DNA Enveloped Viruses

Herpes viruses

Which include

- 5 important human pathogens

Herpes simplex virus 1 (HSV)

HSV-2

Cytomegalovirus (CMV)

Varicella-zoster virus (VZV)

Epstein-Barr virus (EBV)

Characters of Herpes viruses

All of them has similar characters

① DS – DNA

Linear genome

② Icosohedral symmetry

③ Enveloped viruses

④ The are only viruses which acquaint their enveloped by budding from nuclear membrane

⑤ Size (large)

120-200 nm

(Second in size after pox)
Certain Herpes viruses cause latent infection, leading to mean acute disease following by asymptomatic period during which virus remain in latent state.

When exposure to initiating agent or immunosuppression, reactivation of viral replication occurs, leading to disease.

Virion does not contain polymerase enzyme, so replication occurs in nucleus and lead to intra nuclear inclusion body.

Certain Herpes viruses cause cancer in humans, e.g., EBV associated with nasopharyngeal carcinoma, Burkitt's lymphoma.
Transmission and epidemiology

**Characters**
- Route of transmission
- So infection occurs
- Incidence (recent year)
- Primary infection in children
- Congenital Abnormalities
- Lab d x

**Hsv-1**
- By saliva
- Face
- Notice: oral genital sexual practice
- Lead to
- HSV-1 infect genital area
- Not increase
- Early appearance of Ab in childhood indicated that most primary infection with HSV-1 occur in childhood
- HSV-1 and HSV-2 neither of them cause congenital abnormalities by any significant degree (nor cause abortion) because don’t cross the placenta
- Tzank smear staining by giemza stain

**Hsv-2**
- By sexual contact
- Genital area
- HSV-2 infect oral cavity
- Increase
- Ab to HSV-2 not appear until age of sexual activity
<table>
<thead>
<tr>
<th>Characters</th>
<th>varicella zoster</th>
<th>cytomegaloviruses</th>
<th>Epstein Barr ums</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission</td>
<td>-1 respirating droplet</td>
<td>-1 placenta to fetus</td>
<td>Via saliva exchange during kissing</td>
</tr>
<tr>
<td></td>
<td>2- direct contact with lesion</td>
<td>2- birth canal and breast milk in early life</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-3 saliva young adult</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4- via sexual intercourse because the virus present in both semen and cervical secretion</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-5 transmitted by</td>
<td></td>
</tr>
</tbody>
</table>

- Blood transfusion
- Organ transplantation (kidney, bone marrow)
Lab dx of CMV

Lab dx of varicella zoster

Tzank smear (see multinuclear giant cells)

Tissue culture
  - For virus isolation
  - Isolation of virus, we can see cytopathic effect
    - Very slow need 1-2 week
  - Also
    - Most of virus produce latent or remain cell associated

Serology
  - To detect Ab
    - Fourfold Diagnostic
Lab. Dx of EB virus

**Hematological approach**

Absolute lymphocytosis + 30% abnormalities

Atypical lymphocyte (heterophil) which are

- Large
- Lobular nucleus
- Vacculated basophilic cytoplasm

Recognized and destroyed by cytotoxic T-cells

**Immunological approach**

EBV specific Ab test

VC A (viral capsid Ag)

Isolation of the virus from saliva by morphological transformation of cord blood lymphocyte (difficult test)
Disease

**HSV-1**
- A cut gingivostomatitis
- In children more severe
- Keratoconjunctivitis
  - Encephalitis: Involve Temporal lobes
  - High mortality rate
- Herpetic without postural lesion of finger and Hand
- Recurrent Herpes labials (cold sores):
  - Characterized by Mild recurrent
- Disseminated infection:
  - Eosophagitis
  - Pneumonia
  - Occur in immune-compromised patient with depression T-cell function

**HSV-2**
- Cause
- Recurrent infection
- Which include:
  - Neonatal Herpes
  - Genital Herpes

Primary infection

Recurrent infection
Notice 1

HSV-1

Neither cause congenital abnormalities

Because can't cross placation

HSV-2

Or abortion

Notice 2

HSV-1 HSV-2 can distinguish between them by two criteria

Notice 3

cell mediated immunity in limiting or prevent HSV infection

so suppression of CMI reactivation disease and spread of v sever disease

Notice 4

so they differentiate by

① Antigenicity

 HSV-1 HSV-2 morphologically structurally indistinguishable

② Type specific monoclonal Ab

Restricted end nuclease pattern of their genome DNA

③ Other criteria To distinguish Between HSV-1 +HSV-2 location of Lesion

Above the Waist Caused by HSV-1

below the waist Caused By HSV-2

8page
Diseases Varicella zoster

Varicella

Cause

Chicken pox

V Z-properties

Structure

morphology

Identical to H S V

Antigenically different

from H S V

It has

Single serotype

Replication

similar

zoster

cause

shingles

Pathogeneses and immunity to

V Z

v-infect m-m of upper

Resp. tract

blood

skin

lead to vascular Rash

Immunity long life

because

Single serotype but Zoster can occur

With advancing age

page 10
vascular Rash

Multinuclear giant cell

+ intranuclear inclusion Body

Recovery

v. latent in the dorsal root ganglia

Reduce in C M I

virus Reactivation

nerve pain

skin lesion
Clinical finding of VZ infection

(A) varicella
  chicken pox
  characterized by:
  l. p 14 day

Fever
Papule vascular Rash
Then
Croupes appear on trunk
spread to
Head
extremities

(B) Zoster
  shingles present of painfud vesicles
  Along the course of Sensory nerve of head And trunk

complication

Pneumonia
encephalitis
Reye's syndrome which characterized by
liver degeneration this syndrome associated with VZV and influenza B virus infection in children given aspirin.
v. replicate initially in the skin or m.m as initial site of infection

