Infection Basics

Lecture 12
Biology W3310/4310
Virology
Spring 2015

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 literal 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 (antibody positive)
  - 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.
Many virions that land on the skin are inactivated by desiccation, acids (pH 5.5), or other inhibitors formed by our cells or by commensal microorganisms (eg antimicrobial peptides)
Mucosal surfaces are ripe for viral infection

Lined by living cells

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Alimentary tract

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

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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
Urogenital tract
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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

- Localized
- Disseminated and systemic

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Viral spread

- Enterocyte
- Microvillus
- Tight junction
- M cell
- M cell pocket
- Nucleus
- Basement membrane
- Macrophage
- Apical side
- Lymphocyte
Viral spread

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

Days after infection

Relative virus titer

0  2  4  6  8  10  12  14

Primary viremia

Secondary viremia

Passive viremia

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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>
</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

- Virus spread from primary site of infection by entering local nerve endings

- For some (rabies, alpha herpesviruses) neural spread is definitive characteristic of pathogenesis

- For others (poliovirus, reovirus) invasion of the CNS is an infrequent diversion from normal replication and hematogenous spread
Spread of virus in nerves

A

Transport

Transsynaptic spread

Transport

Axon

Replication

Replication

Uptake

Retrograde spread

B

Transsynaptic spread

Transport

Transport

Uptake

Replication

Replication

Anterograde spread

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Movement of virus in nerves
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

- Liver
- Spleen
- Bone marrow
- Adrenal glands
- Renal glomerulus
- Pancreas
- Ileum
- Colon
- CNS
- Connective tissue
- Skeletal & cardiac muscle
- Parenchymatous cells

- Pericyte (glial cell in CNS)
- Neuron
- Basement membrane
- 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

- Replication in endothelial cells
- Transcytosis
- Trafficking lymphocyte or monocyte
- Basement membrane
- Endothelial cell

Capillary lumen

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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
- Urine
- Semen
- Feces
- Mucosal shedding
- Skin lesions
- Blood
- Insect vectors
- Vertical blood supply
- Germline
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/
Primary vaccination: multiple pressure method

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?

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
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
Chikungunya virus infections, US
n=45

PR, USVI, locally transmitted cases (n=44, 1)

http://www.virology.ws/2009/03/18/chikungunya-an-exotic-virus-on-the-move/
Seasonality of virus infections
Seasonal factors that affect influenza virus transmission

- Virus particles are stable; droplet nuclei form at 5°C.
- Virus particles are unstable at 20°C.
- Droplet nuclei take on water and are no longer airborne at 20°C.

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