VIROLOGY

Mechanisms of Viral Pathogenesis

Mechanisms of Viral Pathogenesis:

Interactions between animal viruses and cells

Interactions between animal viruses and cells: bullets

- The properties of a virus and the cell it infects together determine if the cell lives, dies, or remains infected for ever.
- All animal virus–cell interactions can be classified under just six headings:
  - *Null infections*
  - *Abortive infections*
  - *Acutely cytopathogenic infections*
  - *Persistent infections*
  - *Latent infections*
  - *Transforming infections*
- Classification depends on the type of cell infected, and as a result a virus can be classified in more than one category.
- Virus infection can lead to the death of a cell by several mechanisms.

Interactions between animal viruses and cells: points to be kept on mind

1. A prerequisite of any of types of infection is the initial interaction between a virus and its receptor on the surface of the host cell. Hence any cell lacking the receptor is automatically resistant to infection (*Null infections*).

2. Both virus and cell play a vital role in determining the outcome of the interaction. A virus may exhibit, for example, an acutely cytopathogenic infection in one cell type and latency in another.

Interactions between animal viruses and cells: possible outcomes

Type	Viral production	Cell fate
• *Null*	-	-
• *Abortive*	-/+	-
• *Acutely Cytopathogenic*	+	death
• *Persistent*	+	senescence
• *Latent*	-	-
• *Transforming*		
DNA viruses	-	immort./transfor.
RNA viruses	+	immort./transfor.

Mechanisms of Cellular Pathogenesis:
Null and Abortive Infections

- Null infections

  Cells which do not have the appropriate receptors for a particular virus (e.g., rodent cells and poliovirus)

- Abortive infections

  Cells that possesses te appropriate receptors, but are not fully permissive

Mechanisms of Cellular Pathogenesis:
Acutely Cytophatogenic Infections

Direct effects of cytolityc viruses

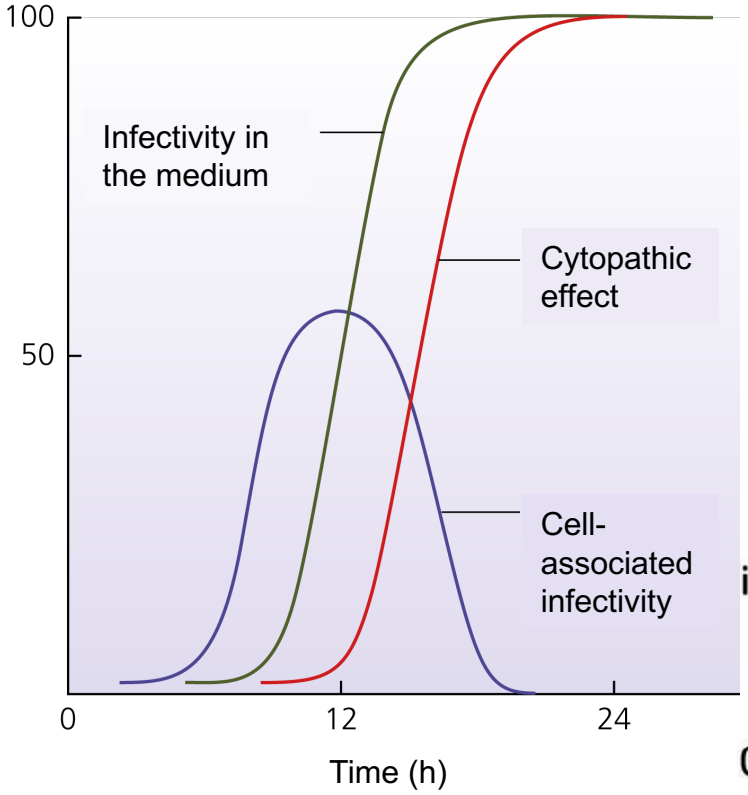
- Cytopathic effect (CPE)
- Inclusion bodies
- Apoptosis
- Dysregulation of cell physiology

Mechanisms of Cellular Pathogenesis: *The CPE*

Cytopathic effect(s):	**Virus(es)**
• Inibition of host protein synthesis	polio, herpes, toga, pox
• Host chromosome margination and DNA degradation	herpes
• Nuclear shrinking	picorna
• Proliferation of nuclear membrane	herpes
• Cell membrane alterations	enveloped viruses
• Vacuoles in the cytoplasm	papova
• Syncytia (cell fusion)	paramyxo, herpes, HIV
• Cell Rounding up and detachment	herpes, rabdo, adeno, picorna

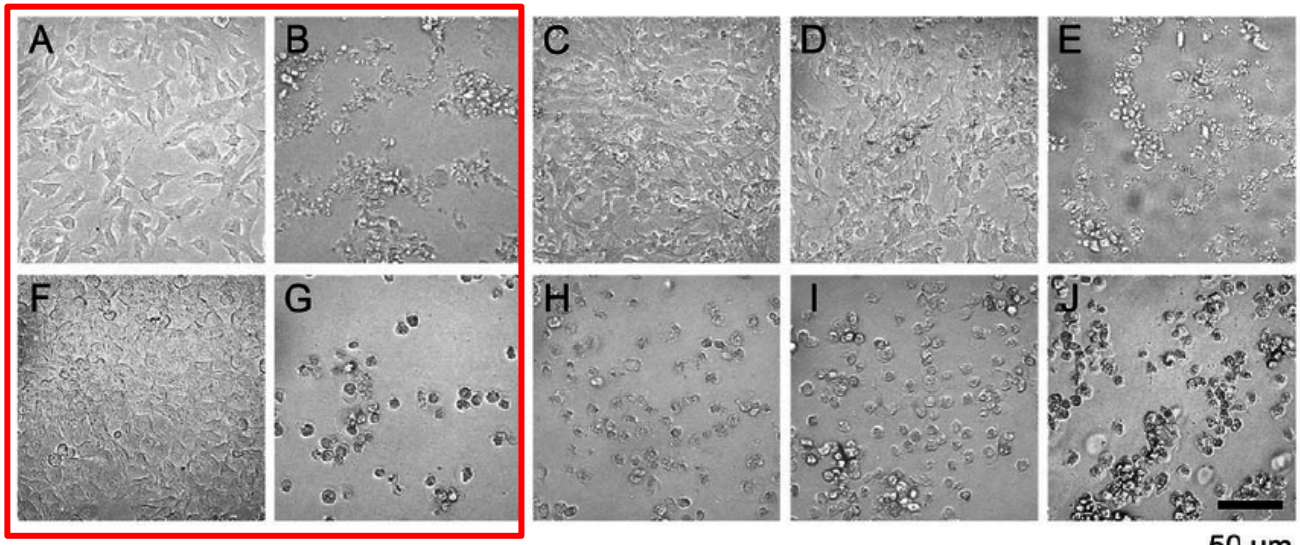
Inclusion bodies:	
• Intranuclear basophils	adeno
• Virion in the cytoplasm (Negri bodies)	rabdo
• “Factories” in the cytoplasm (Guarnieri bodies)	pox
• “Owl eyes” in the nucleus	CMV
• Perinuclear acidophils	reo

Poliovirus infection *in vitro*: an examples of an Acutely Cytopathogenic Infection



Neural Cells

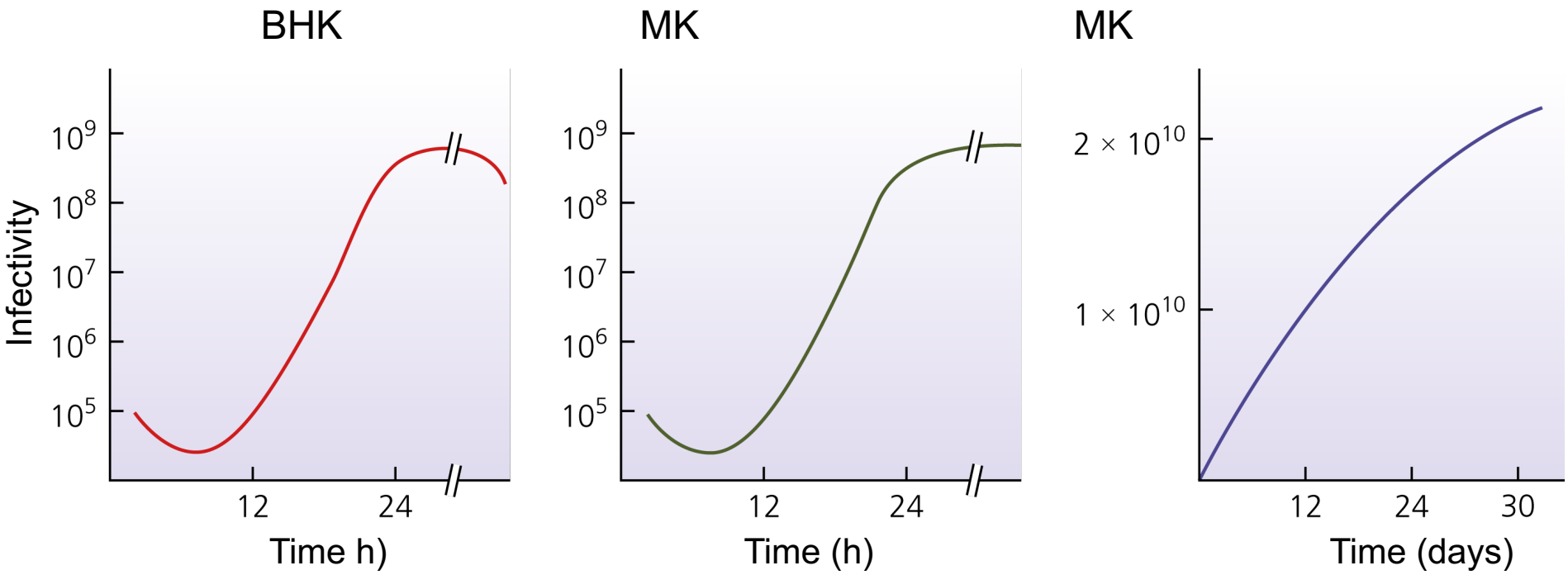
HeLa



Mechanisms of Cellular Pathogenesis:
Persistent Infections

- Persistent infections result in the continuous production of infectious virus.
- This is achieved either by the survival of the infected cell or by a situation in which a minority of cells are initially infected and the spread of virus is limited, so that cell death is counterbalanced by new cells produced by cell division, i.e. no net loss within the culture
- Persistent infections can result from the specific virus–cell interaction (e.g., origin of cell type)
- Persistent infections can result also from interactions between viruses, cells and interferon, or viruses, cells and antibodies

Different types of infection caused by simian virus 5 in BHK and MK cells: an example of persistent infection without CPE determined by the host cell origin



Mechanisms of Cellular Pathogenesis:
Latent Infections

- A latent infection is existing, but not exhibited.
- Thus, in a latenly-infected cell, the viral genome is present, but not infectious progeny is produced.
- Nevertheless, latency is an active infection and some virus-encoded products are always expressed.
- Latent infections always begin as acutely cytophatogenic infections.

Examples of latent infections.

Virus	Synthesis of:			
	State of virus genome	At least one transcribed RNA*	Viral protein(s)	Infectious progeny
Herpes simplex virus	Episomal	+	−	−
Epstein-Barr virus	Episomal	+	+	−
Adeno-associated virus	Integrated	+	+	−

*The amount and nature of gene expression is limited but varies between virus systems, and is strictly controlled.

Mechanisms of Cellular Pathogenesis:
Transforming Infections

A trasforming infection is the result of infection with a variety of DNA viruses or some retroviruses, in which an infected-cell may undergo more rapid multiplication than the other cells in the same culture, concomitant with a change in a wide variety of its properties, i.e. it is transformed.

Animal viruses that can cause transformation of the infected cell

Family	Genome	Proportion of genome integrated	Progeny
Retrovirus	RNA	Whole	+
Polyomavirus	DNA	Part	–
Papillomavirus	DNA	Part	–
Adenovirus	DNA	Part	–
Herpesvirus	DNA	None; episomal	–
Hepadnavirus	DNA	Part	–

Mechanisms of Cellular Pathogenesis:
Transforming Infections

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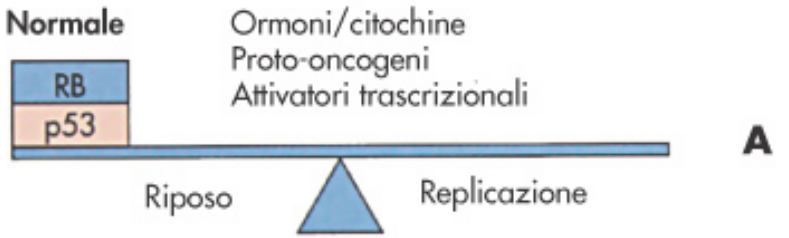
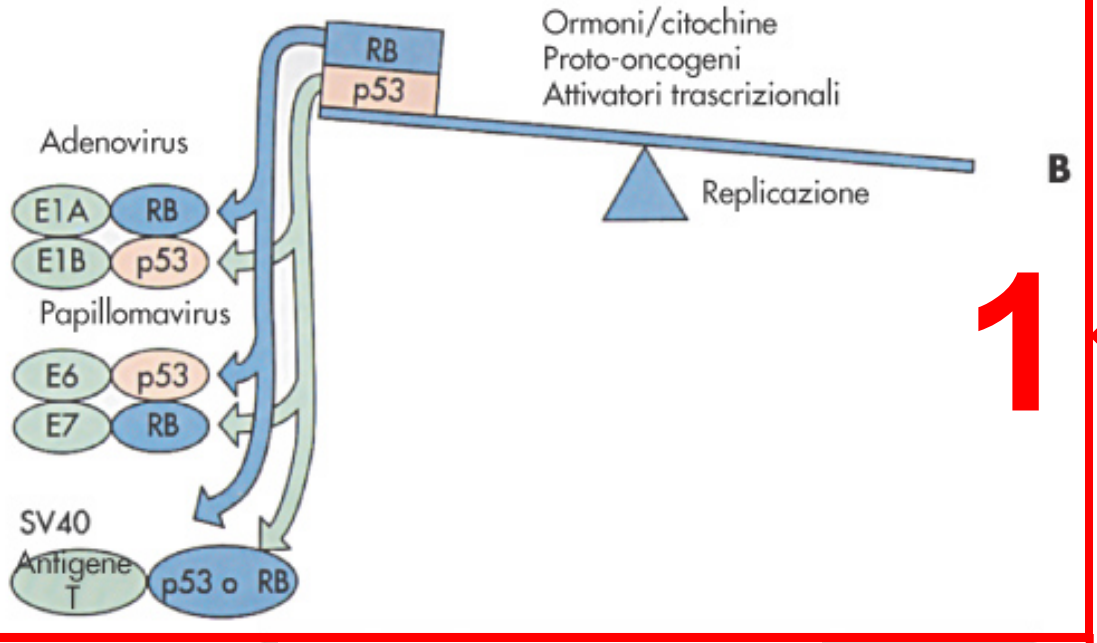
Adenovirus	DNA	Part	–
Herpesvirus	DNA	None; episomal	–
Hepadnavirus	DNA	Part	–

Transformation often preceded by integration of at least part of the viral genome with that of the host

Mechanisms of viral transformation





1

Removing Growth Suppressors

2

Reinforcement of Growth Promoters

Mechanisms of Cellular Pathogenesis:
How do animal viruses kill cells?

