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
<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</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>Cervical lymph node</td>
<td>Laryngitis</td>
<td>Parainfluenza virus, Respiratory syncytial virus, Influenza virus, Adenovirus, Measles, SARS, MERS</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Tracheitis</td>
<td></td>
</tr>
<tr>
<td>Bronchi</td>
<td>Bronchitis</td>
<td></td>
</tr>
<tr>
<td>Bronchioles</td>
<td>Bronchiolitis</td>
<td></td>
</tr>
<tr>
<td>Bronchial lymph node</td>
<td>Bronchopneumonia</td>
<td></td>
</tr>
<tr>
<td>Alveolus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar macrophage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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

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

1. Respiratory tract
2. Alimentary tract
3. Eye
4. Skin
5. 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

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

- Vein
- Great vein
- Postcapillary venule
- Epithelium at body surface
- Lymph node
  - Germinal center
  - Marginal sinus
- Lymphatic capillary
- Basement membrane
- Thoracic lymph duct
- Efferent lymphatic

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Pathogenesis of mousepox

- **Day 0**: Skin: invasion, reproduction
- **Day 1**: Regional lymph node: reproduction
- **Day 2**: Bloodstream: primary viremia
- **Days 3-4**: Spleen and liver: reproduction, necrosis
- **Days 5-6**: Bloodstream: secondary viremia
- **Days 7-11**: Skin: focal infection, reproduction
- **Day 7**: Swelling of foot: primary lesion
- **Days 8-9**: Early rash: papules
- **Day 10**: Severe rash: ulceration

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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?

1. Viral replication in the bloodstream
2. Viral replication at the original site of entry
3. Viral replication in organs distal to the site of entry
4. Viral replication in lymph nodes
5. 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

- Liver, spleen, bone marrow, adrenal glands
- Renal glomerulus, pancreas, ileum, colon
- Liver, spleen, bone marrow, adrenal glands

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

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

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

• The spectrum of tissues infected by a virus
  - Enterotrophic, neurotrophic, hepatotropic
• Ranges from limited to pantropic
• Some determinants: Susceptibility, permissivity, accessibility, defense
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.

1. Susceptibility
2. Club cell tryptase
3. Permissivity
4. Tropism
5. 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
Go to:

m.socrative.com
room number: virus

Which statement about viral transmission is not correct?

1. All virus infections are transmitted by shedding
2. The route is determined by the site of virus shedding
3. Transmission is required to maintain a chain of infection
4. Speaking can produce an aerosol that can transmit infection
5. 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

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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 *A. albopictus*
- One amino acid change in viral E1 glycoprotein
Aedes albopictus

Chikungunya virus infections, US

679 cases, no local transmission (rare before 2006)
Seasonality of virus infections

A Rubella, 1963–1968

B Influenza, 1994–1999

C Poliomyelitis, 1956–1957

Monthly percentage of cases

Latitude

35–70°N (Anchorage AL; 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)