus Retrovirus/ HIV-1/MLV

Contagions

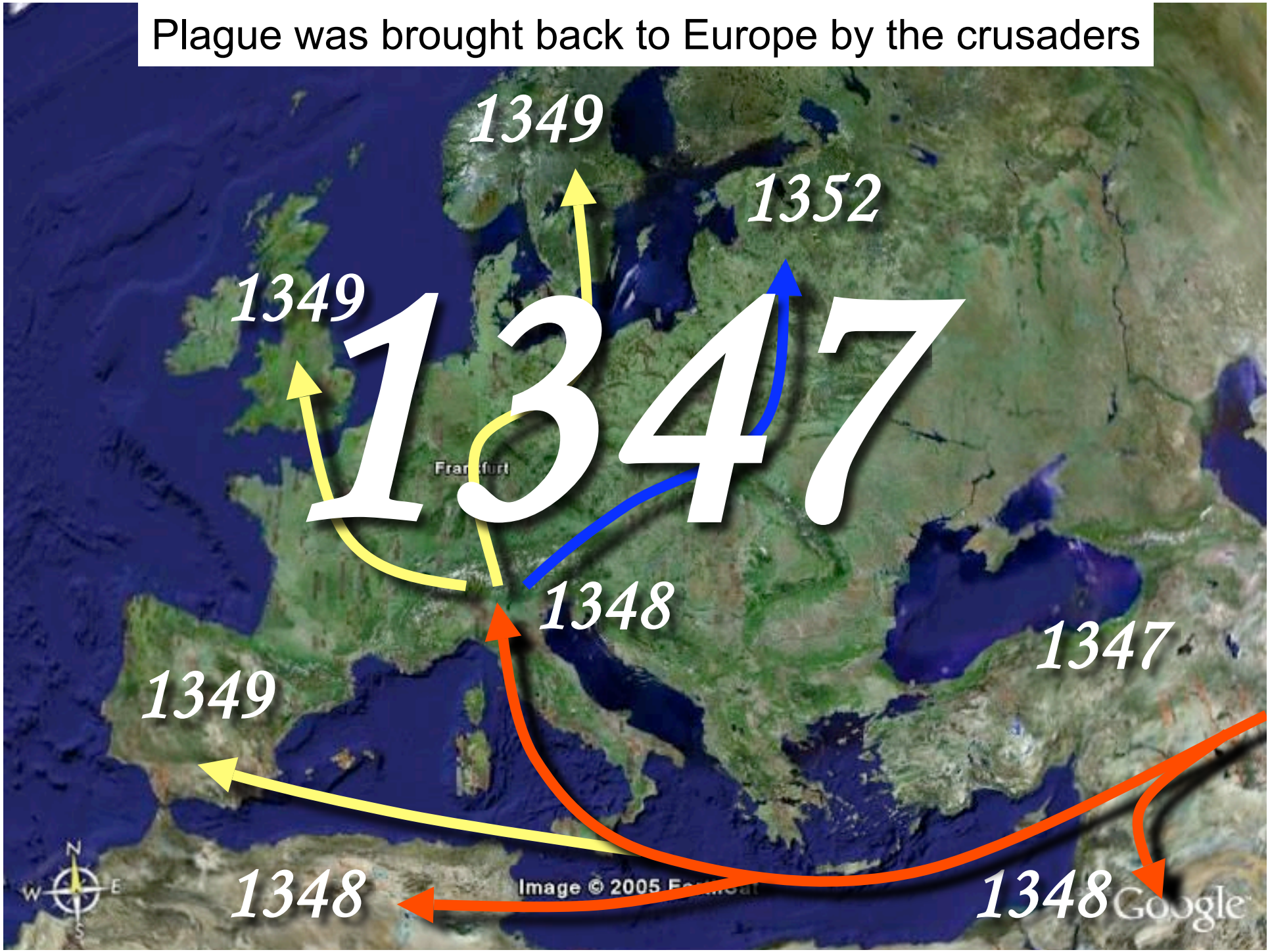
GSH 100

Pest/Plague

Syphilis

AIDS

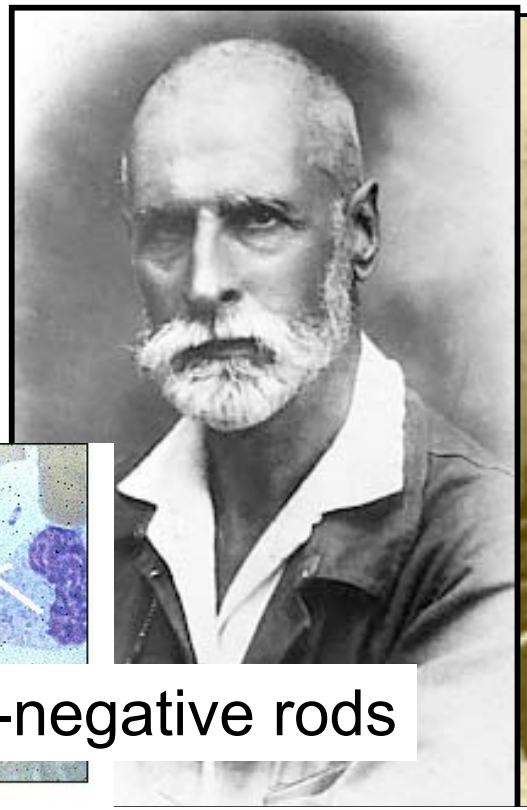
Influenza/Flu

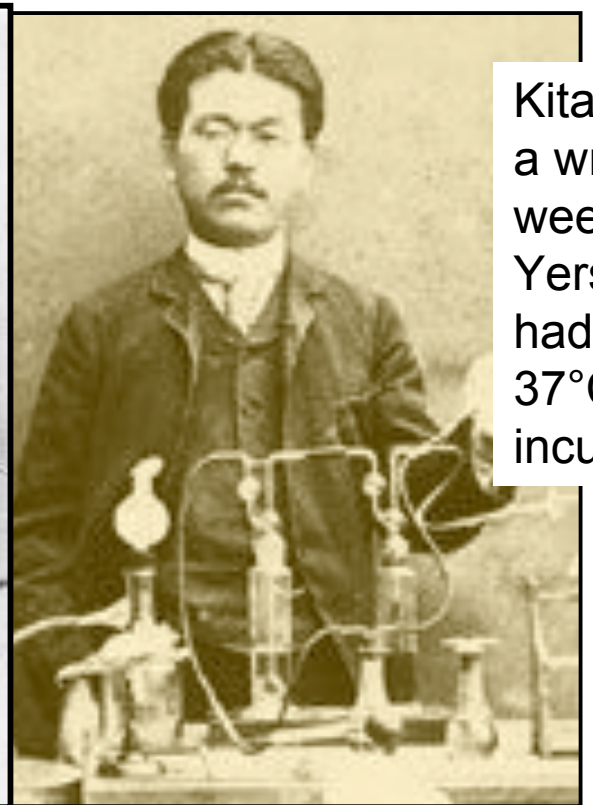

Plague was brought back to Europe by the crusaders
1349
1352
1349
1347
1348
1347
1349
1348
1348
Image © 2005
Google

1890: Pague in China

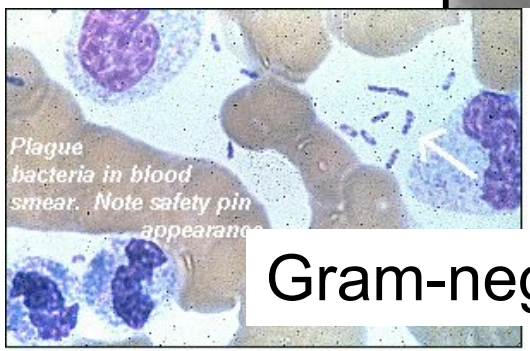
- Alexander Yersin (Pasteur Institut) and Kitasato (Japan)search for the pathogen

Yersin discovered Yersinia pestis as the bacteria grew preferentially at 30°C and he did not have an incubator.

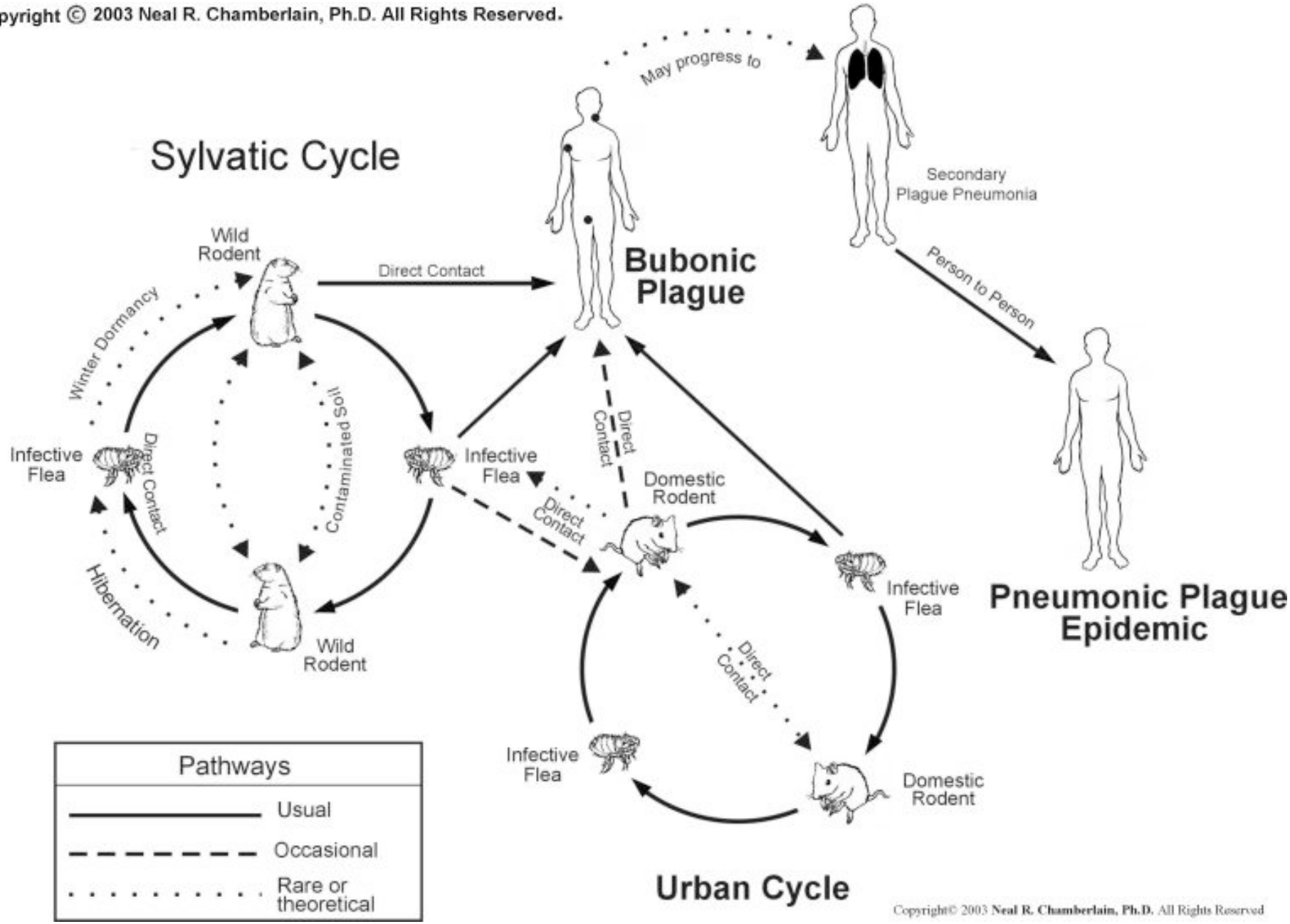




Kitasato published a wrong agent 4 weeks before Yersin, which he had isolated at 37°C in an incubator



Gram-negative rods



Bubos at primary lymph nodes

Manifestations of Plague

- Bubonic plague
- Lung plague
- Septic plague

Transmission by fleas

2000 Flea species, of which 80 are infectable with Y. pestis

200 rodent species support replication of Y. pestis

Y.p. grows in the stomach of the flea

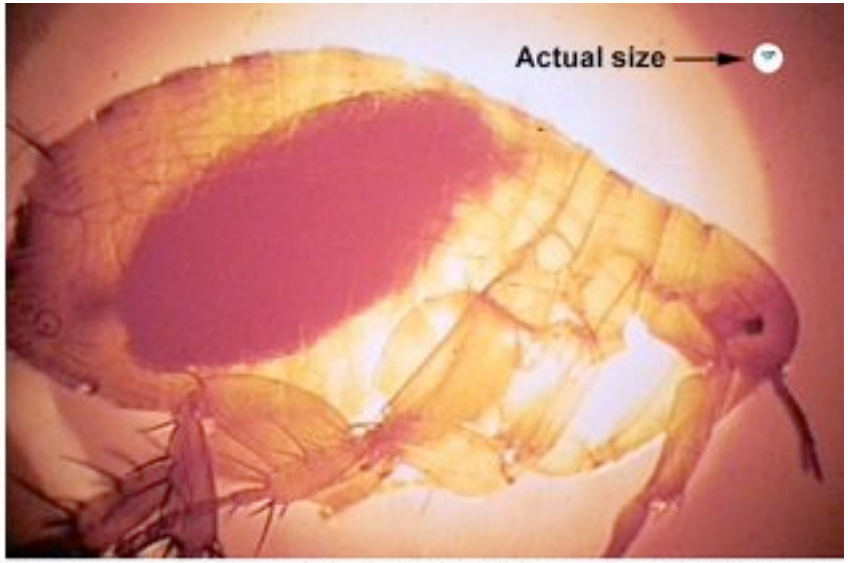
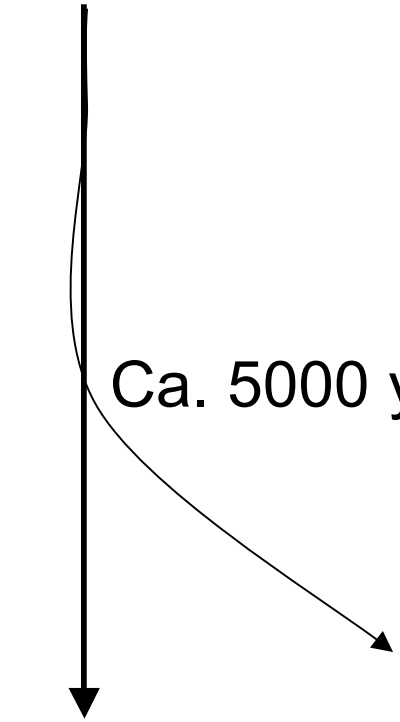