Some mechanisms of viral cytopathology

Mechanism	Virus
Inhibition of host transcription	rhabdoviruses, poliovirus
Competing out of cellular mRNA by excess viral mRNA	Semliki Forest virus
Loss of ability to initiate translation of cellular mRNA	poliovirus, reovirus, influenza virus, adenovirus
Degradation of cellular mRNA	influenza virus, herpes virus
Failure to transport mRNA out of the nucleus	adenovirus, influenza virus
Apoptosis	sindbis virus, Semliki Forest virus, influenza A, B, C viruses, HIV-1*, adenovirus, measles virus
Imbalance in intracellular ion concentrations	Semliki Forest virus, rotavirus

*HIV-1, human immunodeficiency virus type 1.

Mechanisms of Viral Pathogenesis:

Animal virus-host interactions

Animal virus-host interactions: bullets

- It must alwasy keep in mind that viruses are parasite and that the biological success of a virus depends absolutely upon the success of the host species.
- When an animal is infected with a virus, several outcomes are possible, ranging from no disease through short periods of disease to long-lasting disease states.
  The various outcomes can be:
  - *Acute infections*
  - *Subclinical infections*
  - *Persistent and chronic infections*
  - *Latent infections*
  - *Slow progressive diseases*
  - *Tumorigenic infections*
- Any one virus may be found in more than one category (circumstances of the infection).

Animal virus-host interactions: possible outcomes virus infections at the level of the whole organism

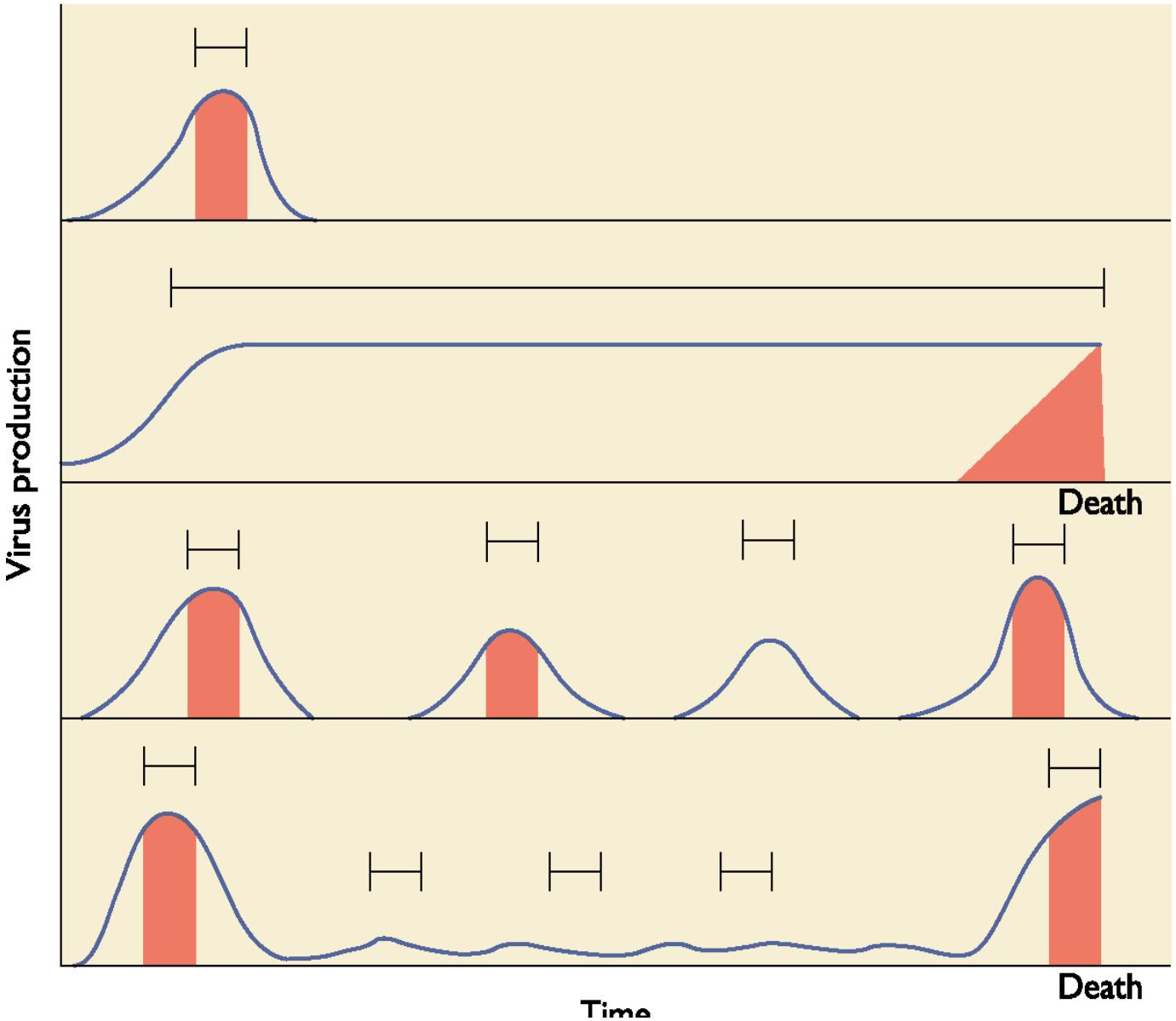
Type of infection	Production of infectious progeny	Cell death	Clinical signs of disease	Duration of infection*	Transmission	Examples**
Acute	+	+	+	Short	Efficient	Measles virus, poliovirus (1% of infections)
Sub-clinical	+	+	–	Short	Efficient	Poliovirus (99% of infections)
Persistent	+	– or +	–	Long (+ immune defect?)	Many opportunities	Rubella virus
Chronic	+	+	+	Long (+ immune defect?)	Many opportunities	Hepatitis B virus
Latent	–	–	–	Long	Many opportunities	Herpes viruses
Slowly progressive disease						
(a)	+	+	Eventually	Long	Many opportunities	HIV-1, TSE agents
(b)	–	+	Eventually	Long	None	Measles virus
Tumourigenic	+	–	+	Long	Many opportunities	Retroviruses, Epstein-Barr virus
	–	–	+	Long	None	Hepatitis B virus, human papillomaviruses

*Short, approximately 3 weeks or less; long, up to a lifetime.

**Examples are given of viruses that have the given type of infection at some point of their life history, and are not intended to convey that they cannot also be classified elsewhere, e.g. herpesviruses switch between latency and acute infection (see text).

HIV-1 human immunodeficiency virus type 1; SSPE, subacute sclerosing panencephalitis; TSE, transmissible spongiform encephalopathy (includes bovine spongiform encephalopathy and Creutzfeld-Jacob disease) – these are not virus infection but prion diseases (see Chapter 28).

Animal virus-host interactions: patterns of infection



Acute infection
- Rhinovirus
- Rotavirus
- Influenza virus

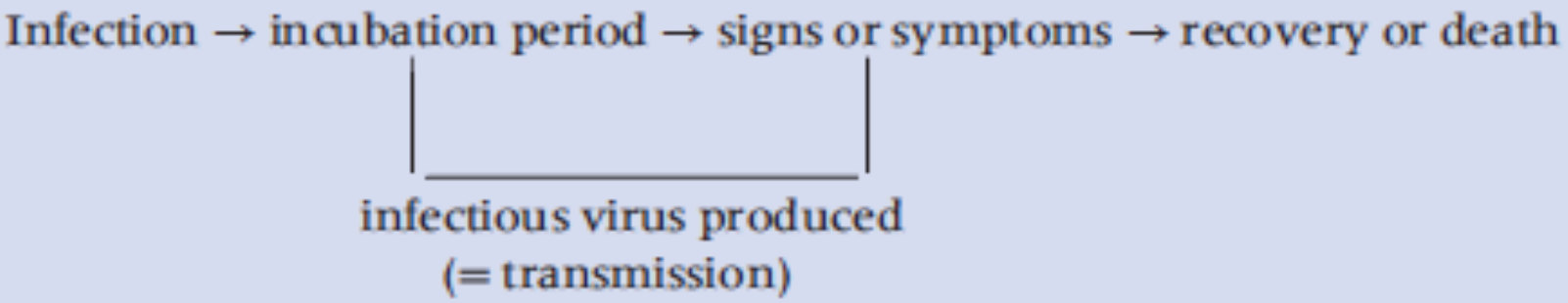
Persistent infection
- Lymphocytic choriomeningitis virus

Latent, reactivating infection
- Herpes simplex virus

Slow virus infection
- Measles SSPE
- Human immunodeficiency virus

Animal virus-host interactions: acute infections

Key points about acute infections

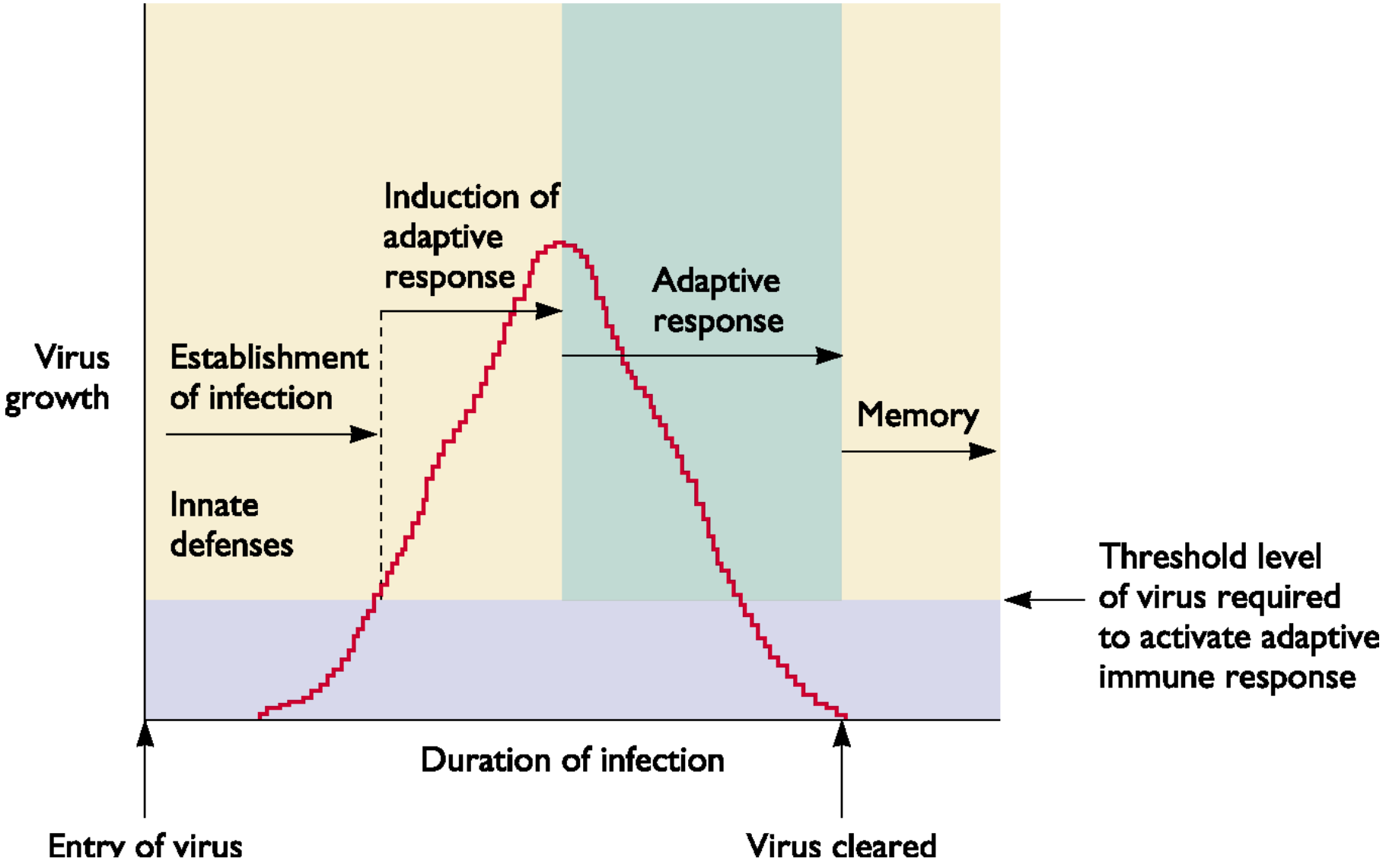


- Rapid onset of viral replication
- Short, but possibly severe course of disease
- Production of large numbers of virus particles
- Immune clearance

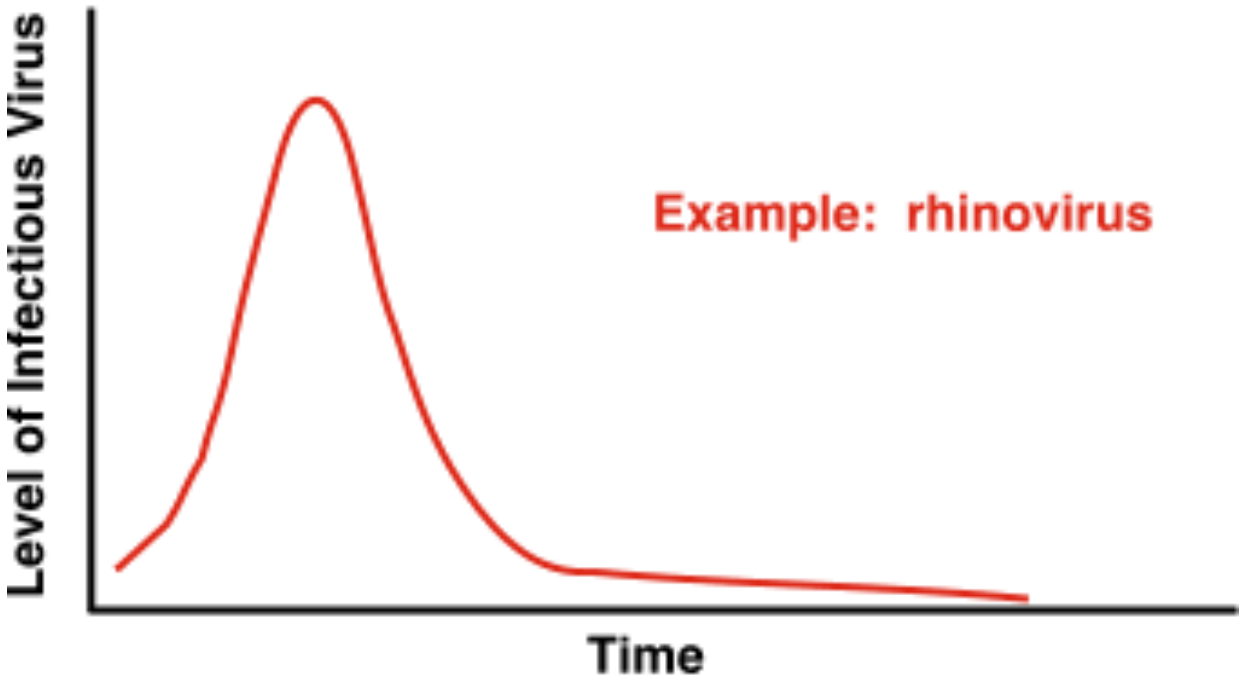
Acute infections *are common public health problems*

