

REVIEW OF VIROLOGY

DEFINITIONS

Attenuated: Made less virulent, usually by passage through an abnormal host.

Capsid: The outer-most component of a virion, the protein coat which protects the nucleic acid from the environment.

Capsomere: The structural protein subunits of the viral capsid.

Defective interfering virus - has deletion mutation which makes it unable to replicate by itself; needs a helper virus for replication but has normal capsid proteins. Can cause cell transformation and may be involved in persistent infections.

Envelope: The structure which some viruses acquire as they leave the host cell. It consists of viral protein components (usually glycoproteins) and host-cell derived lipids and lipoproteins of the cell membrane. Lipid solvents react with the envelope and inactivate the infectivity of the virus.

Genome: The nucleic acid core of the virus, either DNA or RNA. It contains the genetic information of the virus. Some genomes are segmented, others are polycistronic. They may be single-stranded, as is the case with most RNA viruses, or double stranded. Some RNA viruses are + stranded, as in the case of picornaviruses (e.g., polio) and the togaviruses (e.g., WEE).

Icosahedron: A 20-sided polygon.

Latent infection: A form of inapparent infection following a clinical case in which the pathogen is not completely eliminated, but remains viable in the tissues after the host recovers. The host may be infectious.

Nucleoprotein: Proteins associated with the nucleic acid of the viral genome. These are internal proteins and may be structural, or enzymes such as RNA-dependent DNA polymerase.

Prion: An infectious proteinaceous particle; virus-like but with no nucleic acid content.

Provirus: Naked viral nucleic acid intracellularly located. It may remain dormant in the host cell or it may become integrated into the host cell genome.

Uncoating: The process whereby the viral genome is freed into the internal milieu of the host cell. After this process occurs the viral genes are read and synthesis of early proteins, etc. begins.

Viroids: Small naked RNA molecules capable of causing disease in plants and perhaps animals.

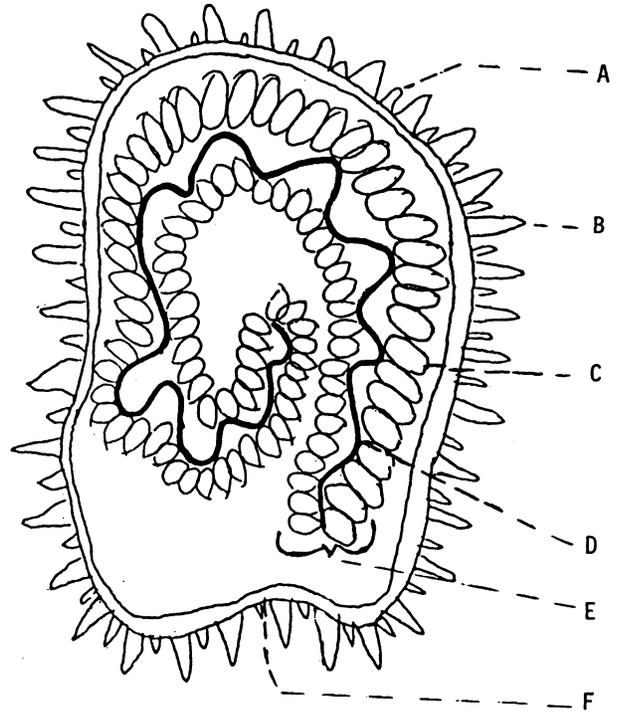
VIRUS STRUCTURE

The outermost component of a virion is the capsid, made up of protein subunits called capsomers. The capsid serves four important functions: (1) it protects the viral genome, (2) it aids in infection by attaching the virion to susceptible cells, (3) it is the stimulus for antibody production, (4) it serves as the antigen in serologic tests and (5) responsible for tissue tropism in naked viruses such as polio.

The viral genome, the other major component of every virion, is found inside the virus particle and may be either double-stranded or single stranded DNA, or single-stranded or double-stranded RNA. Once introduced into a susceptible cell, the viral genome provides the genetic information needed for production of new virions in a cell. The cell contributes cellular structures (ribosomes), energy, and enzymes for the synthesis of viral macromolecules. Since viruses lack most of these essential components, they must invade and make use of living cells in order to be replicated.

Animal virions are either naked or enveloped. A naked virion consists of nucleic acid enclosed in a protein shell known as the capsid; nucleic acid and capsid together are termed nucleocapsid. An enveloped virion in turn consists of a nucleocapsid surrounded by a structure called the envelope. The envelope consists of viral protein components (usually glycoproteins), and host cell-derived lipids and lipoproteins. Lipid solvents react with the lipid-containing envelope to inactivate the infectivity of the virus. The capsid and the envelope contribute antigens useful in vaccine development and in serologic tests.

Label the components of the virus.



- A. _____
- B. _____
- C. _____
- D. _____
- E. _____
- F. _____

VIRAL CLASSIFICATION

All naked animal virus particles resemble icosahedra. Enveloped animal virions exhibit a large variety of shapes (symmetry). In many cases, a nucleocapsid that is distinctly icosahedral or helical, depending on the virus, is surrounded by an envelope which gives the particle the appearance of a sphere, e.g., influenza virus. Other enveloped animal viruses are shaped like a bullet, e.g., rabies virus; and still others look like bricks, e.g., poxviruses.

