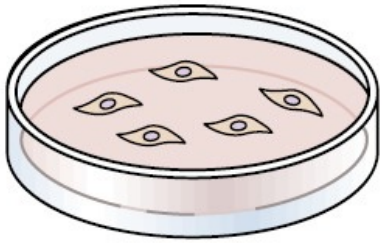
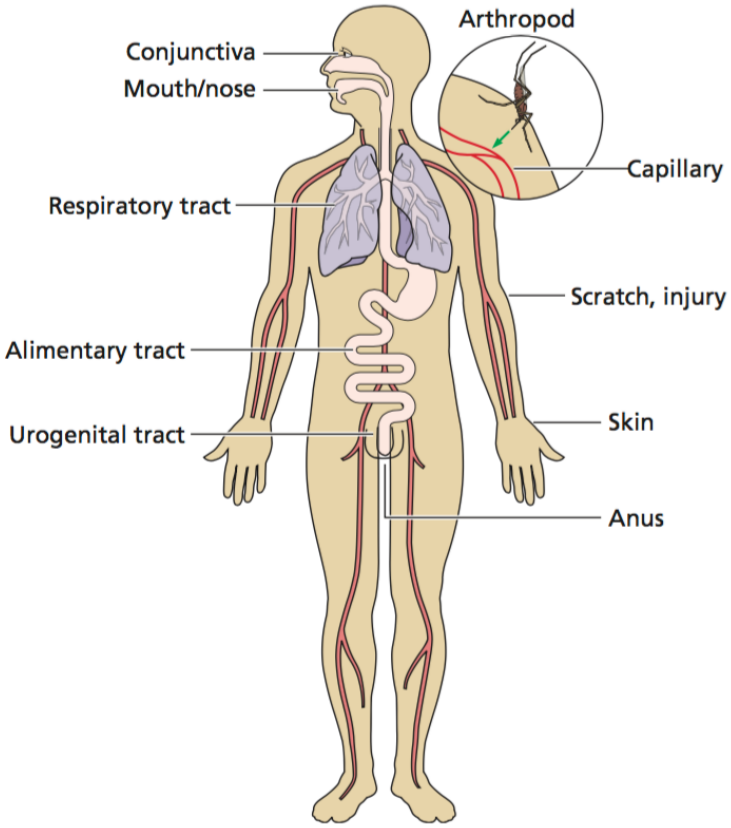
Infection Basics

Lecture 12
Biology 3310/4310
Virology
Spring 2017

Before I came here I was confused about this subject. Having listened to your lecture, I am still confused—but at a higher level.
–Enrico Fermi

The nature of host-parasite interactions





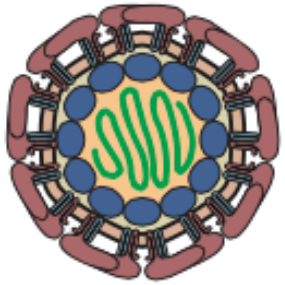
The viral genome must establish itself

in a host population to endure

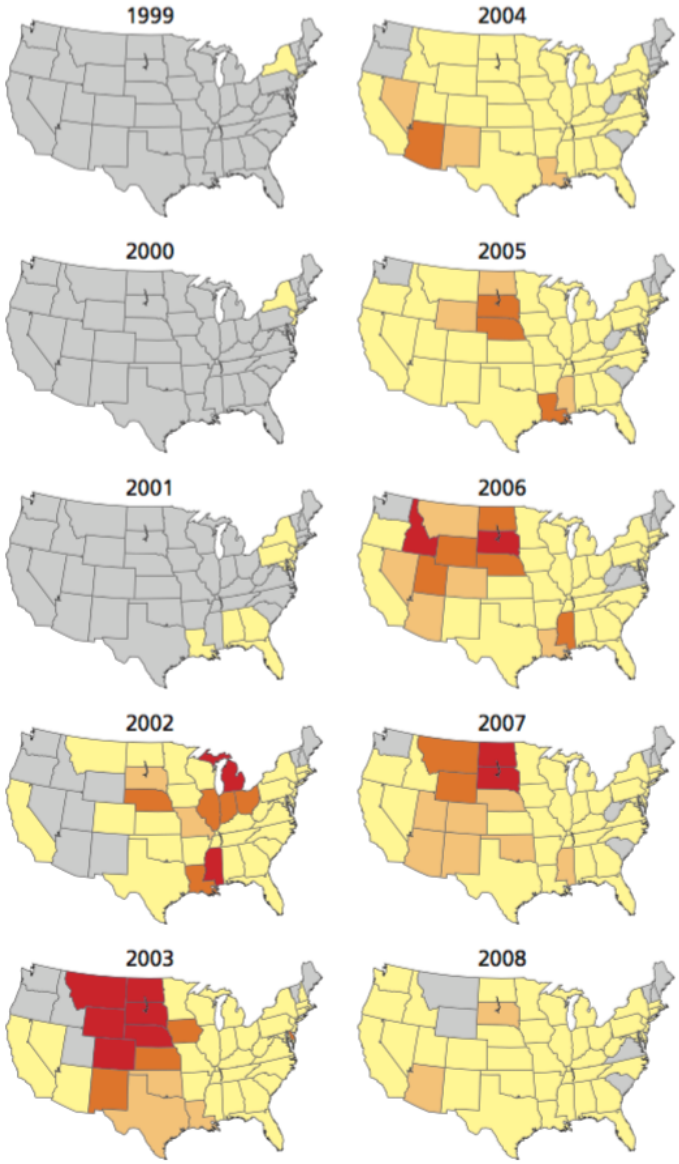
We live and prosper in a cloud of viruses

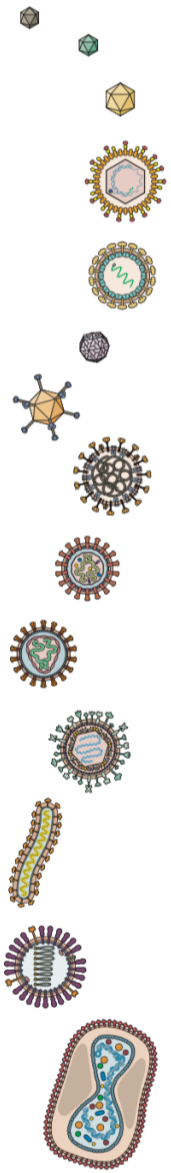
- Most infections have no consequence
- If we do get infected, many infections are *inapparent*

Example: West Nile virus infection



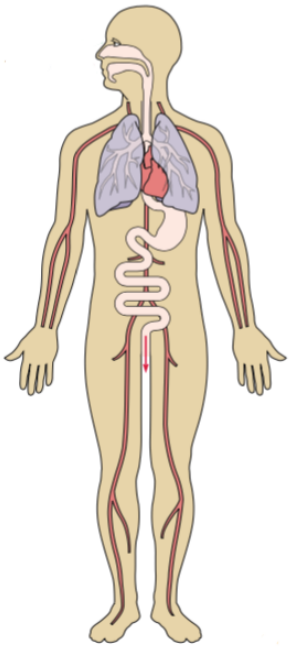
- WNV spread across the US in less than 4 years (’99)
  - By October 2004 about 1 million people were infected (Ab+)
  - Febrile illness developed in 20% of infected people
  - Neuroinvasive illness developed in 1% of infected people
- Many people were infected with no obvious disease
  - Inability to stop an epidemic because it can’t be recognized early





Viral pathogenesis

- *Pathogenesis*: the process of producing a disease
- Two components of viral disease:
  - Effects of viral replication on the host
  - Effects of host response on virus and host

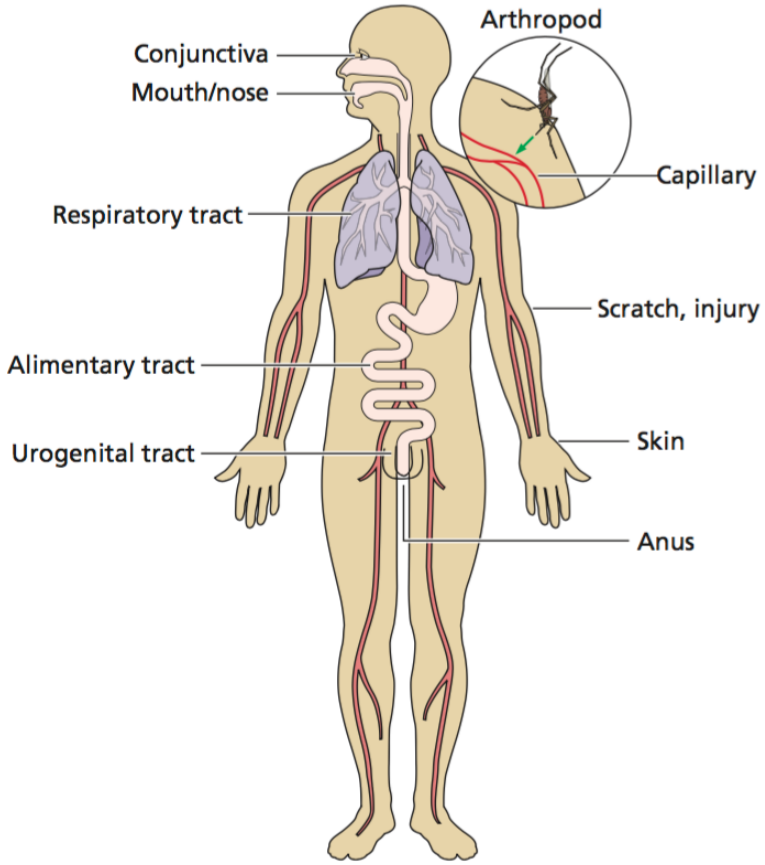


Fundamental questions of viral pathogenesis

- How does a virus particle enter the host?
- What is the initial host response?
- Where does primary replication occur?
- How does the infection spread in the host?
- What organs and tissues are infected?
- Is the infection cleared from the host or is a persistent infection established?
- How is the virus transmitted to other hosts?

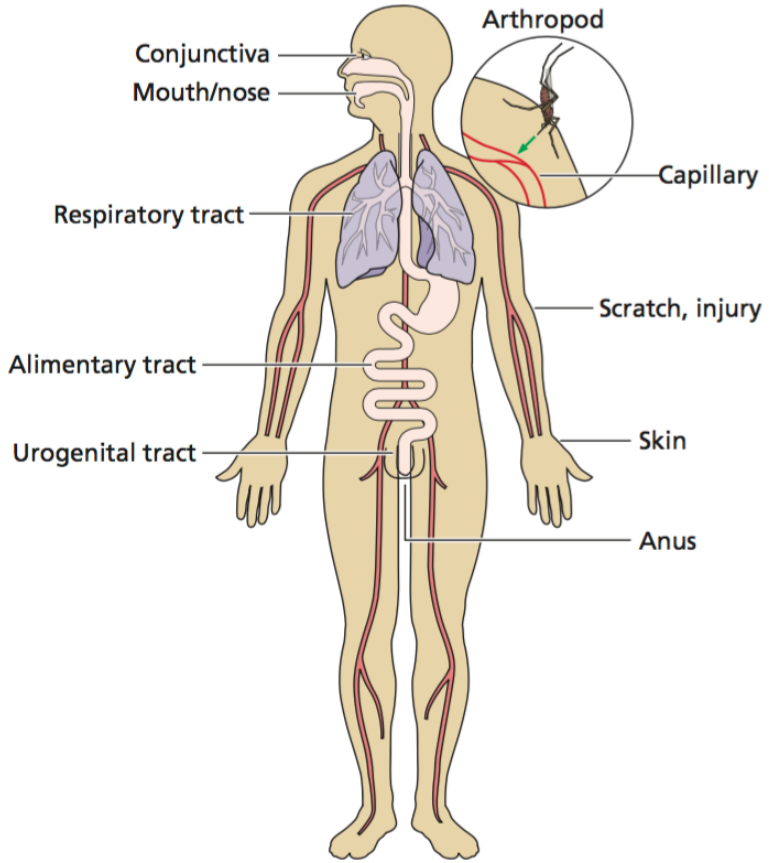
Three requirements for a successful infection