Image: Xenopsylla chepsis (oriental rat flea) engorged with blood

Biofilm formed by bacteria blocks entrance into flea stomach

- Flea sucks in vain, increases biting frequency, finally starves

Genomics elucidates origin of plague



Ca. 5000 years

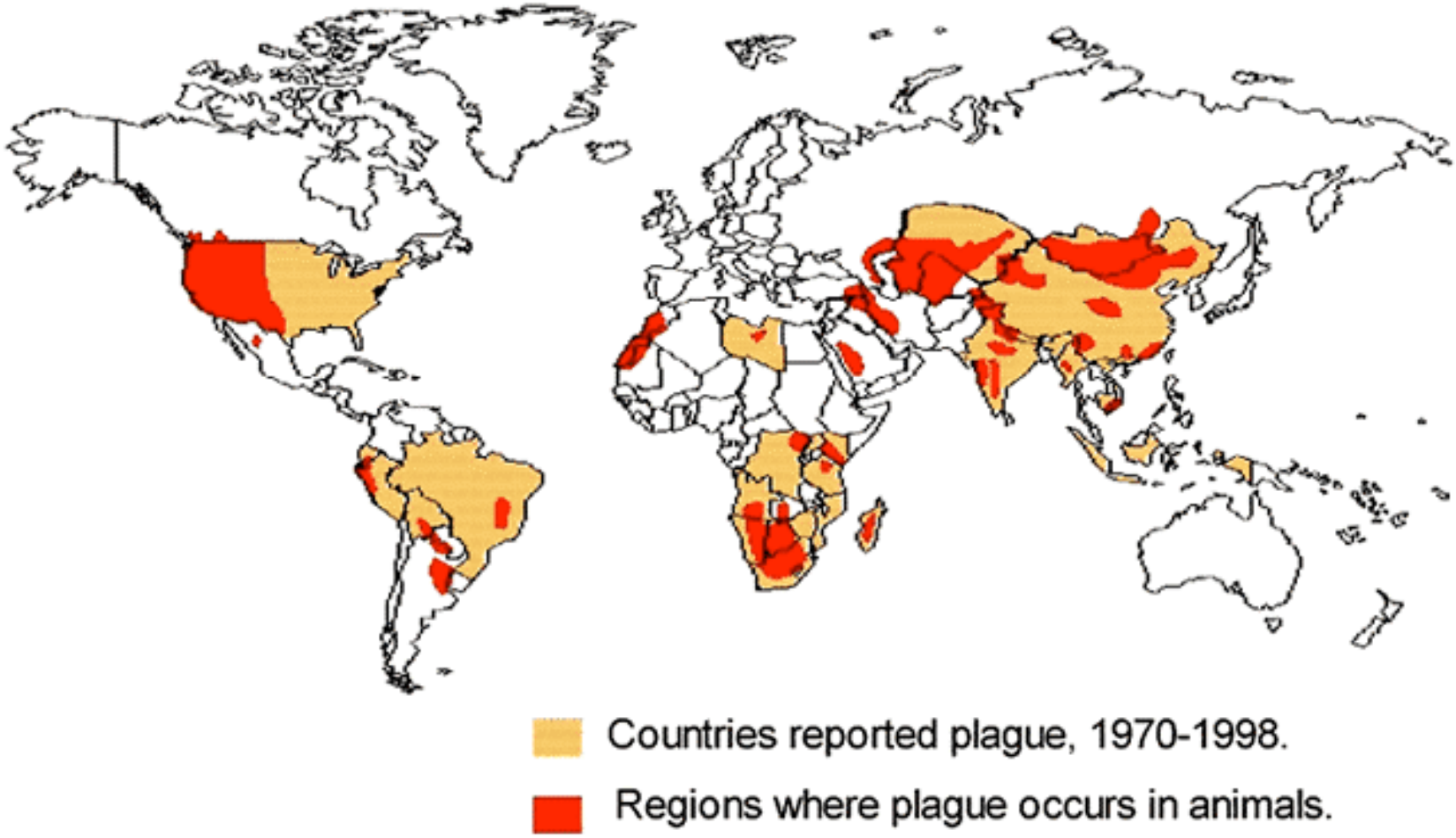
Yersinia entercolitica

Y. pestis

>97% Homology
Insgesamt 4000 Gene

Adaptation to growth in flea and transmission by bite
+ 2 Plasmide
+ 32 Genes
- 317 Genes

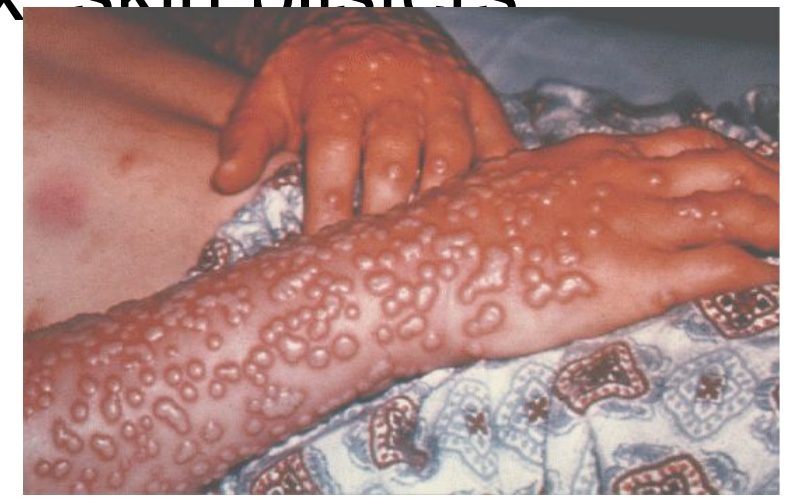
World Distribution of Plague, 1998



Plague not Smallpox !

GSH 100

- Smallpox caused by a virus: Variola
- Smallpox has been irradicated since the 70tees
- There is an effective vaccine: Vaccinia
- Smallpox: skin blisters



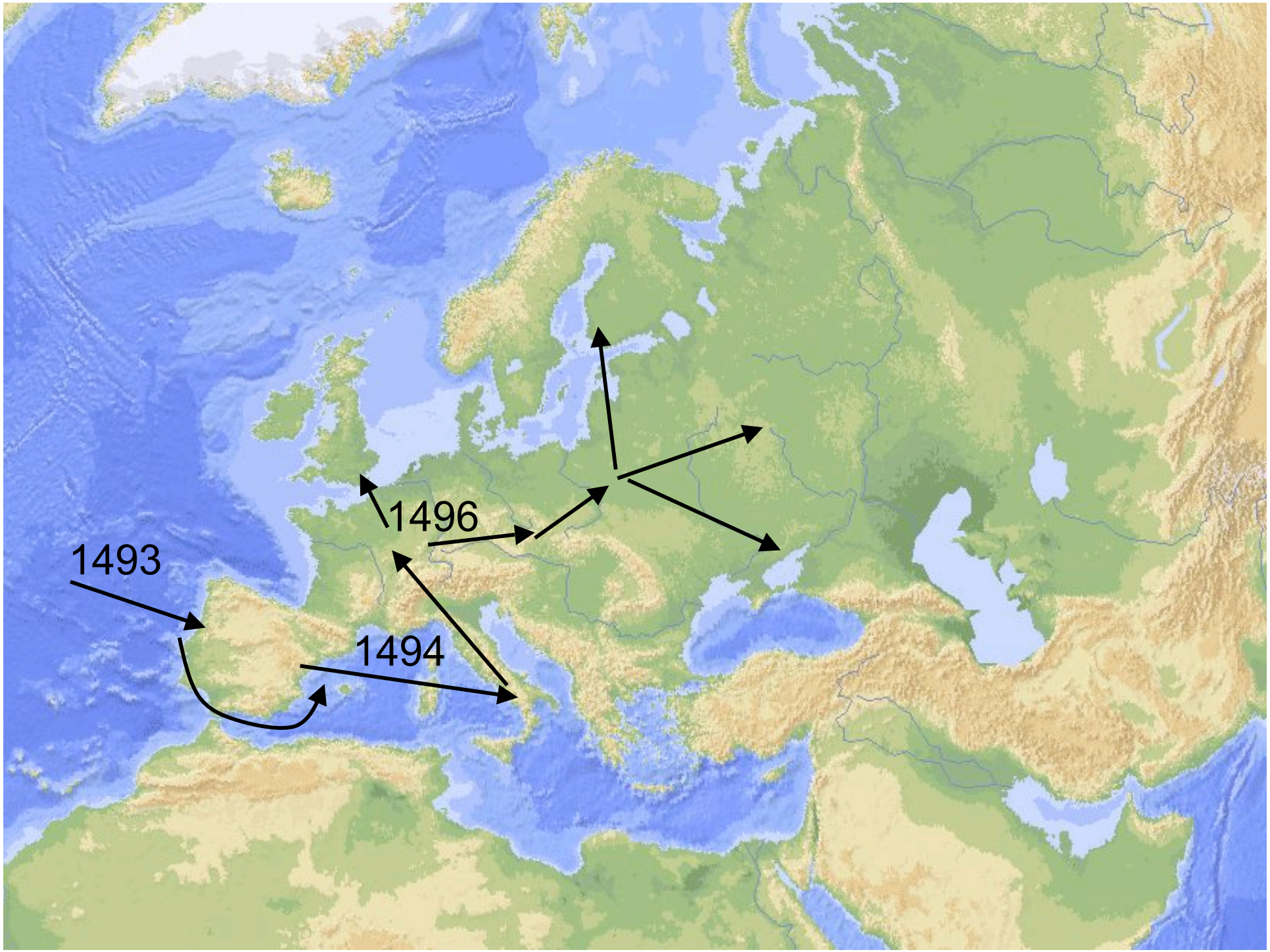
Syphilis
=Lues

Agent: Treponema pallidum
subspezies pallidum

Columbus Souvenir

GSH 100

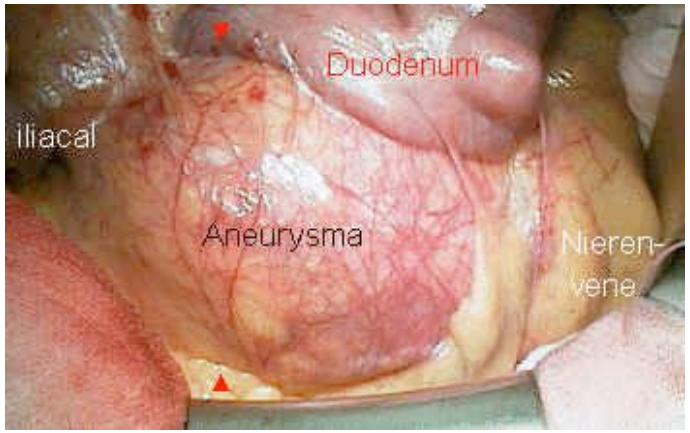
- 1493 Columbus returns from Haiti, sailors distribute syphilis in Spanish harbors
- Among Indians a lokal, less pathogenic variant was endemic: Frambesia
- 1494 Spanish soldiers help Karl VIII to conquer Naples, on his way back he carries the disease to France, Karl dies of syphilis 1498. Syphilis spreads eastwards throughout Europe.


1493
1494
1496

Clinical manifestation

- Incubation 21 days-> primary chancre lasts ca 6 weeks, local Lymphadenopathy
- Secondary s., generalized lymphadenopathy, rash, contagious

Tertiary S.



Gummas (Skin, bone, liver), cardiovascular manifestations, (aortic aneurysm)

Tertiary S.; Neurolues

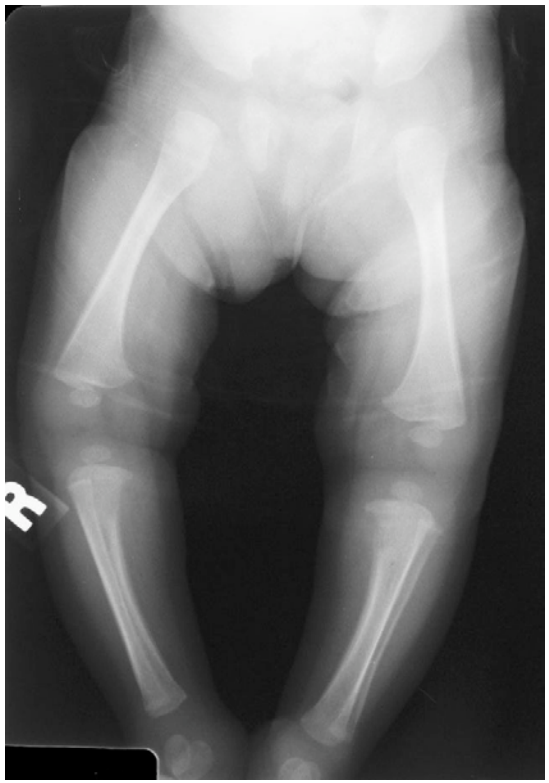
- Tabes dorsalis - spinal chord nerve degeneration

  Heinrich Heine
- General paralysis (Progressive Paralyse) with psychiatric symptoms, reduced vision and intelligence

  Nietsche

Congenital Syphilis

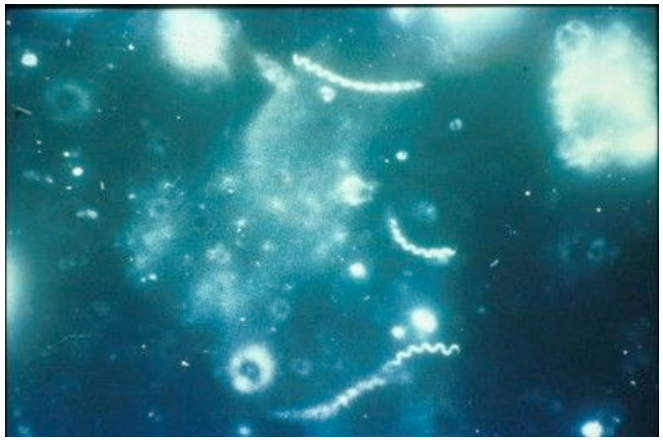
40 % abortions



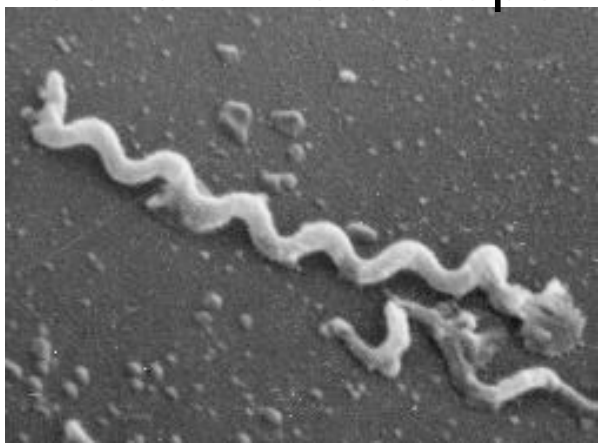
The infectious agent was discovered

- 1905 by Schaudinn and Hoffmann in Berlin
- Treponema (Spirocheta) pallidum
- Difficult to stain bacteria, do not grow in culture!