Taxonomic classification of viruses is based on the relatively constant physical and chemical properties of virions. Some of the criteria used for classification are (1) type of nucleic acid found in the virion (DNA or RNA) and whether the nucleic acid is single-stranded or double-stranded, (2) shape of the viral nucleocapsid (icosahedral or helical), (3) nature of the outermost viral component (naked or enveloped), and (4) antigenic properties.

Viruses are classified on the basis of

1. _____
2. _____
3. _____
4. _____

MAJOR HUMAN VIRUS GROUPS

DNA viruses

1. Herpes
 - a. simplex I & II
 - b. varicella
 - c. cytomegalo
 - d. Epstein-Barr
2. Hepadna (Hepatitis B)
3. Adeno
4. Pox
5. Papova
6. Parvo

RNA viruses

1. Picorna

- a. Entero
 - 1. Polio
 - 2. Coxsackie
 - 3. ECHO
 - 4. Hepatitis A
- b. Rhino

2. Toga

- a. WEE, EEE, VEE
- b. SLE, Dengue, Yellow fever
- c. Rubella

3. Rhabdo

4. Orthomyxo

5. Paramyxo

- a. Parainfluenza
- b. Mumps
- c. Measles
- d. Respiratory syncytial

6. Reo

- a. Reo
- b. Rota

7. Arena (LCM)

8. Bunya

9. Corona

10. Retro

- a. Oncorna
- b. HIV

Uncertain NA type

- 1. Slow Viruses,
- 2. prions (protein only)
- 3. non A/non B Hepatitis

The table below is a helpful way to group the viruses. There are 6 families of DNA-containing viruses, Herpes, Hepadna, Adeno, Papova, Pox and Parvo (The HHAPPPy viruses). If one can remember these and the generalities associated with the DNA viruses, then any other virus will be the opposite. As nothing is ever that simple, the table also contains the exceptions to that rule, e.g., if all DNA viruses are Double stranded and Naked, then the RNA viruses should all be single stranded and enveloped; and they are with the exception of the REO (dsRNA) and Picorna (naked RNA) as noted in the table.

VIRUS CLASSIFICATION

<u>Virus Type</u>	<u>Generalities</u>	<u>Exceptions</u>
DNA Viruses	Double Stranded, linear	Parvo*
<div style="border: 1px solid black; padding: 2px; display: inline-block;"> Herpes Hepadna Adeno Papova Pox Parvo </div>	Naked	Pox and Herpes
	Nuclear site for Replication	Pox
	Icosahedral (cubic) symmetry	Pox (complex)
<hr/>		
RNA Viruses**	Single Stranded	REO
<div style="border: 1px solid black; padding: 2px; display: inline-block;"> Paramyxo Toga Picorna Corona Rhabdo Orthomyxo Arena Bunya Retro REO Flavi </div>	Enveloped	REO and Picorna
	Helical symmetry	REO, Picorna, Toga
	Cytoplasmic site for replication	Orthomyxo and Retro (nuclear + cytoplasmic)

* Parvoviruses are circular, SS DNA
 Hepadnaviruses are circular, DS DNA

** The first 5 viruses listed are polycistronic single RNA strands; the remaining viruses have segmented genomes

VIRAL REPLICATION

STEPS

ACTIVITY

- | | |
|--|---|
| 1. Adsorption | -virus attaches to specific receptors on cell membrane
-interaction is, at first, reversible, then becomes irreversible |
| 2. Penetration | -virus particle is actively taken up by cell through a process called pinocytosis or phagocytosis |
| 3. Uncoating | -takes place at cell membrane or vesicles
-viral nucleic acid is released inside of cell by cell host enzymes |
| 4. Intracellular replication of viral components | |
| A. RNA viruses | -picorna and toga-viruses - the genome is +RNA and serves as mRNA
-others (e.g., myxo [ortho & para], rhabdo) carry viral RNA dependent RNA polymerase which synthesizes +mRNA from viral -RNA strands.
-early proteins are enzymes for viral RNA synthesis or inhibitors of cellular synthetic events.
-late proteins are viral structural proteins and assembly proteins synthesized in response to the viral genome |
| B. DNA viruses | |
| 1. RNA synthesis | -host cell supplies transcriptase, pox has its own DNA dependent RNA polymerase |
| 2. Early protein synthesis | -synthesis of enzymes for DNA synthesis, tumor antigens, etc. |

The first step in viral replication is _____.

Antibody to viral capsid/nucleic acid blocks this process.

Early viral proteins are _____

_____ ;

late proteins are _____

_____ .

3. Viral DNA synthesis -many new copies of viral DNA
4. Late protein synthesis -viral capsid proteins(structural)
5. Assembly: -newly synthesized viral nucleic acid and protein assembled inside cell
-viral envelope added (usually from cell membrane)
-new viruses released from cell by budding or lysis
6. Effects of Viruses on Cells -lytic viruses inhibit cell RNA, DNA, protein synthesis
-tumor viruses transform cells
-latent viruses (herpes) probably do not alter host cell greatly

The template for early proteins in a Herpes infected cell is provided by viral RNA/newly synthesized RNA.

