BBS2711
VIROLOGY

VIRAL PATHOGENESIS

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Evolutionary conflict is the basis of viral pathogenesis

Both the host & the virus are seeking a reproductive advantage

- new viruses are evolving continuously.
- natural selection favours viruses with low pathogenicity/ virulence (so they don't eradicate their hosts)
  - most viral infections are asymptomatic
  - disease is an “unusual” consequence of infection.

DEFINITIONS

Pathogenicity [Gr. "pathos", pain]: ability to cause disease

Pathogen: organism able to cause disease

Pathogenesis: means by which organism produces disease in host.

A result of:
- injury to discrete populations of cells
- in particular target organs
- producing signs & symptoms of disease in a given host.

Virulence: “capacity” to produce disease

Extent of disease dependent on:

VIRUS **dose**
route of entry
replication efficiency

HOST factors which modify viral pathogenesis 1

• **Virus receptors** - genetically determined or due to the state of differentiation.

1. HIV-1. The primary cellular receptor for HIV-1 (CD4) is found only on T helper cells and monocytes, and the HIV entry cofactors (CCR5, CXCR4) are likewise expressed on these cell types.
   - people with two copies of a mutant CCR5 allele have a reduced susceptibility to HIV-1 infection.

2. Rhinovirus. The rhinovirus receptor (ICAM-1) is found on epithelium of upper respiratory tract.

• **Age**

certain infections are more severe in different age groups.

less severe before puberty, e.g. EBV infections and mononucleosis, measles, VZV (chickenpox) and polio
- immune system maturity
- hormonal influences

HOST factors which modify viral pathogenesis 2

• Metabolic state.

Generalized malnutrition or Vitamin A deficiency increase susceptibility to, and severity of, measles infection.

Pregnancy (with its associated change in hormonal balance) can also lead to altered susceptibility to certain viruses.

• "Altered" immune responses

Impaired

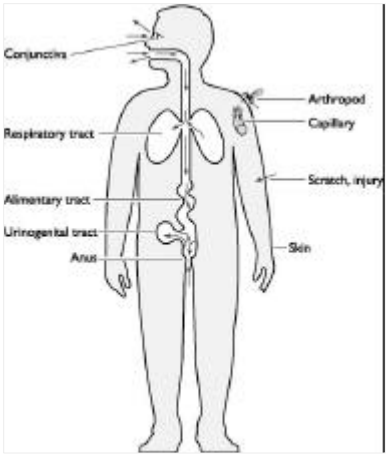
1.genetically determined, e.g. agammaglobulinemia
2.acquired as a consequence of infection, e.g. HIV
3.iatrogenically (therapeutically) acquired, e.g. after transplant

Enhanced

1. auto-immunity
2. higher incidence of DHF in females

Despite diversity of both viruses and hosts
- common overall strategies in viral-host interactions

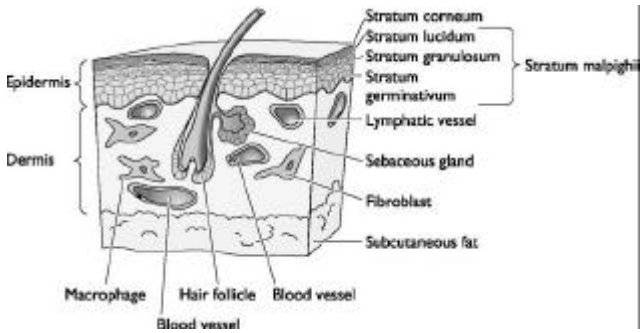
Loosely categorized as:
- Routes of entry
- Localization and spread
- Shedding of virus and transmission



Routes of entry

- skin
- respiratory tract
- gastrointestinal tract
- genitourinary tract
- conjunctiva

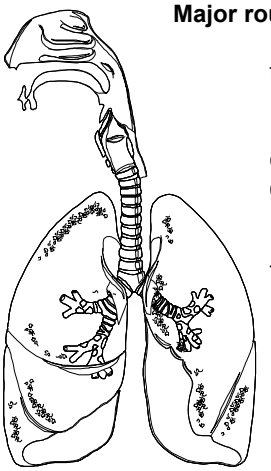
Skin



May be penetrated by viruses as a result of
- mechanical trauma (HPV,HIV, HSV, HBV, poxvirus)
- by injection (HBV, HIV)
- by the bite of an infected mosquito (arboviruses)
  either mechanical or true insect-borne
- by the bite of an infected animal (rabies)