- Serious epidemics affecting millions each year (Influenza, Norovirus, Zika virus)
- Acute infections are difficult problems: by the time you feel ill, the infection may be over and has spread

The course of typical acute infection: rapid and self-limiting



Animal virus-host interactions: acute infections



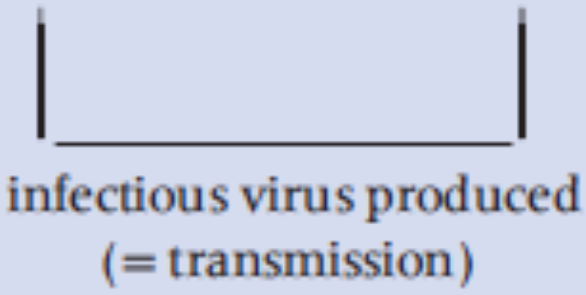
Acute infection followed by clearance of virus

- productive infection
- viremia (circulating virus)
- clearance by immune system
- example: rhinovirus (common cold), influenza, measle, poliovirus, rotavirus

Animal virus-host interactions: subclinical infections

Key points about subclinical infections

Infection → incubation period → *no* signs or symptoms → clearance of virus



Subclinical, Inapparent or silent infections

- Successful infections, no symptoms or disease
- Sufficient virus particles produced to spread in the population
- How do we know?
- Well adapted pathogens: is the sign of a highly-evolved relationship between a virus and its natural host

  E.g. - >90% of poliovirus infections are inapparent

Animal virus-host interactions: persistent and chronic infections

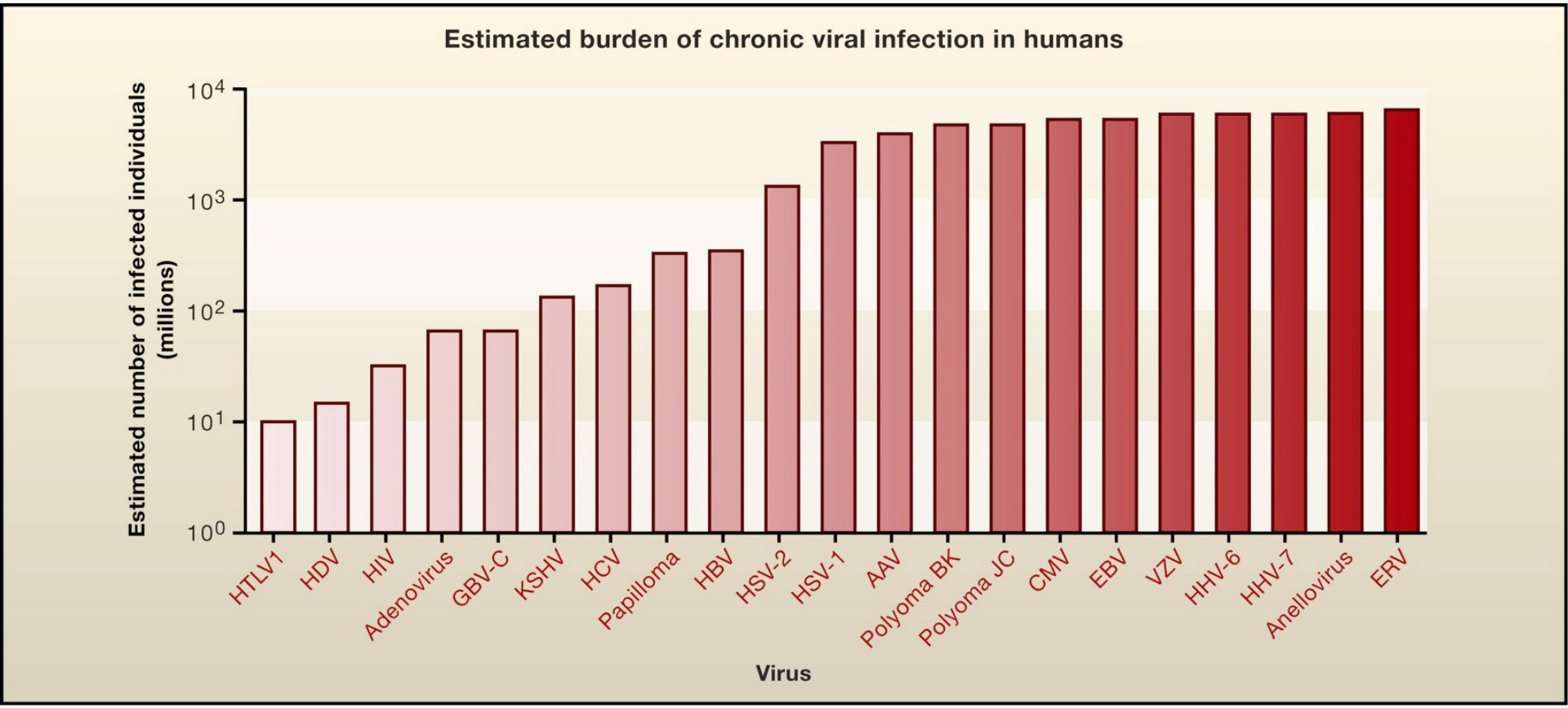
Persistent and chronic infections:

- Occur when primary infection is not cleared by immune system
- Virions, protein, genomes continue to be produced
- Viral genomes may remain after proteins are not detected
- No single mechanism
- When cytopathic effects are absent and host defenses are reduced, persistent infection is likely
- Viral immune modulation

Acute vs persistent infections

- Acute infection - rapid and self-limiting
- Persistent infection - long term, life of host
- Most persistent infections probably begin as an acute infection

Animal virus-host interactions: persistent and chronic infections



Animal virus-host interactions: persistent infections of humans

Virus	Site(s) of persistence	Consequence(s)
Adenovirus	Adenoids, tonsils, lymphocytes	None known
Epstein-Barr virus	B cells, nasopharyngeal epithelia	Burkitt's lymphoma, Hodgkin's disease
Human cytomegalovirus	Kidneys, salivary gland, lymphocytes,[a] macrophages,[a] stem cells,[a] stromal cells[a]	Pneumonia, retinitis
Hepatitis B virus	Liver, lymphocytes	Cirrhosis, hepatocellular carcinoma
Hepatitis C virus	Liver	Cirrhosis, hepatocellular carcinoma
Human immunodeficiency virus	$CD4^+$ T cells, macrophages, microglia	AIDS
Herpes simplex virus types 1 and 2	Sensory and autonomic ganglia	Cold sore, genital herpes
Human T lymphotropic virus types 1 and 2	T cells	Leukemia, brain infections
Papillomavirus	Skin, epithelial cells	Papillomas, carcinomas
Polyomavirus BK	Kidneys	Hemorrhagic cystitis
Polyomavirus JC	Kidneys, central nervous system	Progressive multifocal leukoencephalopathy
Measles virus	Central nervous system	Subacute sclerosing panencephalitis, measles inclusion body encephalitis
Rubella virus	Central nervous system	Progressive rubella panencephalitis
Varicella-zoster virus	Sensory ganglia	Zoster (shingles), postherpetic neuralgia

[a]Proposed but not certain.

Key points about persistent and chronic human infections

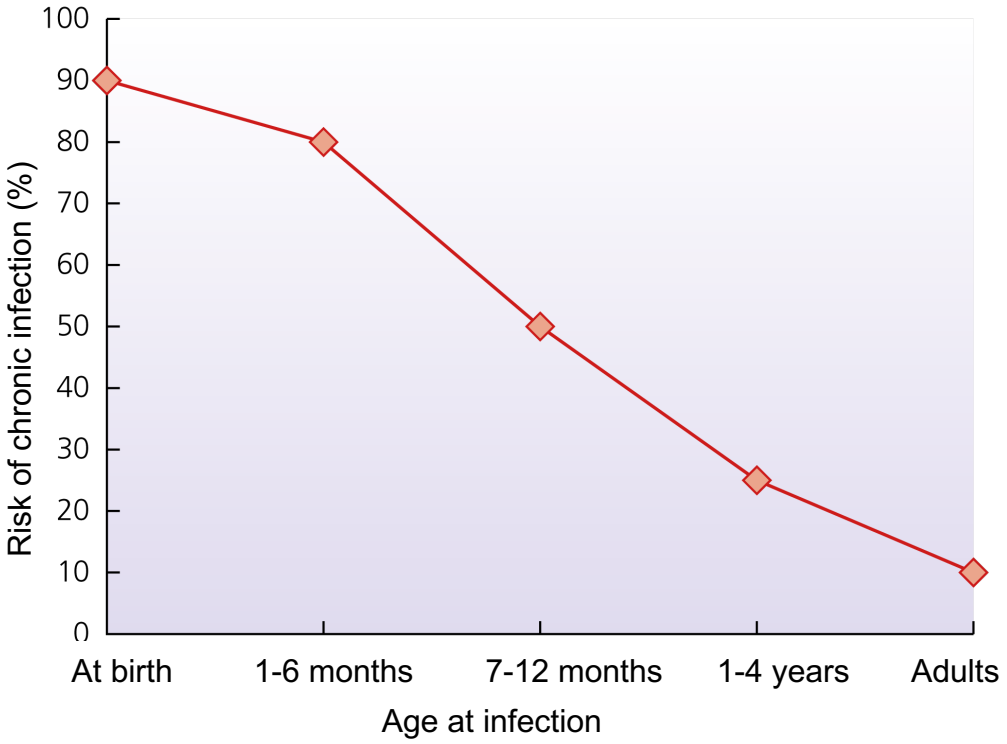
- Most result from the ***virus modulating the immune system in some way*** (e.g. immunosuppression, down-regulation of interferons, down-regulation of MHC proteins, infection early in life); a few result from congenital immunodeficiency.
- Because chronic infections yield large numbers of infected cells and large amounts of viral antigen for years, immune responses can have pathological rather than beneficial consequences.

Animal virus-host interactions:
HBV as an example of chronic infection

Infection of *adults* by hepatitis B virus: chances of progression of liver infection and disease.

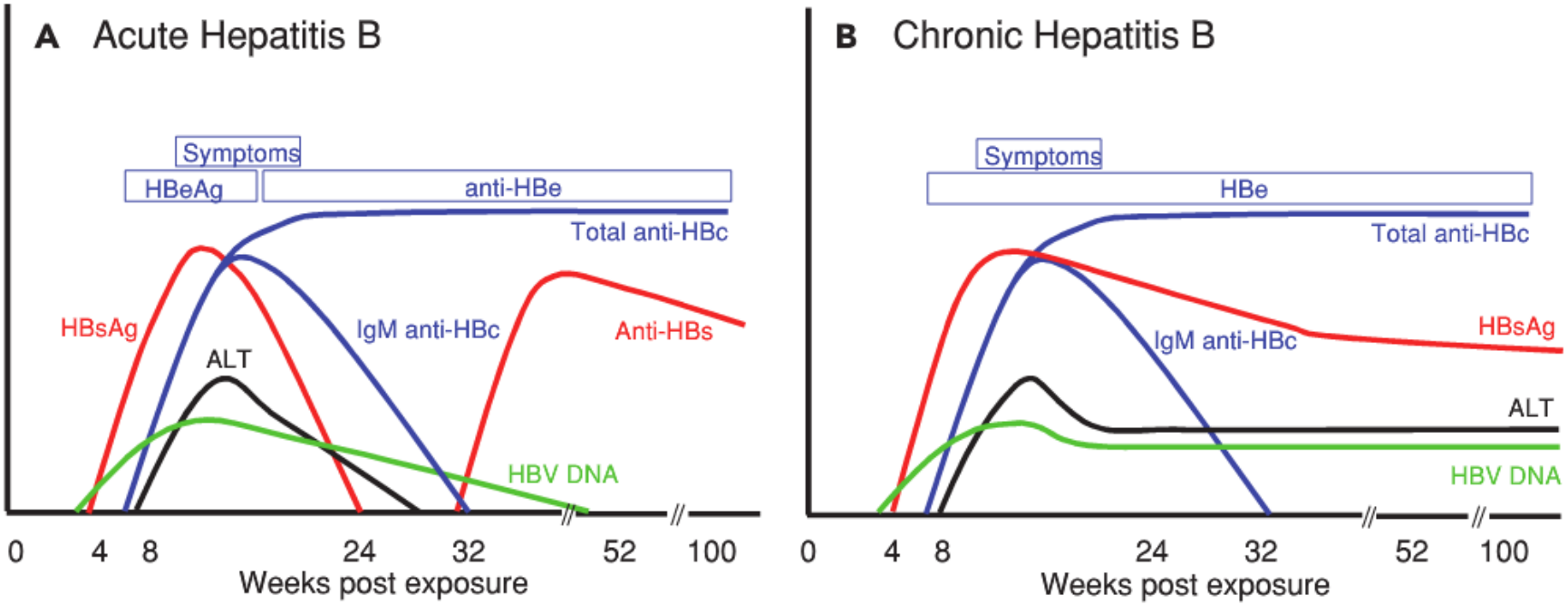
Approximate percentage of infected* adults who develop the type of infection listed	Type of infection
100%	Acute or Subclinical
↓	↓
10%	Chronic
↓	↓
1%	Liver cirrhosis
↓	↓
0.1%	Liver cancer (primary hepatocellular carcinoma)

*Figures are expressed as a proportion of all people shown to be infected. Current estimates are that approximately 30% of people exposed to hepatitis B virus become infected.