Migrate up Neuron becomes latent in the sensory ganglion cells

HSV-1 in trigeminal ganglia and HSV-2 in the lumber sacral ganglia

Virus reactivated by sun light, Hormones, Trauma, Stress and Fever

Virus migrates down the neuron and replicates in the skin causing lesions

Multinucleated Giant cell found in the base of the lesions

vesicle ruptures, transmit v. to other individuals

W contain serous Fluid, V. and cell debris

Vesicles
Replication cycle of Herpes viruses..... (not in case CMV)

HSV
VZV
CMV
EBV

attach to fibroblast growth factor Receptor on the cell surface

Entry → uncoat → DNA nucleus

Early V. mRNA transcription by cell RNA polymerase

Translated into early non-structural protein in the cytoplasm e.g.
Thymidin kinase and DNA polymerase

Replicate DNA genome

To Which time Early protein synthesis is shut off and

Exit the cell via Tubules or vacuoles to exterior

Obtain Envelope

Budding through nuclear membrane

New Visions Assembly which by

Late protein synthesis begin and trans ported to the nucleuses where
Cytomegalovirus (CMV)

Cause:

1. Cytomegalic inclusion disease (CID) in fetus
   - Characterized by:
     - Microcephaly
     - Many organs affected
     - Cause congenital abnormalities
     - (wide spread) include:
       - Seizure
       - Jaundice
       - Mental retardation
       - Deafness
       - Hepatosplenomegaly

2. Heterophile negative mononucleosis (HNM) in adult
   - Found in adult of children
   - Is asymptomatic except in immunocompromised patient
   - Characterized by:
     - Fever
     - Lethargy
     - Mental retardation
     - Deafness
     - Hepatosplenomegaly
     - Purpura

3. Pneumonia in immune compromised patient
   - Characterized by:
     - Pneumonia
     - Hepatitis
     - In
     - Immunocompromized patient
     - Renal or B.M transplant

14 page
Epstein – Barr virus mainly infect lymphoid cell primarily B - lymphocyte

Diseases

1. infectious mononucleosis (I. M)
2. Burkitt's lymphoma
3. B cells lymphoma
4. nasopharyngeal carcinoma

Characterized by

- Fever
- Sore throat
- Lymphoadenopathy
- Spleenomegaly
- Anorexia
- Lethargy
- Hepatitis
- Encephalitis
- Spleen rupture

Other property of EBV

- Structure to morphology
- Agic Different
- Viral capsid Ag (VCA) +
  Early Ag (EA) +
  EBNA (EB nuclear Ag)

Some but not all genes are transcribed and only subset are translated to protein

Helpful in DX
Other properties of cytomegalovirus

CMV enters latent state in Kidney for years and can reactivate when CMI decreases

Leukocyte

Kidney for years

CMV enters latent state in

Properties

Morphology structure
Similar to herpes v.

CMI more important than humoral immunity because depression - CMI leads to systemic disease

Antigenical
Different from herpes v.

EBV pathogenesis

Initial infection in oropharynx (Epithelial cells, Lymphoid tissue)

Spread to Blood

Infection of B-lymphocyte

T. lymphocyte react against B lymphocyte which appear as Atypical lymphocyte in Blood smear

1. Few copies of V. DNA integrated
2. Many copies in the cytoplasm

v. remain Latent
Immunity to EBV

- IgM and IgG to Viral capsid Ag (VCA)
- Immunity against 2nd Episodes of Infectious mononucleosis based on Ab to V. membrane Ag
- Non specific Hetrophil Abs they donot react with EBV - Ags…. it seenlikely that EBV infection ( also HBV and serum sickness) because these viruses modifies a cell membrane constituent so that it becomes antigenic and induce this Het. Ab. That mean these Ab not specific against EBV. Infection disappear after 6m.
Pox viruses

They are largest and most complex viruses (250-300 nm)

Import. Properties

Brick – shape particles

DS – DNA linear

Lipoprotein envelope

Disk – shape core within double membrane

Contain DNA – dependant RNA polymerase within particle

Which help the viral replication in cytoplasm

+ 

The virus not need to cellular RNA polymerase which located in the nucleus

Pox viruses

Family include 3 viruses medically important

Small pox v. also called variola v. which eradicated by vaccination

Becaucen

Vaccinia virus

Molluscum contagious virus

Singles stable serotype for that vaccine in successes

18 page
Summary of Replication cycle of pox v.

v. penetrate the cell → Uncoating → V. DNA dependent RNA polymerase → Synthesis Early mRNA → Translated to Early non structural protein → Enzyme Required for v. DNA replication

Notice, all steps of v. replication occurs in cytoplasm ….. which unusual for DNA virus

Virions assembled and acquired Envelopes by budding from cell memb. → Late structural Protein forming → Release

……..
Pathogenesis and immunity of pox v.

- v. infect upper Resp. tract and Local Lymph Nodes
- Blood (primary viremin)
- Internal organs (Reticuloendothelial organs)
- re-enter Blood (second viremia)
- spread to skin
- rash due to v. replication in the skin
- crust in 2-3 week

all then steps occure during 1.p 7-14 day
Immunity

Long – life

Transmission and epidemiology by

Aerosol

Direct contact

Lab dx

Isolation of v. on tissue culture
detection by IFT

Prevention by vaccine eradication which depend on 5 critical Factors

1 v. has single stable serotype

2 No. animal reservoir and human is only the host

3 Ab response is protective

4 disease in easily recognized clinically

5 no carrier state or subclinical infection

Clinical Find

1.p 7-14 day

sudden onset of prodromal syndrome – suchas

fever

malaise

Followed by Rash on the Face

Spread over all the body

RX

Rifampsin

inhibit v. DNA dependent RNA poly – merase