Dark field



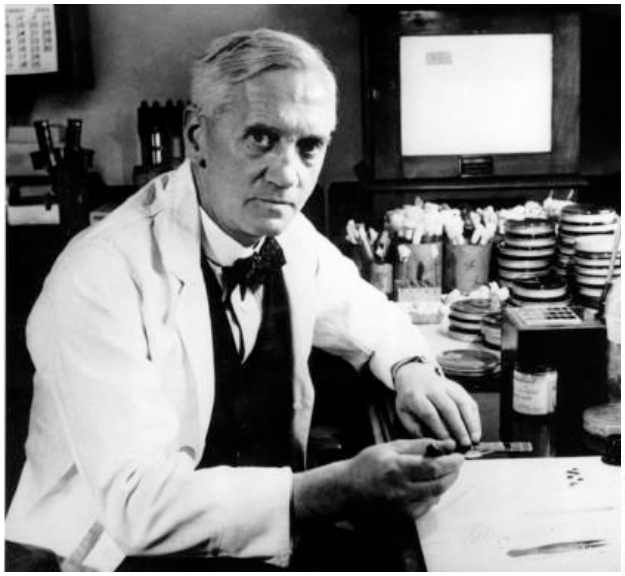
Electron microscope

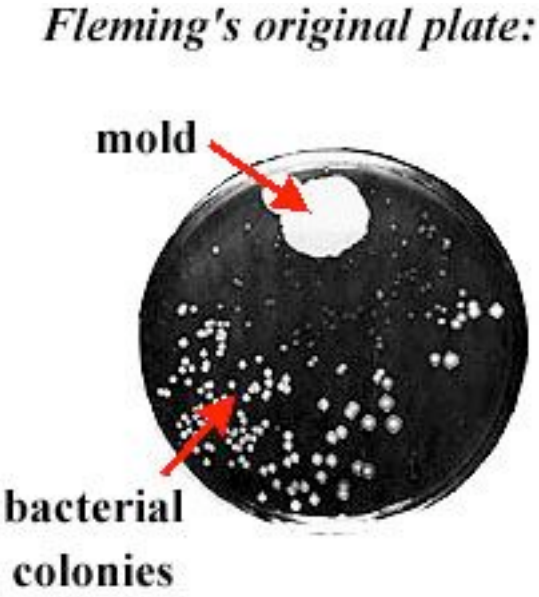


Fritz Schaudinn

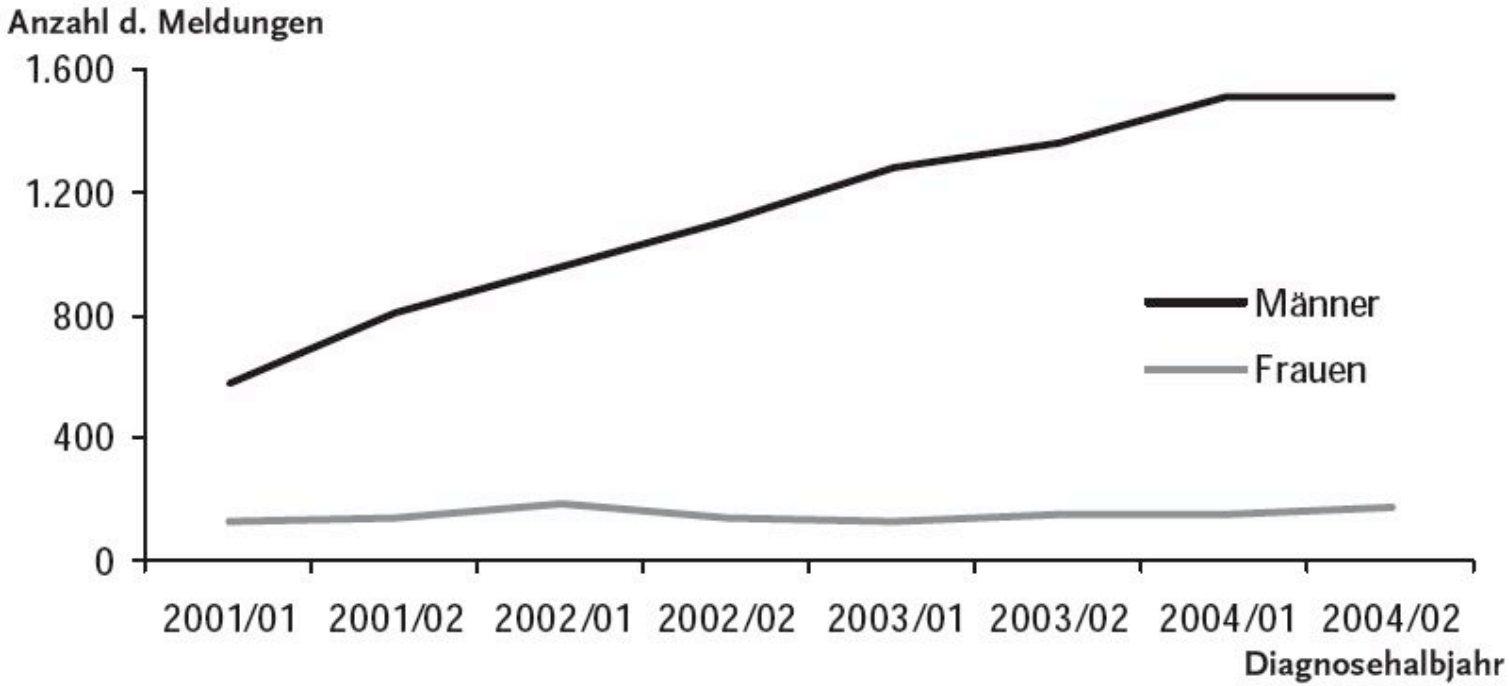
Antibiotics

- 1929: Fleming discovers Penicillin
- 1939: Flory purifies P. and tests in clinically
- 1943: industrial production initiated in the US





Situation in Germany

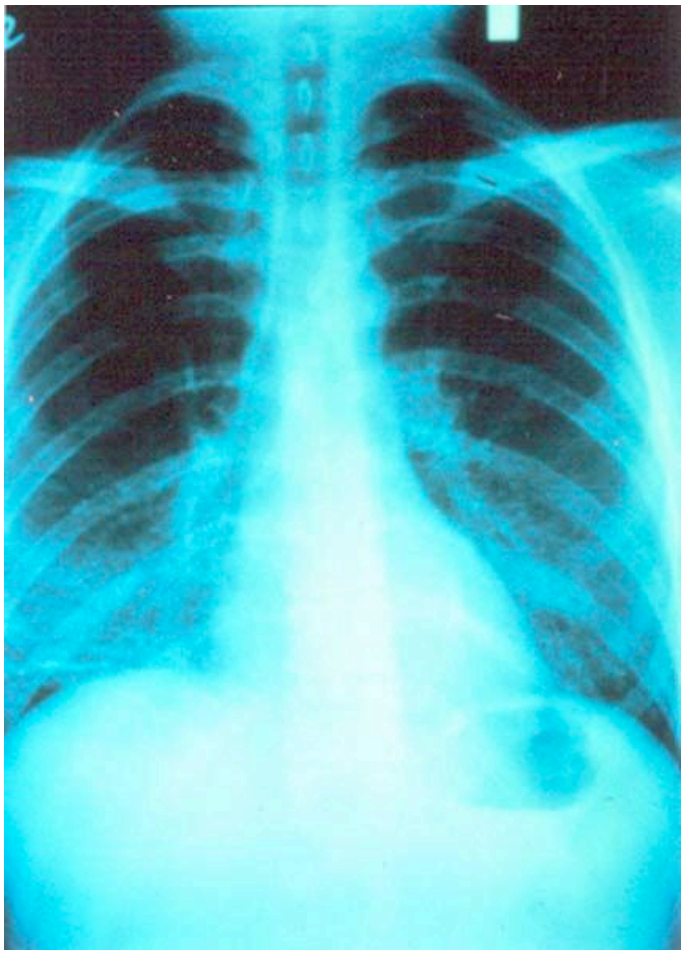


HISTORY of the AIDS pandemic

History I

New York, 1981:
Cluster of Kaposi‘s sarcoma in MSM

California, 1981:
Cluster of PCP in MSM



*MSM: Men who have sex with men

History II

1982: Incidence of Kaposi and PCP was also increasing in drug addicts.

In Africa wasting/slim disease was emerging.

Slim disease
Wasting disease

Discovery of the virus:

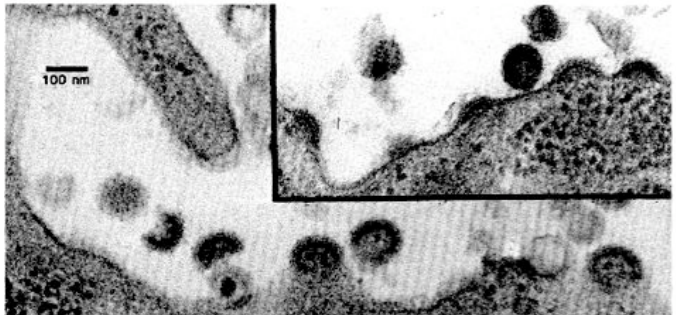
1983 Luc Montagne (left) discovers AIDS virus (LAV) and sends a sample to Robert Gallo.

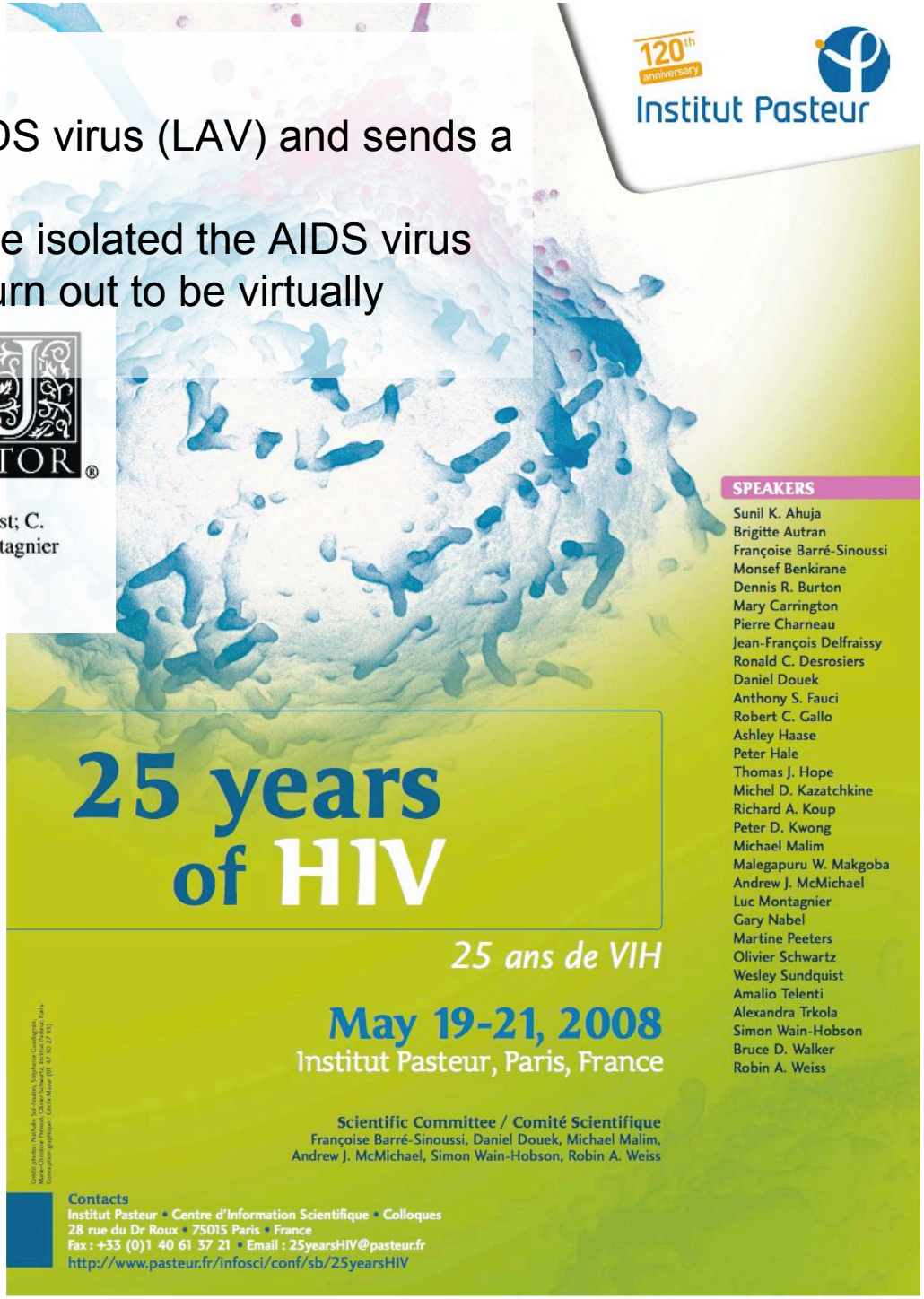
1984 Robert Gallo (right) claims to have isolated the AIDS virus and calls it HTLVIII. LAV and HTLVIII turn out to be virtually sequence identical.

Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome (AIDS)

F. Barre-Sinoussi; J. C. Chermann; F. Rey; M. T. Nugeyre; S. Chamaret; J. Gruest; C. Dauguet; C. Axler-Blin; F. Vezinet-Brun; C. Rouzioux; W. Rozenbaum; L. Montagnier

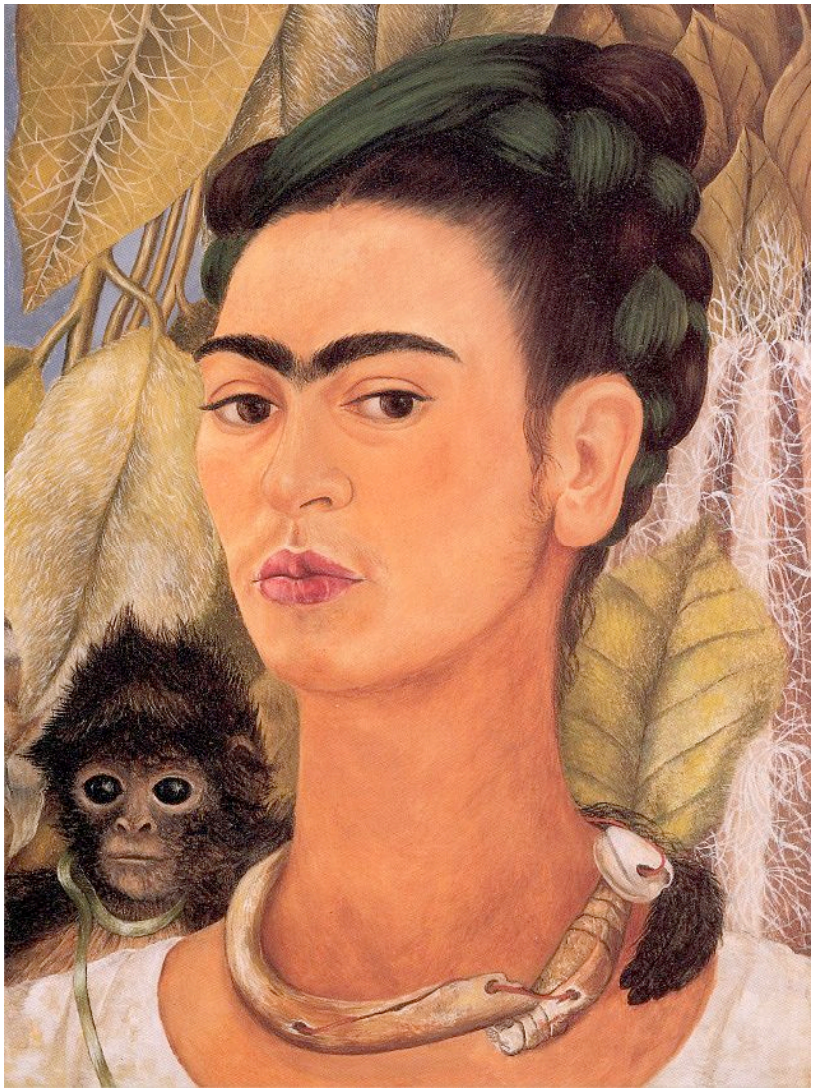
Science, New Series, Vol. 220, No. 4599 (May 20, 1983), 868-871.