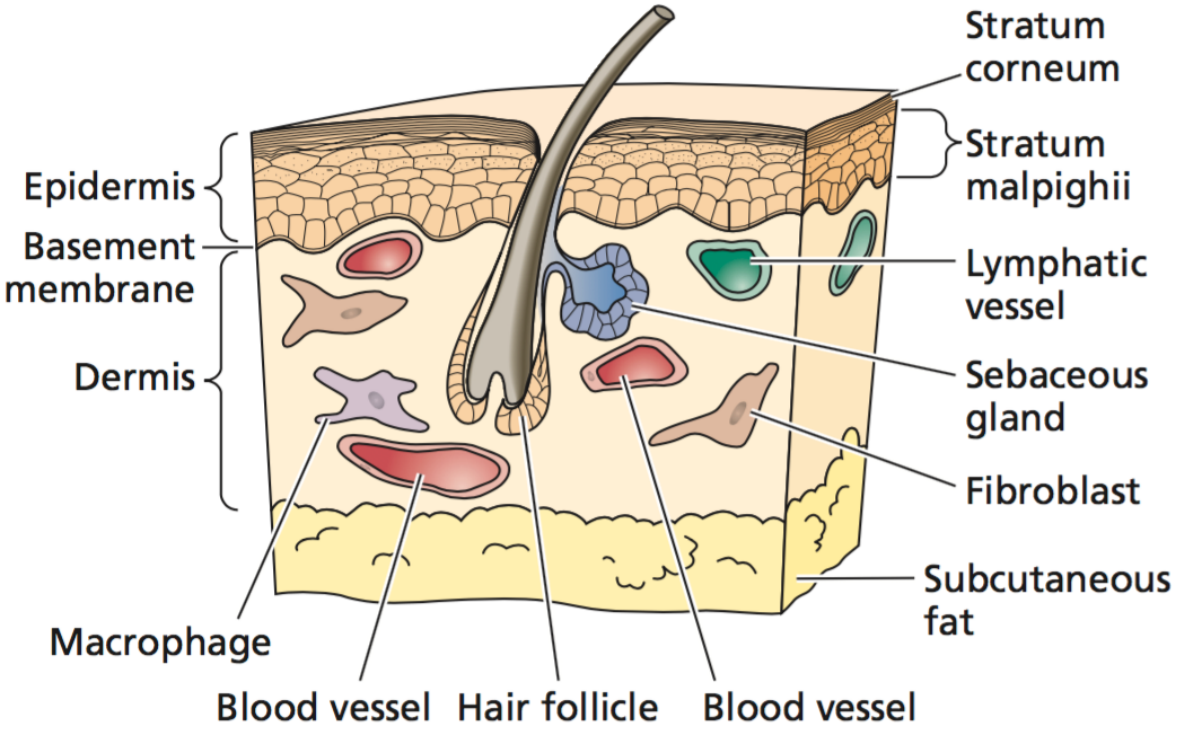
- Enough virus
- Cells accessible, susceptible, permissive
- Local antiviral defense absent or overcome

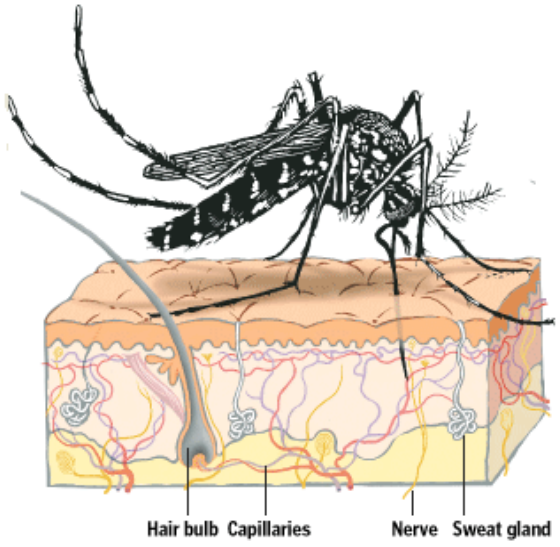


Gaining access: site of entry is critical

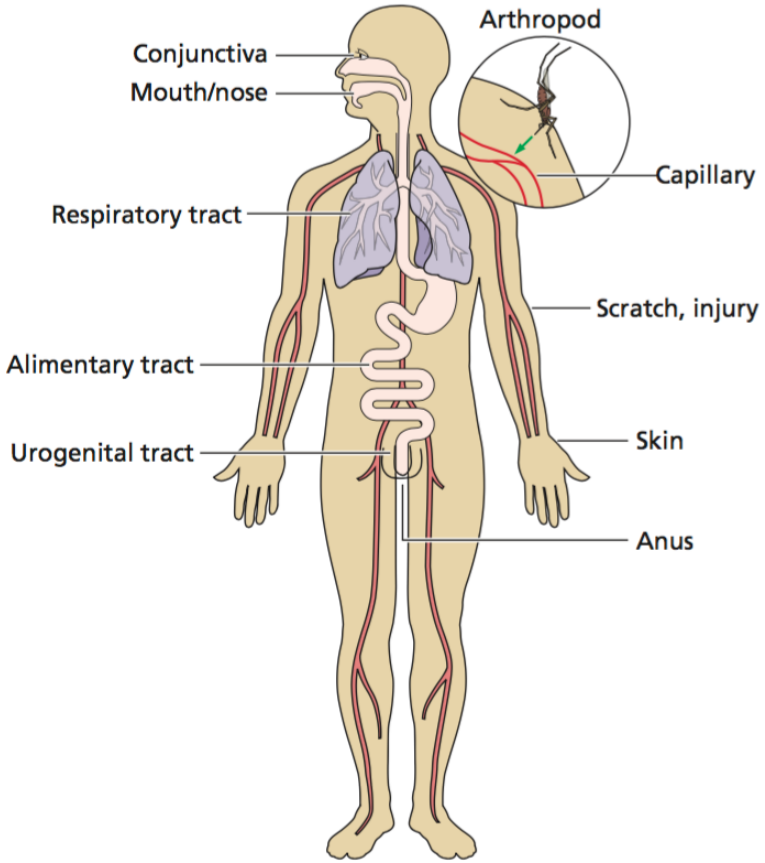
The human body presents only a
limited spectrum
of entry sites for viral infection.