REPLICATION OF SPECIFIC RNA VIRUSES

1. Picornavirus and Togavirus
e.g. polio, rubella, WEE
-viral RNA is single stranded piece of messenger RNA (+mRNA)
-naked viral RNA can infect cells
-viral RNA (+mRNA) gets to polysomes to make new viral proteins
-new proteins made as one long protein, then cleaved to viral specific proteins
-replicase (RNA-dependent RNA polymerase), an enzyme which copies +mRNA and makes a negative strand of mRNA
-the -mRNA is then used as template to make new viral RNA (+mRNA)

The template for late proteins in a polio infected cell is provided for by viral RNA/newly synthesized RNA.

The template for poliovirus RNA is +mRNA/-mRNA.

2. Orthomyxovirus
(influenza virus)

- viral RNA is fragmented into 8 pieces of (-mRNA)
- virus carries into cell a transcriptase enzyme (RNA dependent RNA polymerase)
- transcriptase copies (-mRNA) to make (+mRNA) for viral proteins
- (+mRNA) is also template for new viral (-mRNA)

3. Paramyxoviruses and Rhabdoviruses
(mumps, measles, rabies)

- viral RNA is single-stranded (-mRNA), not segmented
- virus carries transcriptase like the influenza virus; similar replication cycle

4. Diplornavirus
(reovirus and retrovirus)

- viral RNA is double-stranded and composed of ten fragments
- virus carries transcriptase

5. Retroviruses
(RNA tumor viruses)

- viral RNA is single stranded
- virus carries reverse transcriptase (RNA-dependent DNA polymerase)
- transcriptase copies viral RNA into DNA
- DNA is integrated into host genome and serves as template for new viral RNA

The RNA dependent RNA polymerase found in influenza virus is also called

_____;
it converts -RNA into +RNA template for protein synthesis.

The template for mumps capsid is provided for by viral RNA/newly synthesized RNA.

REPLICATION OF SPECIFIC DNA VIRUSES

1. Herpesvirus

- replicates inside nucleus
- viral envelope obtained from nuclear membrane

2. Adenovirus

- replicates inside nucleus

3. Poxvirus

- replicates in cytoplasm; complex cycle
- virus carries many enzymes into cell

4. Papovavirus

- replicates in nucleus, circular DNA

RNA dependent RNA polymerase is a part of the following viruses

1. _____
2. _____
3. _____
4. _____

VIRAL ENZYMES

VIRUS

Negative RNA
ex orthomyxo
paramyxvo
rhabdo

Retrovirus

Pox

Herpes

Reoviruses including
Rotovirus

ENZYMES

RNA polymerase

Reverse transcriptase

More than a dozen

Thymidine kinase*
DNA polymerase*

RNA polymerase

* produced in cell not brought in with virion

INTERFERENCE WITH VIRAL REPLICATION

1. Interferon (IFN)

- a group of proteins made by cells in response to viruses, synthetic nucleotides (poly r:IC), foreign cells that interferes with viral replication

Interferon produced by a macrophage would be an $\alpha/\beta/\gamma$ interferon.

IFN species

Leukocyte (alpha), fibroblast (beta), lymphocyte (gamma/immune)

- cell genome has information for IFN: if one inhibits cell metabolism with actinomycin D, no IFN produced
- IFN induces cells to make products which inhibit viral or foreign cell replication
- IFN released from cells, spreads to other cells and induces new IFN

Interferon is effective against

- A. DNA viruses
- B. RNA viruses
- C. Both
- D. Neither

(answer at bottom of page)

IFN induced products

1. protein kinase which inactivates elongation factor-2 by phosphorylation
2. A phosphodiesterase which inhibits peptide elongation
3. Oligoisoadenylate which activates a cellular RNase to degrade viral mRNA

Interferon inhibits viral replication by inducing cellular production of

1. _____
2. _____
3. _____

Biologic Activities of interferon

1. antiviral
 2. Inhibition of cell growth
 3. Immune modulation
 - a. NK
 - b. ADCC
 - c. macrophage activation
- ### 2. Specific Antibody

1. IgG, A, M
2. Neutralize by interfering with the functions of viral capsid or envelop proteins. The antibodies block
 - absorption
 - penetration
 - uncoating (rare)

(answer = C)

3. Chemical Inhibitors

- a. Amantadine
 - for influenza viruses
 - inhibits viral penetration and/or attachment
- b. 5-iododeoxyuridine-(idoxuridine)
 - inhibits DNA viruses, esp. herpes
 - inhibits DNA synthesis by inhibiting thymidylate synthetase
- c. Ara-C (cytosine arabinoside, vidarabine)
 - inhibits DNA viruses (herpes and pox)
 - must be phosphorylated in the host cell to form a competitive inhibitor for DNA polymerase
- d. Ara-A (adenosine arabinoside)
 - inhibits DNA viruses, esp. herpes
 - competitive inhibitor for DNA polymerase
 - causes premature termination of the DNA chain
 - Ara-ATP competes with dATP
- e. Acyclovir (acycloguanosine)
 - inhibits DNA polymerase
 - herpesvirus specific thymidine kinase phosphorylates drug to active form therefore acyclovir is better vs. herpes that code for their own kinase (i.e., simplex & zoster) than vs. CMV & EB that use host cell enzyme
- f. Ribavirin (virazole)
 - active vs both DNA and RNA viruses
 - interferes with viral mRNA
- g. Azidothymidine
 - incorporated into DNA by viral reverse transcriptase; it causes nucleic acid chain termination

Most chemical viral inhibitors are active against DNA/RNA viruses.