Origin HIV

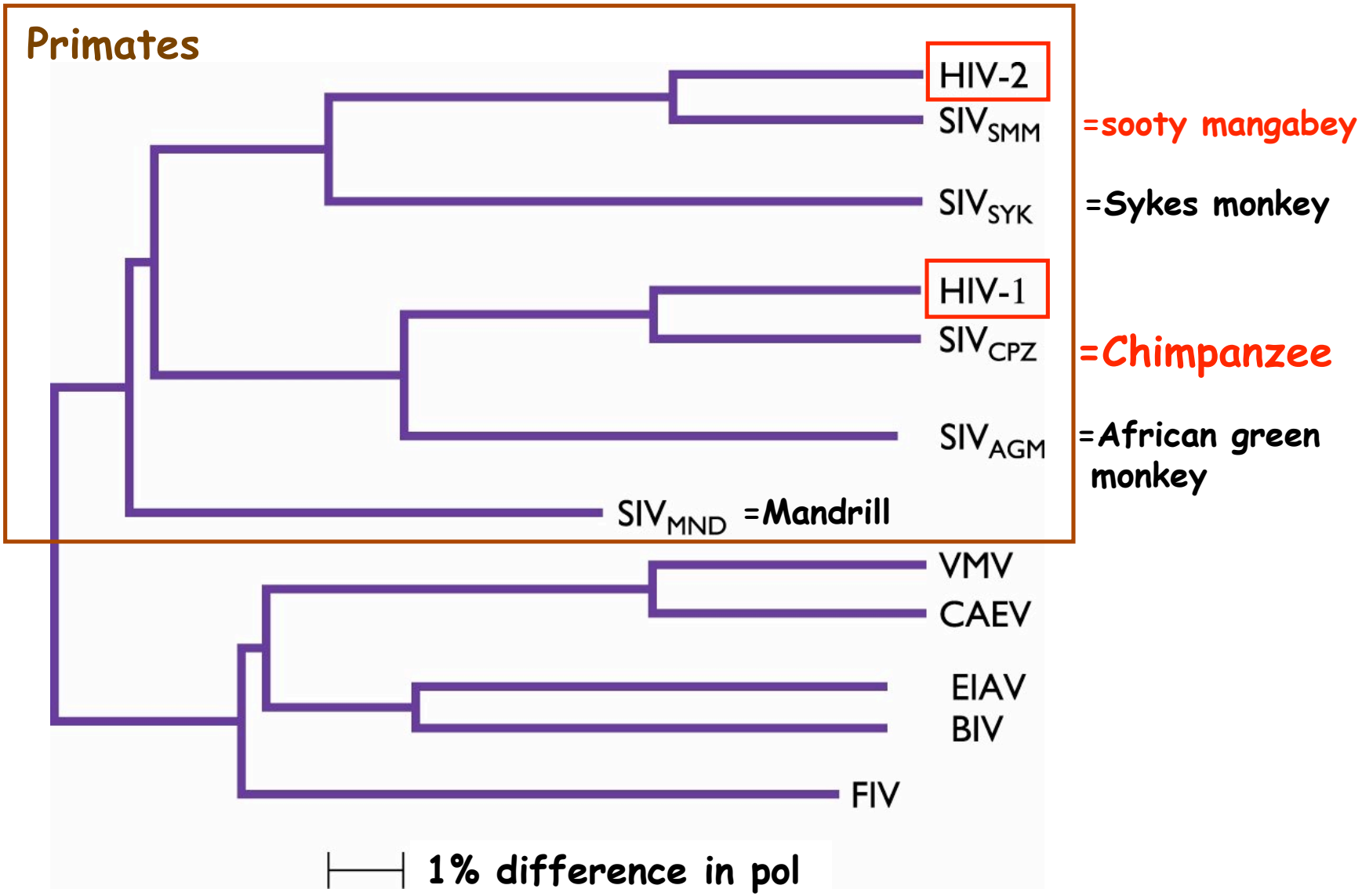
Non-human primate SIV:
SIVcpz -> HIV-1
SIVsm -> HIV-2



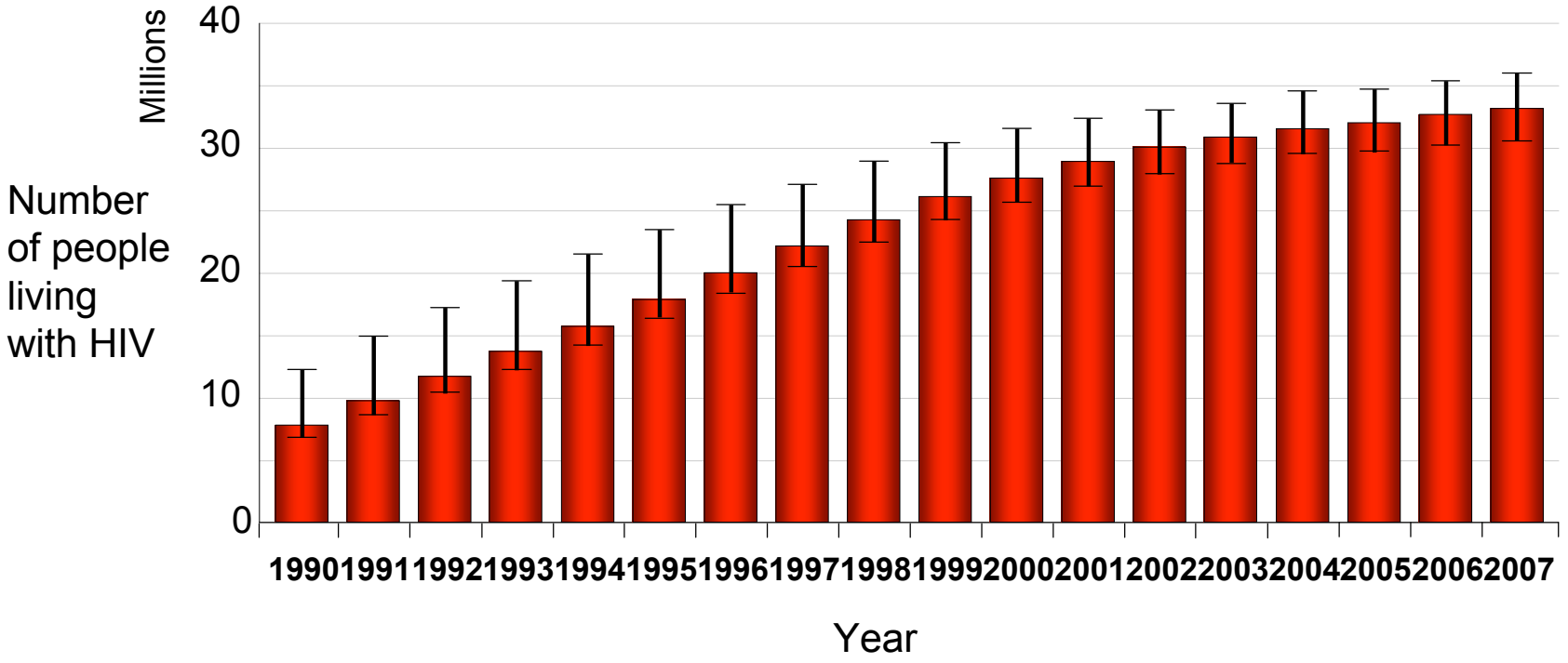
Ca 1930->Final transfer of virus to humans, spread enhanced by work camps and vaccine programmes