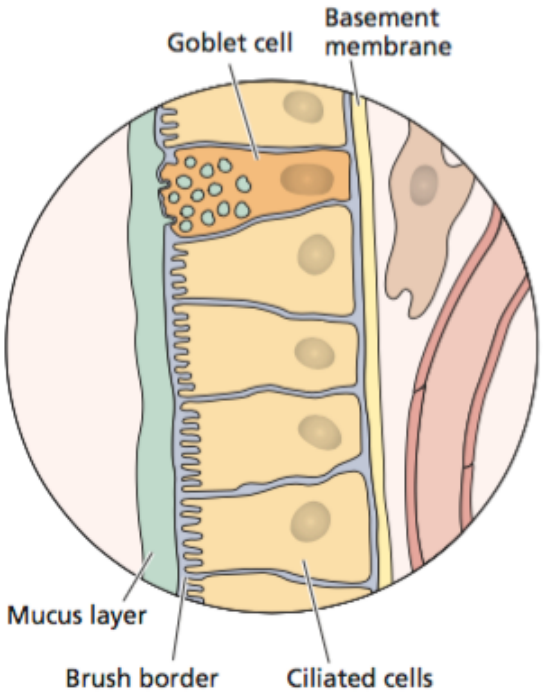


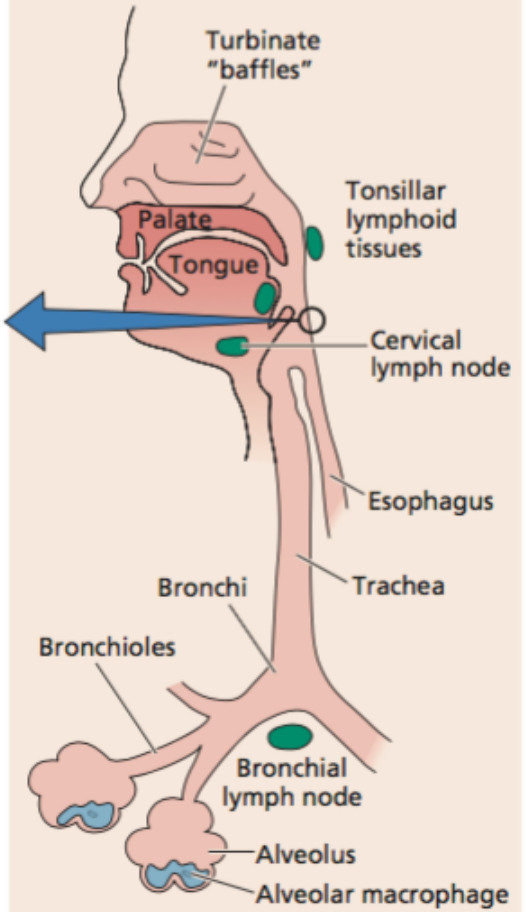


Mucosal surfaces are ripe for viral infection



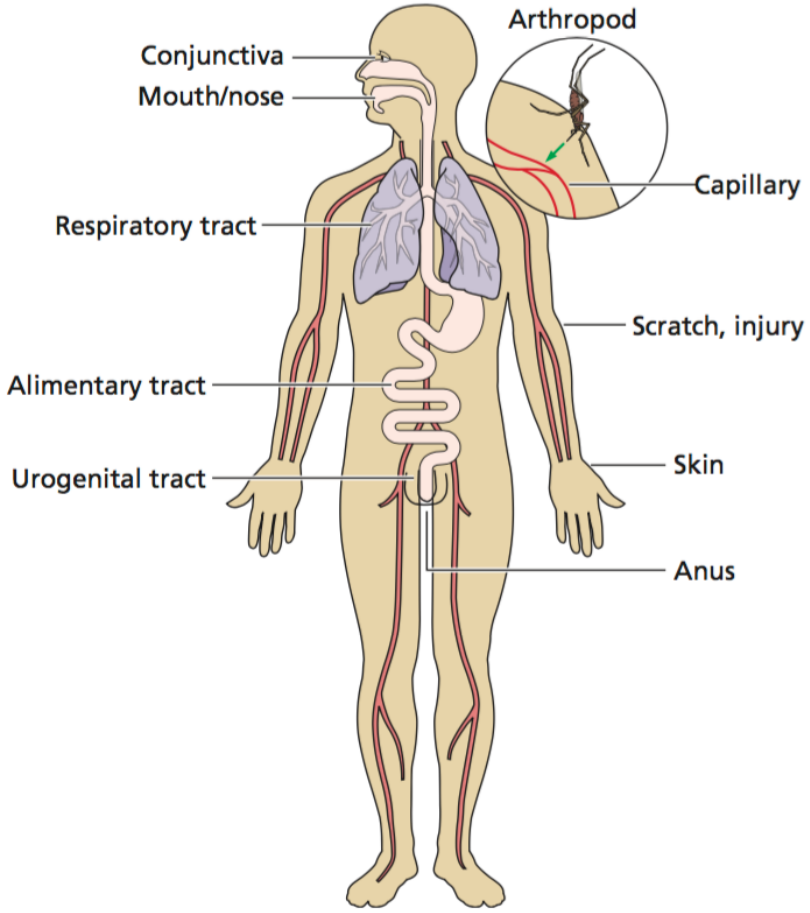
Lined by living cells

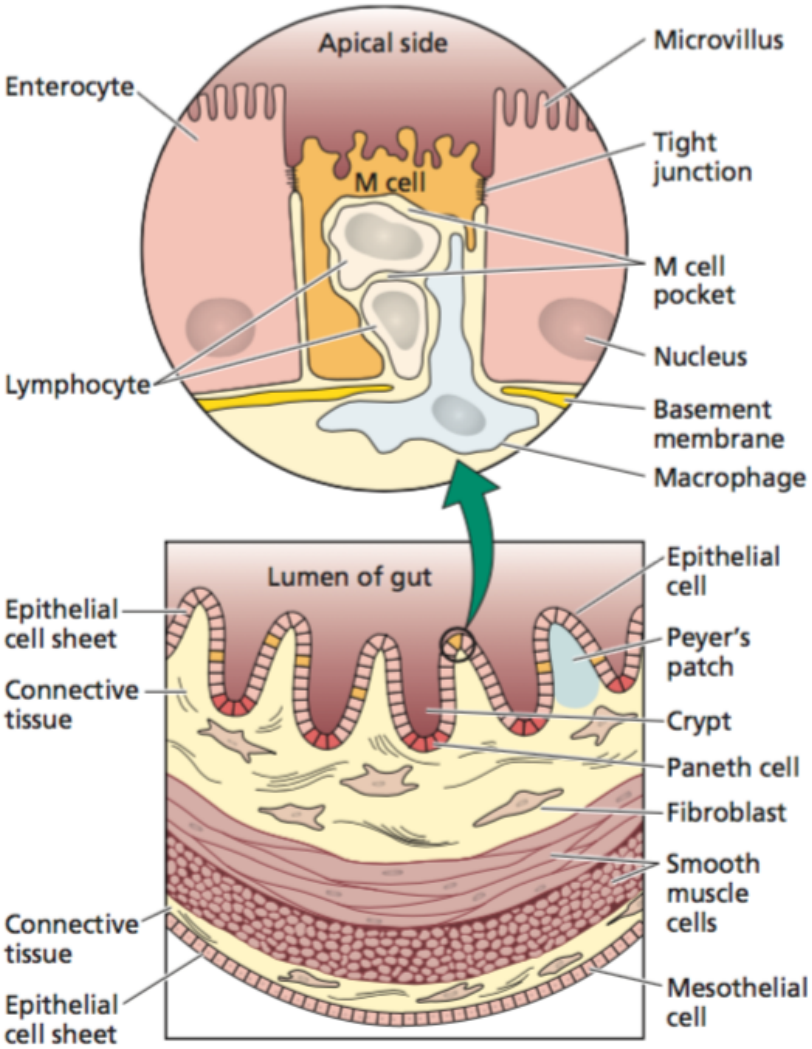


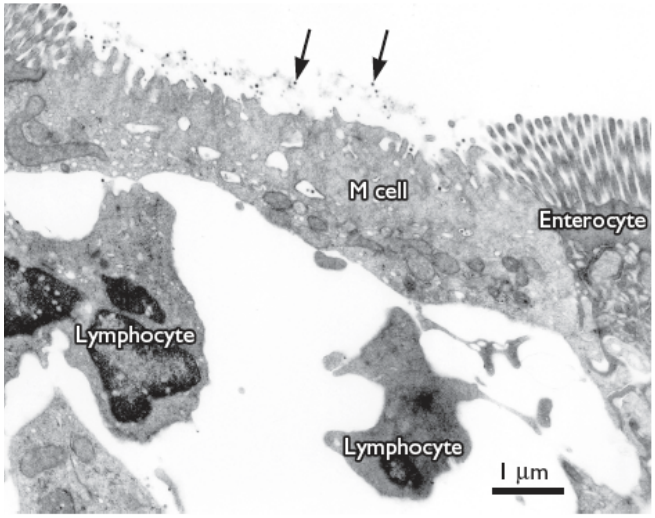


Site of reproduction	Clinical manifestation	Virus
Turbinate "baffles"	Rhinitis (common cold)	Rhinovirus Coronavirus Parainfluenza virus Respiratory syncytial virus Influenza virus Adenovirus Herpes simplex virus Epstein-Barr virus
Tonsillar lymphoid tissues	Pharyngitis	
Palate Tongue		
Cervical lymph node	Laryngitis	
Esophagus		
Trachea	Tracheitis	Parainfluenza virus Respiratory syncytial virus Influenza virus Adenovirus Measles SARS MERS
Bronchi	Bronchitis	
Bronchioles	Bronchiolitis	
Bronchial lymph node	Bronchopneumonia	
Alveolus Alveolar macrophage		

Alimentary tract





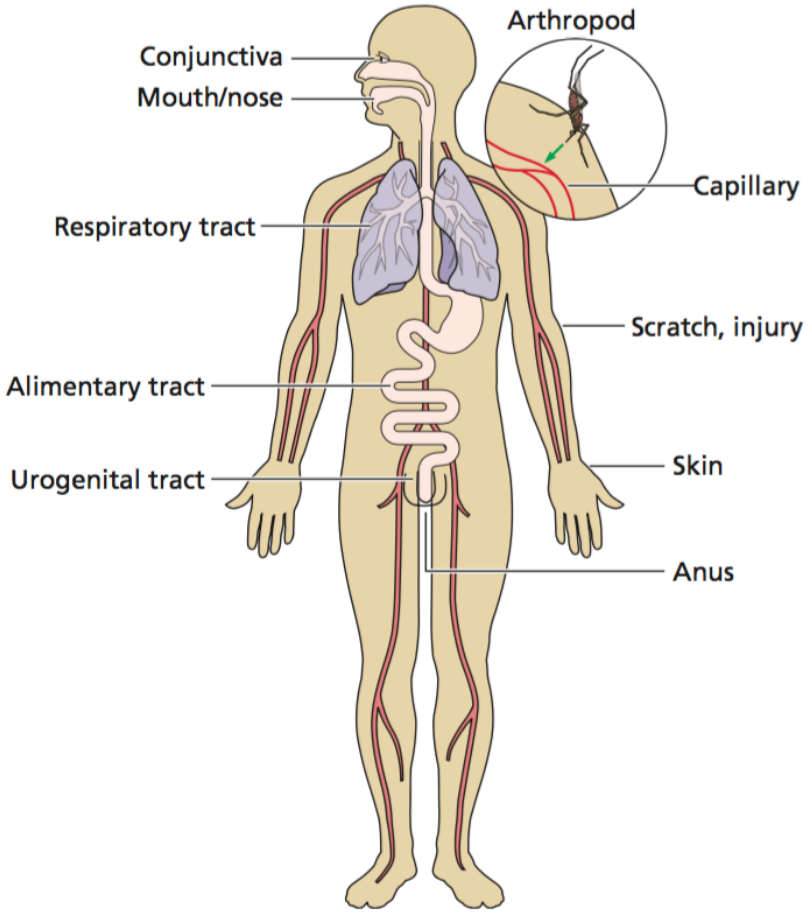


The small intestine

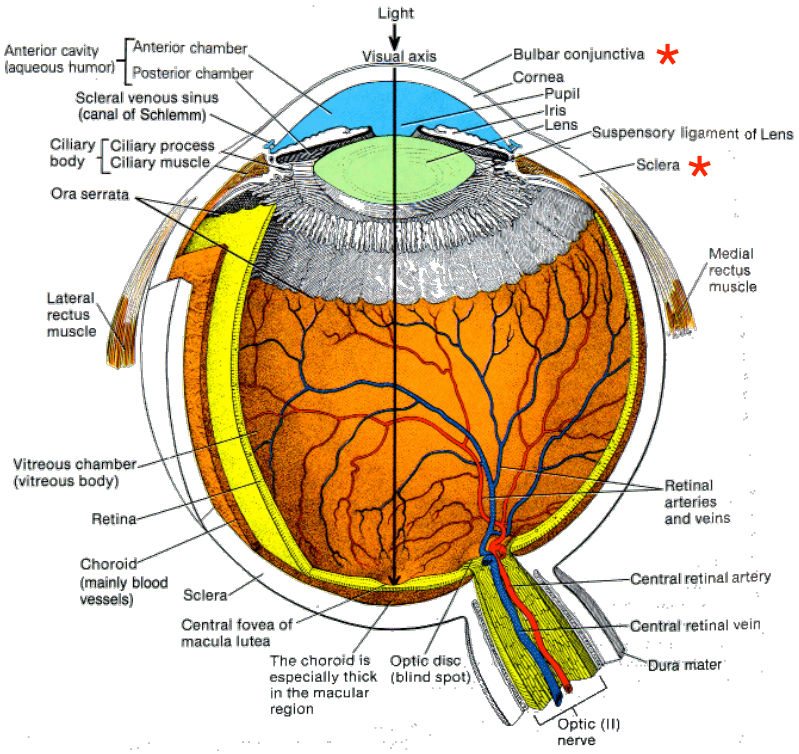
- A selectively permeable barrier
- Polarized epithelial cells
- Direct contact with outside world
- Direct contact with the immune system and the nervous system

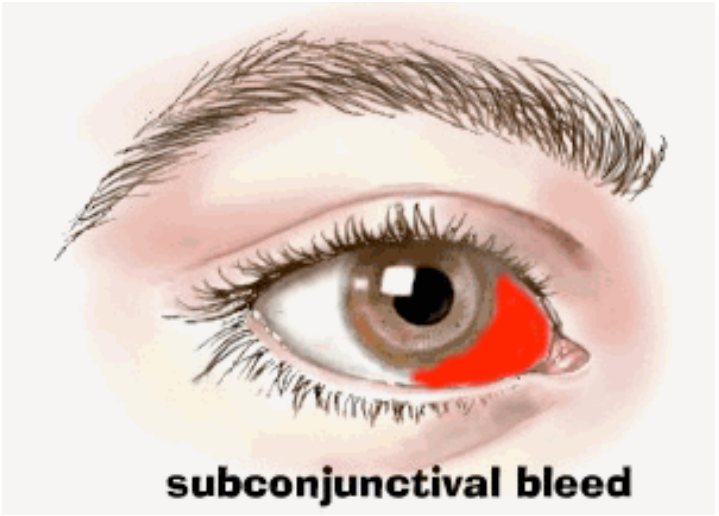
Urogenital tract

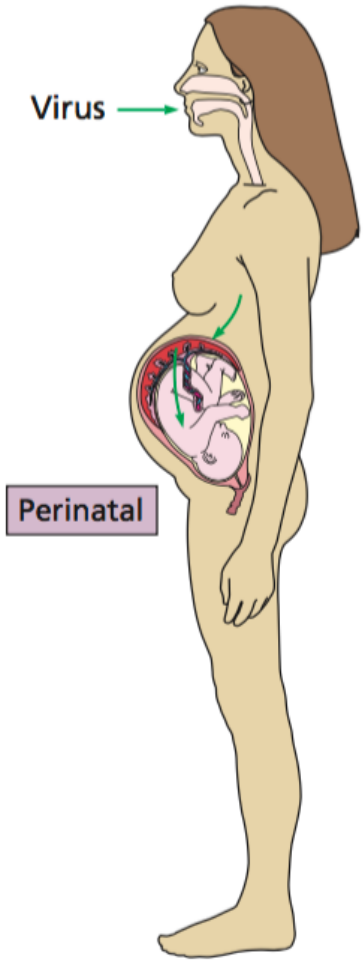
- Protected by mucus, low pH
- Minute abrasions from sexual activity may allow viruses to enter
- Some viruses produce local lesions (HPV)
- Some viruses spread from urogenital tract (HIV, HSV)



Eye







The fetus

- Transplacental vs perinatal infection
- TORCH pathogens: Toxoplasma, rubella, cytomegalovirus, HIV, other
- Zika virus

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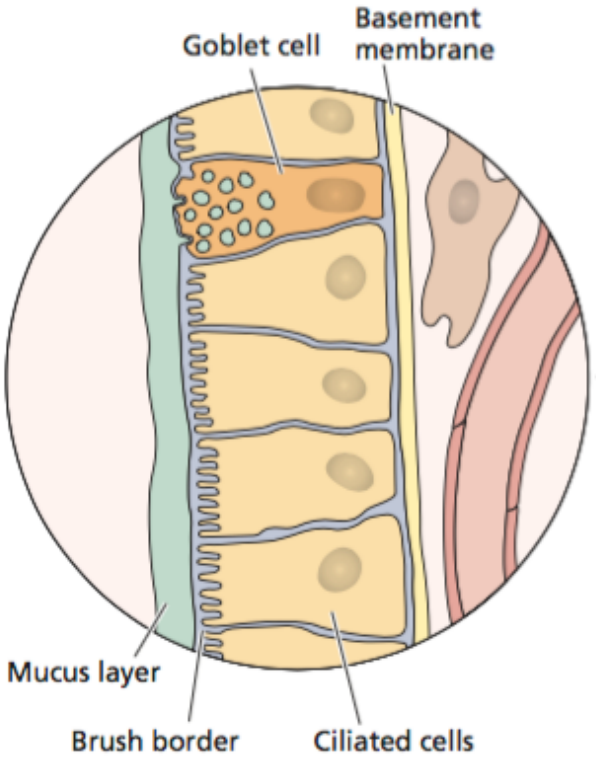
The outer layer of which of the following is dead but can still serve as a portal of virus entry?