Acyclovir is relatively specific for

Herpes because _____

_____.

VIRAL IMMUNOTHERAPY AND PROPHYLAXIS

I. Active, Artificial Immunity

A. Recommended for all persons in US

Disease	Condition of Vaccine
1. Rubella*	live attenuated
2. Measles*	live attenuated
3. Mumps*	live attenuated
4. Polio	
(Sabin)**	live attenuated
(Salk)**	inactive

Live viral vaccines are NOT recommended for immunosuppressed individuals.

B. Recommended for special conditions (epidemic, military, travel, exposure)

Disease	Condition of Vaccine
1. Rabies***	inactive
2. Yellow Fever	live attenuated
3. Influenza**	inactive
4. Adenovirus**	active
5. Togavirus	inactive
6. Chickenpox	live attenuated
7. Hepatitis B	inactive

MMR vaccine combination consists of

- _____
- _____
- _____

Live viral vaccines induce immunity of long duration.

*May be combined; all are a single antigenic type

**May be polyvalent

***Usually given with immune serum

II. PASSIVE, ARTIFICIAL IMMUNITY-use of immune serum or gamma globulin. Used only under special circumstances.

- | | |
|----------------------|----------------|
| 1. Rabies | 4. Rubeola |
| 2. Rubella | 5. Mumps |
| 3. Hepatitis A and B | 6. Chicken Pox |
| | 7. Polio |

Polyvalent viral vaccines include

- _____
- _____
- _____

This type of treatment may be effective in disease prevention; it is of little value after onset of disease.

III. New approaches to acquired immunity is the use of

- viral subunit particles
- synthesis of viral peptides:
 - in bacteria via cDNA technology
 - by other, non-pathogenic hybrid viruses (e.g. vaccinia)

HERPESVIRUSES

Properties of the group

Enveloped ds DNA viruses with icosahedral nucleocapsid; replicate in the nucleus

Herpes hominis (simplex) Serotypes 1 & 2

Epidemiology

1. Man is the only known natural host
2. Most have been infected by type 1, many adults by type 2
3. Spread through close contact

Clinical features

Primary herpes hominis

An acute illness, commonly seen in young children, characterized by fever, and small vesicular lesions of mouth, lips, face, conjunctiva, etc.

Recurrent or secondary herpes simplex: (fever blisters, cold sores) A vesico-ulcerative rash which may be triggered by trauma, emotional disturbances, menses, fever etc.

Disseminated herpes hominis

(neonatal herpes): A rare illness of early infancy characterized by a high fever, jaundice and encephalitis

Other diseases

- Aseptic meningitis
- Encephalitis
- Keratoconjunctivitis
- Genital herpes simplex, particularly associated with serotype 2

Treatment

Nucleic acid analogs, such as Ara A (Vidarabine) and Ara C are used for herpetic encephalitis and ocular diseases. Acyclovir is also good; latent infections are refractory

Diagnosis

Culture is necessary as most people will have neutralizing antibodies; can use immunofluorescent stain, or observation of multinucleated giant cells in lesion

Herpes viruses

1. are DNA/RNA.
2. are single/double stranded.
3. are naked/enveloped.
4. multiply in the nucleus/cytoplasm.
5. have helical/cubic symmetry.

Drugs that are effective against

herpesviruses include

1. _____
2. _____
3. _____

Varicella (chickenpox or Herpes zoster)

Serotype

There is only one serotype of the varicella-zoster virus

Epidemiology

1. Man is the natural host
2. The overall incidence of infection is very high.
3. Transmission probably follows inhalation of infective aerosols, or direct skin contact

Clinical features

1. The onset is sudden, with a rash progressing from macules to papules to vesicles. Pustules do not develop; there is no scarring
2. The lesions appear in successive crops over 3 to 4 days
3. The lesions are distributed chiefly on the trunk and face

Zoster (Herpes zoster or shingles)

Epidemiology

This disease occurs chiefly in adults, most of whom give a history of having had varicella. Infection is communicable from as early as 5 days before to one week after the rash first appears

Pathogenesis

The virus probably persists in cells of the root ganglia after an attack of varicella, and is activated later with a resultant inflammatory reaction along the nerve followed by destruction of the epithelial cells served by that nerve

Clinical features

1. Erythematous maculopapular lesions develop, and on the trunk these have a band-like distribution
2. A disseminated form of disease is sometimes seen in patients who have received immunosuppressive therapy or radiotherapy

Herpes zoster causes

- A. chicken pox
- B. cold sores
- C. shingles
- D. all of the above
- E. A and C only

(answer at bottom)

(answer = E)

Infectious mononucleosis

Etiologic agent (Epstein-Barr)

herpesvirus.