The risk of becoming a carrier who is chronically infected with HCBV depends on the age at which an individual is infected

Animal virus-host interactions: HBV as a chronic infection



- Transmitted by exposure to blood (childbirth, transfusion, sex, drug use, tattooing, nosocomial).
- Main target is hepatocyte.
- 95% of adults, 5-10% newborns resolve acute infection.
- ~350 million worldwide have chronic HBV.
- Virus is not cytopathic for hepatocytes.
- CTL kill infected hepatocytes.
- During chronic infection, fibrosis leads to cirrhosis, liver failure.
- **Hepatocellular carcinoma** after 20-30 yr of chronic (often asymptomatic) infection

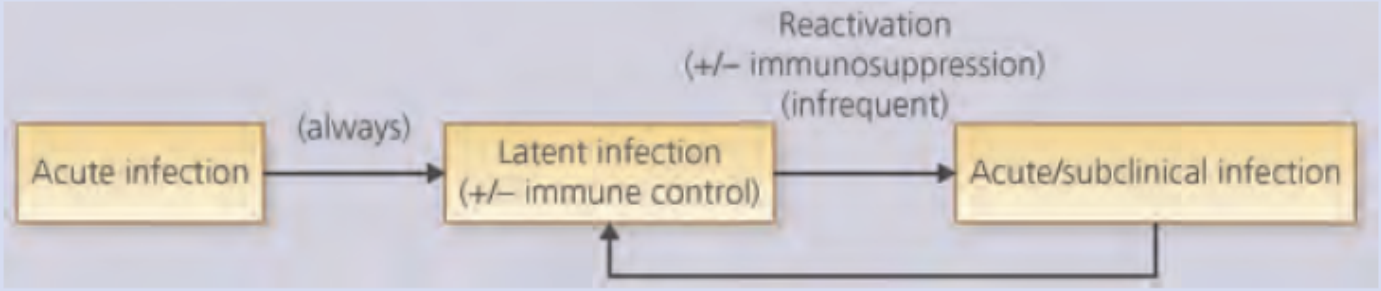
Animal virus-host interactions: latent infections

"An inefficient virus kills its host. A clever virus stays with it."
(J. Lovelock)

- Latent infections are an important facet of the interaction of certain viruses with their hosts.
- The ability to establish a latent infection means that the virus can maintain its genome in the host for the entire life of the host, being reactivated periodically to produce new viruses which can infect new hosts.
- This can be seen as a highly evolved virus–host interaction

Animal virus-host interactions: latent infections

Key points about latent infections



Latent infections are lifelong infections.

- During latency, viral gene products that promote productive replication are not made or found in low concentrations.
- Cells harboring the latent viral genome are poorly recognized by the immune system.
- Viral genome persists intact so that productive infection can be initiated to spread infection to new hosts

- This can be seen as a highly evolved virus–host interaction

Animal virus-host interactions: latent infections

Examples of latent infections.

Virus	Synthesis of:			
	State of virus genome	At least one transcribed RNA*	Viral protein(s)	Infectious progeny
Herpes simplex virus	Episomal	+	−	−
Epstein-Barr virus	Episomal	+	+	−
Adeno-associated virus	Integrated	+	+	−

*The amount and nature of gene expression is limited but varies between virus systems, and is strictly controlled.

State of the viral genome in latent infections

- Non-replicating DNA in a non-dividing cells: HSV, VZV in neurons
- Autonomous self-replicating DNA in dividing cell: EBV, CMV, KSHV
- Integrated into host chromosome, replicates with host: AAV (chr 19)

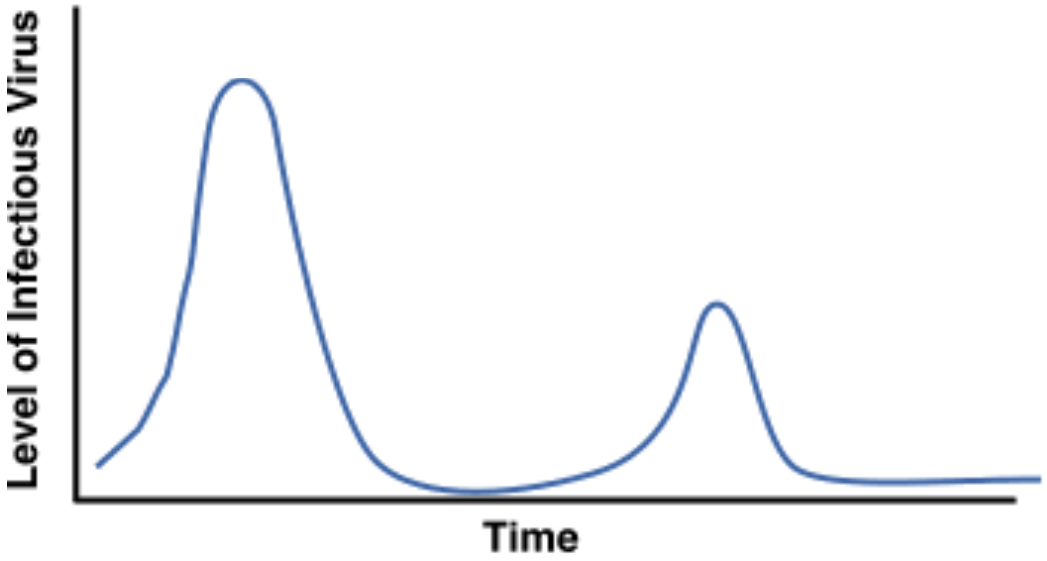
Animal virus-host interactions: Herpesviruses latent infections

The establishment of latent infections in man with herpes viruses and the breakdown of latency (reactivation).

Virus	Primary acute infection	Site of latency	Stimulus for reactivation	Reactivated acute infection
HSV-1	Stomatitis: infection of the mouth and tongue	Dorsal root ganglion of the trigeminal (cranial) nerve	e.g. strong sunlight, menstruation, stress	Cold sore*
HSV-2	Genital lesions	Dorsal root ganglion of the sacral region of the spinal cord	Not known, though probably similar to HSV-1	Genital lesions (and infection of neonates)
VZV	Chicken-pox: generalized infection with fluid-filled vesicles over the body surface	Any dorsal root ganglion of the central nervous system	Release of immune control, e.g. in the elderly	Zoster (shingles)
EBV	Child: subclinical Adult: glandular fever (IM: acute)***	B cells and possibly throat epithelium	Not known; frequent	Subclinical**
CMV	Prenatal:**** Child: subclinical Adult: subclinical	Salivary glands and probably other sites	Frequent	In all body fluids, especially during the immunosuppression that accompanies pregnancy. A major cause of death in AIDS and transplant surgery

*10–40% of reactivations are subclinical; varies between individuals.
**EBV also causes cancer: nasopharyngeal carcinoma and Burkitt's lymphoma (see Chapter 25).
***IM: an example of a more severe clinical disease that occurs when primary infection takes place after childhood – a common microbiological problem of the (over-) sanitized world. 'Mononucleosis' refers to the uncommonly large numbers of mononuclear cells (mainly lymphocytes) that are found in the blood.
****The foetus is only at risk when its mother gets a primary infection.
Abbreviations: AIDS, acquired immune deficiency syndrome; CMV, cytomegalovirus ('cytomegalo' refers to the characteristic swollen cell cytopathology caused by CMV to cells of the kidney, lungs and liver); EBV, Epstein-Barr virus; HSV, herpes simplex virus; IM, infectious mononucleosis; VZV, varicella-zoster virus.

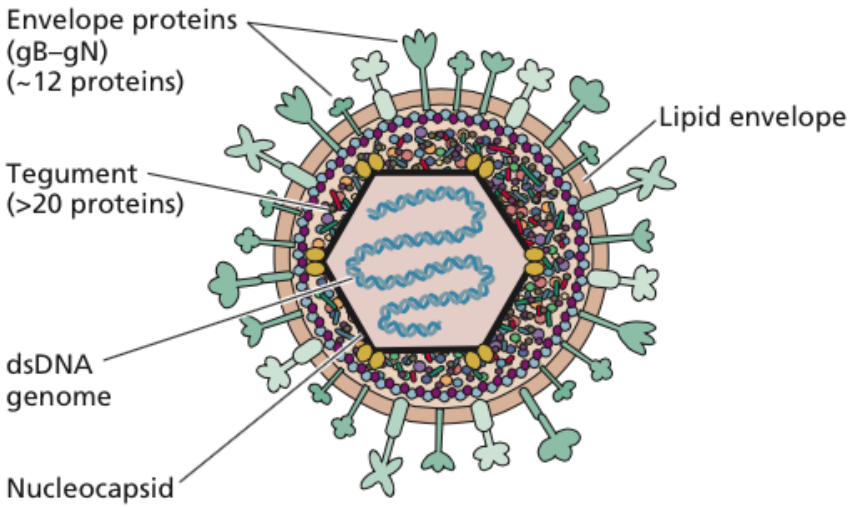
Animal virus-host interactions:
HSV-1 as an example of latent infection



- acute infection followed by latent infection and periodic reactivation;
- initial productive infection with viremia;
- viral persistence in non-infectious form;
- intermittent reactivation with productive infection;

HSV latency is maintained through the combined action of viral RNAs (LATs and miRNAs) which downregulate viral lytic gene expression and the host immune response that recognizes and responds to signs of reactivation before a clinically apparent event can occur.

Animal virus-host interactions: HSV-1 as a latent infection

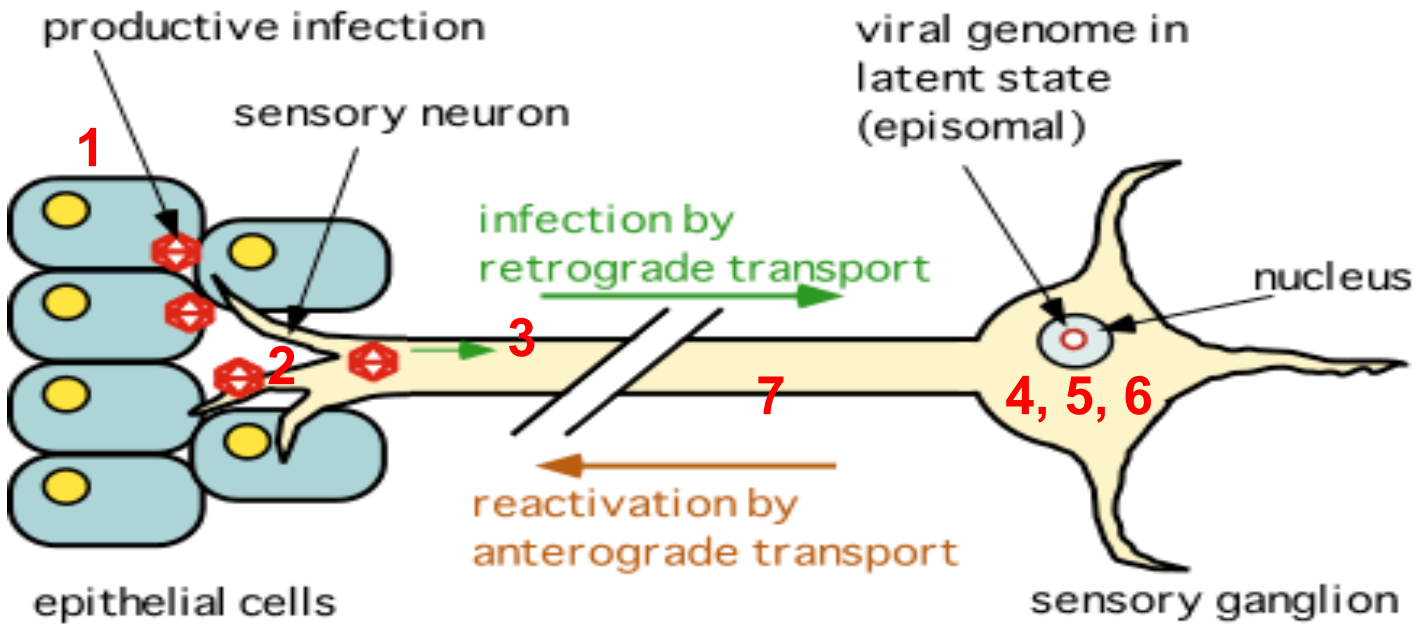


US >80% seropositive with genomes in PNS

- Millions carry latent viral genomes in nervous system without symptoms
- 40 million experience recurrent herpes diseases
- HSV-1, HSV-2
- A very well-adapted pathogen

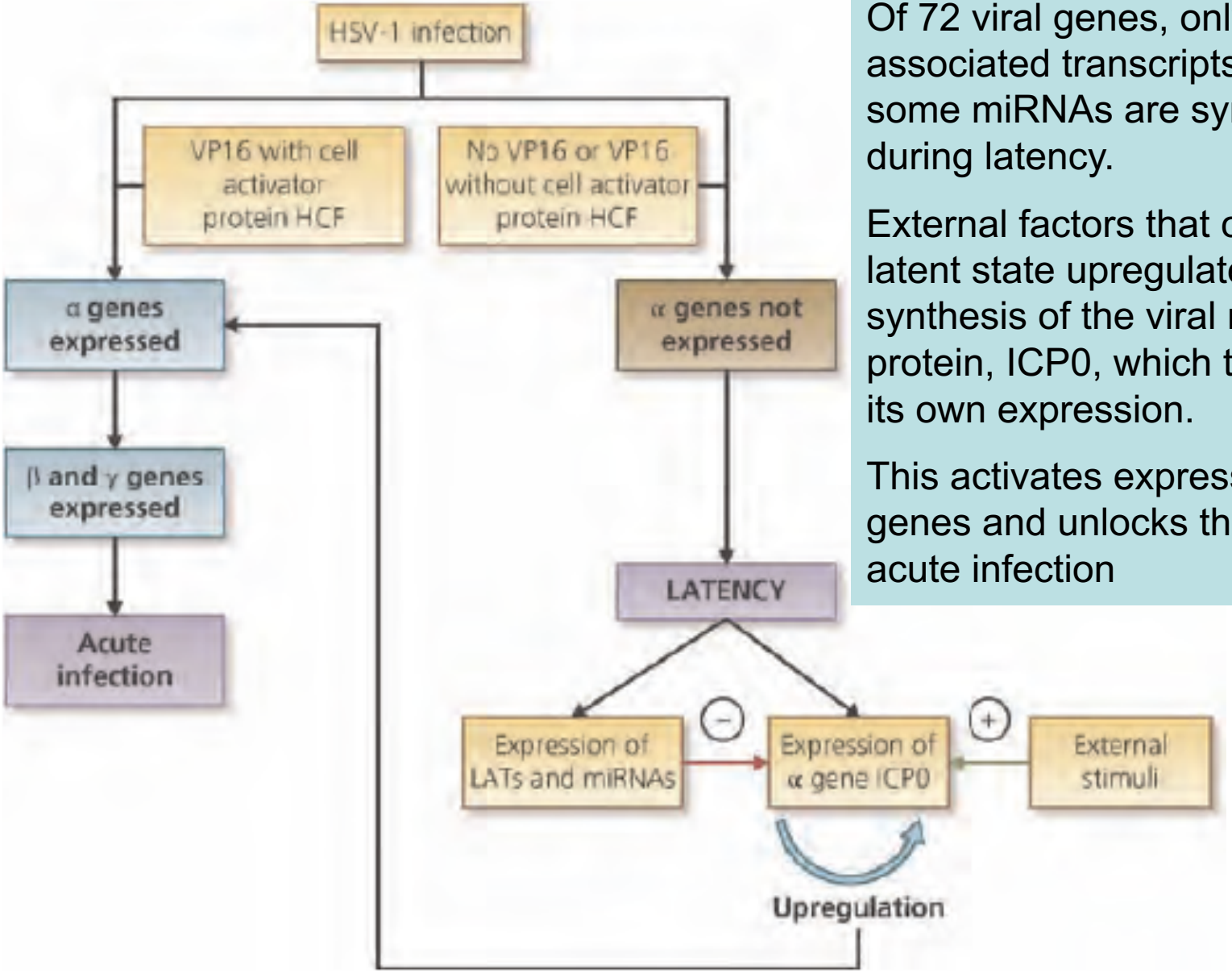
Herpes is forever - drugs and vaccines cannot cure a latent infection