Generally viruses do not multiply locally but are carried away from site of infection:
by bloodstream (HBV, arboviruses)
or migration along nerves (rabies)

Respiratory Tract

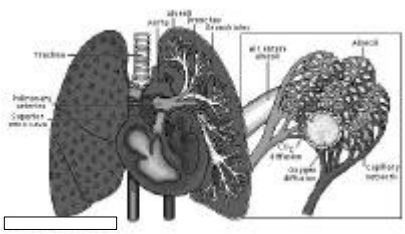


Major route of invasion:

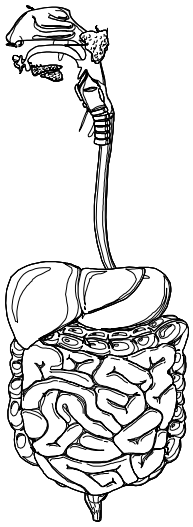
for viruses causing local respiratory infections
- flu, RSV, rhinoviruses

others causing asymptomatic initial infection then generalized spread
- measles, mumps, chickenpox, enteroviruses

Transmission usually by droplet infection in aerosols



Gastrointestinal Tract



Entry via GI tract may involve

- local infection (rotavirus, coronavirus, adenovirus) or
- invasion of the host to produce systemic illness (enteroviruses, hepatitis A)

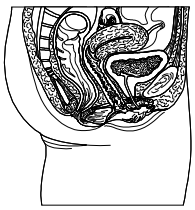
- due to invasion of tissues underlying the mucosal layer

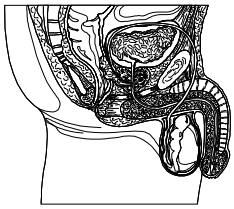
Virus survival depends on:

acid stability
resistance to bile salts
inactivation by proteolytic enzymes
- in some cases a requirement!

Most non-enveloped
survival mechanism for coronaviruses in presence of bile salts unknown

Genitourinary Tract





Tears or abrasions allow viral entry

Sexually transmitted viruses

- HIV
- herpes simplex (mostly HSV II)
- papillomaviruses (genital warts)
- hepatitis B virus.

Nature of cervical mucus, the pH of vaginal secretions and the chemical composition of urine all play a role in host defence.

LOCALIZATION AND SPREAD

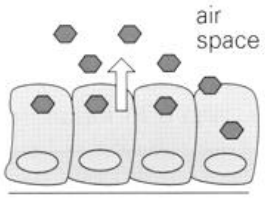
Localization versus systemic spread

- many viruses multiply in epithelial cells at site of entry
- produce a spreading infection
- then shed directly to exterior

  • respiratory infections – influenza, rhinoviruses and RSV

  • gastrointestinal infections caused by rotaviruses

  • dermatologic infections of the papillomaviruses



surface infection
failure to spread to deeper tissues (e.g. influenza virus in respiratory epithelium*)

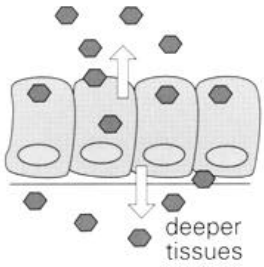
LOCALIZATION AND SPREAD

Localization versus systemic spread

polarized infection of epithelial cells and spread

• targeting of viral budding to apical or basal surfaces of polarized cells may define subsequent spread

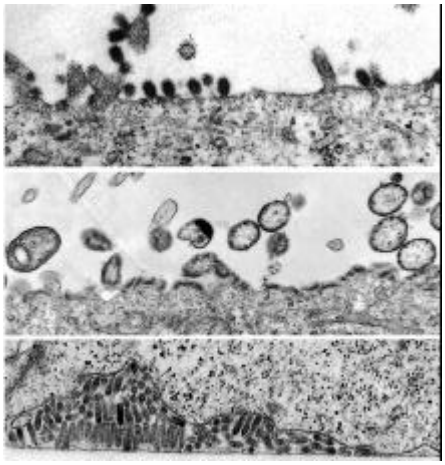
  • by viral glycoproteins? (secreted proteins carry signals for targeting)



invasion of deeper tissues
(e.g. herpes simplex virus)

Viruses employ a similar mechanism for virion targeting:

Baso-lateral budding	rhabdo retro
Apical budding	orthomyxo paramyxo alpha



Influenza

Measles

VSV

Learning objectives

- ***The factors that underlie the disease potential of viral infections***
- ***The main portals of entry for viruses and examples of each***
- ***The consequences of infection at epithelial cell surfaces***
  - particularly the distinction between localized and systemically spread infections