Epidemiology

1. Man is the natural host
2. Infection is most common in young adults
3. Incidence of infection is high
4. Mode of transmission; inhalation of infective aerosols during close personal association
5. Viruses associated with Burkitts lymphoma and nasopharyngeal carcinoma

Serodiagnosis

The heterophile agglutination test detects a IgM hemagglutinin vs sheep RBC

Cytomegalic inclusion disease

Etiologic agent

Cytomegalovirus; multiple serotypes are known

Epidemiology

1. Man is the only known natural host
2. The virus can be transmitted across the placenta and cause congenital infection. The mode of postnatal transmission is unclear, but the virus is excreted in saliva, semen, milk and urine

Clinical features

1. Intrauterine infections may cause death of the fetus, or result in congenital disease which is frequently fatal. In those who survive, hepatosplenomegaly with jaundice, blood dyscrasias, mental retardation, microcephaly and chorioretinitis are common sequelae
2. Postnatal infections are usually symptomless in infants and children, but occasionally hepatitis, pneumonitis or acquired hemolytic anemia develop
3. In patients with malignancies, AIDS, or those receiving immunosuppressive therapy, hepatitis, pneumonitis, infectious mononucleosis-like disease (with negative heterophile), pneumonia, or even generalized disease may develop, possibly resulting from the activation of latent virus

Positive heterophile hemagglutinating antibodies are seen in diseases with infectious mononucleosis-like symptoms caused by

- A. Cytomegalovirus
- B. Epstein-Barr virus
- C. Both
- D. Neither

(answer at bottom)

Epstein-Barr virus is associated with what two human malignancies (see p. 207)?

1. _____
2. _____

(answer = B)

ADENOVIRUSES

Properties of the group

1. Naked viruses, which have an icosahedral nucleocapsid, contain double-stranded DNA and replicate in the nucleus
2. There are more than 40 human serotypes, some cause tumors in animals

Diseases caused by adenoviruses

A. Pharyngo-conjunctival fever

1. Particularly common in military recruits; in the general population, only about 5% of all respiratory illness is caused by adenoviruses
2. The mode of transmission is via infective aerosols or fresh fomites
3. Bronchitis and pneumonia sometimes occur, the latter usually in infants

B. Epidemic keratoconjunctivitis

1. Associated with serotype 8
2. Outbreaks in certain industries are associated with minor ocular trauma resulting from dusty atmosphere

C. Exanthem

Adenovirus is possibly responsible for a rubelliform rash

D. Hemorrhagic Cystitis

Particularly in children

Adenoviruses are

1. DNA/RNA.
2. single/double stranded.
3. naked/enveloped.
4. multiply in the nucleus/cytoplasm.
5. helical/cubic symmetry.

Diseases caused by Parvoviruses include

1. _____
2. _____
3. _____

PARVOVIRUSES

Properties of the group

1. Naked, single stranded DNA

Diseases caused by parvoviruses

1. Fifth disease (erythema infectiosum)
 - a. primarily a disease of children
 - b. Polyarthritits in adults
2. Spontaneous abortion

PAPOVAVIRUSES

Properties of the group

Naked viruses, which have an icosahedral nucleocapsid, contain dsDNA, and replicate in the nucleus

Papilloma virus

Several serotypes affect humans

Epidemiology

1. Man is the only known host
2. The mode of transmission is presumably by direct contact

Pathogenesis and pathology

Replication occurs in the epithelial cells of the skin, virus causes a benign neoplasm. Papilloma #16 has a high association with cervical carcinoma

Clinical features

The common wart; condyloma acuminatum

Polyoma virus

Causes many different malignancies in several animal species

Vacuolating virus

A simian virus (SV40) causes tumors when inoculated into newborn animals. Also transforms cells in culture

JC virus

Has been isolated from immunocompromised individuals and from the brains of patients with progressive multifocal leukoencephalopathy. Most humans have specific antibody vs. the JC virus

The papovavirus responsible for the common wart is _____.

The papovavirus associated with progressive multifocal leukoencephalopathy is

_____.

Papilloma virus serotype 16 is associated with

_____.

POXVIRUSES

Properties of the group

Complex ellipsoid viruses, which contain double-stranded DNA, replicate in the cytoplasm; virion contains many enzymes (e.g. RNA polymerase)

Smallpox

Epidemiology

1. Man is the only natural host; disease has been eradicated from the planet
2. Smallpox is transmitted by inhalation of infective aerosols through personal association, or by contaminated fomites such as bedding

Treatment

Methisazone, which is of value prophylactically, is also useful in treating dermal complications following vaccination. It blocks synthesis of certain viral proteins thus inhibiting viral replication

Artificially-acquired immunity

Active (vaccination)

Immunization is carried out with live vaccinia virus

Molluscum contagiosum

Epidemiology

Infection probably occurs through minor abrasions, and in swimming pools

Clinical features

Multiple discrete benign tumors appear on the skin anywhere except on the palms and soles; the lesions last for several months, and then disappear spontaneously

Poxviruses are

1. DNA/RNA.
2. single/double stranded.
3. naked/enveloped.
4. multiply in the cytoplasm/nucleus.
5. helical/cubic/complex symmetry.