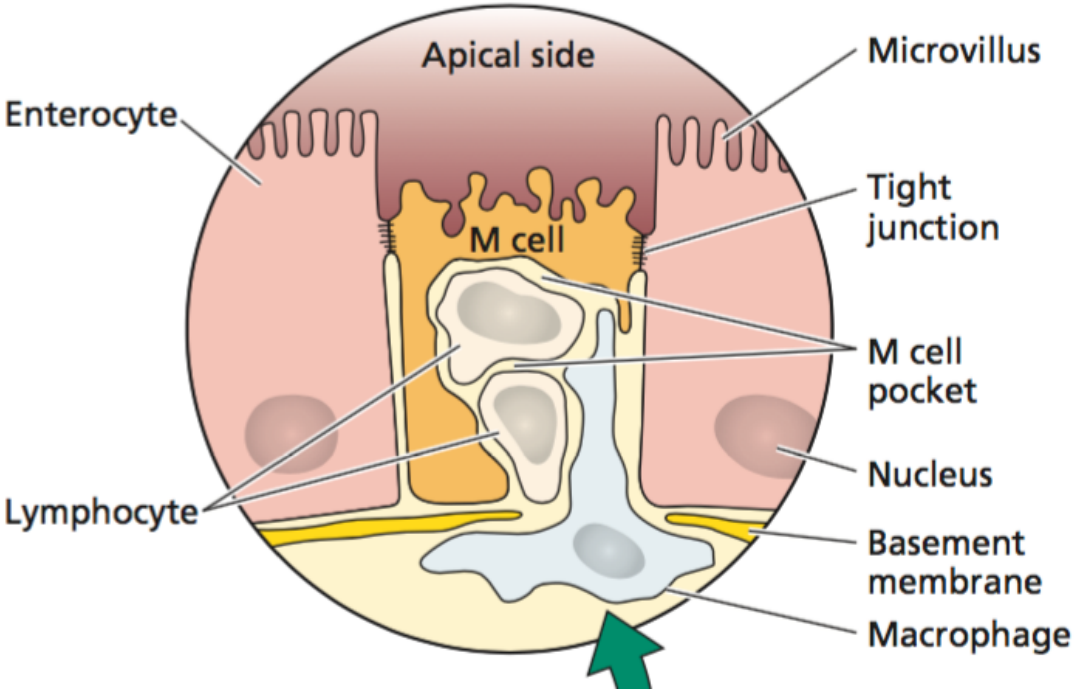
A. Respiratory tract
B. Alimentary tract
C. Eye
D. Skin
E. Urogenital tract

Viral spread

- After replication at the site of entry, viruses may remain **localized**: virus spreads within the epithelium and is contained by tissue structure and immune system
- Some viruses spread beyond the primary site: **disseminated**; if many organs are infected, **systemic**
- Physical and immune barriers must be breached

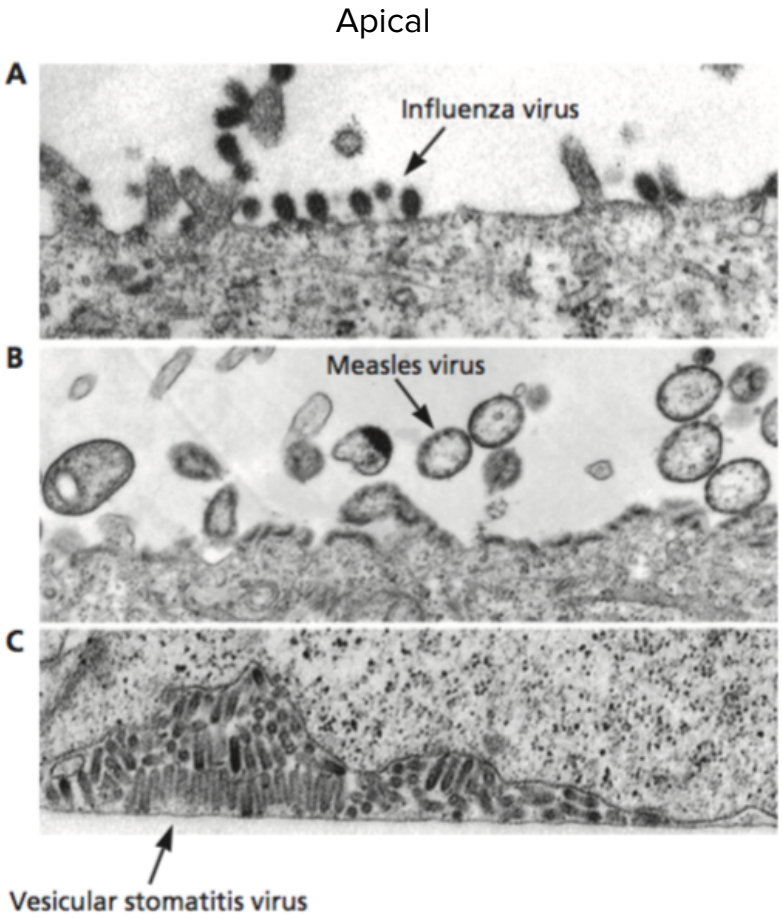


Viral spread

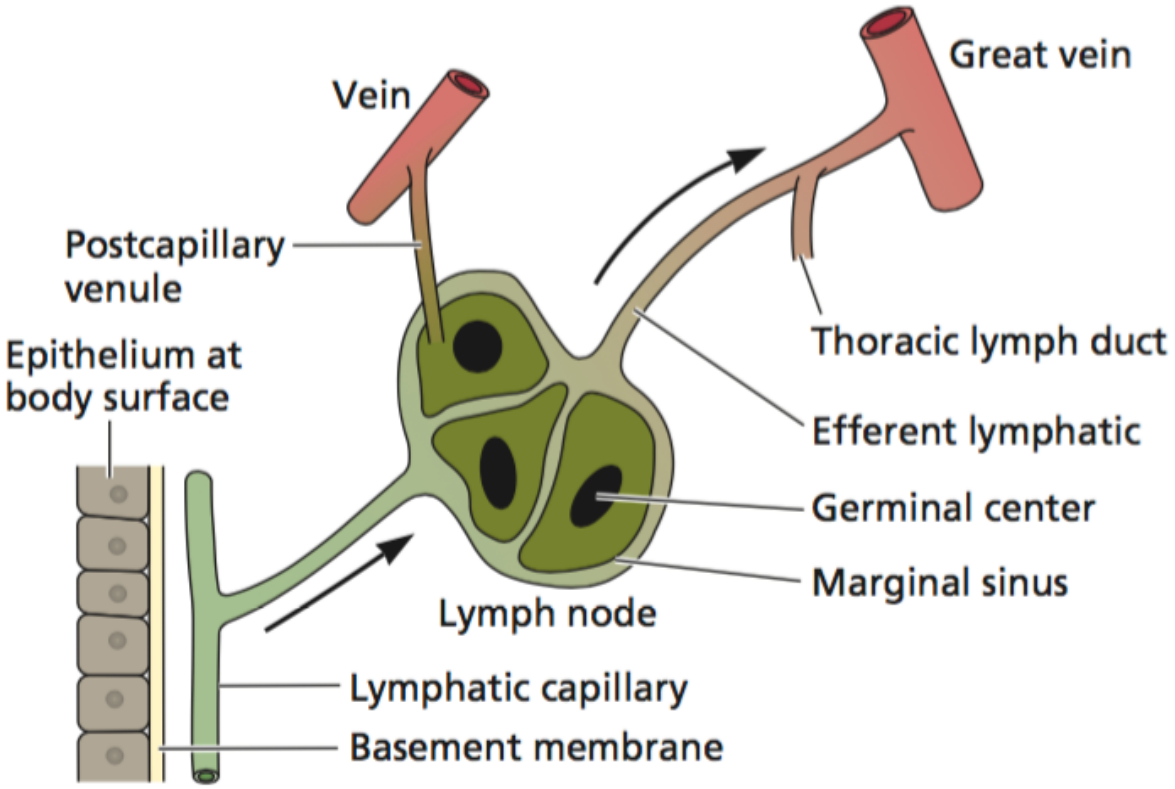


Viral spread

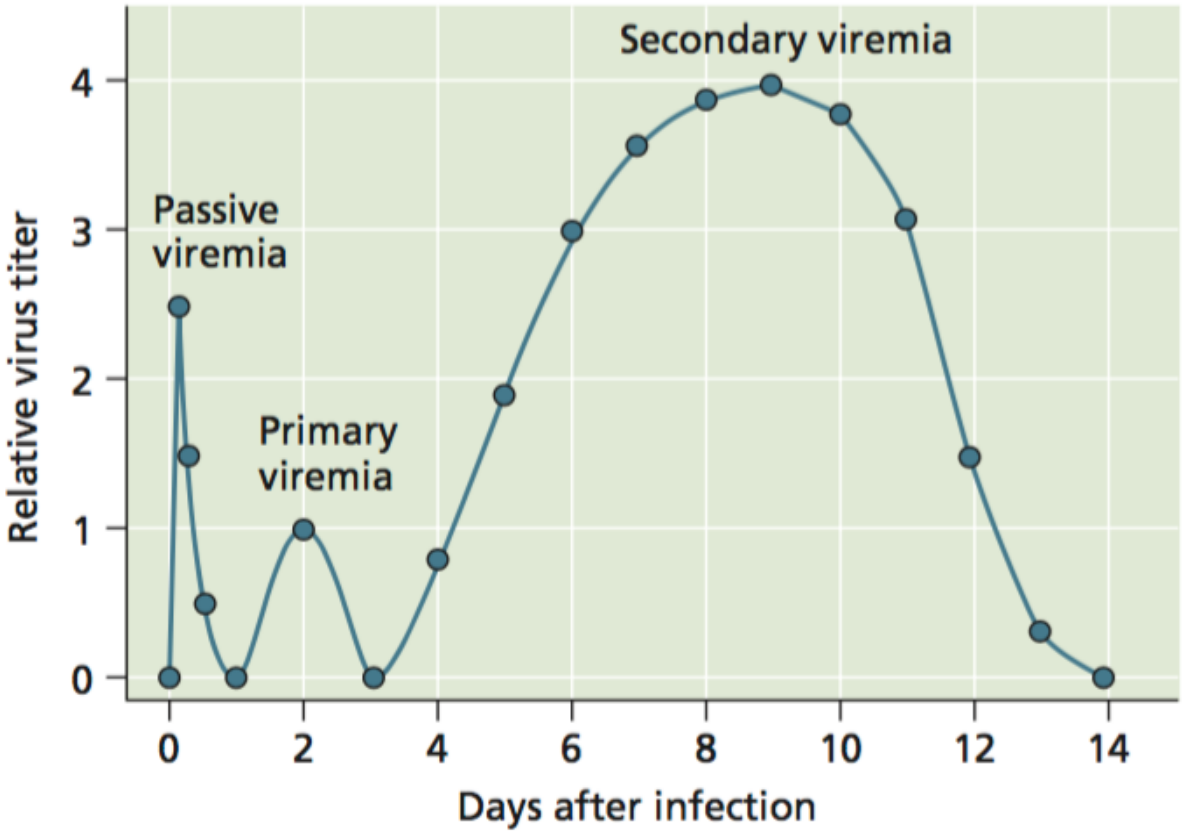
- Apical release facilitates virus dispersal (poliovirus)
- Basolateral release provides access to underlying tissues, may facilitate systemic spread
- Sendai virus