First positive human sera:
-> Afrika 1959
-> USA 1969
-> Europa 1976

Phylogeny Lentiviruses

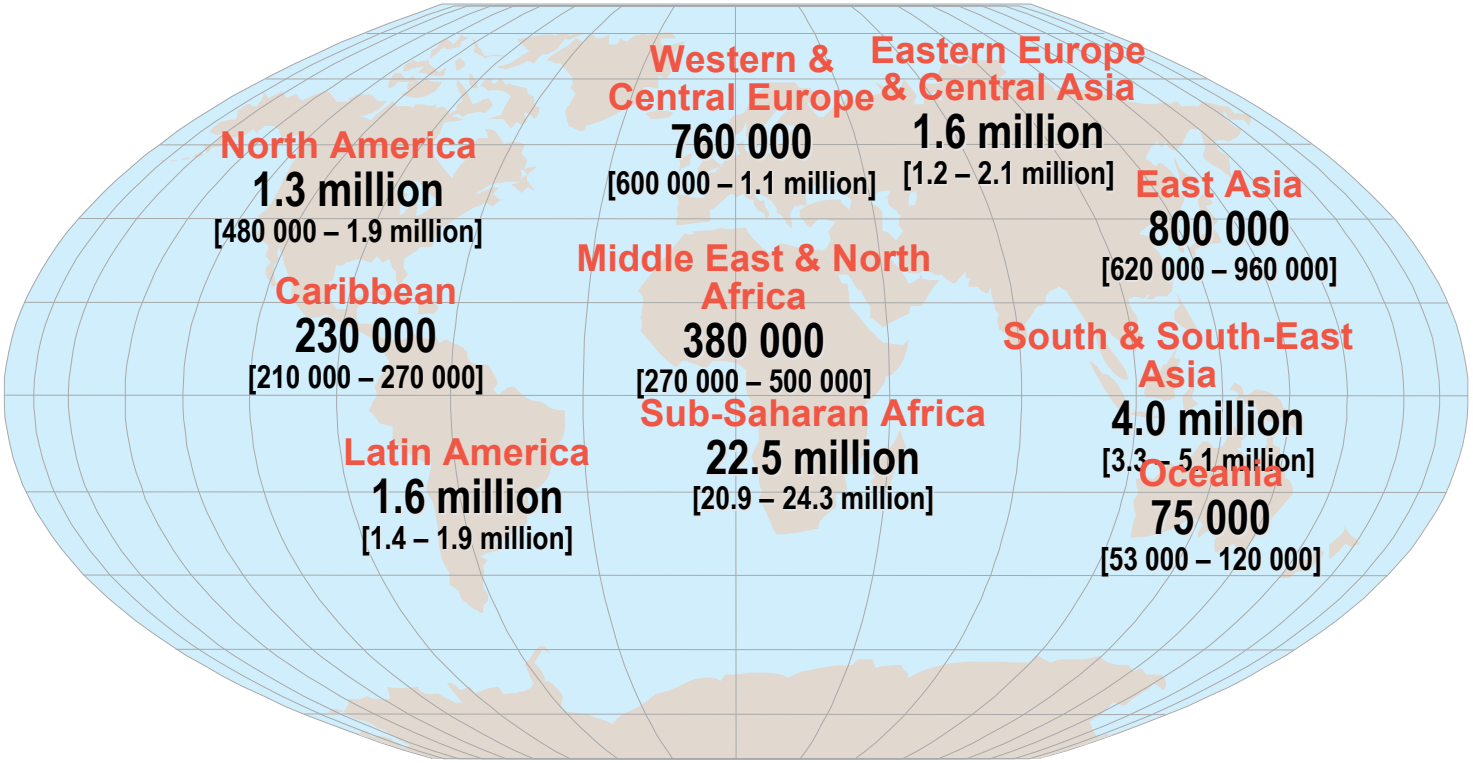


Estimated number of people living with HIV globally, (Prevalence) 1990–2007



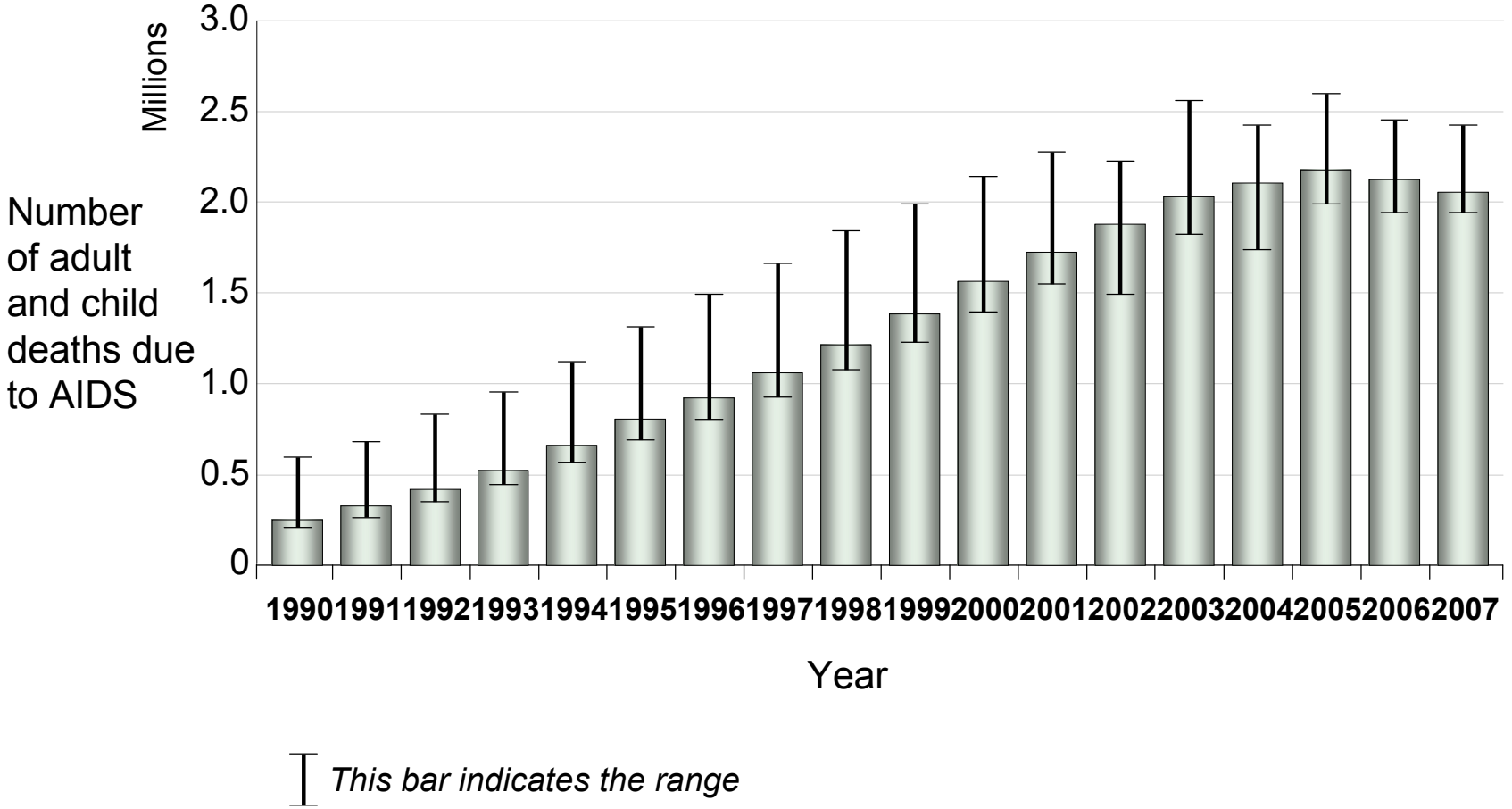
UNAIDS, 2007,

Adults and children estimated to be living with HIV, 2007

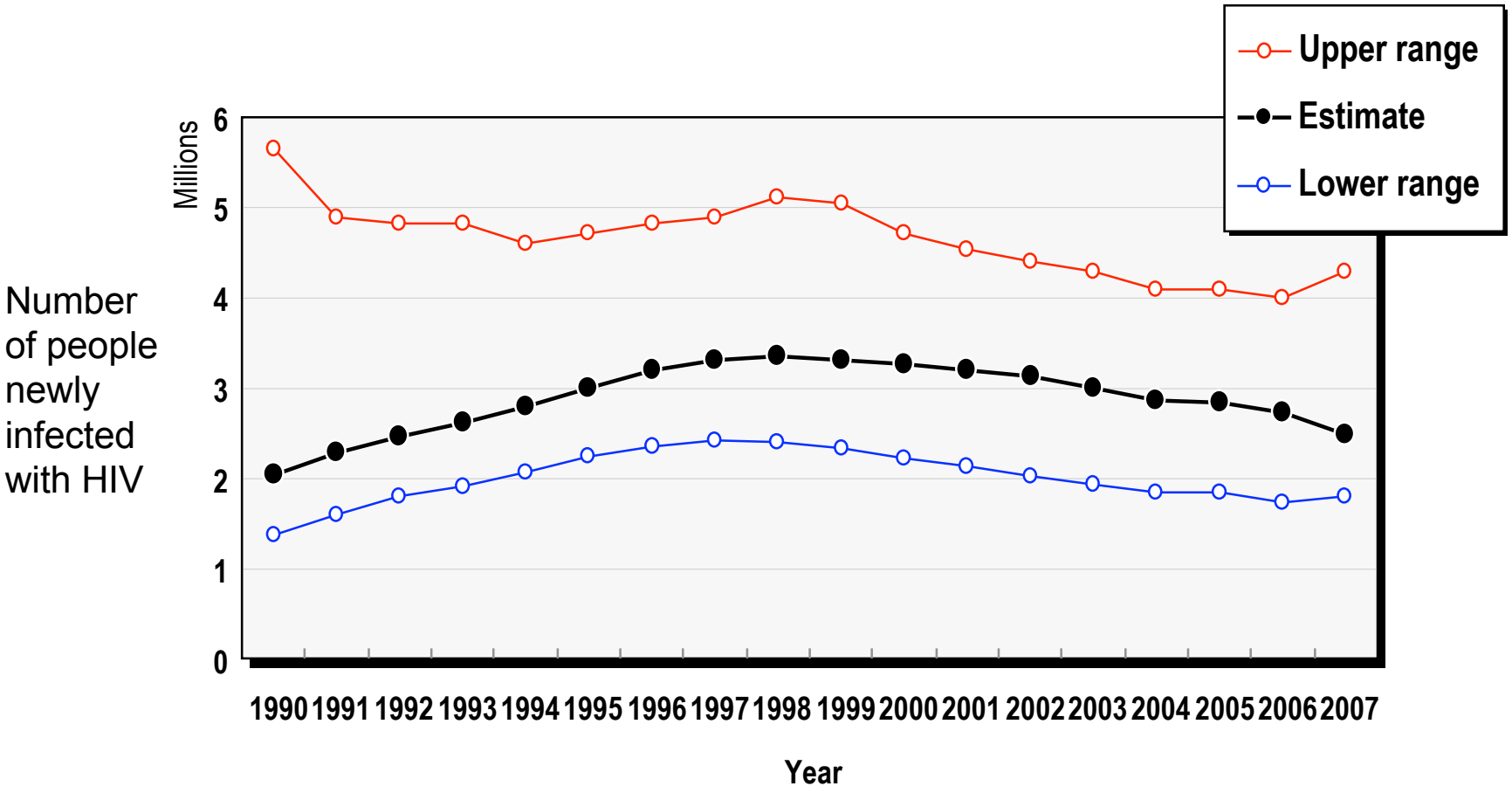


Total: 33.2 (30.6 – 36.1) million

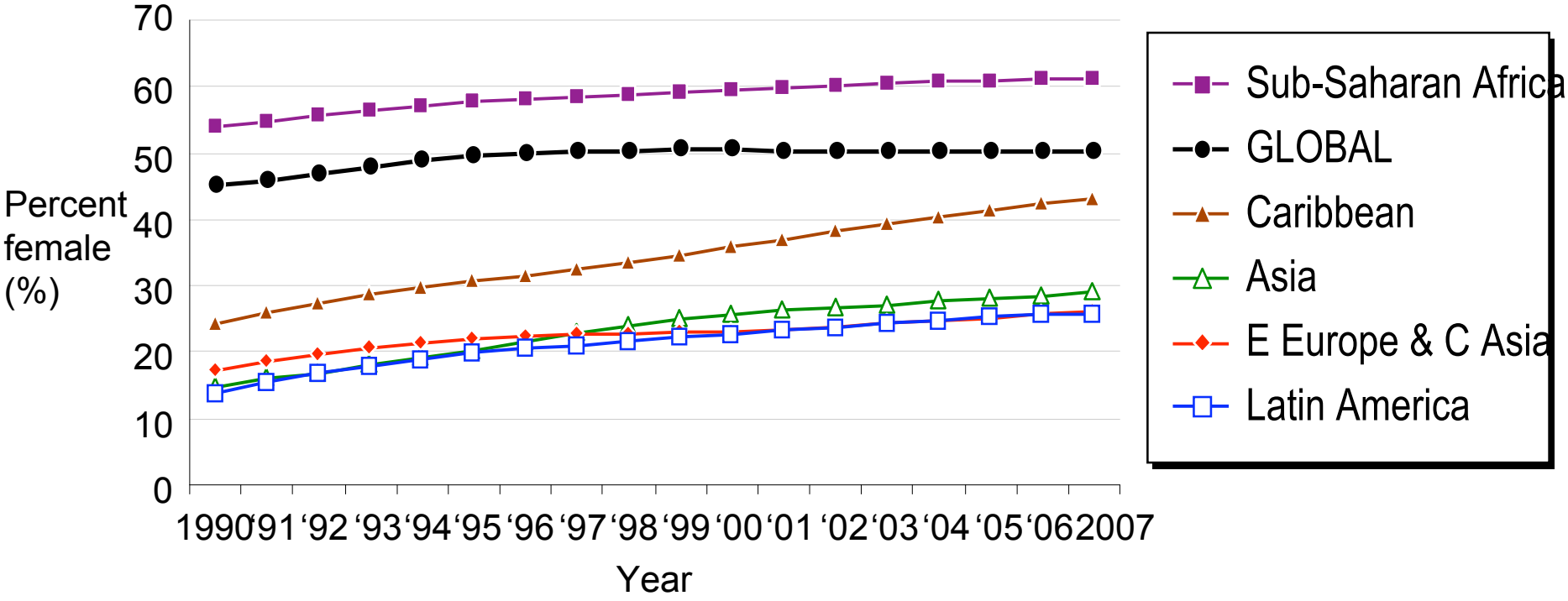
Estimated number of adult and child deaths due to AIDS globally, (Mortality) 1990–2007



Estimated number of people newly infected with HIV globally, (Incidence) 1990–2007

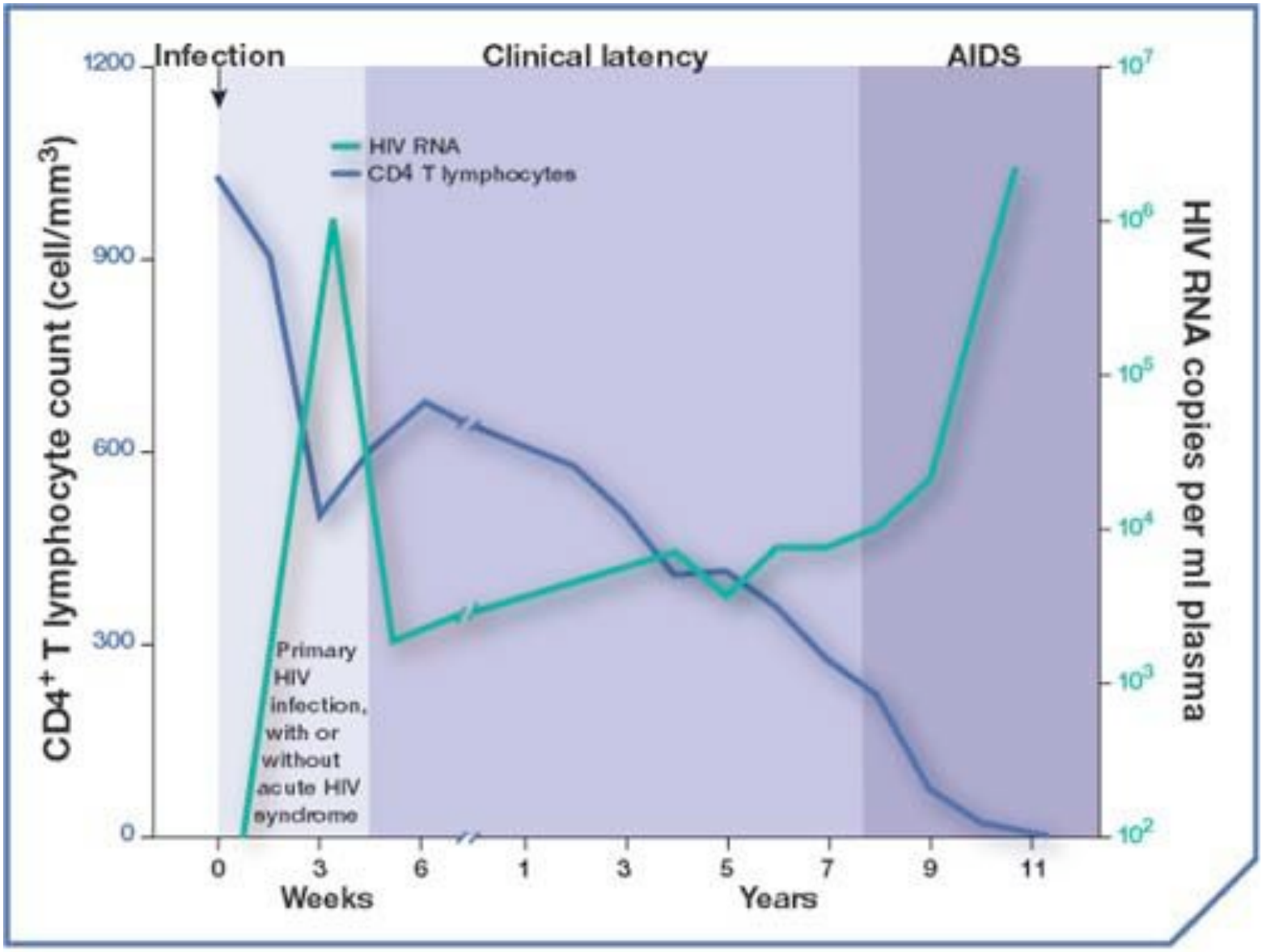


Percent of adults (15+) living with HIV who are female, 1990–2007



Clinical Course of HIV infection

Clinical course



Primary HIV-Infection

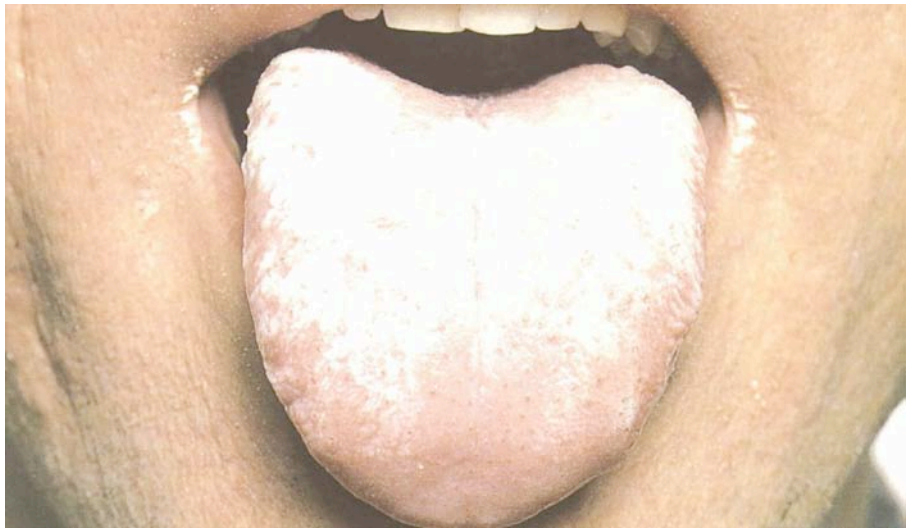
Exanthema und
lymphadenopathy

AIDS

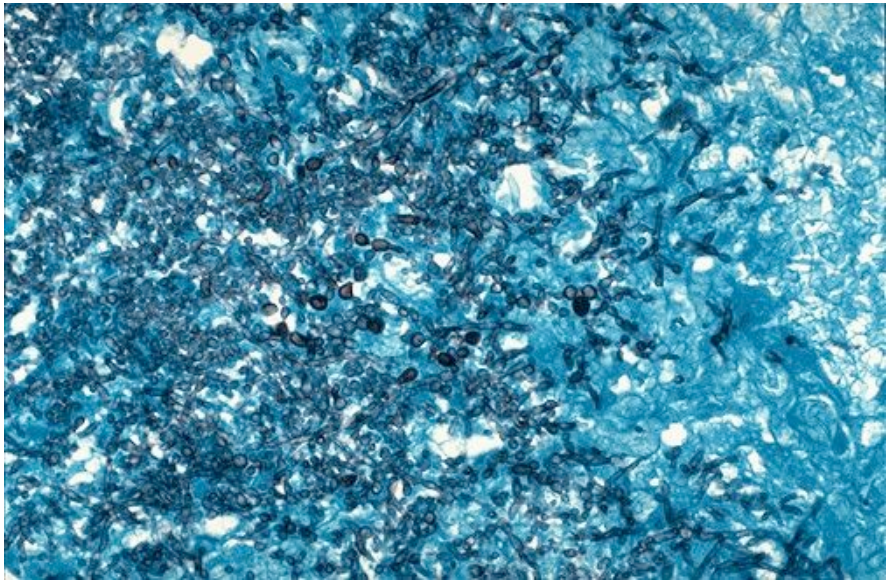
1. Opportunistic infections
   - Candida-Infections (Soor)
   - Gastrointestinal infections (Cryptosporidien)
   - Pneumonia(PCP, atyp. Mykobacterien, TBC)
   - Eye infections (CMV)
   - Brain infections (Cryptococcus)