ORTHOMYXOVIRUSES

Properties of the group

1. Enveloped viruses, helical nucleocapsid, contain 8 distinct segments of single-stranded RNA and replicate in both nucleus and cytoplasm 2. Orthomyxoviruses cause influenza

Serotypes

1. There are 3 serotypes: A, B and C.
2. Each contains 2 surface antigens (H and N):
 - a. A hemagglutinin (H) which enables the virion to attach to receptors on the cell surface
 - b. A neuraminidase (N) which facilitates the release of progeny virus from infected cells
3. The 2 surface antigens of serotypes A and B undergo frequent antigenic changes (caused by point mutations) resulting in antigenic "drift"
4. Antigen "shift" is a much more drastic change which is caused by recombination of RNA segments of the viral (human or animal) genome
5. All known pandemics have been caused by serotype A/B/C influenza virus (answer at bottom, right)

Reye's syndrome (encephalopathy and fatty liver) is associated with type B, and perhaps also with other viruses (e.g. chickenpox). Salicylates may also be involved in the pathogenesis of the disease.

Serodiagnosis

Using the hemagglutination-inhibition technique, the patient's serum can be tested for antibody against a particular strain of virus

Antiviral therapy

Amantadine hydrochloride (Symmetrel) is used as a prophylactic drug before or immediately after exposure to infection. It acts by blocking penetration of the virus into cells and also blocks uncoating of the virus

Artificially-acquired immunity

Induced by egg-derived/subunit vaccines inactivated by formalin

Influenza is an ssRNA virus whose genome is in _____ segments. It agglutinates RBCs through the action of its _____; the enzyme _____ facilitates progeny release.

(Pandemics = A)

PARAMYXOVIRUSES

Properties of the group

Enveloped viruses, helical nucleocapsid, contain single-stranded RNA, and replicated in the cytoplasm. The measles virus is known to replicate in both nucleus and cytoplasm

Parainfluenzavirus infections

The viruses cause a variety of upper and lower respiratory tract illnesses; cold-like ills, pharyngitis, bronchitis, bronchiolitis and pneumonia. In young children, the viruses are the commonest cause of acute laryngotracheobronchitis (croup)

Respiratory Syncytial Virus (RSV) Infection

1. In the infant, severe necrotizing bronchiolitis can occur
bacterial complications are common
2. RSV is the most common cause of viral pneumonia in infants
3. Reinfection occurs commonly, but is usually mild and confined to the upper respiratory tract, frequently resulting in the common cold syndrome
4. Ribavirin is used in therapy in patients likely to have serious disease and sequellae (e.g., patients with a history of coronary heart disease)

Mumps

1. Sudden onset of swelling of the parotid glands, usually bilateral
2. Submaxillary and sublingual glands may also be involved
3. Inflammation of the testis (orchitis) often occurs in males past puberty, but testicular atrophy or sterility is rare
4. Meningitis is a relatively common complication

Respiratory syncytial virus is the most common cause of _____

_____.

Complications of mumps infection include

1. _____
2. _____

Paramyxovirus infections with agents such as RSV can be treated with _____.

This chemotherapeutic is very expensive, hence treatment is limited to patients in which the disease may be

life-threatening.

Measles

1. Cytopathic effect = multinucleated giant cells with nonspecific cytoplasmic and nuclear inclusions
2. Prodromal signs are photophobia, fever, cough, coryza, conjunctivitis and appearance of Koplik's spots in the mouth
3. Viremia
4. After 3 days, a rash starts on the head and spreads to chest, trunk and limbs in the next day or two; the rash disappears slowly
5. May have a transient depression of cell mediated immune responses
6. Complications are fairly common, and sometimes severe: These include - otitis media and pneumonia
7. Encephalomyelitis: rare, occurs 1 to 2 weeks after the rash, and is associated with a high mortality rate
8. Subacute sclerosing panencephalitis may be a post-infection sequela
9. May be transient depression of cell mediated immunity during infections

Prodromal signs of measles include

1. _____
2. _____
3. _____
4. _____
5. _____

Complications of measles include

1. _____
2. _____
3. _____
4. _____

ARENAVIRUSES

Properties of the group

Enveloped RNA viruses

Lymphocytic choriomeningitis

A disease usually manifest as "aseptic" meningitis or a mild influenza-like illness, rarely as a severe encephalomyelitis. The natural host of the virus is the mouse

ARTHROPOD-BORNE VIRAL DISEASES

Classification

1. The arboviruses encompass a heterogeneous collection of some 400 viruses related only by the epidemiological fact that they are arthropod-borne
2. The so-called 'arboviruses' alternate between an invertebrate vector and a vertebrate reservoir
3. Arboviruses belong to several viral families: Togaviridae, Bunyaviridae, Reoviridae, Arenaviridae, Flaviviridae and others

Epidemiology

1. The cycle of transmission of these viruses is from arthropod to vertebrate host and back to arthropod
2. The arthropods involved are commonly mosquitoes, but sometimes ticks, sandflies and gnats act as vectors
3. The natural hosts, which act as reservoirs, include birds, reptiles, mammals and, rarely, man

BUNYAVIRIDAE

Bunyamwera viruses are enveloped, spherical viruses with helical symmetry. They are similar ecologically to the togaviruses and are arthropod-borne (arboviruses). The single-stranded RNA is composed of three segments. The pathogenesis of disease is similar to the togaviruses (encephalitis). One group of this diverse family of viruses which has been associated with encephalitis in humans is California viruses, first found in California and more recently in other parts of the USA