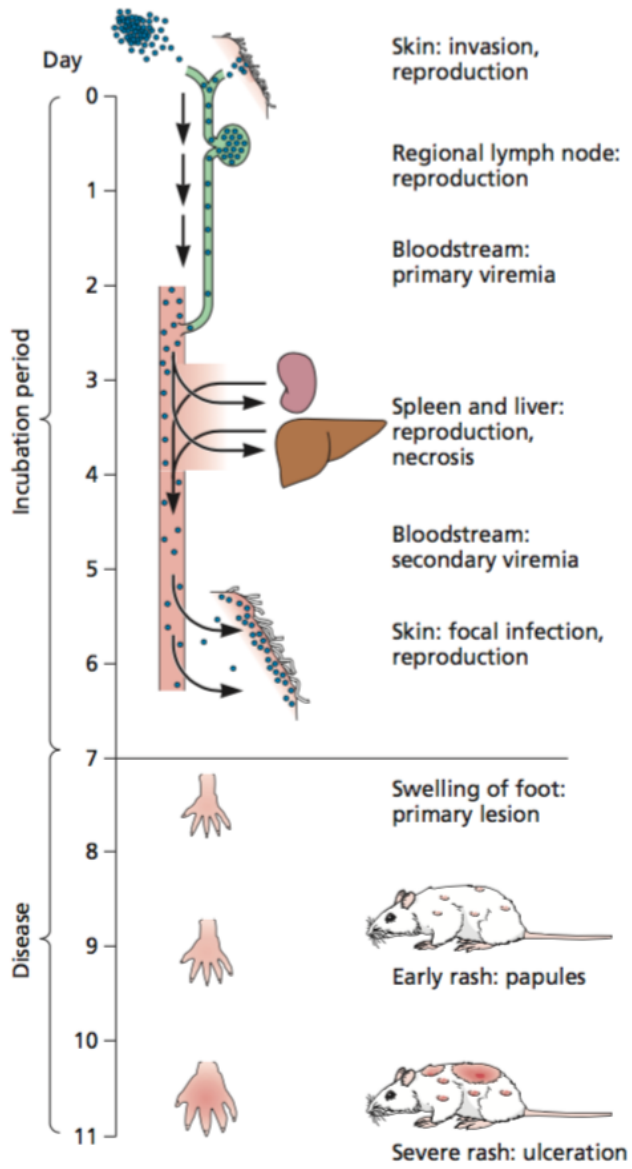
Hematogenous spread

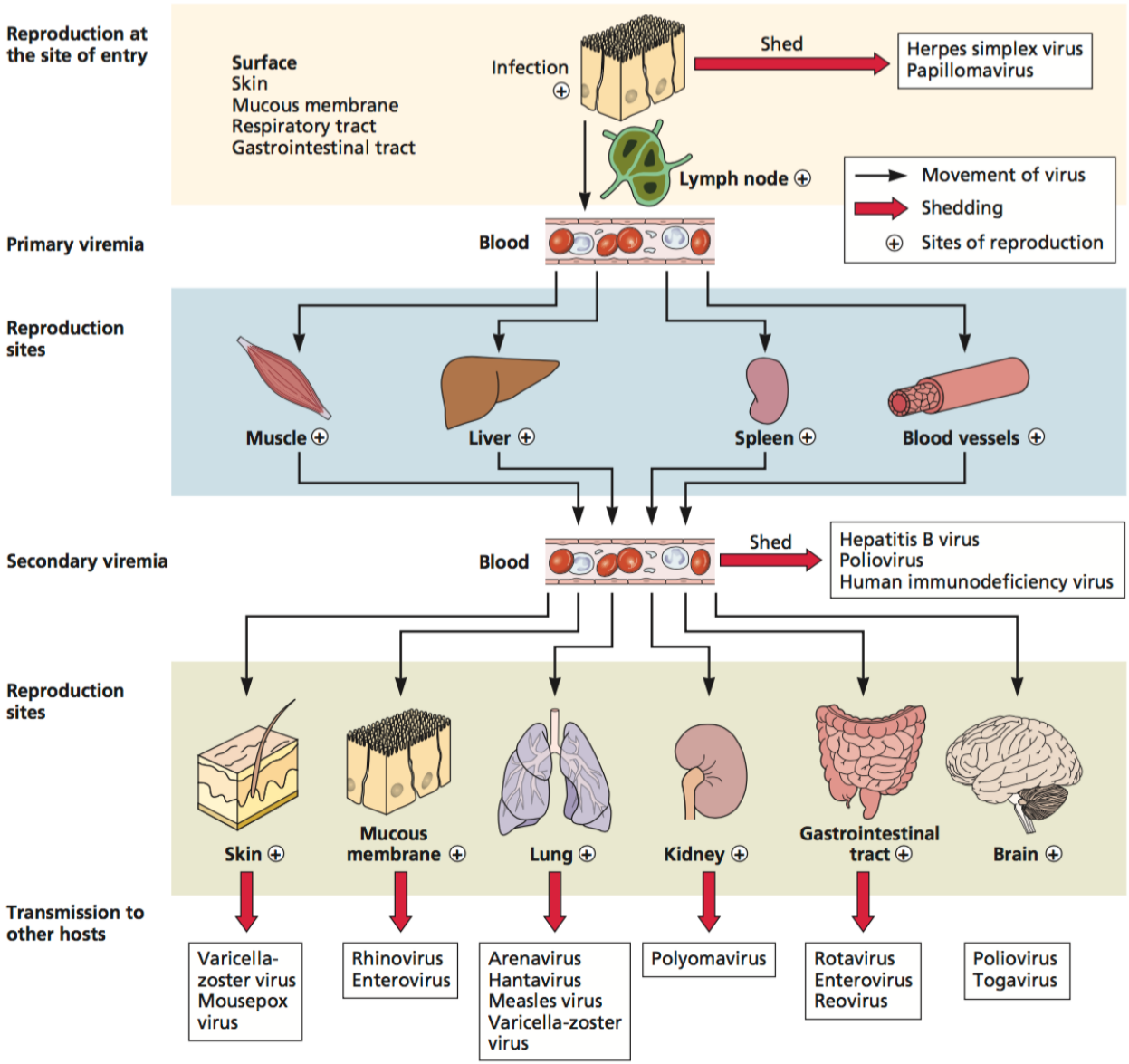


Viremia



Pathogenesis of mousepox





Viruses that cause skin rashes in humans

Virus	Disease	Features
Coxsackievirus A16	Hand-foot-and-mouth disease	Maculopapular rash
Measles virus	Measles	Maculopapular rash
Parvovirus	Erythema infectiosum	Maculopapular rash
Rubella virus	German measles	Maculopapular rash
Varicella-zoster virus	Chickenpox, shingles	Vesicular rash
Zika virus	ZIKV illness	Maculopapular rash

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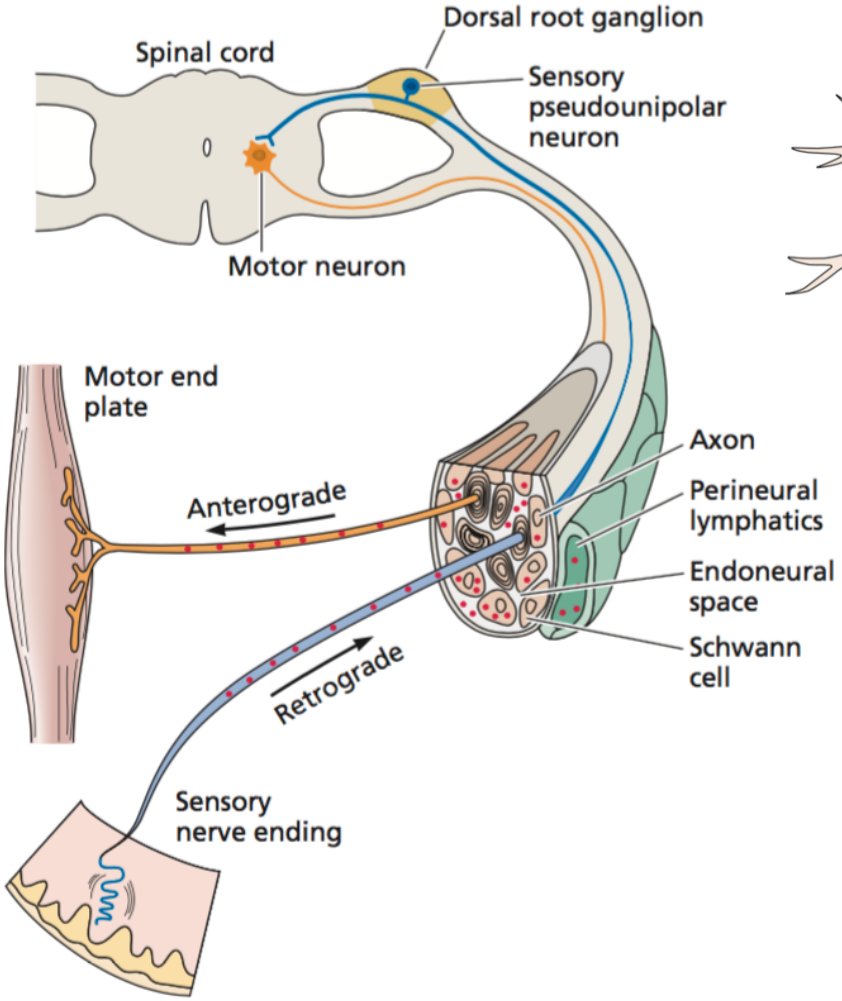
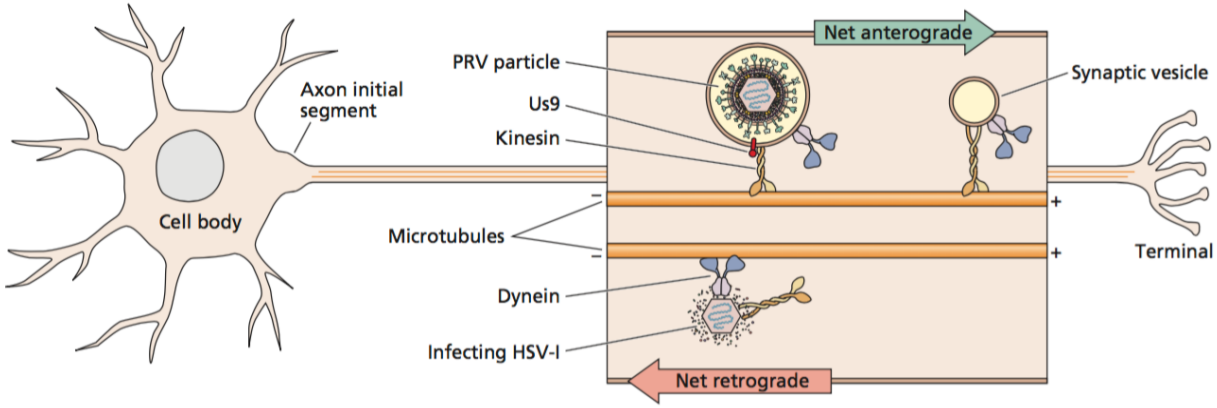
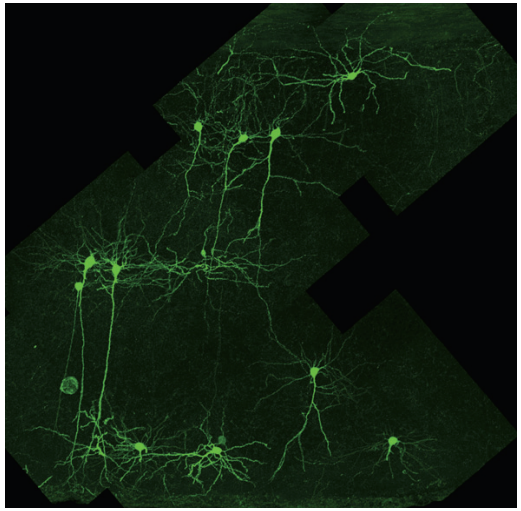
In general, secondary viremia is a consequence of which of the following events?