2. Opportunistic Tumors
   - Kaposi‘s sarkoma
   - AIDS-reladed lymphoma (ARL, B-cell, NHL)

Candidiasis

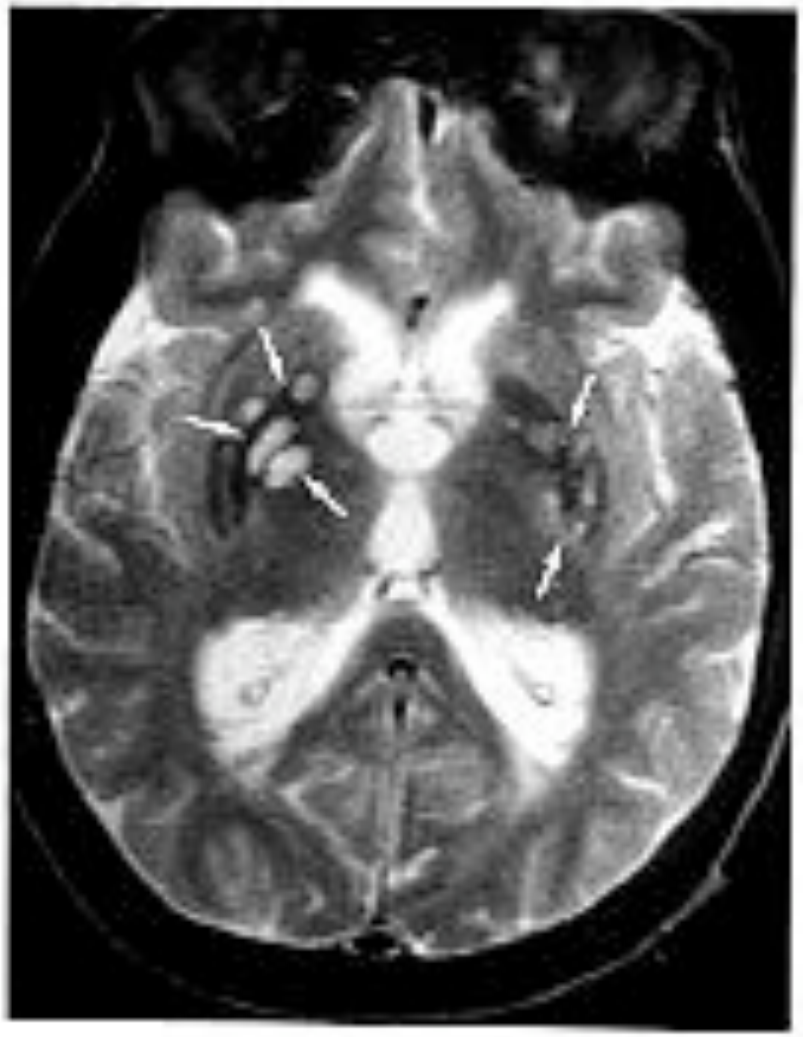


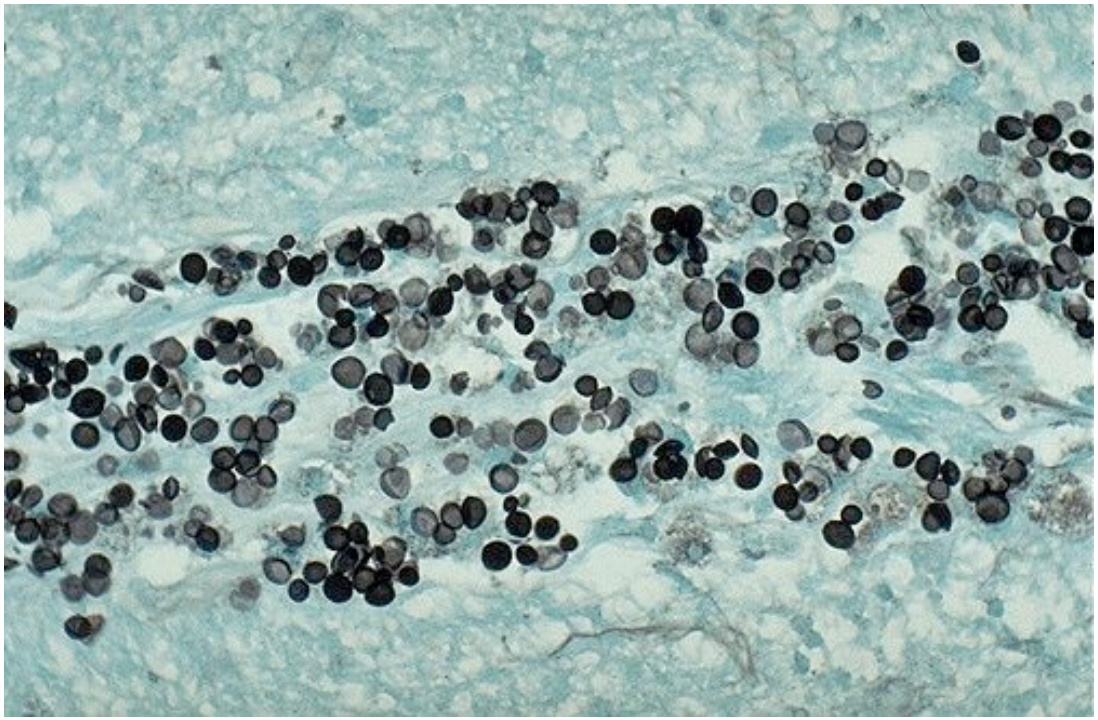
Oral Candidiasis



Candida albicans as an invasive process in the esophagus with GMS staining

Cryptococcus infection

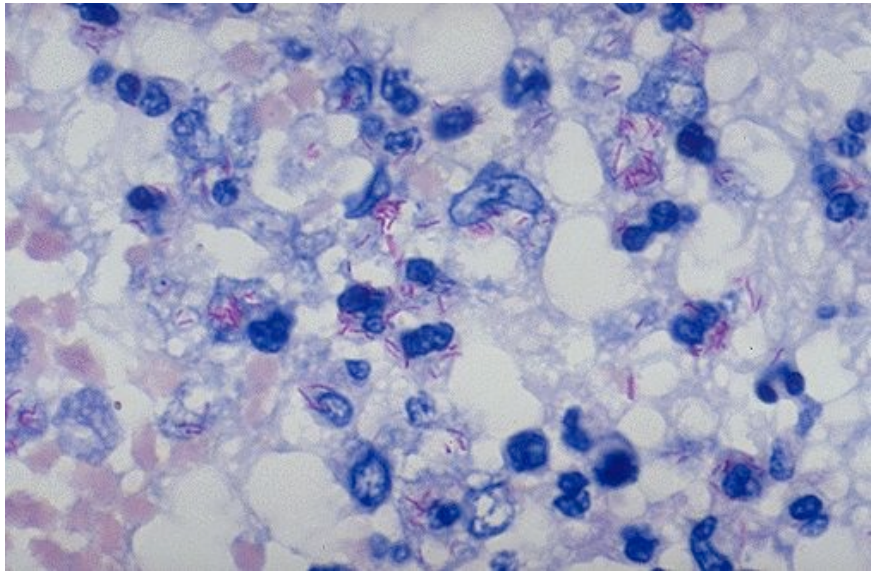




Cryptococcus neoformans
- here lacking a capsule,
- nucleus stains well with GMS staining
- meninges in a case of cryptococcal meningitis

Severe tuberculosis

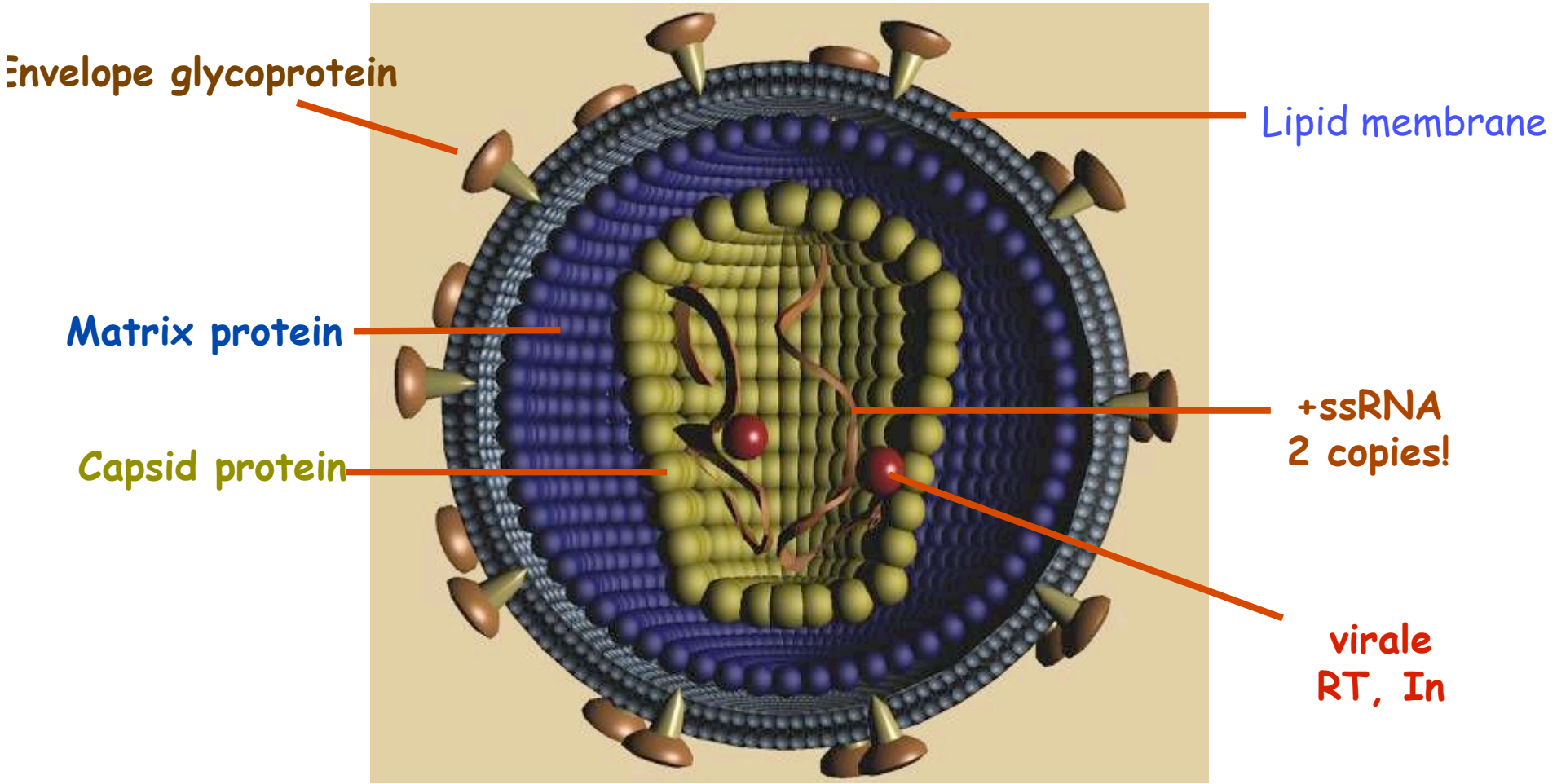
Miliary tuberculosis



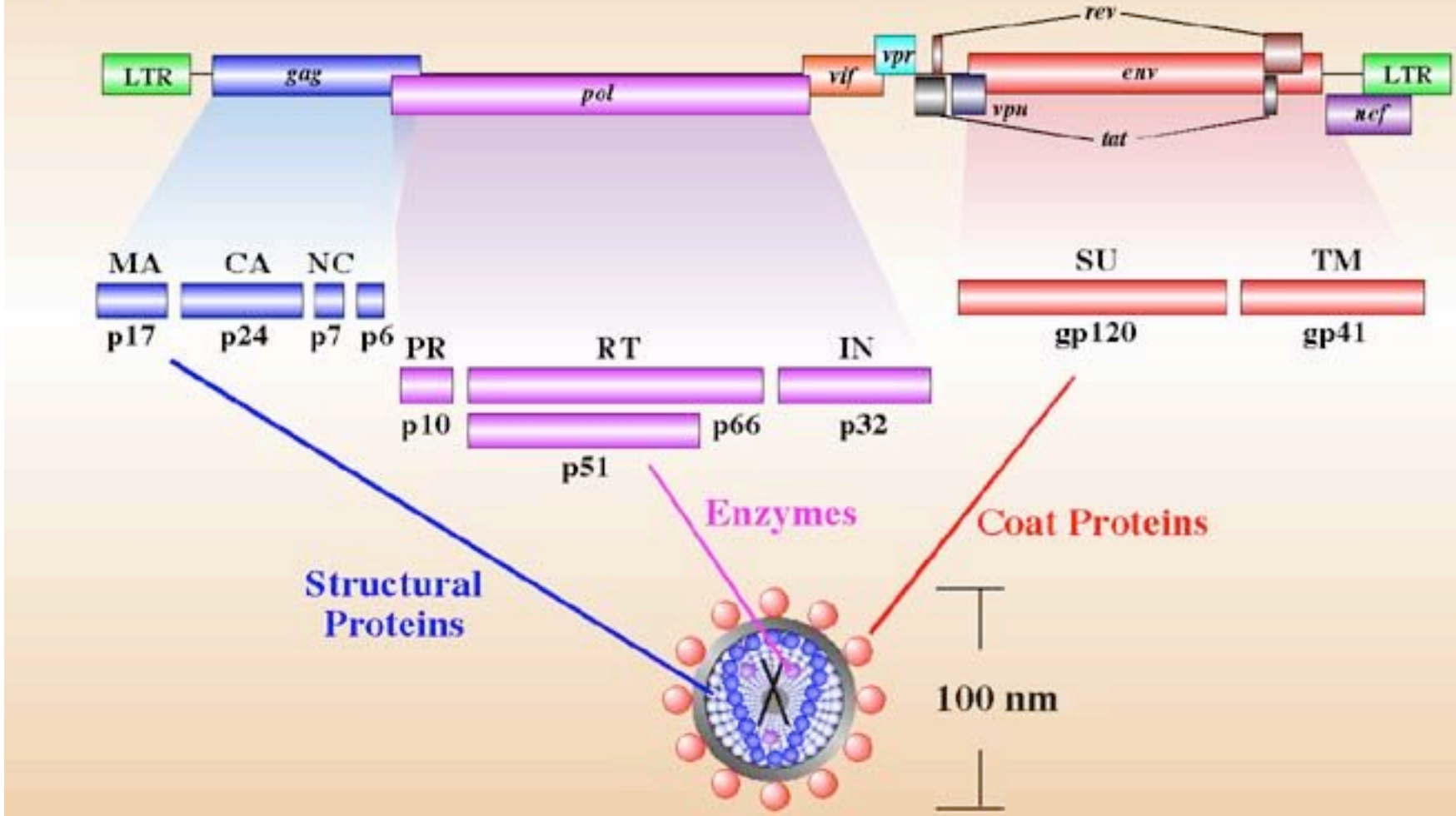
Mycobacterium tuberculosis infection of lung is shown here with numerous red rods seen with acid fast staining.