Arthropod-borne viral diseases belong to the following viral families

1. _____
2. _____
3. _____
4. _____

TOGAVIRIDAE

Arbovirus encephalitis

Most arboviruses are antigenic groups A or B; rubella belongs here. They are enveloped ssRNA viruses with (+mRNA) genome

1. These encephalitides in the USA include Venezuelan, Western and Eastern equine viruses
2. The usual reservoir is birds, and the vector is the mosquito
3. Clinical findings include fever, chills, headache, widespread muscular aches, drowsiness, nuchal rigidity, convulsions, paralysis, coma and death. (EEE has 50-70% mortality rate)

Yellow fever

1. The natural host is the monkey, and the vector is the Aedes mosquito; two forms of yellow fever, the urban and the jungle (sylvatic), are recognized
2. In the urban type of yellow fever, man is the main reservoir, and the transmission cycle is man-mosquito-man
3. In the jungle type, the monkey is the main reservoir, and the cycle is monkey-mosquito-monkey with man being infected occasionally
4. The outstanding feature in cases of yellow fever is the extent of damage to liver and kidney in severe cases

Dengue

1. The onset of illness is characterized by fever, chills, headache, conjunctivitis, lymphadenitis, severe pain in the back, muscles and joints ('break-bone fever')
2. Fever often falls, then rises again within a week ("saddleback curve")
3. Dengue hemorrhagic fever is a severe disease with a 10% mortality which occurs in individuals who have passive maternal antibody or have recovered from a previous attack by a different dengue serotype. Virus/antibody complexes form early in the disease; they activate complement and disseminated intravascular coagulation and shock result

Clinical signs of viral encephalitis

include

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____

RUBELLA VIRUS

Properties

Enveloped virus, which contains single-stranded RNA, and replicates in the cytoplasm. There is only one serotype. The rubella virus is classified with Togaviruses; however, it is not an arthropod-borne disease, but rather is droplet spread

Clinical feature of postnatal rubella

1. There is enlargement of lymph nodes with conjunctivitis, often followed by a fine macular rash; slight fever may occur
2. The main risk of this infection is that it may occur in a non-immune woman during the first trimester of pregnancy, with serious consequences for the fetus

Clinical features of prenatal rubella

1. The risk of congenital malformations is greatest when the mother is infected during the first trimester of pregnancy
2. One or more of the following features may be present:
 - a. Blindness
 - b. Deafness
 - c. Congenital heart defects
 - d. Mental retardation (often with microcephaly)

Rubella virus is

1. DNA/RNA.
2. single/double stranded.
3. naked/enveloped.
4. multiplied in the nucleus/cytoplasm.

Replication of Rubella virus occurs in the following stages (see p. 181)

1. _____
2. _____
3. _____
4. _____

RHABDOVIRUSES

Properties of the group

1. Bullet-shaped enveloped viruses, which contain single-stranded RNA, have a helical nucleocapsid, replicate in the cytoplasm, and are released by budding.
2. The group includes the virus responsible for rabies

Rabies

Serotypes: There is only one serotype of rabies virus

Epidemiology

1. The natural hosts include many kinds of mammals and bats
2. The usual mode of transmission is by inoculation (bite). Infection may rarely result from inhalation of infective aerosols from bat secretions

Pathogenesis

1. Virus spreads along nerves to the CNS.
2. The virus causes destruction of nerve cells and demyelination; the highest concentration is usually found in the hippocampus

Artificially-acquired immunity

Vaccines

1. Virus is grown in human diploid cells and inactivated. Weekly, SubQ injections for 4 to 6 weeks are adequate. Human cell source virus has resulted in significant decrease in neurologic complications of vaccination
2. Passive antibody in the form of rabies immune globulin is also available

Treatment

1. Detain animal for observation
2. Wound must be thoroughly cleansed
3. Inject rabies immune globulin (human origin) into the wound and I M
4. Start the vaccine immediately at another site

THE NEGRI BODY IS THE INCLUSION SEEN IN THE CYTOPLASM OF CELLS IN THE HIPPOCAMPUS AND OTHER CNS AREAS.

The replication cycle of the rabies virus includes the following stages

(see p. 182)

1. _____
2. _____
3. _____
4. _____

PICORNAVIRUSES

There are 2 groups of small (pico) RNA viruses, the enteroviruses and the rhinoviruses

ENTEROVIRUSES

Properties of the group

1. Naked viruses, icosahedral nucleocapsid, contain single-stranded RNA, and replicate in the cytoplasm
2. There are 4 subgroups: polioviruses, coxsackieviruses, echoviruses, and hepatitis A

Pathology

1. Most infections are subclinical
2. Virus multiplies first in the pharynx, small intestines and local lymph nodes
3. Viremia follows, with spread of virus to the brain and spinal cord

Polioviruses

1. A formalin-inactivated viral vaccine (Salk) containing all 3 serotypes is available for injection
2. A live attenuated viral vaccine (Sabin) containing either a single serotype or all 3 are given orally. It induces sIgA in addition to IgG and IgM and imparts immunity of long duration. May be dangerous in immunosuppressed individuals (use Salk vaccine)
3. Clinical diseases
 - a. Most cases are subclinical
 - b. Aseptic meningitis
 - c. Poliomyelitis-an acute disease which causes flaccid paralysis. The virus replicates in many cells in the body. The target cells are the motor neurons in the CNS where destruction causes paralysis