A. Viral replication in the bloodstream
B. Viral replication at the original site of entry
C. Viral replication in organs distal to the site of entry
D. Viral replication in lymph nodes
E. All of the above

Neural spread



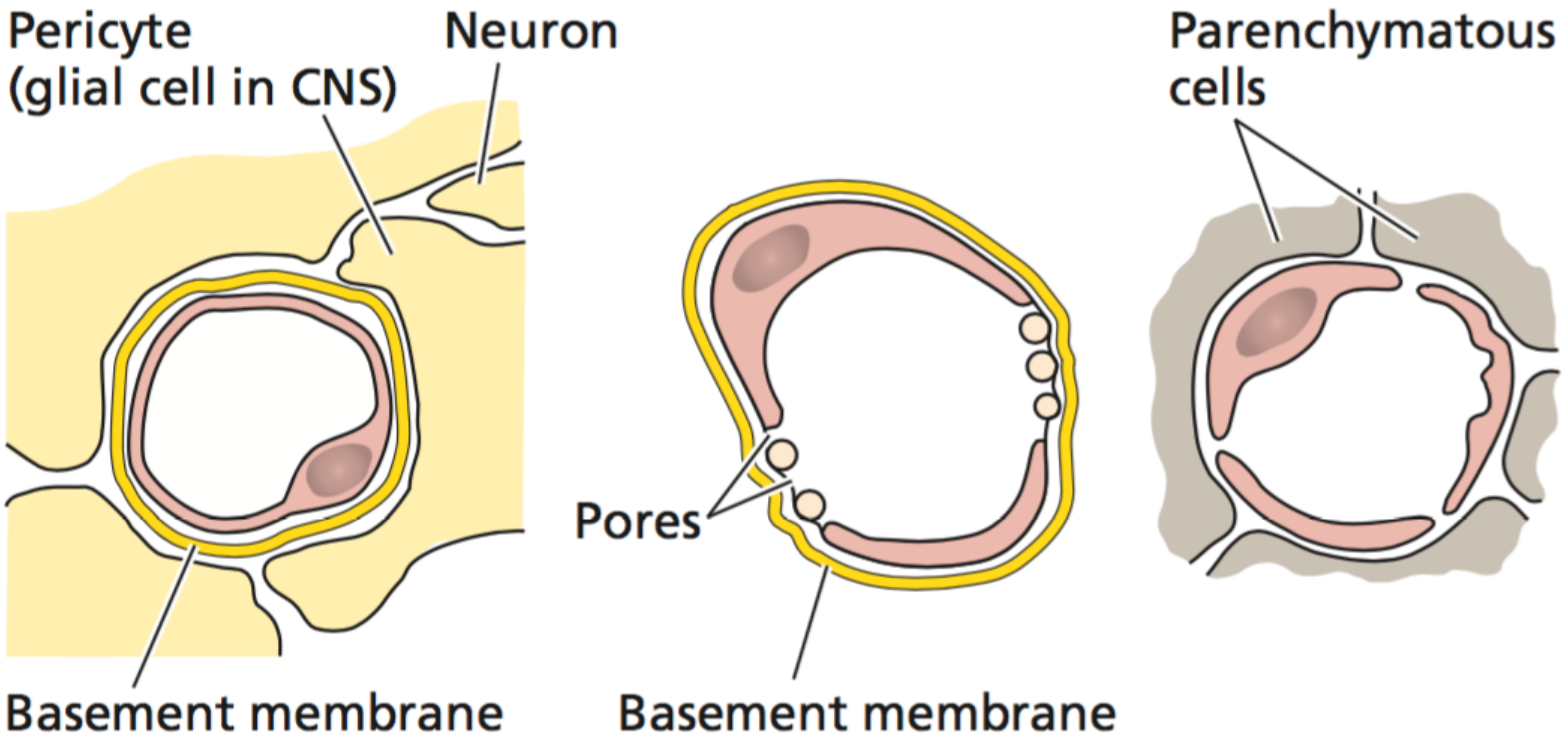




Infections of the CNS

- **Neurotropic** virus can infect neural cells; infection may occur by neural or hematogenous spread from a peripheral site
- **Neuroinvasive** virus can enter the CNS after infection of a peripheral site
- **Neurovirulent** virus can cause disease of nervous tissue
- HSV: low neuroinvasiveness, high neurovirulence
- Mumps: high neuroinvasivness, low neurovirulence
- Rabies: high neuroinvasiveness, high neurovirulence