The HI-Virus and Immunopathogenesis

HIV Particle

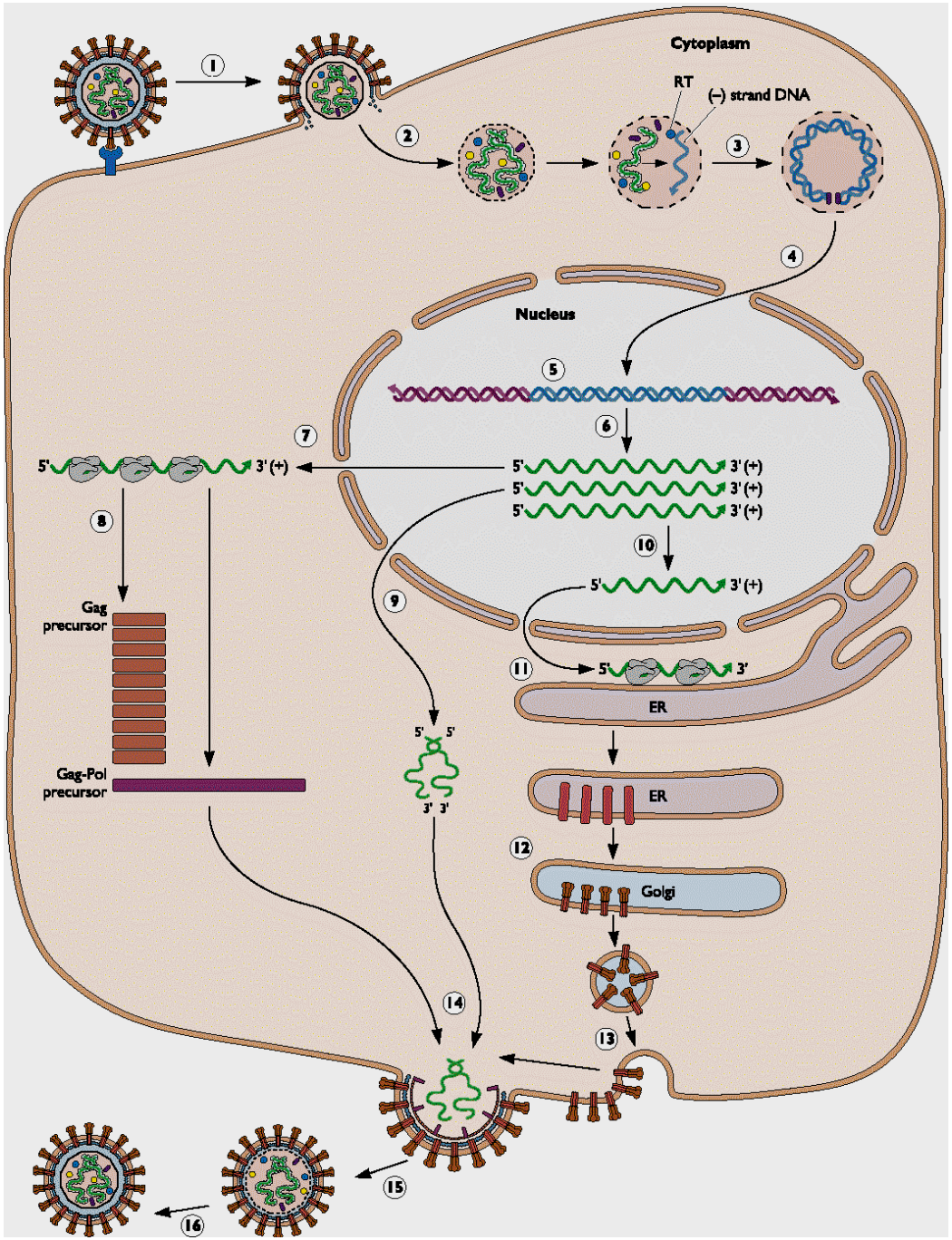


Genomic Organization of HIV-1



MWCHO

HIV replication cycle

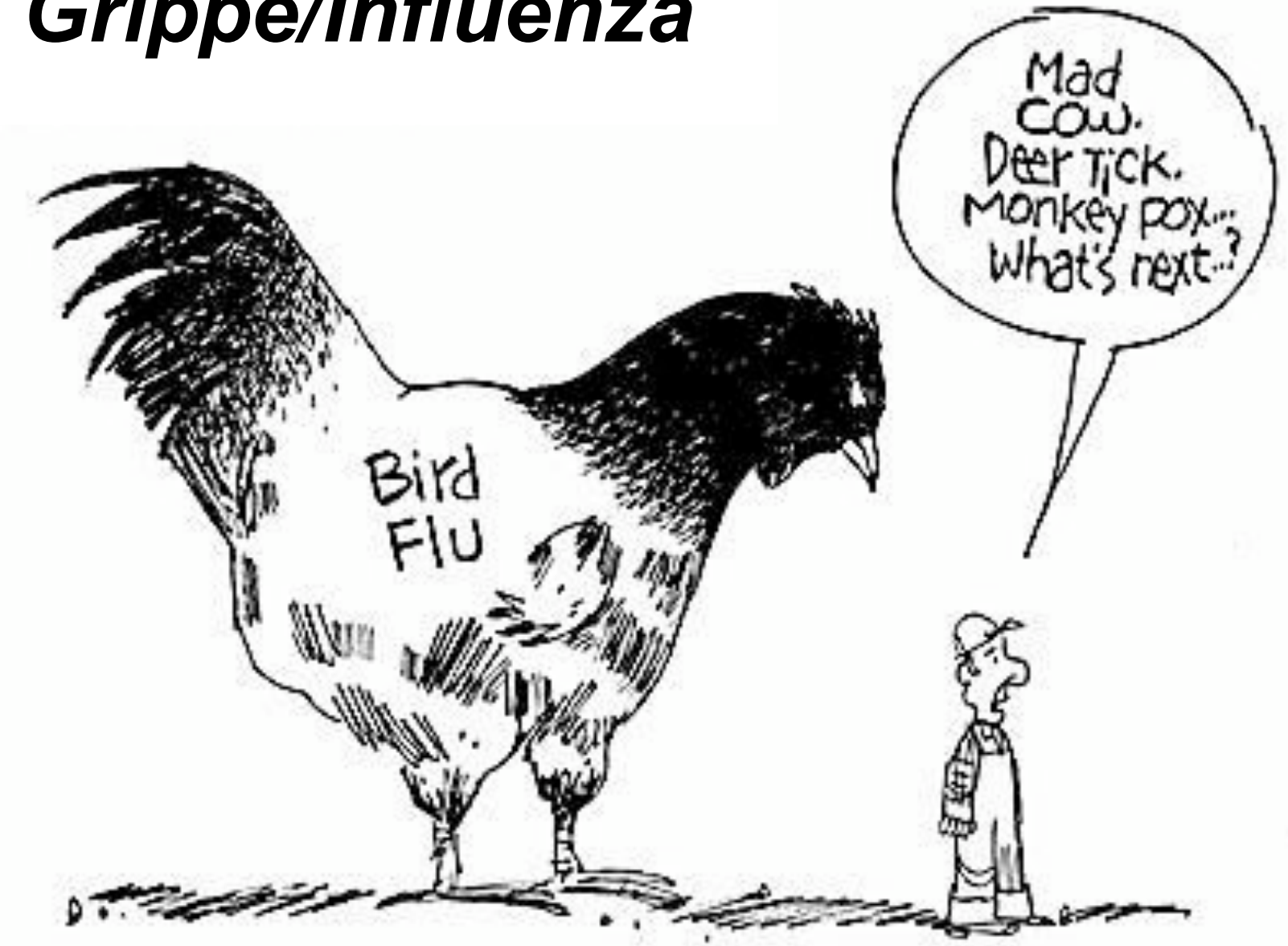


HIV-associated Immunodeficiency

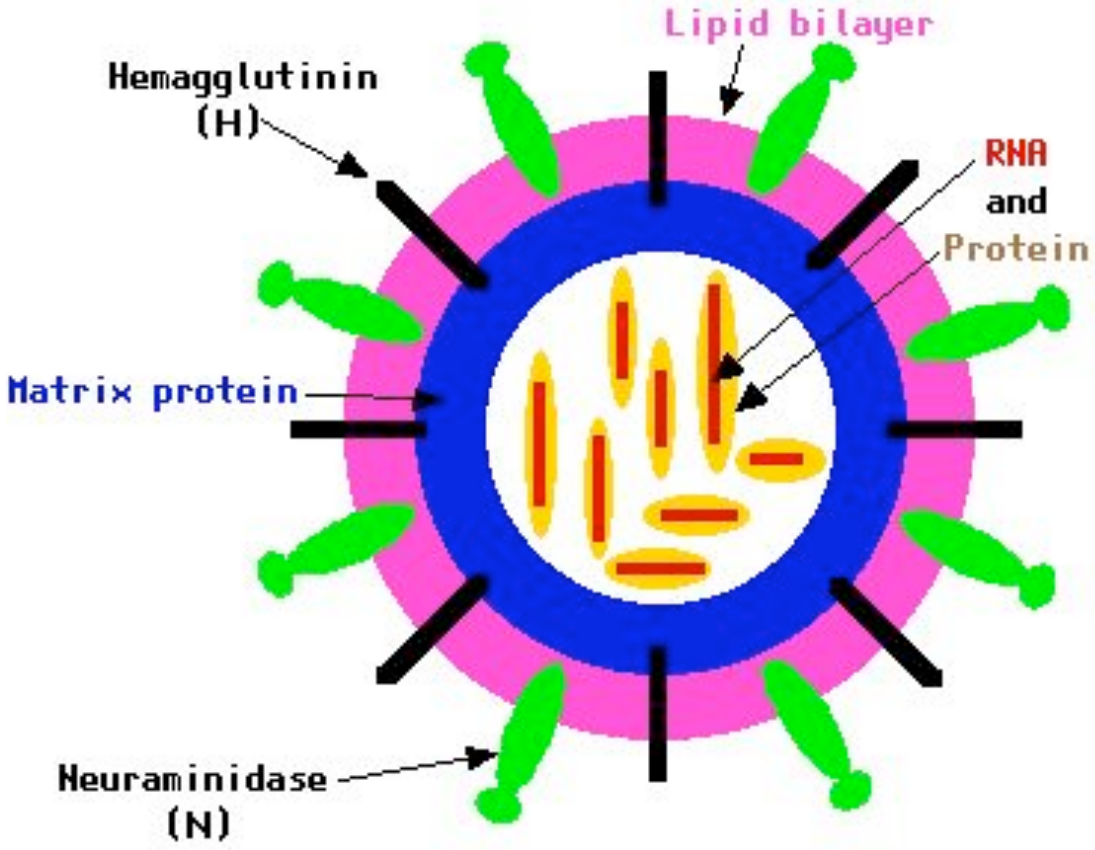
- Reduction of number of T helper cells
- Narrowing of repertoire of T helper cells
- (especially loss of HIV-specific T helper cells)
- Pertubation of immune function (Th1->Th2 shift; chronic immune activation)

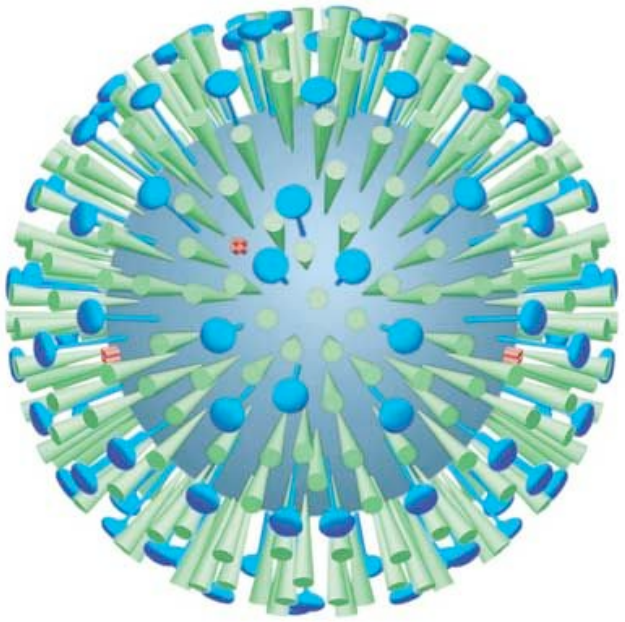
However: the origin is HIV-1 replication, because if HIV-1 replication suppressed the immune system (CD4 counts, less repertoire) regenerates!!!

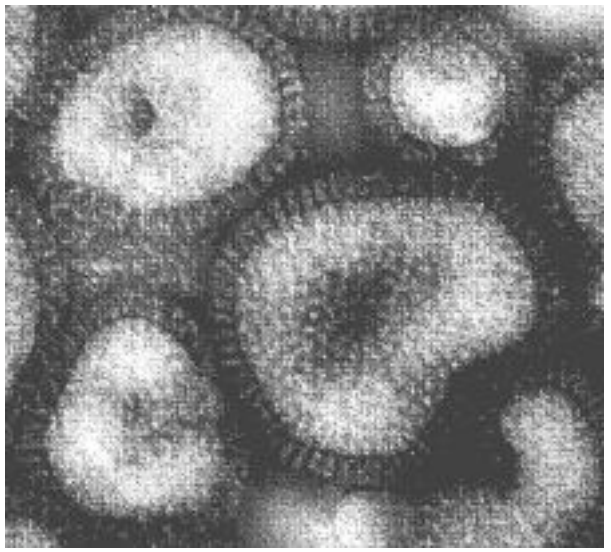
Grippe/Influenza



Virus: 1933 initially described by Smith, Andrewes, Laidlaw:
bacteria-free filtrate transmitted infection to ferret
negative strand RNA virus







Tropism of surface glycoproteins H and N of the Flu virus

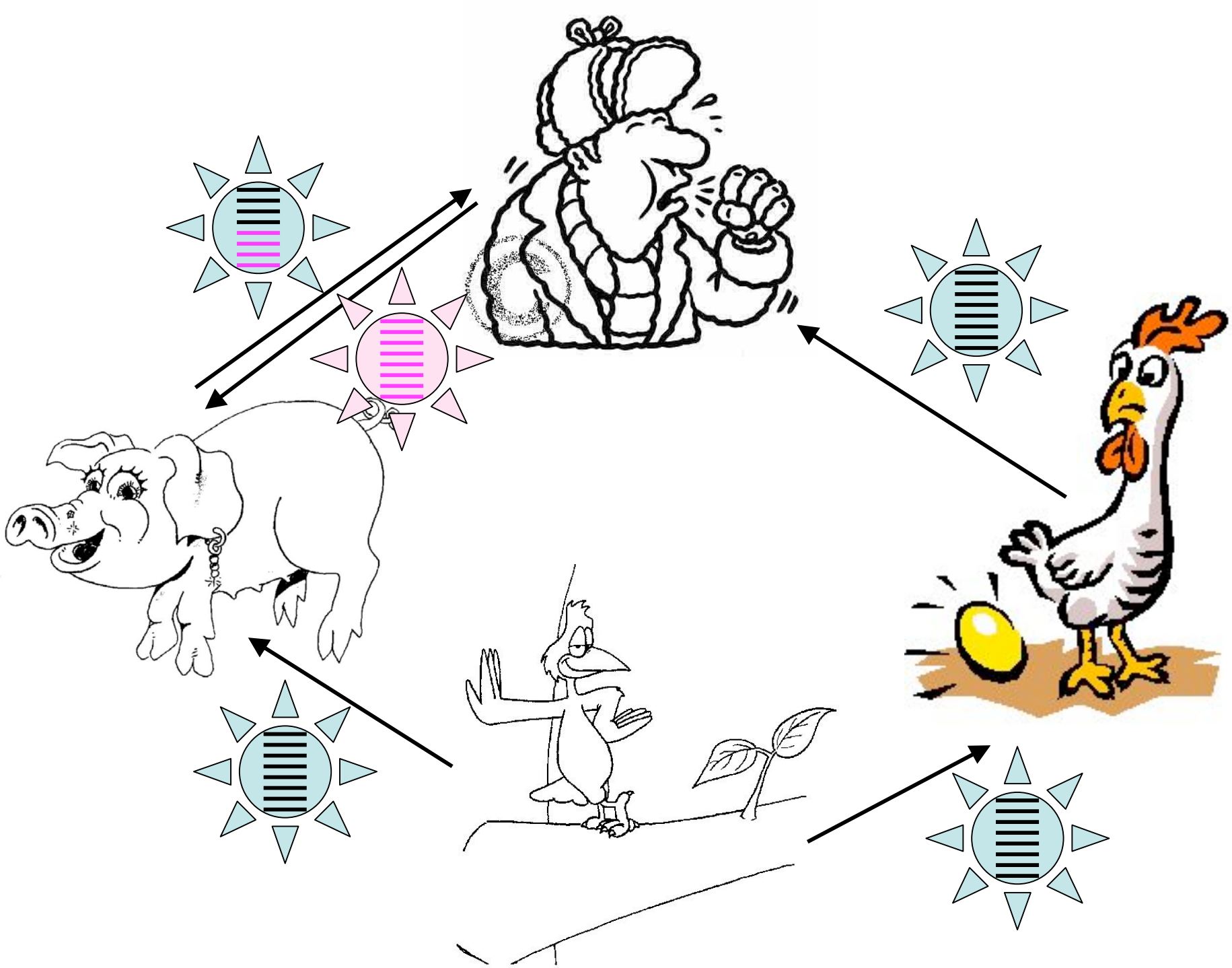
Hämagglutinin		Neuraminidase	
H1	(Mensch, Schwein)	N1	(Mensch, Schwein)
H2	(Mensch, Schwein)	N2	(Mensch, Schwein)
H3	(Mensch, Schwein, Pferd)	N3	
H4		N4	
H5	(Mensch, Schwein?)	N5	
H6		N6	
H7	(Mensch, Pferd)	N7	(Mensch, Pferd)
H8		N8	(Pferd)
H9	(Mensch, Schwein?)	N9	(Mensch)
H10			
H11			
H12			
H13			
H14			
H15			
H16			