Animal virus-host interactions:
HSV-1 as an example of latent infection



1. Productive infection of epithelial cells
2. Virus infects sensory neurons
3. Virus travels to sensory ganglion by neuronal retrograde transport
4. Virus establishes latent infection in sensory ganglion
5. Limited expression of viral genes, latency associated transcripts (LATs), miRNAs viral genome present in episomal state
6. Virus may be reactivated by changes in physiological status of the neuron (neuron damage, immunosuppression, hormonal changes, stress, UV)
7. Changes lead to activation of viral gene expression and productive infection

HSV-1 latency and reactivation: molecular control of latency

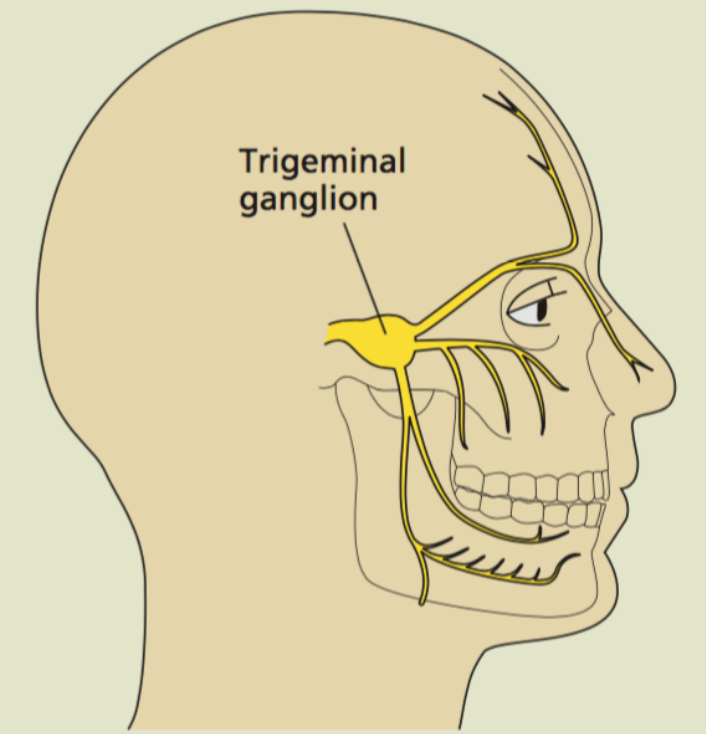


Of 72 viral genes, only the latency-associated transcripts (LATs) and some miRNAs are synthesized during latency.

External factors that can break the latent state upregulate the synthesis of the viral non-structural protein, ICP0, which then enhances its own expression.

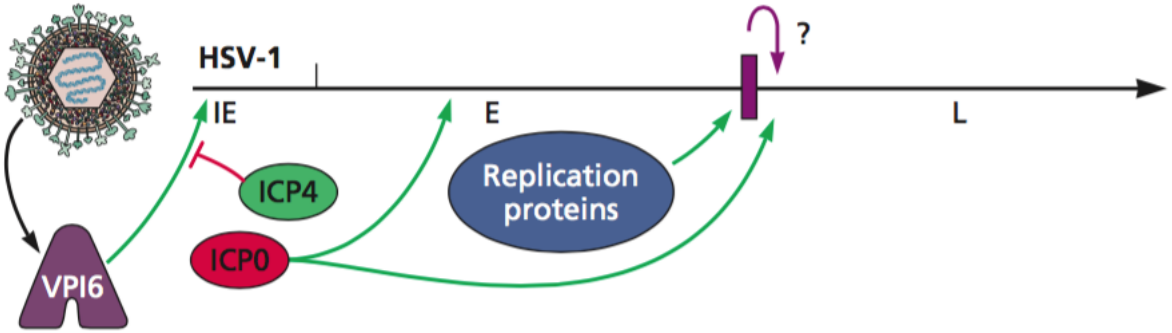
This activates expression of IE genes and unlocks the pathway to acute infection

HSV-1 latency and reactivation: post-infection events in neurons



- Viral genome silenced, coated with nucleosomes
- Multiple copies of episomal viral DNA remain in nucleus
- No further replication needed to persist - neurons do not divide
- Latency associated transcript (LATs)
- Only LATs and miRNAs are made in latently infected neurons
- No proteins translated from LATs
- RNA silencing to maintain viral genome in latent state
- LATs suppress IE mRNA expression (ICP0) and host cell apoptosis, thus preventing self-programmed cell death

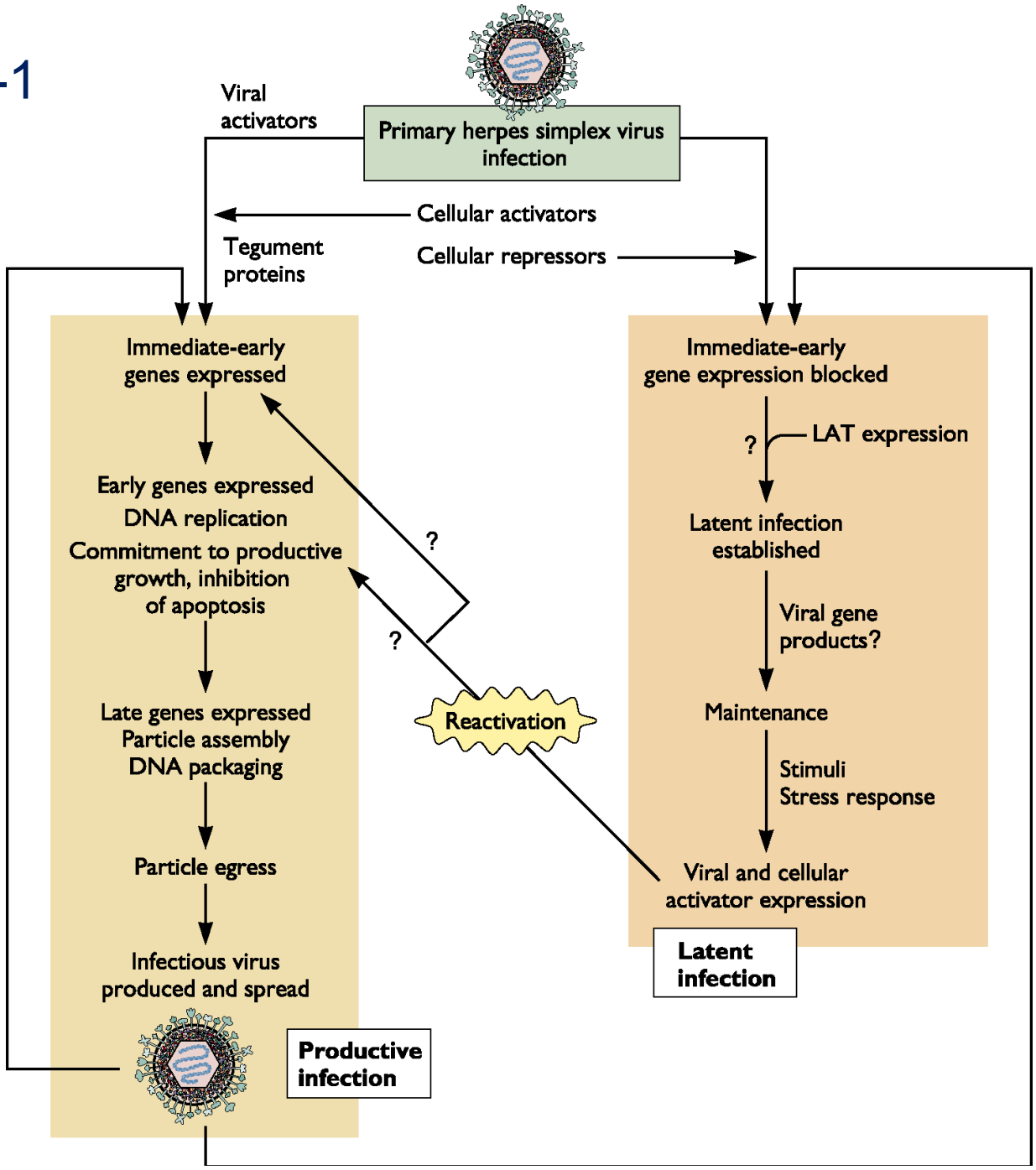
HSV-1 latency and reactivation: reactivation in neurons



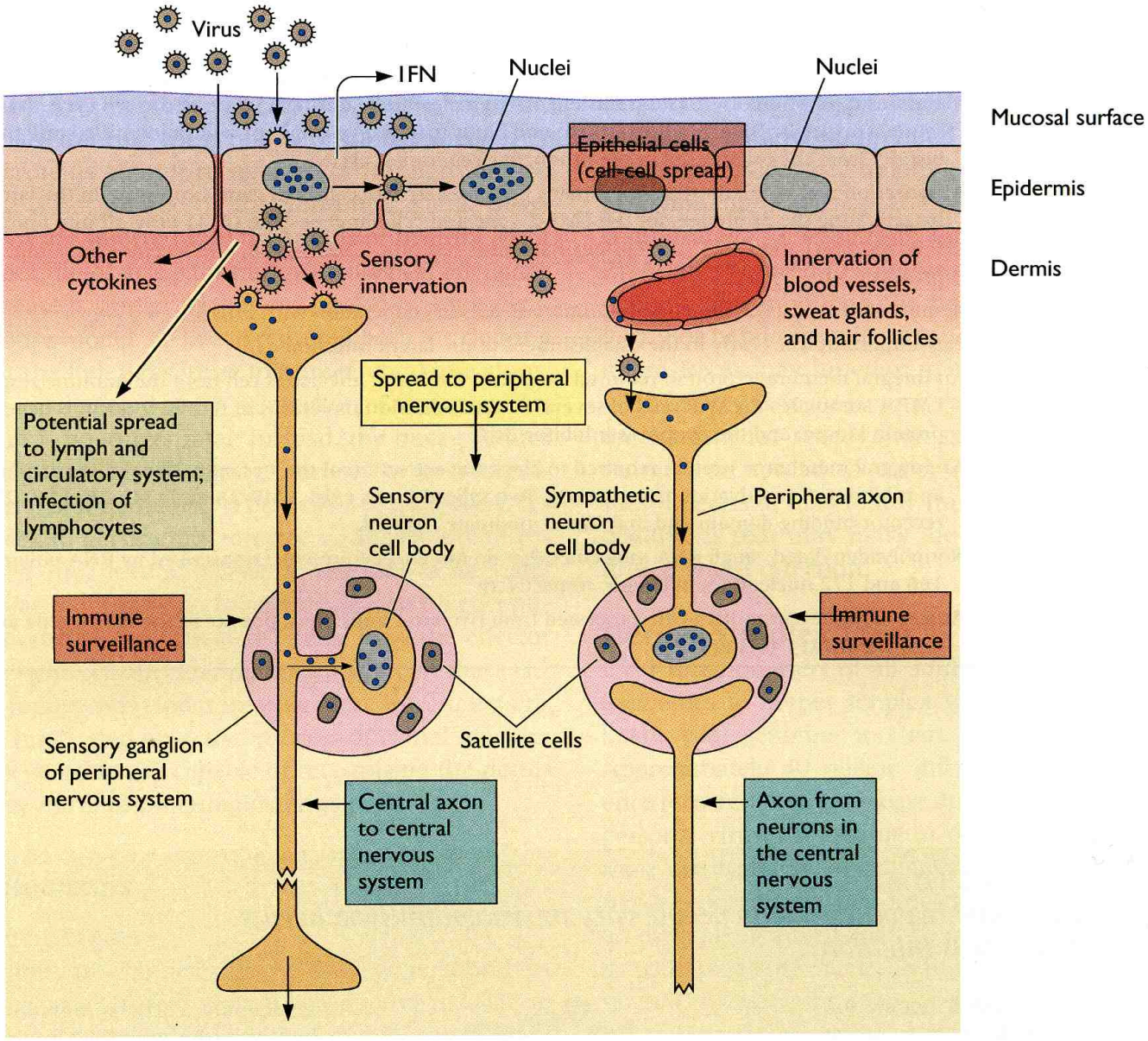
Small number of neurons in ganglion reactivate

- Virions appear in mucosal tissue innervated by latently infected ganglia, blisters ensue (not always)
- This is how infection is transmitted (intimate contact)
- Immune response is too slow (viral antagonism) to prevent shedding
- Some reactivate every 2-3 weeks; others never
- *Triggers of reactivation:* sunburn (UV), physical or emotional stress, nerve damage, hormonal imbalance, steroids
- Stimulate production of viral proteins needed to activate viral transcription program
- Immediate early proteins: ICP0 can reactivate viral gene expression