Tissue invasion



Capillary

CNS, connective tissue, skeletal & cardiac muscle

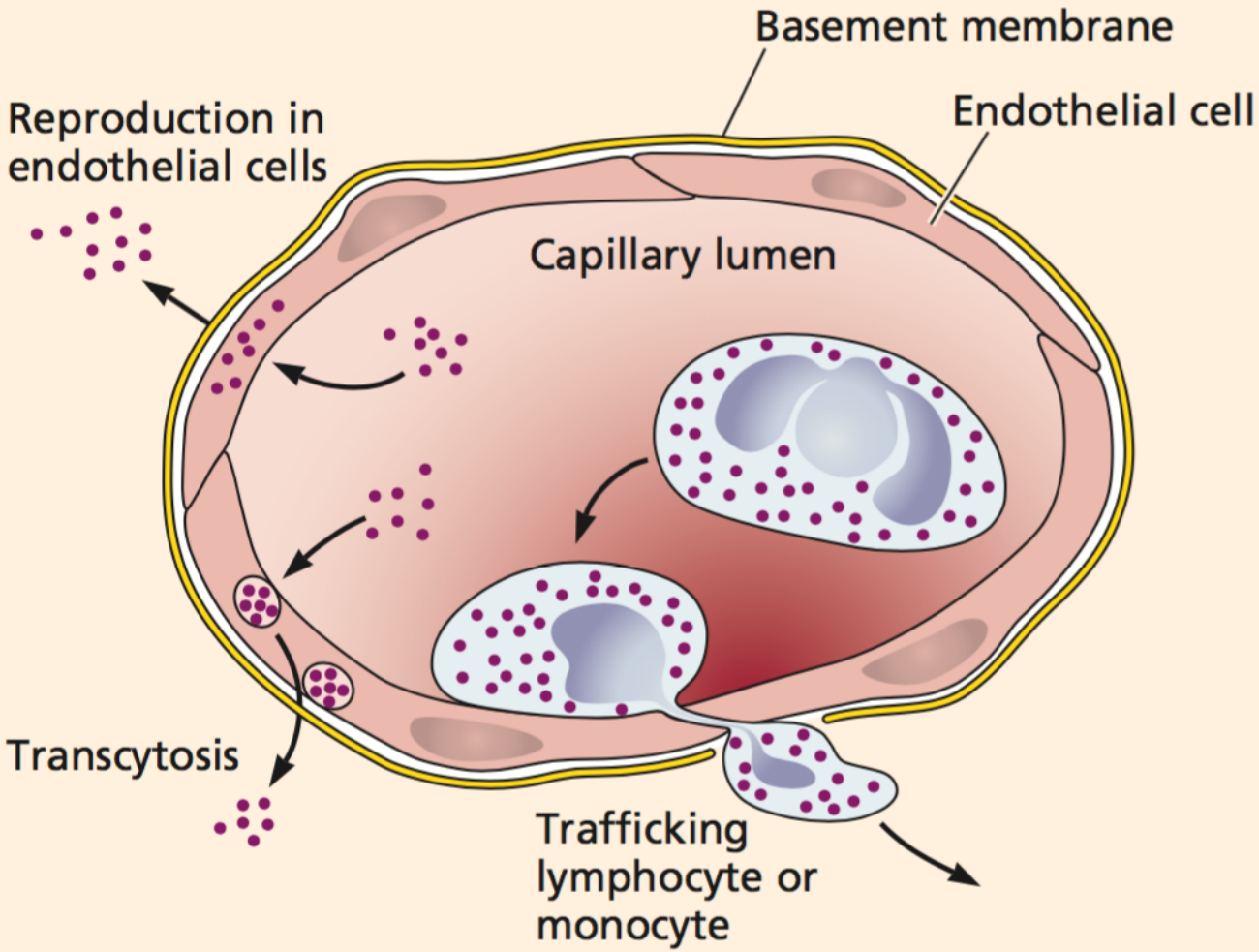
Venule

Renal glomerulus, pancreas, ileum, colon

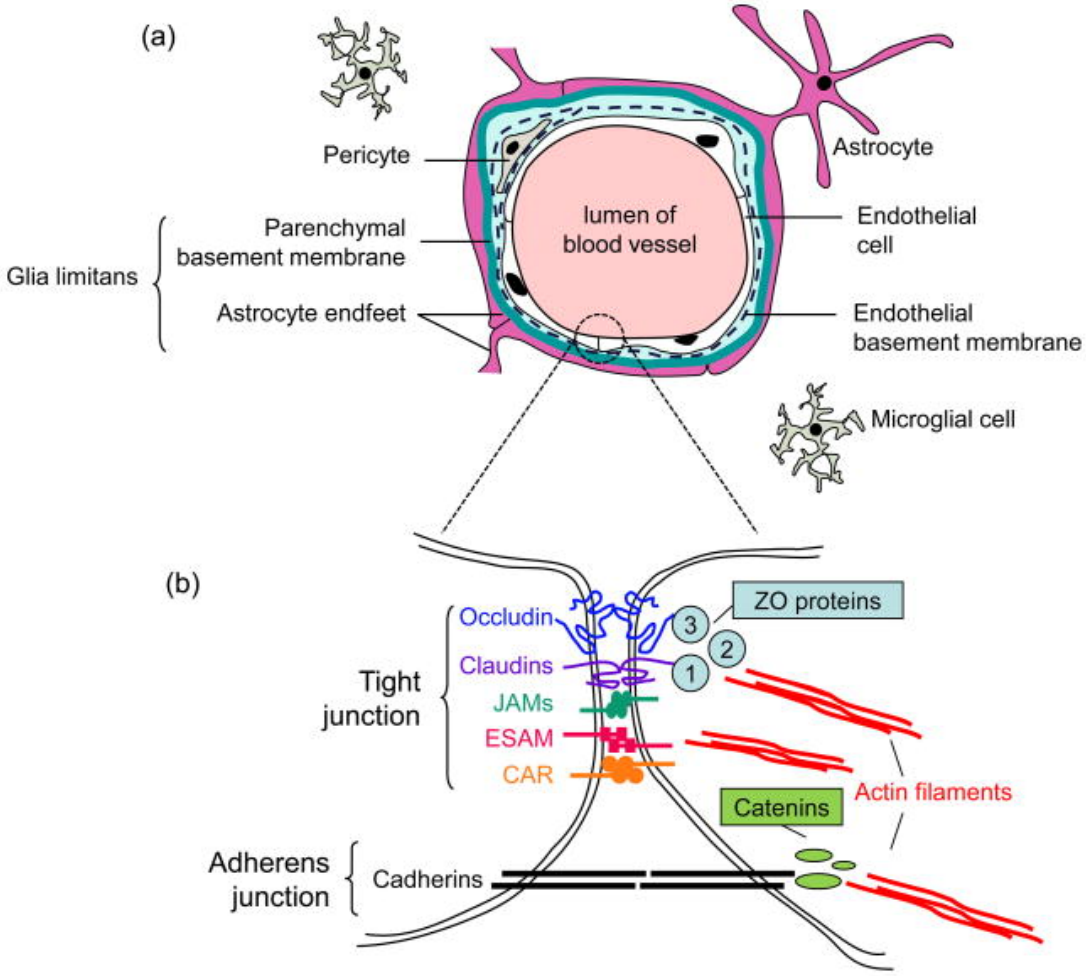
Sinusoid

Liver, spleen, bone marrow, adrenal glands

Blood-brain junction

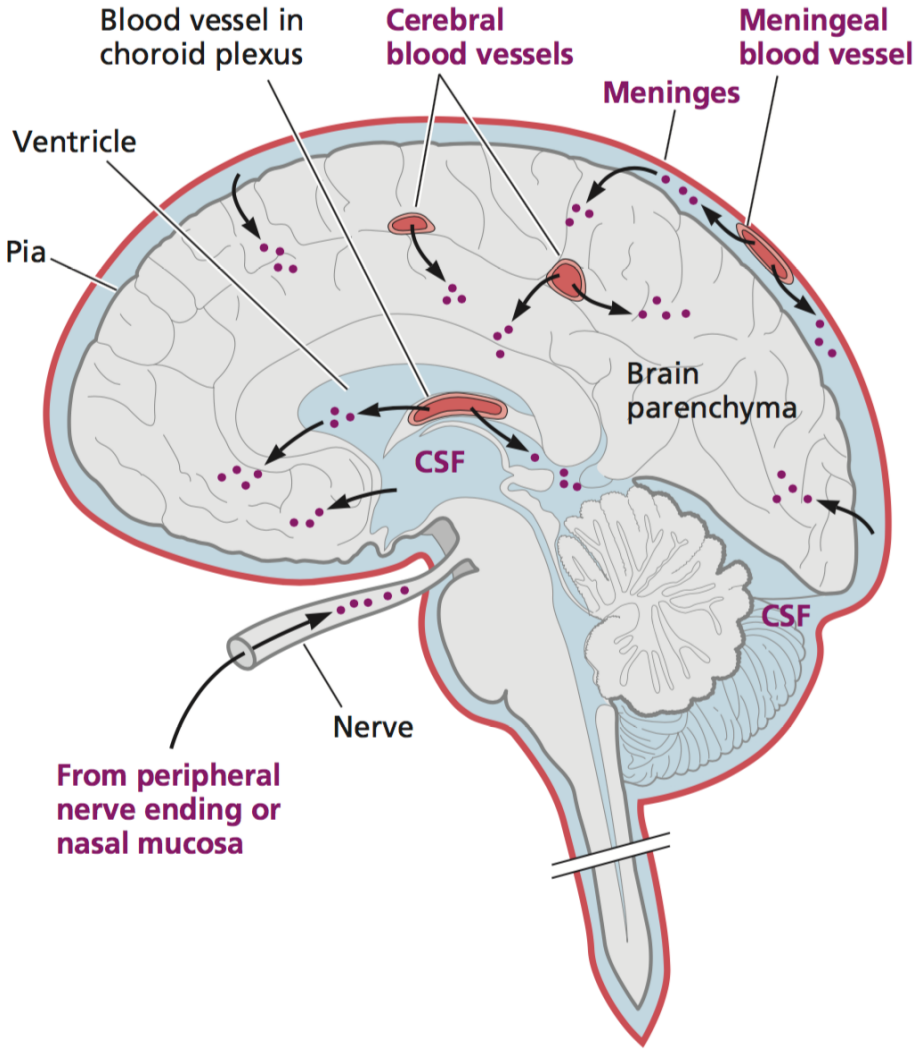


Blood-brain junction



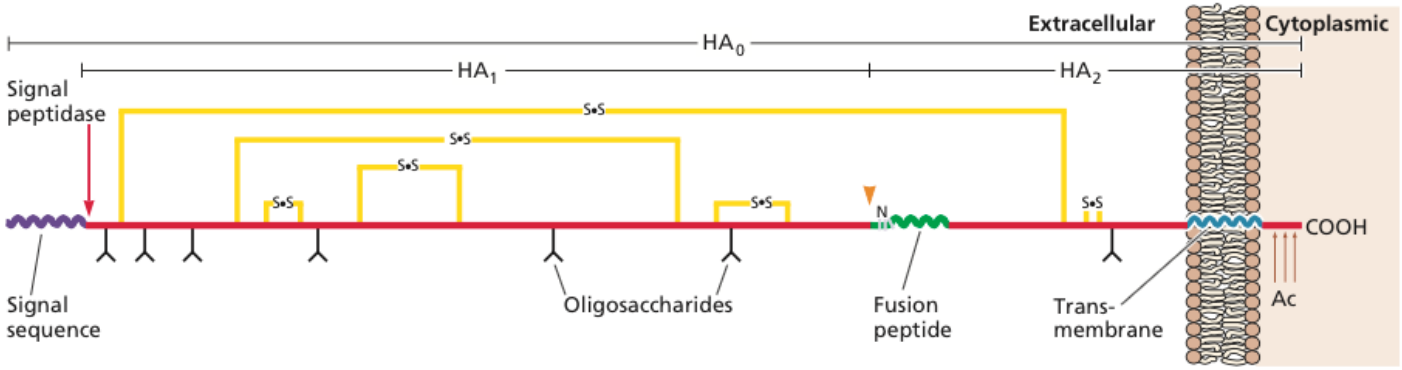
https://www.ncbi.nlm.nih.gov/pubmed/22564250

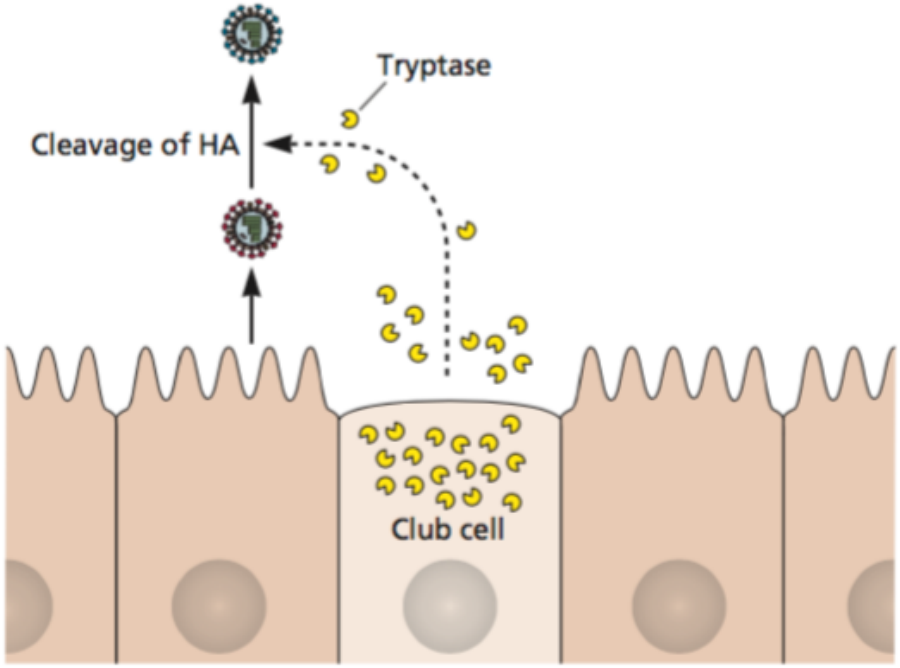
Tissue invasion: CNS



Tissue tropism

- The spectrum of tissues infected by a virus
  - Enterotropic, neurotropic, hepatotropic
- Ranges from limited to pantropic
- Some determinants: Susceptibility, permissivity, accessibility, defense





H5N1

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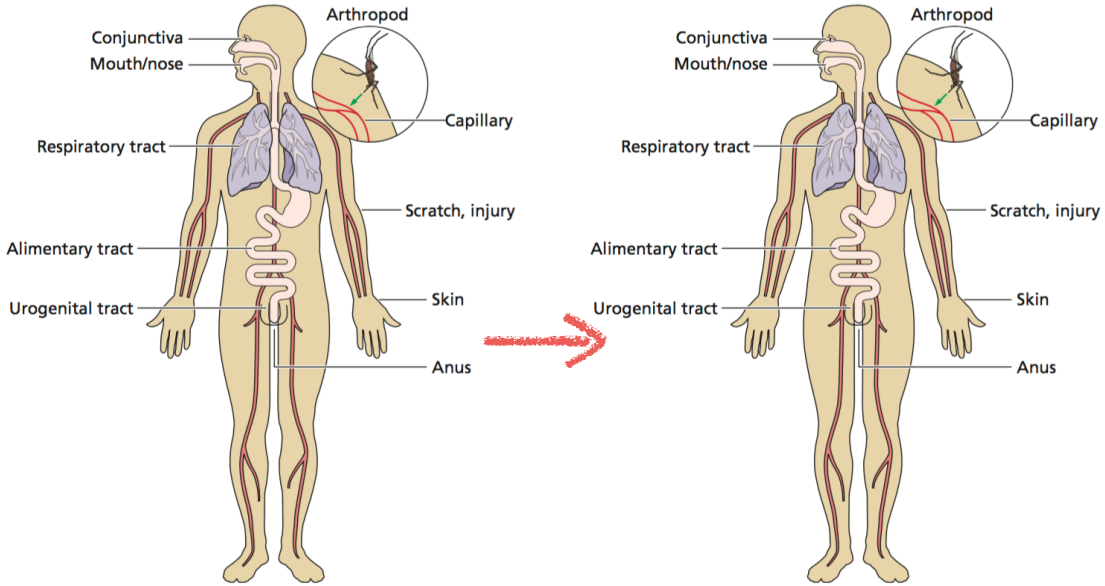
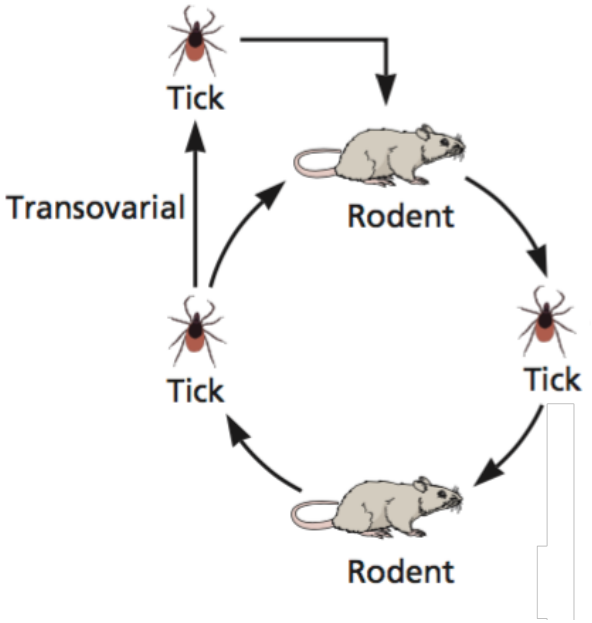
Insertion of multiple basic amino acids at the HA cleavage site allows influenza virus to infect many organs. This means that the _____ of the virus has changed.

A. Susceptibility
B. Club cell tryptase
C. Permissivity
D. Tropism
E. All of the above

Transmission of infection

- Spread of infection from one susceptible host to another; required to maintain chain of infection
- Two general patterns





Transmission terms

- *Horizontal transmission* - between members of same species (*zoonotic* - different species)
- *Iatrogenic* - activity of health care worker leads to infection of patient
- *Nosocomial* - when an individual is infected while in hospital or health care facility
- *Vertical transmission* - transfer of infection between parent and offspring
- *Germ line transmission* - agent is transmitted as part of the genome (e.g. proviral DNA)

Virus shedding

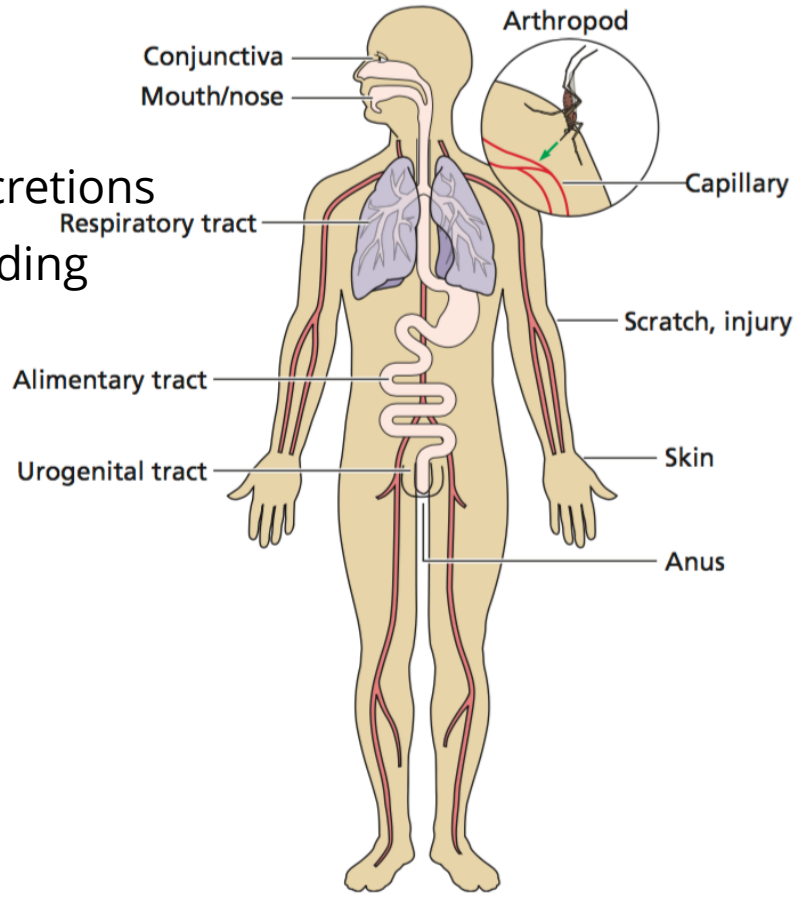
Respiratory secretions

Mucosal shedding

Urine

Semen

Feces



Skin lesions

Blood

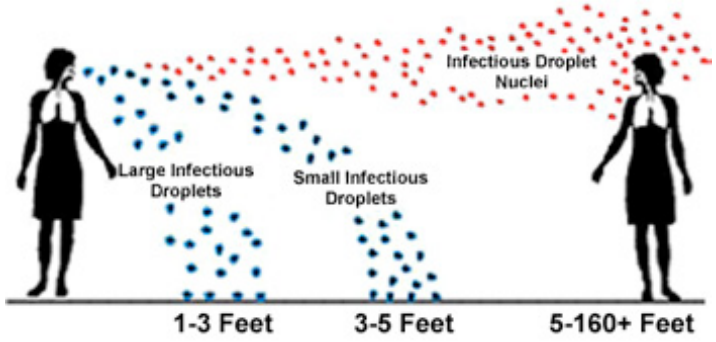
Blood supply

Insect vectors

Germline

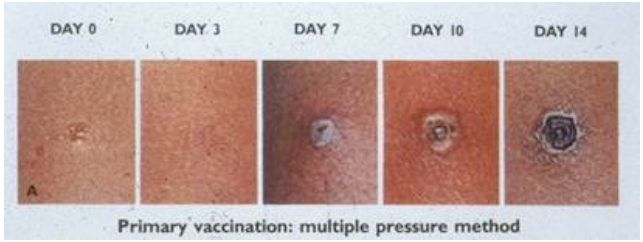
Vertical

Virus shedding



- Respiratory secretions - aerosols produced by coughing, sneezing, speaking
- Nasal secretions contaminating hands, tissues

