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

Gaining access: site of entry is critical
Mucosal surfaces are ripe for viral infection

Lined by living cells
<table>
<thead>
<tr>
<th>Site of reproduction</th>
<th>Clinical manifestation</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turbinate &quot;baffles&quot;</td>
<td>Rhinitis (common cold)</td>
<td>Rhinovirus, Coronavirus, Parainfluenza virus, Respiratory syncytial virus</td>
</tr>
<tr>
<td>Tonsillar lymphoid tissues</td>
<td>Pharyngitis</td>
<td>Influenza virus, Adenovirus, Herpes simplex virus, Epstein-Barr virus</td>
</tr>
<tr>
<td>Palate, Tongue</td>
<td>Laryngitis</td>
<td></td>
</tr>
<tr>
<td>Cervical lymph node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus, Trachea</td>
<td>Tracheitis</td>
<td>Parainfluenza virus, Respiratory syncytial virus, Influenza virus</td>
</tr>
<tr>
<td>Bronchi, Bronchioles</td>
<td>Bronchitis</td>
<td>Adenovirus, Measles, SARS, MERS</td>
</tr>
<tr>
<td>Bronchial lymph node</td>
<td>Bronchiolitis</td>
<td></td>
</tr>
<tr>
<td>Alveolus, Alveolar macrophage</td>
<td>Bronchopneumonia</td>
<td></td>
</tr>
</tbody>
</table>
Alimentary tract

- Conjunctiva
- Mouth/nose
- Respiratory tract
- Alimentary tract
- Urogenital tract
- Arthropod
- Capillary
- Scratch, injury
- Skin
- Anus

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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
• 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

subconjunctival bleed
The fetus

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

![Graph showing the progression of viremia over time. The graph indicates three phases: Passive viremia, Primary viremia, and Secondary viremia. The y-axis represents the relative virus titer, and the x-axis represents days after infection.]
Pathogenesis of mousepox
# Viruses that cause skin rashes in humans

<table>
<thead>
<tr>
<th>Virus</th>
<th>Disease</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coxsackievirus A16</td>
<td>Hand-foot-and-mouth disease</td>
<td>Maculopapular rash</td>
</tr>
<tr>
<td>Measles virus</td>
<td>Measles</td>
<td>Maculopapular rash</td>
</tr>
<tr>
<td>Parvovirus</td>
<td>Erythema infectiosum</td>
<td>Maculopapular rash</td>
</tr>
<tr>
<td>Rubella virus</td>
<td>German measles</td>
<td>Maculopapular rash</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
<td>Chickenpox, shingles</td>
<td>Vesicular rash</td>
</tr>
<tr>
<td>Zika virus</td>
<td>ZIKV illness</td>
<td>Maculopapular rash</td>
</tr>
</tbody>
</table>
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

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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 neuroinvasiveness, low neurovirulence
- Rabies: high neuroinvasiveness, high neurovirulence
Tissue invasion

- Pericyte (glial cell in CNS)
- Neuron
- Parenchymatous cells

**Capillary**
- CNS, connective tissue, skeletal & cardiac muscle

**Venule**
- Renal glomerulus, pancreas, ileum, colon

**Sinusoid**
- Liver, spleen, bone marrow, adrenal glands

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Blood-brain junction

(a)
- Pericyte
- Parenchymal basement membrane
- Astrocyte endfeet
- Endothelial cell
- Endothelial basement membrane
- Microglial cell

(b)
- Tight junction
  - Occludin
  - Claudins
  - JAMs
  - ESAM
  - CAR
- Adherens junction
  - Cadherins
- ZO proteins
- Catenins
- Actin filaments

Tissue invasion: CNS

Blood vessel in choroid plexus
Cerebral blood vessels
Meningeal blood vessel
Meninges
Ventricle
Pia
Brain parenchyma
CSF
Nerve
From peripheral nerve ending or nasal mucosa
Tissue tropism

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

m.socrative.com
room number: virus

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

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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
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
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

A Rubella, 1963–1968

B Influenza, 1994–1999

C Poliomyelitis, 1956–1957

Latitude

35–70°N (Anchorage AK; 61°N)

10–35°N (Tel Aviv, Israel; 32°N)

10°N–10°S (Bogata, Columbia; 4°N)

10–25°S (Rio de Janiero, Brazil; 22°S)

25–55°S (Perth, Australia; 31°S)

Monthly percentage of cases