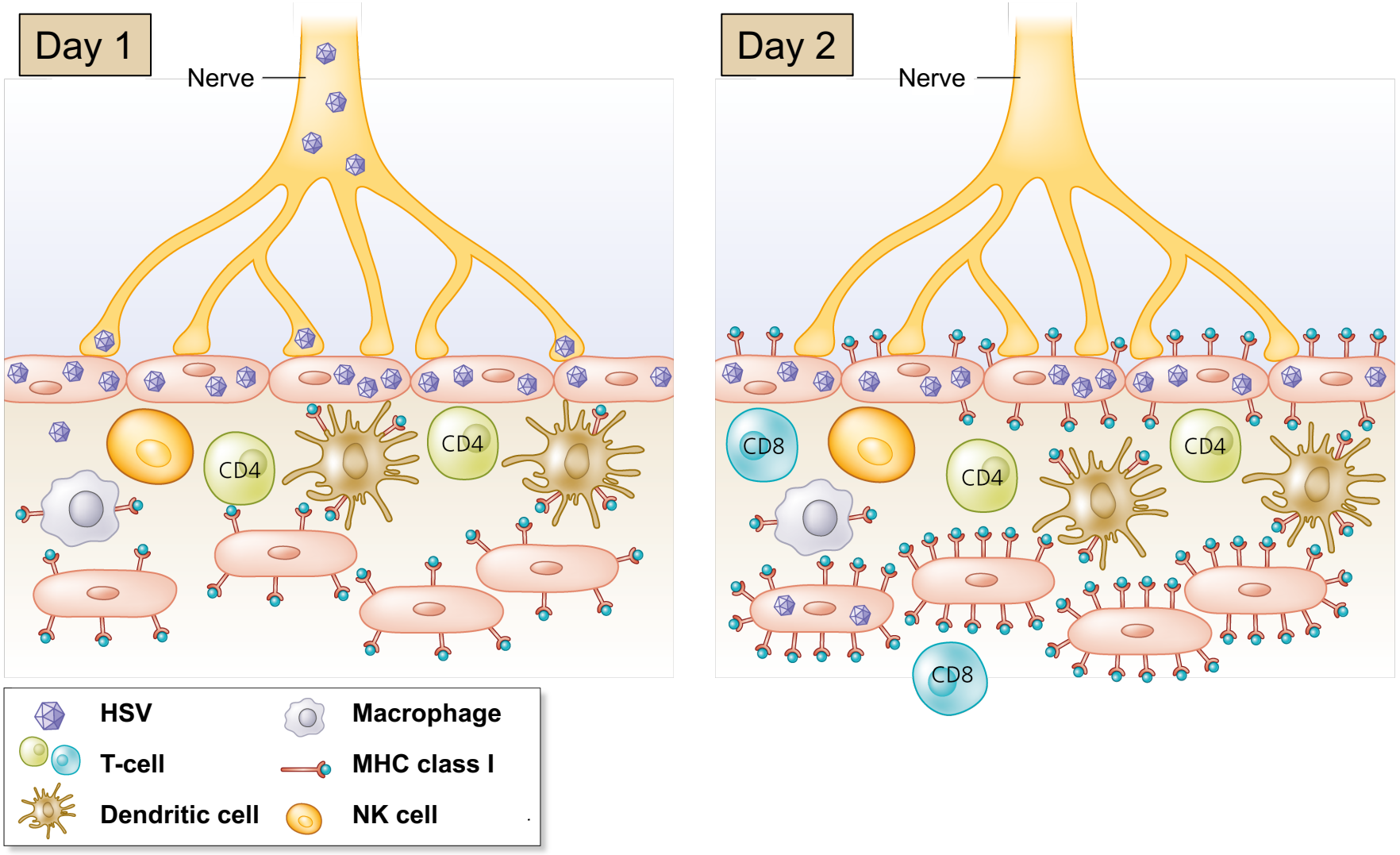
Reactivation of HSV-1 from latency



HSV-1 primary infection of a sensory ganglion



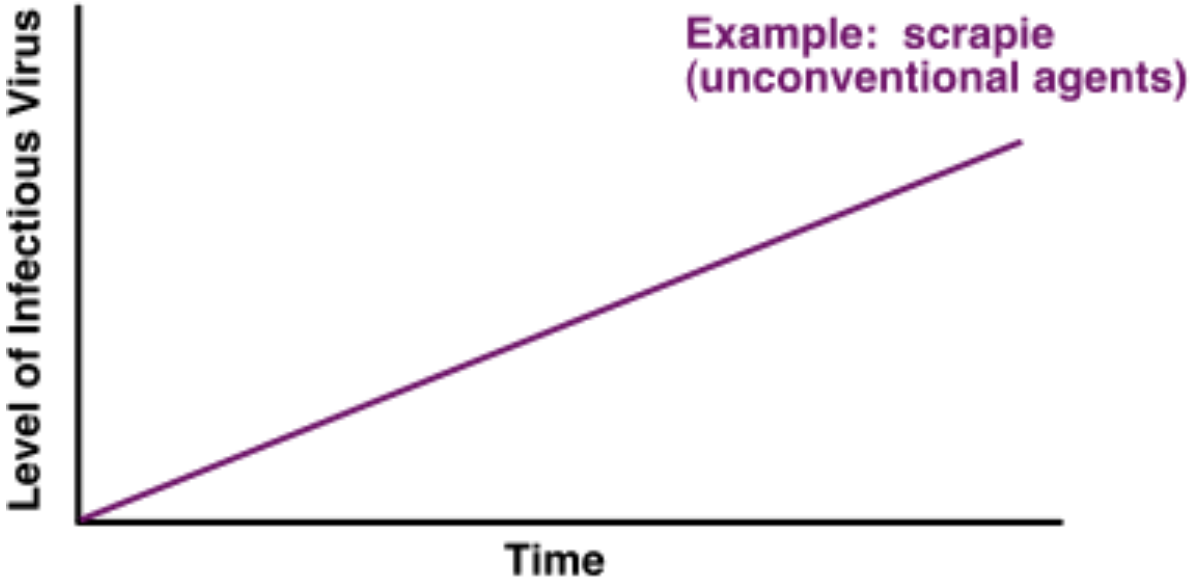
HSV-1 reactivation and the response of the immune system



Animal virus-host interactions: slowly progressive diseases

- As their name implies, these are diseases that take many years to manifest, while virus multiplication proceeds at the normal rate.
- There are two categories: slowly progressive diseases caused by viruses and those classed as spongiform encephalopathies.
- The viruses are subdivided into those that make infectious progeny throughout (e.g. **HIV-1**) and those whose genomes become defective during the long incubation period and hence are noninfectious (e.g. measles virus causing **subacute sclerosing panencephalitis** or **SSPE**).
- The transmissible spongiform encephalopathies are believed to be caused by a novel type of infectious entity that is stable aberrant conformer of a cell protein called PrP (Prion).

Animal virus-host interactions: slowly progressive diseases that are infectious



Slowly progressive virus disease that is infectious characterized by continuous and slowing increasing production of infectious agent with time

Prion diseases are the subject of widespread interest and concern as threats to public health following an epidemic of bovine spongiform encephalopathy (*BSE*) in the United Kingdom in the 1980s and 1990s that spread to other countries, and the associated emergence of a new human disease, variant Creutzfeld-Jakob disease (*variant CJD*).

Animal virus-host interactions: slowly progressive diseases that are non-infectious

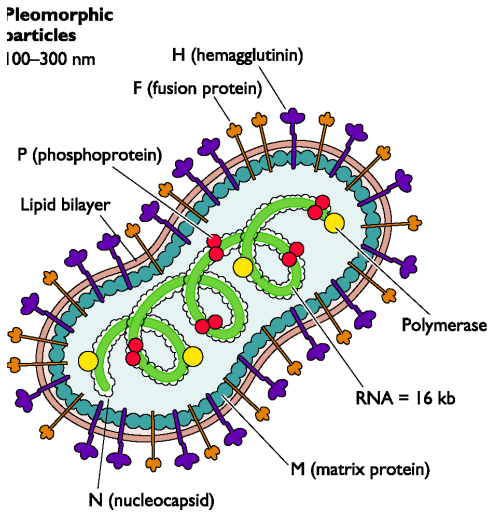
Comparison of acute and slowly progressive measles virus infections

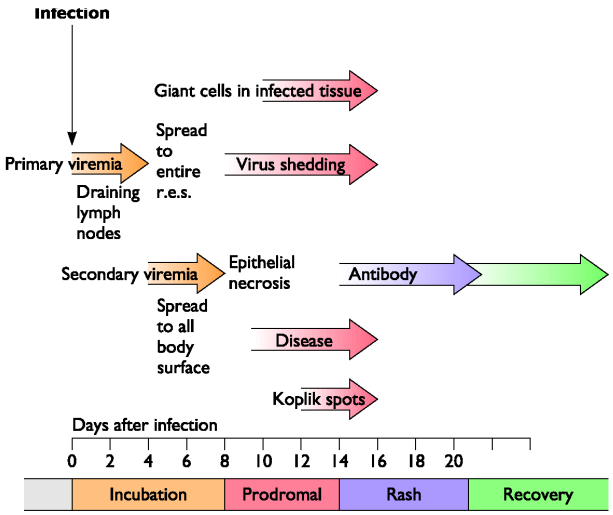
Acute measles virus infection

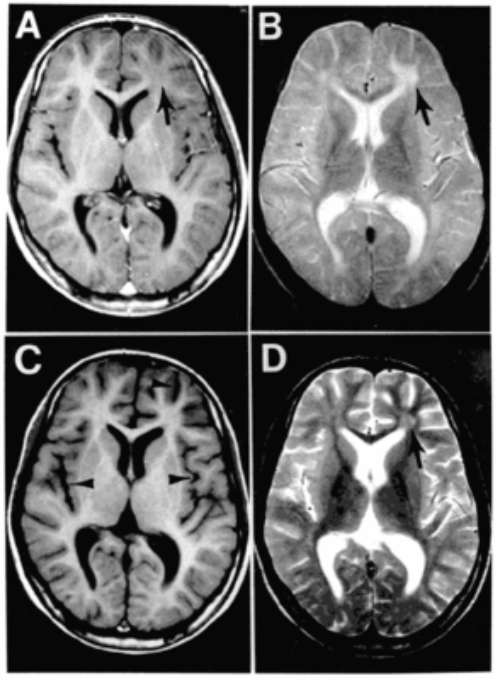
- A common acute childhood infection worldwide before mass immunization was established
- Respiratory transmission
- Systemic infection
- 100% disease – a diagnostic smooth skin rash

Sub-acute sclerosing panencephalitis (SSPE)

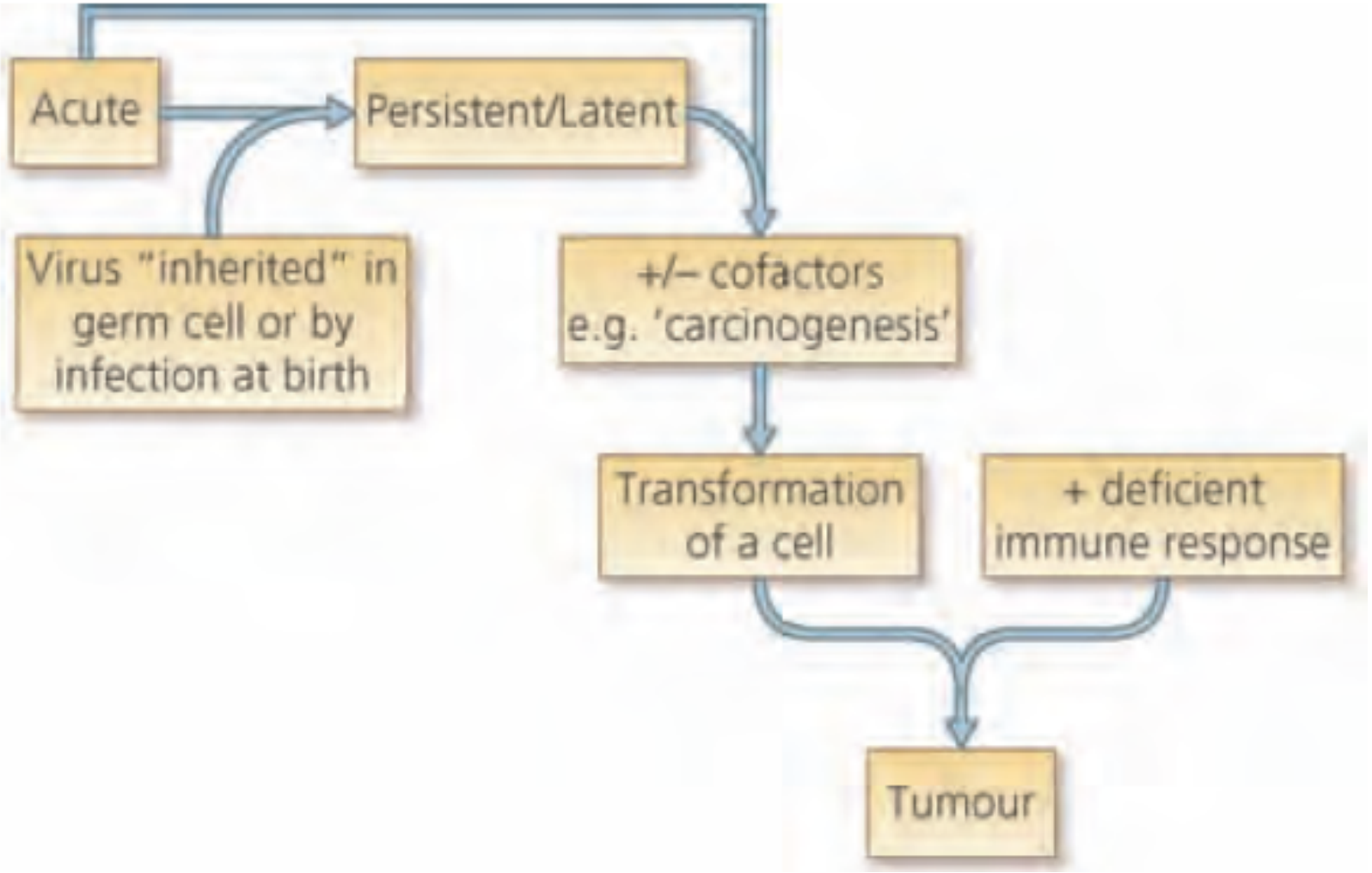
- Very rare, affecting about 6–22 per 10^6 cases of acute measles
- A sequel to acute measles
- Brain infection and disease
- Incubation period of 2–6 years
- Associated with measles infection early in life (<2 y old)
- Invariably fatal







Animal virus-host interactions: tumorigenic infections



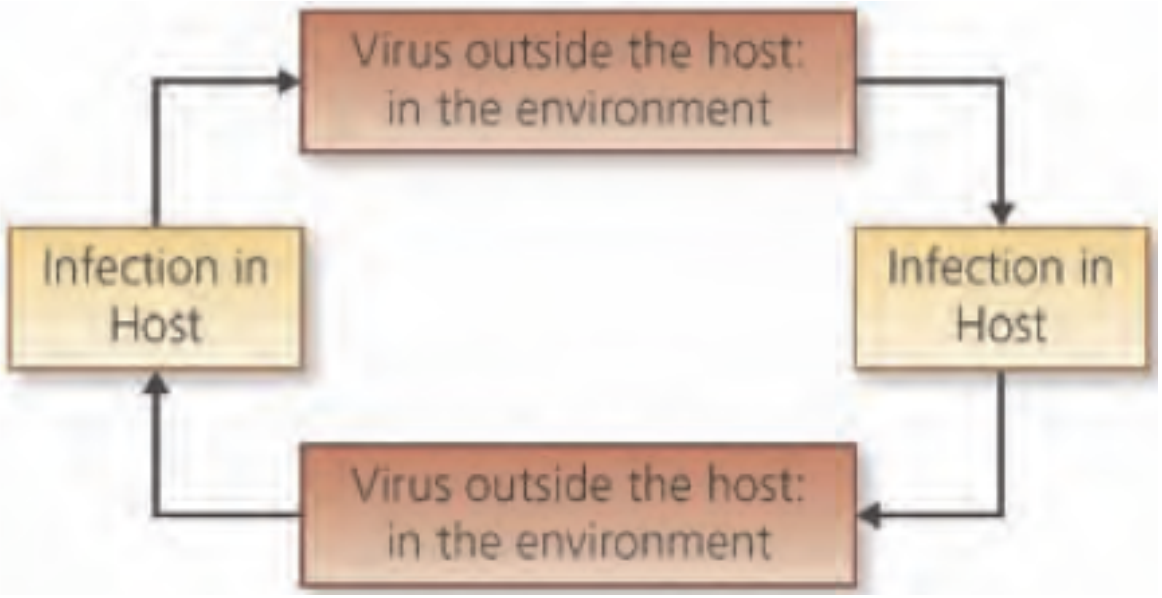
The relationship between virus infection and tumourigenesis

Mechanisms of Viral Pathogenesis:

Transmission and epidemiology of viral diseases

Transmission and epidemiology of viral diseases

Virus transmission cycles



- A virus spends time both within and outside its host.
- Some viruses spend most of their existence in the environment whilst others are predominantly host-associated.
- Most viruses are spread horizontally (person–person) but vertical spread from mother-to-foetus or baby is an important route for some viruses.