Large Pandemias of the 20. century

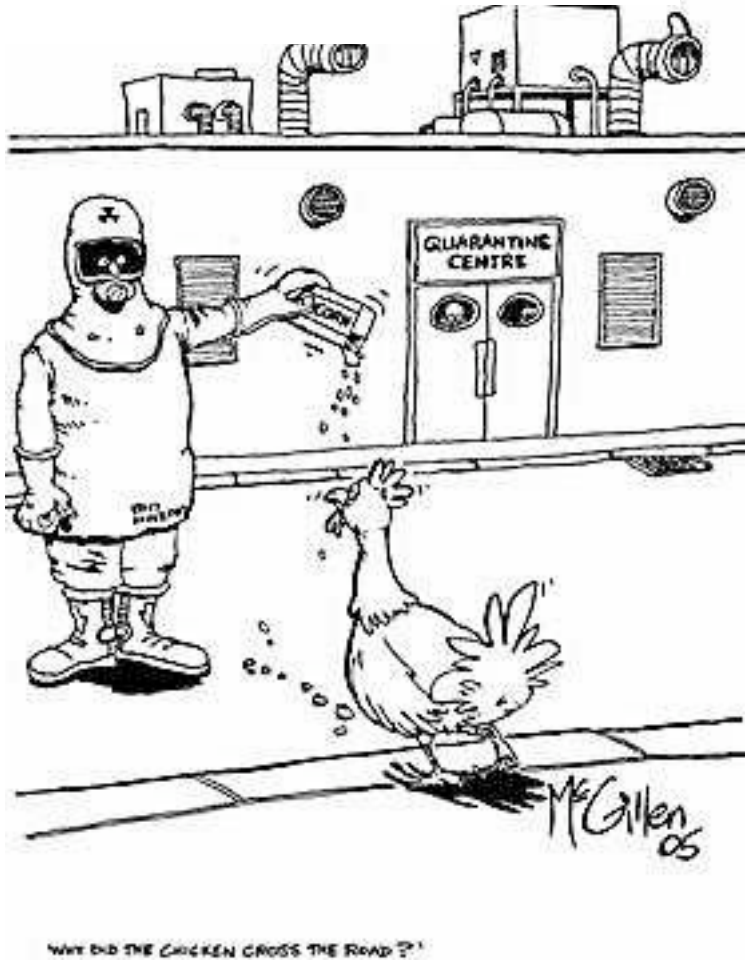
Year	Strain	Subtype	
1918		H1N1	Pandemie der Spanischen Grippe
1957	A/Singapore/57	H2N2	Pandemie, Ansiatische Grippe
1962	A/Japan/62	H2N2	Epidemie
1964	A/Taiwan/64	H2N2	Epidemie
1968	A/Aichi/68	H3N2	Pandemie "Hong Kong" Grippe
1976	A/New Jersey/76	H1N1	Schweinegrippe in Rekruen

1918

- 20 Mio deaths

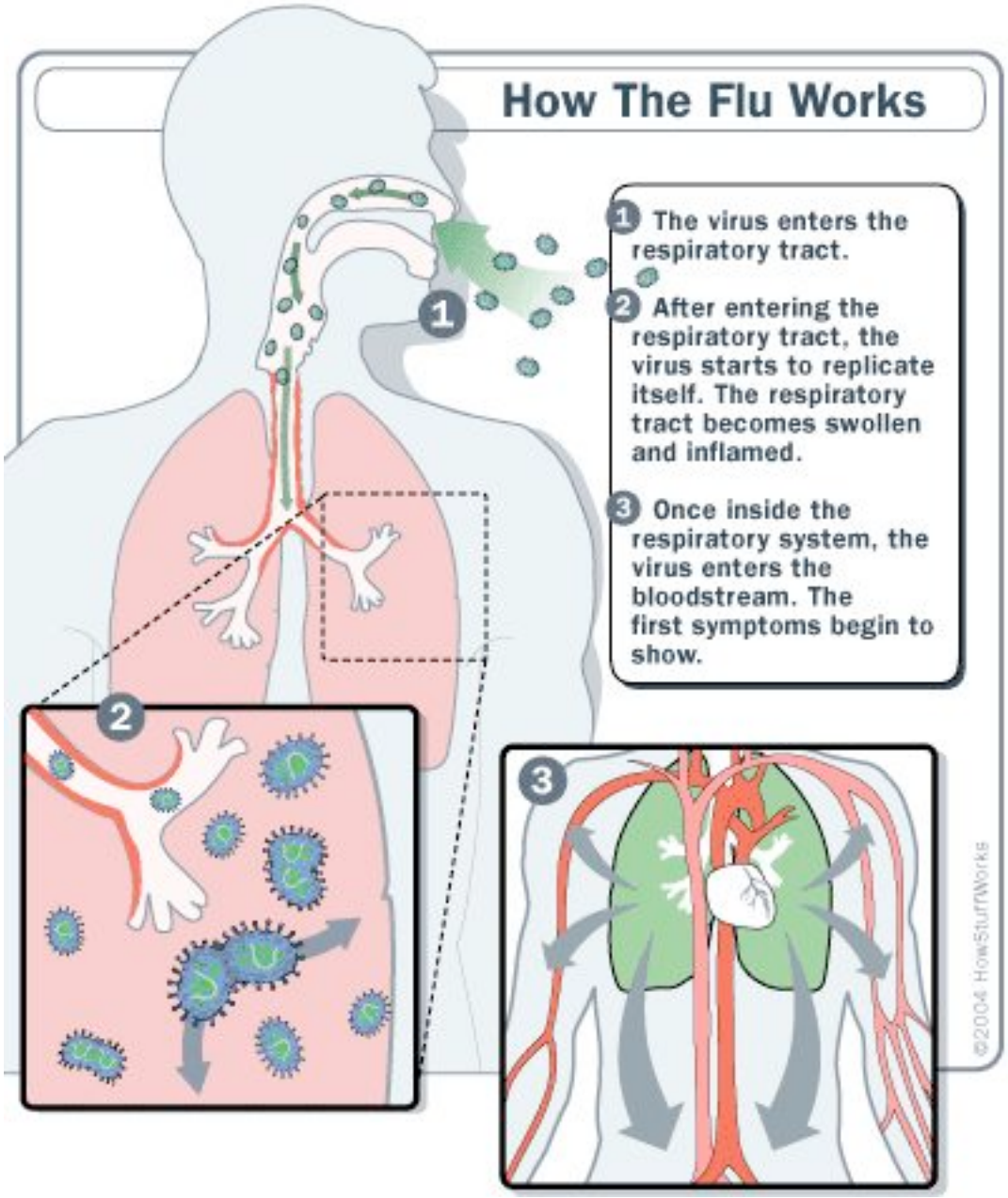


Prevention, vaccine and culling



Strains used in vaccines for the flu seasons shown. * As the 86–87 season got underway, it was found that A/Chile/83 no longer gave protection so A/Taiwan/86 was offered as a second shot late in that season.

Season	H1N1	H3N2	Type B
86–87	A/Chile/83*	A/Mississippi/85	B/Ann Arbor/86
87–88	A/Taiwan/86	A/Leningrad/86	B/Ann Arbor/86
88–89	A/Taiwan/86	A/Sichuan/87	B/Victoria/87
89–90	A/Taiwan/86	A/Shanghai/87	B/Yamagata/88
90–91	A/Taiwan/86	A/Shanghai/89	B/Yamagata/88
91–92	A/Taiwan/86	A/Beijing/89	B/Panama/90
92–93	A/Texas/91	A/Beijing/89	B/Panama/90
93–94	unchanged	unchanged	unchanged
94–95	A/Texas/91	A/Shandong/93	B/Panama/90
95–96	A/Texas/91	A/Johannesburg/94	B/Harbin/94
96–97	A/Texas/91	A/Nanchang/95	B/Harbin/94
97–98	A/Johannesburg/96	A/Nanchang/95	B/Harbin/94
98–99	A/Beijing/95	A/Sydney/97	B/Beijing/93
99–00	A/Beijing/95	A/Sydney/97	B/Yamanashi/98
00–01	A/New Caledonia/99	A/Panama/99	B/Yamanashi/98
01–02	A/New Caledonia/99	A/Panama/99	B/Victoria/00 or similar
02–03	A/New Caledonia/99	A/Moscow/99	B/Hong Kong/2001
03–04	A/New Caledonia/99	A/Moscow/99	B/Hong Kong/2001
04–05	A/New Caledonia/99	A/Fujian/2002	B/Shanghai/2002
05–06	A/New Caledonia/99	A/California/2004	B/Shanghai/2002


How The Flu Works
1 The virus enters the respiratory tract.
2 After entering the respiratory tract, the virus starts to replicate itself. The respiratory tract becomes swollen and inflamed.
3 Once inside the respiratory system, the virus enters the bloodstream. The first symptoms begin to show.
1
2
3
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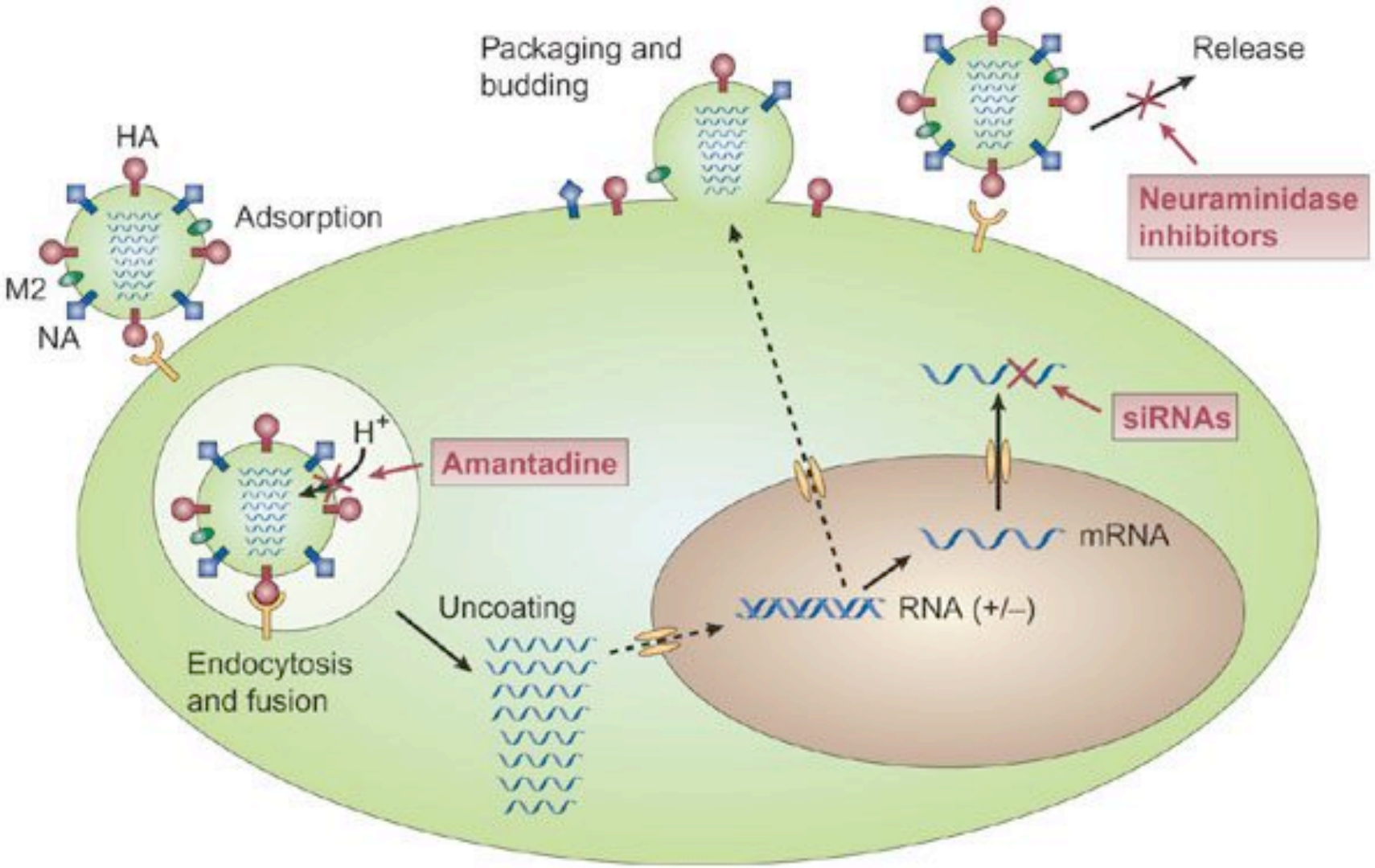
Cold or Flu?

How do you know if you have a cold or the flu? Here are symptoms of the two illnesses

SYMPTOM	COLD	FLU
Fever	Rare	Usually high, sudden onset Lasts 3 - 4 days
Headaches	Rare	Frequent
Aches & Pains	Slight	Usual often quite severe
Weakness	Rare / mild	Moderate to extreme Can last up to one month
Bedridden	Rarely	Frequently lasts 5 to 10 days
Sniffles	Common	Sometimes
Sneezing	Usual	Sometimes
Sore Throat	Common	Sometimes
Cough	Sometimes Mild to moderate	Usual can become severe
Complications	Sinus or ear infection	Pneumonia, kidney failure, heart failure, can be life threatening

Flu virus replication cycle and antivirals



Mortality in

2002/2003	17.000
2003/2004	6.000
2004/2005	20.000

Quelle: RKI; Stand 4.10.2005

How do new infectious diseases emerge?

by

•Mutations of an existing pathogen that changes it's phenotype (Yersinia enterocolitica -> Yersinia pestis (3000-5000 years ago)

•Entry of a pathogen into a new geographic area (Treponema pertenue, Frambrösie -> Treponema pallidum, Syphillis)

•Transfer of an animal pathogen to humans (Flu, SIV).