http://www.virology.ws/2013/01/23/slow-motion-sneezing/



Morbidity and Mortality Weekly Report (*MMWR*)

Secondary and Tertiary Transmission of Vaccinia Virus After Sexual Contact with a Smallpox Vaccinee — San Diego, California, 2012

Weekly
March 1, 2013 / 62(08);145-147

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6208a2.htm

Vaccinia Virus Infection After Sexual Contact with a Military Smallpox Vaccinee --- Washington, 2010

Weekly
July 2, 2010 / 59(25);773-775

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5925a2.htm?s_cid=mm5925a2_w

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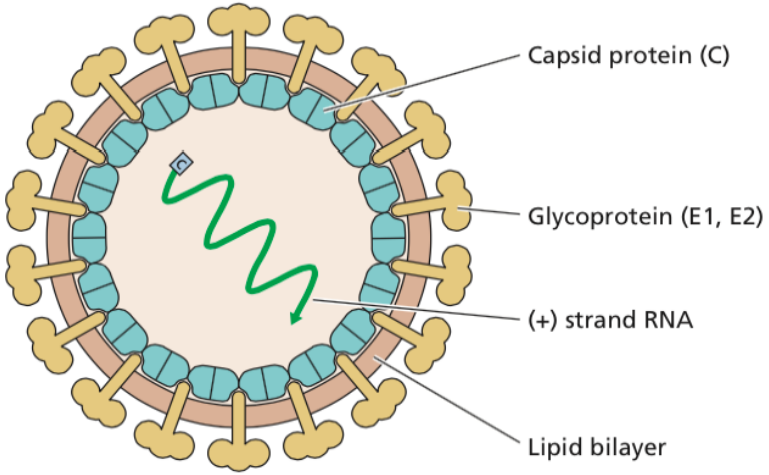
Which statement about viral transmission is not correct?

A. All virus infections are transmitted by shedding
B. The route is determined by the site of virus shedding
C. Transmission is required to maintain a chain of infection
D. Speaking can produce an aerosol that can transmit infection
E. Horizontal transmission is among members of one species

Geography and season

- Geography may restrict presence of virus - requirement for specific vector or animal reservoir
- Chikungunya virus - how vector can affect localization of viral infection

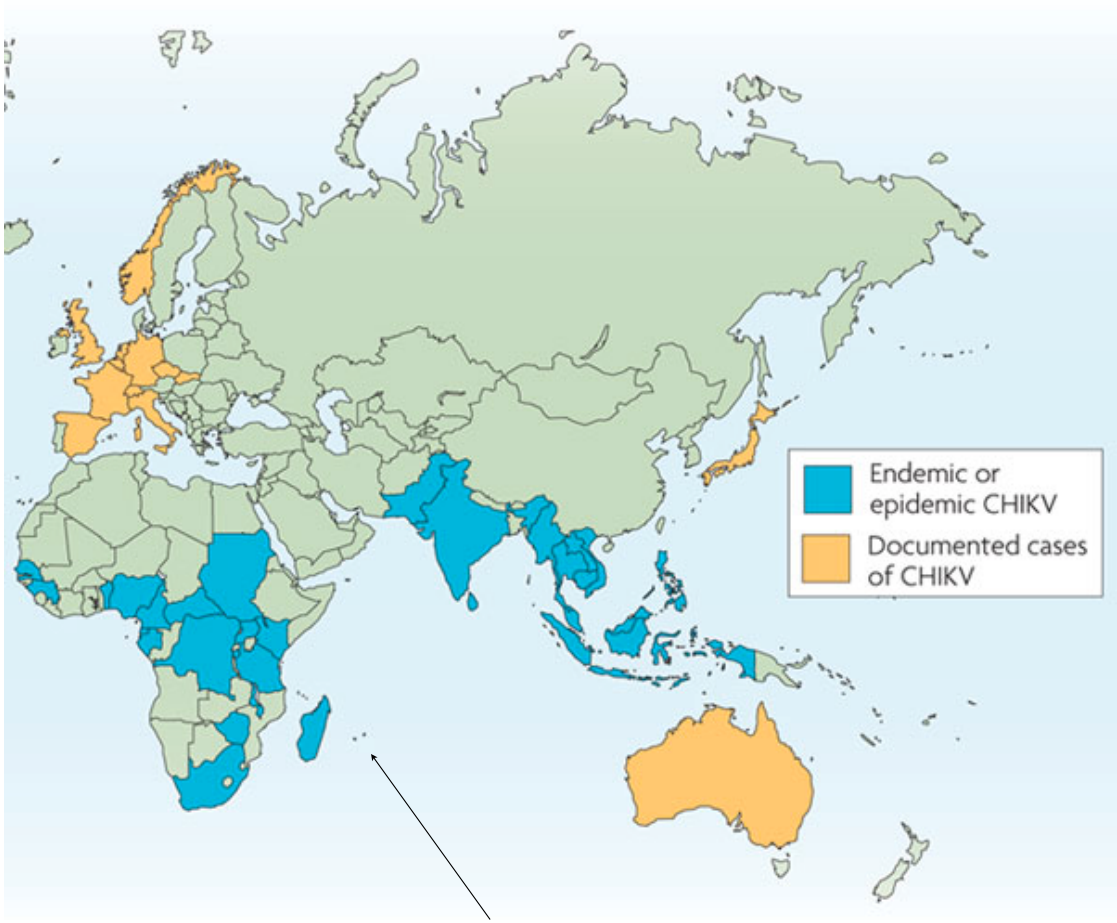
Chikungunya virus



- Togavirus, alphavirus genus
- Spread by *Aedes aegypti*
- Rash, fever, joint pains

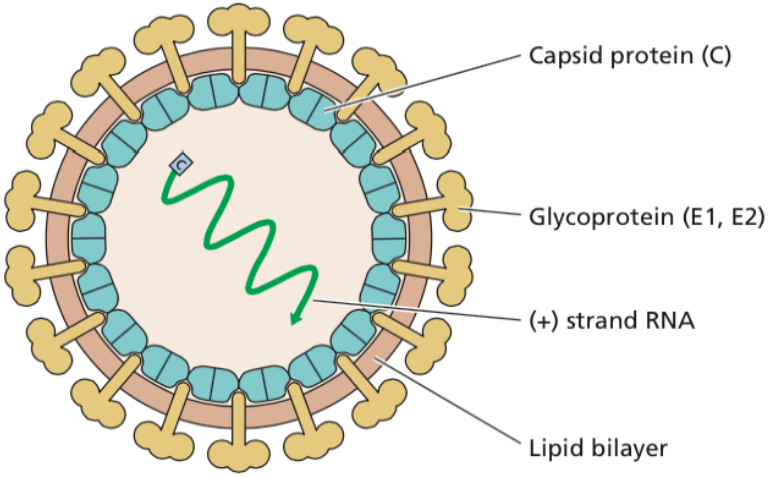
Chikungunya virus

- Asia, Africa, never Europe or US
- 2004 - outbreaks spread from Kenya to India
- 2007 - outbreak in Italy, first in Europe



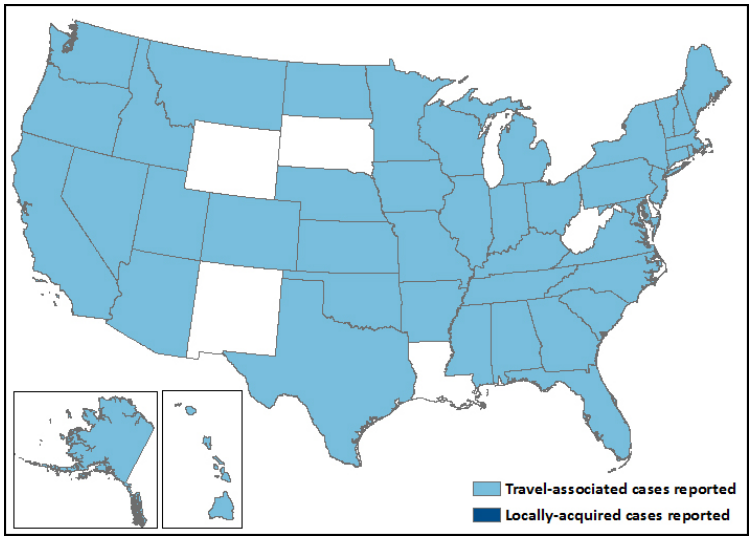
Réunion

Chikungunya virus



- Recent outbreaks associated with *Aedes albopictus*
- One amino acid change in viral E1 glycoprotein

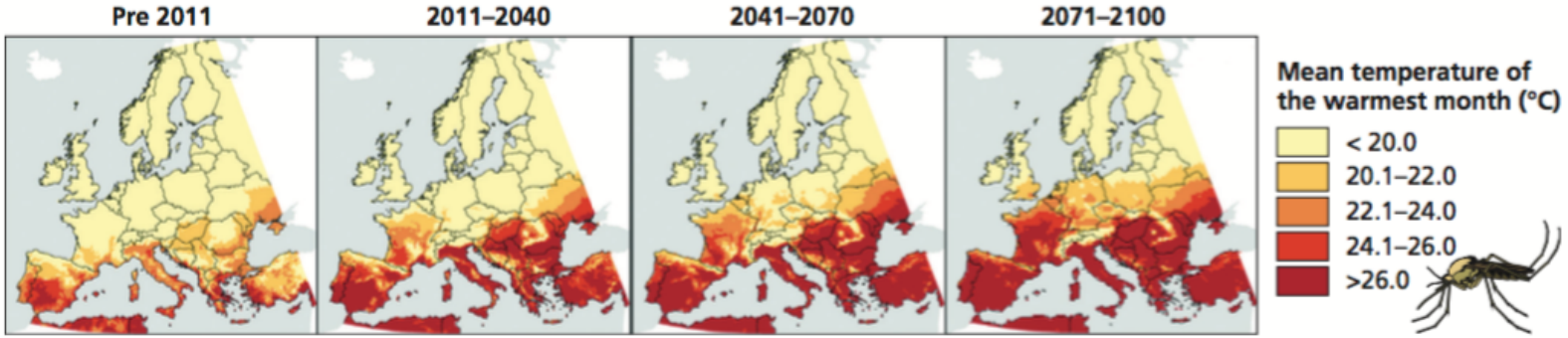
Aedes albopictus



Chikungunya virus infections, US

679 cases, no local transmission
(rare before 2006)

A. albopictus range



Seasonality of virus infections