Transmission and epidemiology of viral diseases

Routes of transmission in humans

Route of transmission	Examples
Respiratory	Paramyxoviruses, influenza viruses, picornaviruses, varicella-zoster virus
Fecal-oral	Picornaviruses, rotavirus, adenovirus
Contact: lesions, saliva, fomites	Herpes simplex virus, rhinovirus, poxvirus, adenovirus
Zoonoses: insects, animals	Togaviruses (arthropod bite), flaviviruses (arthropod bite), bunyaviruses (urine, arthropod bite), arenaviruses (urine), rabies virus (animal bite)
Blood	Human immunodeficiency virus, human T-lymphotropic virus, hepatitis B virus, hepatitis C virus, cytomegalovirus
Sexual contact	Herpes simplex virus, human papillomavirus
Maternal-neonatal	Rubella virus, cytomegalovirus, echovirus, herpes simplex virus, varicella-zoster virus
Germ line	Retroviruses

Transmission and epidemiology of viral diseases

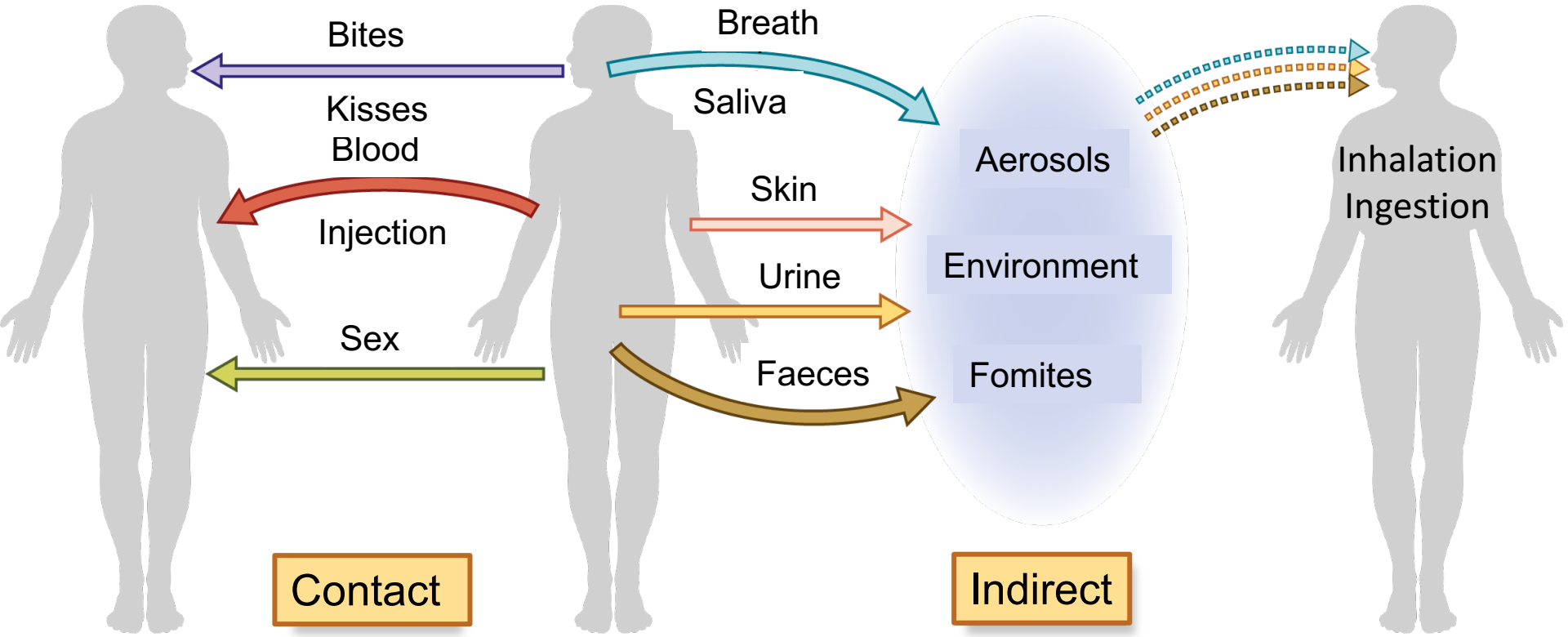
Routes of horizontal transmission in humans

Summary of horizontal transmission routes

- Respiratory route: entry via nose and mouth, e.g. rhinovirus, influenza virus
- Faecal-oral route: entry via mouth into the gastrointestinal tract, e.g. poliovirus, rotavirus
- Conjunctival route: entry into eye, e.g. some adenoviruses, possibly other respiratory viruses
- Via saliva or urine: e.g. Epstein-Barr virus, cytomegalovirus, Lassa fever virus
- Via fomites: e.g. hepatitis A virus
- Sexual route: entry into body via sexual activity, e.g. HIV-1, HBV, papillomavirus
- Mechanical route: entry into body via skin puncture, e.g. papillomavirus, arboviruses, HIV-1, HBV

Transmission and epidemiology of viral diseases

Routes of horizontal transmission in humans



Horizontal transmission occurs between individuals of a species by a variety of routes.

Each virus has evolved to utilize particular route(s) of transmission, but this does not prevent a virus from transmitting via an atypical route under special circumstances.

Transmission and epidemiology of viral diseases

Routes of vertical transmission in humans

Examples of vertical transmission of viruses in humans

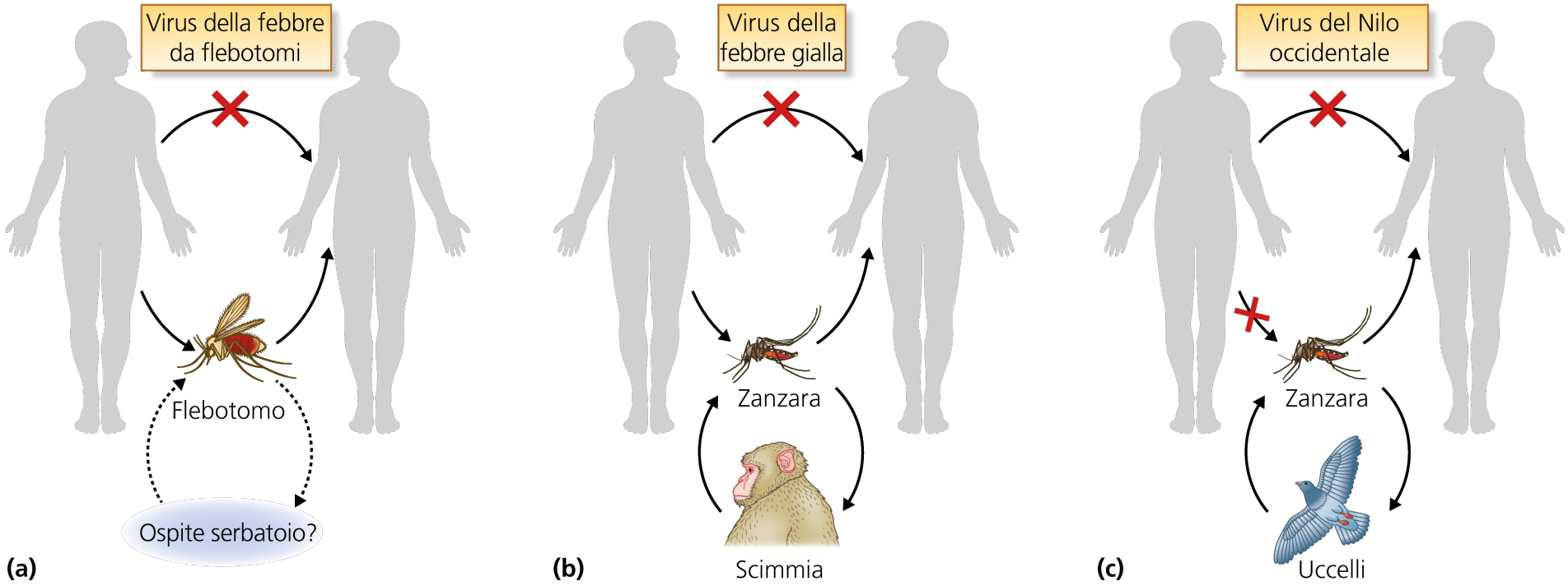
Virus	Possible modes of infection			Possible adverse outcomes		
	Trans-placental	During birth*	After birth†	Death of foetus	Clinical disease after birth	Persistent infection
Rubella	+	−	−	+	Congenital abnormality	+
CMV (Primary maternal)	+	−	−	?	Congenital abnormality	+
CMV (Reactivated maternal)	−	+ (2% of all babies)	+	na	−	+
HIV-1	+	+ Up to 15% of babies born to infected mothers without preventive treatment	+	−	AIDS	+
HBV	+	+	+	−	−	+
HSV (genital)	(+)	+	−	+	Herpes lesions	+
HPV (various types)	−	+	−	−	−	+

*A Caesarean delivery can help avoid infection; †from breast milk; (+) small minority of cases; na, not applicable; ?, not known.
Abbreviations: CMV, cytomegalovirus; HBV, hepatitis B virus; HIV-1, human immunodeficiency virus type 1; HSV, herpes simplex viruses; HPV, human papillomavirus.

- Vertical transmission occurs between mother and foetus/baby in utero, during delivery or breast feeding.
- Infection in a foetus can have severe consequences because of the absence of fully functional immune responses.

Transmission and epidemiology of viral diseases

Vector-borne viruses and zoonotic transmission



- *Arboviruses* (Arthropod-borne viruses) are spread from person to person, or from other species into humans, by biting insects.
- Some infections are *zoonoses* in which a virus is spread from a non-human animal to humans without sustained onward transmission between humans.

Transmission and epidemiology of viral diseases

The study of the occurrence, distribution and control of diseases

- **Prevalence:** the proportion or percentage of individuals in the population having a disease.
- **Incidence:** the total number of cases of disease in a population
- **Morbidity:** incidence of illness in a population.
- **Mortality:** incidence of death in a population.

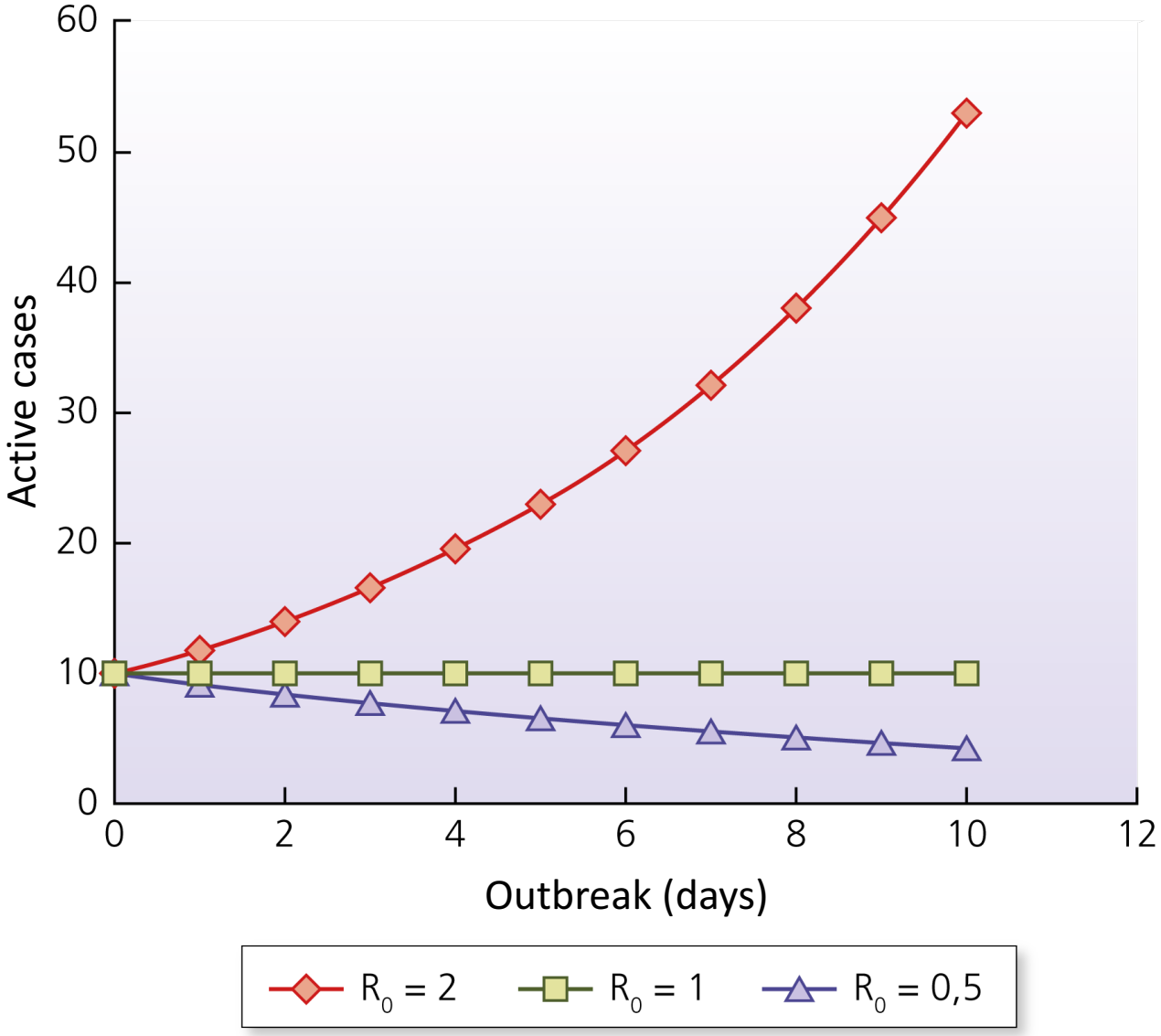
Transmission and epidemiology of viral diseases

R_0 and the epidemiology of a viral diseases

R_0 (basic reproductive number) measures the average number of infections initiated by an infected individual.

An epidemic will spread if R_0 >1

Disease	Transmission	R_0
Measles	Airborne	12–18
Diphtheria	Saliva	6–7
Smallpox	Airborne droplet	5–7
Polio	Fecal-oral route	5–7
Rubella	Airborne droplet	5–7
Mumps	Airborne droplet	4–7
HIV/AIDS	Sexual contact	2–5
Pertussis	Airborne droplet	5.5
SARS	Airborne droplet	2–5
Influenza (1918 pandemic strain)	Airborne droplet	2–3
Ebola (2014 Ebola outbreak)	Bodily fluids	1.5-2.5



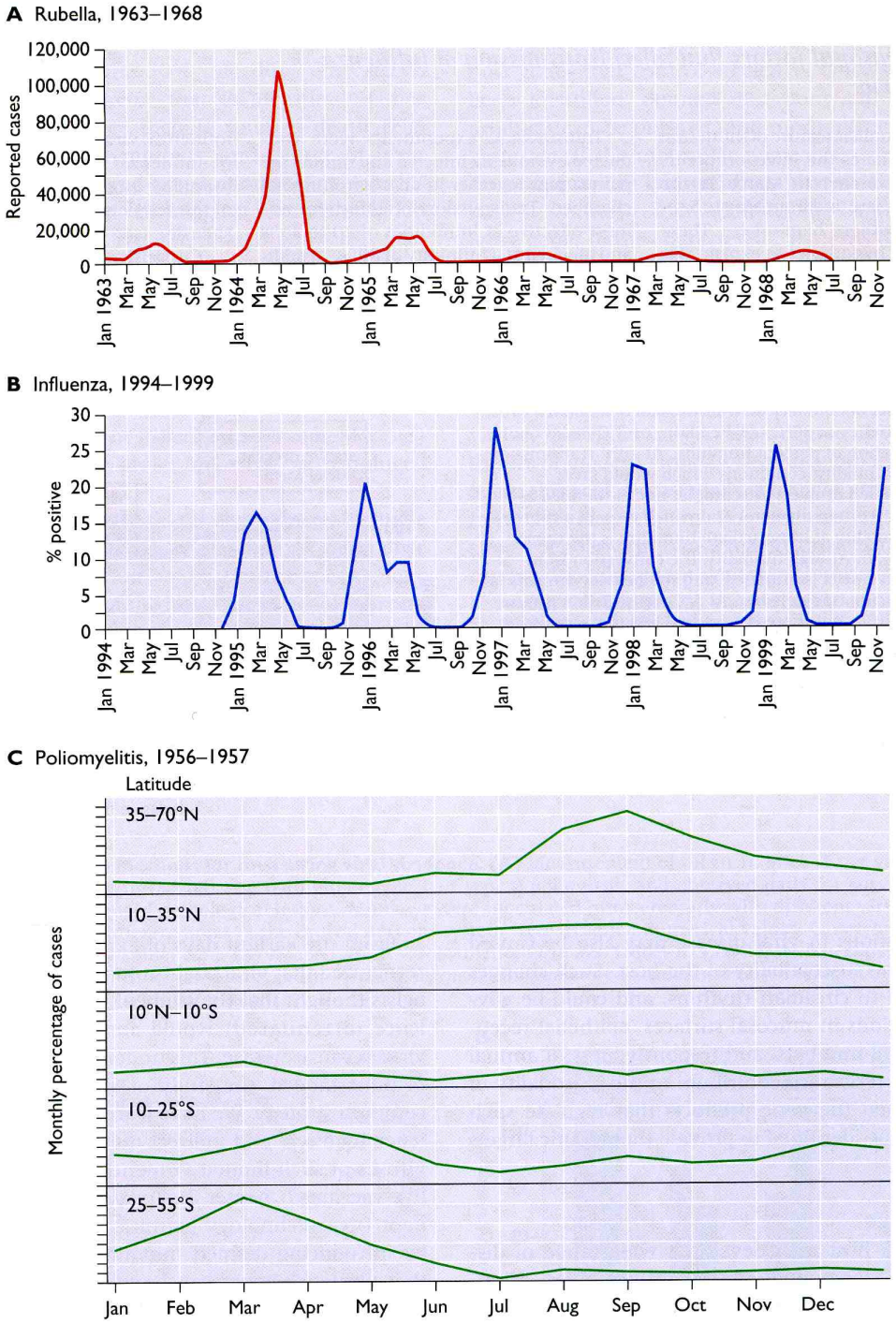
Transmission and epidemiology of viral diseases

- **Mechanisms of viral transmission:**
  Aerosol, infected things, direct contact, sexual contact, transplant, blood-transfusion, zoonosis.
- **Factors influencing viral transmission:**
  Environmental persistence of virions;
  Viral replication in body fluids
- **Risk factors:**
  Age, health, immune status, work, travels, life style
- **Populations characteristics:**
  Percentage of susceptible serum-negative individuals
- **Geography/Season:**
- **Prevention and control:**
  Quarantine, vector elimination, immunization (natural infection, vaccination), antiviral therapy

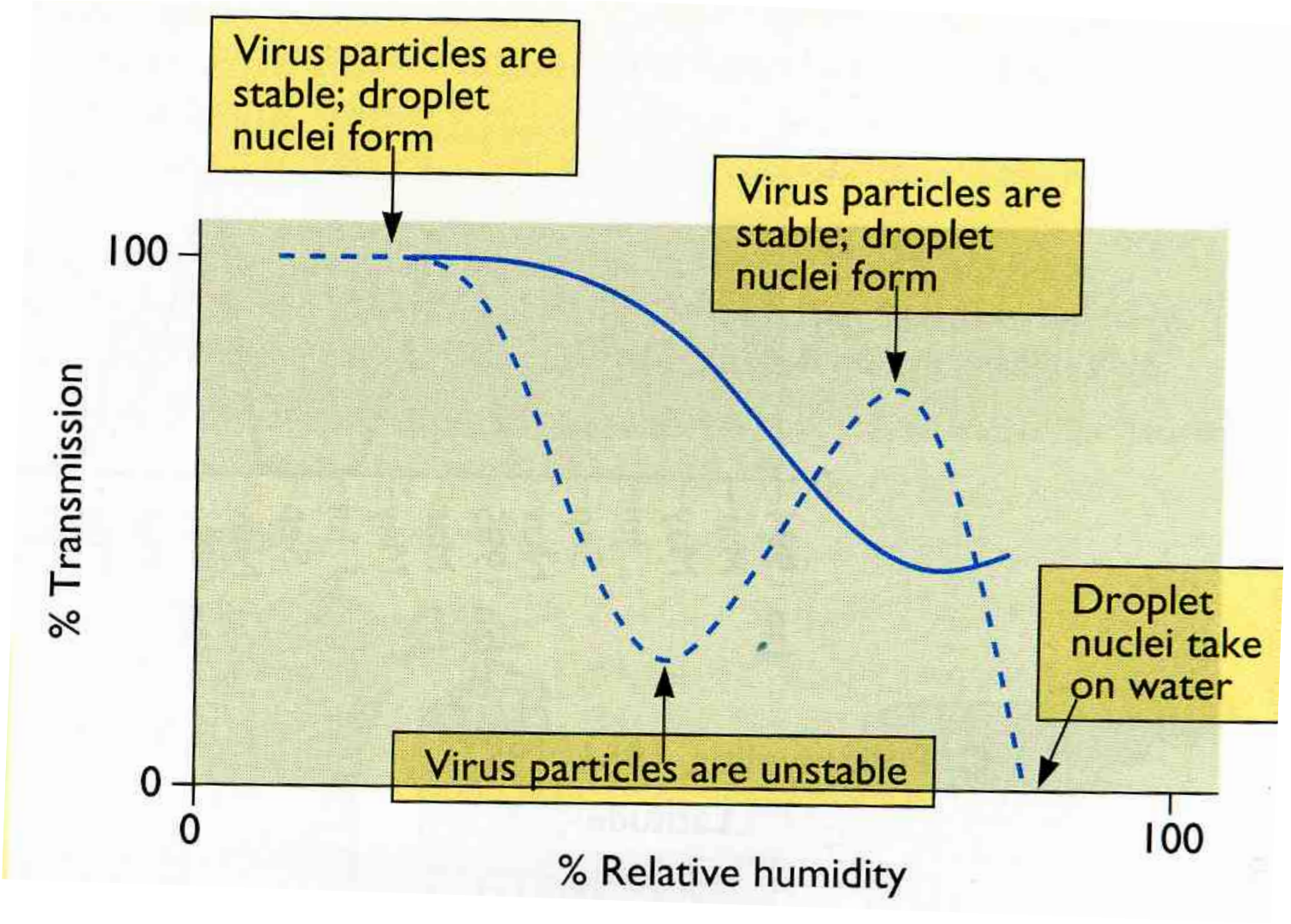
Table 2.5 The many components of epidemiology

Mechanisms of transmission
Aerosol
Food and water
Fomites
Body secretions
Sexual activity
Birth
Transfusion or transplantation
Zoonoses (animals, insects)
Factors that promote transmission
Virion stability
Presence in aerosols and secretions
Asymptomatic shedding
Ineffective immune response
Geography and season
Vector ecology (habitat and season)
School year
Home-heating season
Risk factors
Age
Health
Immunity
Occupation
Travel
Lifestyle
Children (school, day care centers)
Sexual activity
Critical population size
Numbers of seronegative susceptible individuals
Means of control
Quarantine
Vector elimination
Immunization
Antivirals

Acute viral infections with seasonal variation in incidence



Effect of humidity on transmission of influenza virus



Transmission and epidemiology of viral diseases

The study of the occurrence, distribution and control of diseases

- **Outbreak:** the occurrence of a large number of cases of a disease in a new site and in a short period of time (HAV).
- **Endemic:** disease constantly present, usually in low numbers.
- **Epidemic:** the occurrence of a disease in unusually high numbers due to the introduction of new viral strain in a naive population (Influenza).
- **Pandemic:** a worldwide epidemic due to the introduction of a new virus (HIV, SARS, Influenza)

Transmission and epidemiology of viral diseases

Classification of disease by incidence

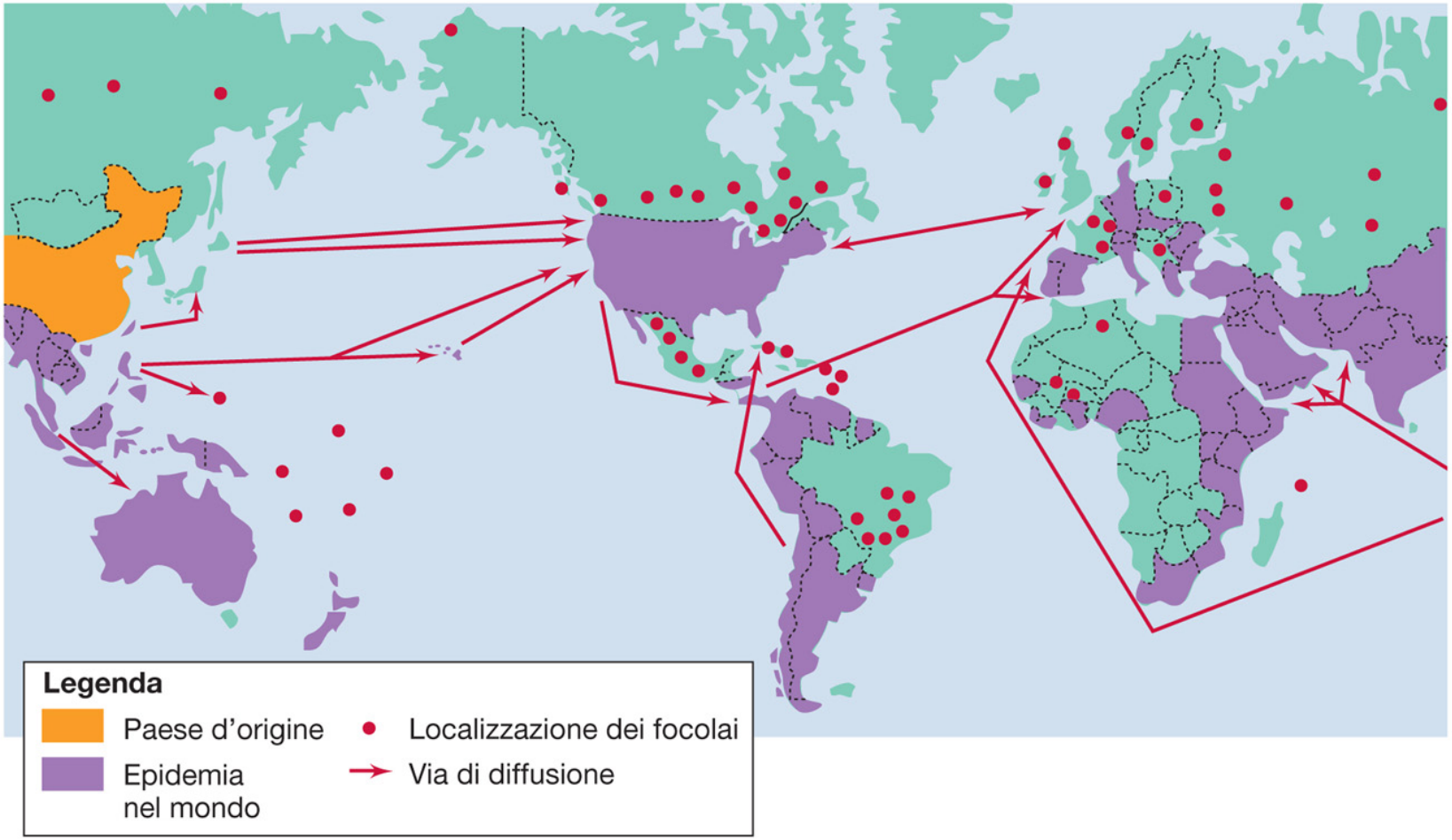
Endemic disease

Epidemic disease

Pandemic disease

Transmission and epidemiology of viral diseases

The spread of the Asian influenza pandemic of 1957



Transmission and epidemiology of viral diseases

Recent outbreaks of emerging and reemerging infectious diseases

Transmission and epidemiology of viral diseases

Prevention and control

- **Quarantine**
- **Public health measures**
  - Directed against the reservoirs (domestic animals, wild animal, insect, humans)
  - Directed against transmission (food, water, air)
  - Education (STDs)
- **Immunization**
  - Natural infection
  - Vaccination
- **Antiviral therapy**

Transmission and epidemiology of viral diseases

Prevention and control of viral diseases

Vaccines:
the proven best defense
against viruses

Antiviral drugs:
small molecules that block
virus replication