There are 5 virus groups classified as small RNA viruses

1. _____
2. _____
3. _____
4. _____
5. _____

- A. Salk vaccine
- B. Sabin vaccine
- C. Both
- D. Neither

1. Confers intestinal immunity
2. Confers immunity to viremic phase of infection
3. Not recommended for patients with Bruton's disease

(answers on next page)

Coxsackieviruses

These viruses are classified as either A or B depending on their pathogenicity for mice

Clinical features:

Infection may be inapparent, or result in illness ranging in severity as far as lethal disease. Several different forms of illness can develop as follows:

1. Herpangina (vesicular pharyngitis) is the commonest manifestation of infection by A-serotypes
2. "Aseptic" meningitis can be caused by some A-serotypes or any B-serotypes
3. Epidemic myalgia is a common manifestation of infection by B-serotypes
4. Myocarditis or pericarditis can occur in infants from a B-serotype infection, and B-serotypes occasionally cause a cardiomyopathy in children or adults

Echoviruses

Clinical features

1. Meningitis is commonly caused by echoviruses, but permanent paralysis is very rare
2. Skin rashes, pharyngitis and fever may occur
3. Echoviruses are a cause of a cold-like disease
4. Gastroenteritis and infantile diarrhea have been associated with echovirus infection

Hepatitis A is considered to be in this group as well. (cf section on hepatitis viruses for more information on this agent)

answers

- 1 = B
- 2 = C
- 3 = B
- 4 = A
- 5 = A, B
- 6 = B
- 7 = B

Match the disease with the Coxsackie virus.

serotype A

serotype B

_____ 4. vesicular pharyngitis

_____ 5. aseptic meningitis

_____ 6. myocarditis

_____ 7. pericarditis

(answers at left, bottom)

RHINOVIRUSES

Properties of the group

Naked icosahedral viruses, contain single-stranded RNA

Serotypes:

More than 100 serotypes are known

1. These viruses are the commonest cause of the common cold (rhinitis, rhinorrhea)
2. Rhinoviruses usually remain localized in the nasal mucosa

Artificially-acquired immunity

In view of the number of serotypes, the development of a vaccine is not practicable

CALICIVIRIDAE

Norwalk agent

RNA virus which is single stranded. Etiologically associated with epidemic acute gastroenteritis in children and adults

REOVIRUSES

Properties of the group

1. Naked icosahedral viruses, contain double-stranded RNA
2. Reoviruses can be isolated from feces and respiratory secretions of healthy persons, as well as from patients with a variety of illnesses, e.g., rhinitis
3. Rotaviruses cause gastroenteritis in human infants and lower animals

CORONAVIRUSES

Enveloped helical viruses, contain RNA

Coronaviruses are a common cause of a cold-like disease in adults, but they do not seem to be an important cause of acute respiratory illness in children

Match the disease with the virus

- A. Norwalk agent
- B. Reovirus
- C. Rhinovirus
- D. Rotovirus

1. Rhinitis
 2. Gastroenteritis in adults
 3. Gastroenteritis in infants
- (answers at bottom)

Viruses with dsRNA include

1. _____
2. _____

- Answers
1. B, C
 2. A
 - D. D

HEPATITIS VIRUSES

Viral hepatitis types A and B

Three particular forms of viral hepatitis can be distinguished clinically; these are hepatitis type A (infectious hepatitis or short-incubation hepatitis) = RNA virus; hepatitis type B (serum hepatitis or long-incubation hepatitis) = DNA virus and; hepatitis non-A non-B (disease resembles that of type B). There are multiple antigenic subtypes of hepatitis B and nonA/nonB virus; hepatitis A is now enterovirus 72 (a single antigenic variety)

Clinical features

Incubation period

Type A: 10 to 50 days
Type B: 50 to 180 days
Non A, Non B: 50 to 180 days

Signs and symptoms

The illness is characterized by malaise, anorexia, nausea, vomiting, diarrhea, fever and also jaundice which may or may not appear between two days and three weeks after onset

Type A: In young children, infection frequently remains inapparent or develops into a mild illness without jaundice; in older age groups, infection often leads to icterus or more severe disease

Type B: The Dane particle is the infectious entity. Infection may remain inapparent. Many cases continue to chronic hepatitis with surface antigen carrier state. Primary hepatocellular carcinoma may develop

Laboratory Diagnosis

Serum from the patient is examined for the presence of: Hepatitis A = Ab vs the virus; Hepatitis B = surface Ag-HBsAg, core Ag-HBcAg, and HBeAg
Non A, Non B Hepatitis = by exclusion

Which of the following viral hepatitis agents can be transmitted via transfusion?

- A. Hepatitis A
- B. Hepatitis B
- C. Non-A Non-B
- D. All of the above
- E. A and C only

(answer at bottom)

The Hepadnaviruses are _____
_____.

DELTA HEPATITIS

A unique antigen:antibody system has been observed in some Hepatitis B infections. The antigen is termed the Delta Agent. It is believed to be a defective virus that replicates only in Hepatitis B-infected cells.

(answer = D)

Antiviral therapy

There is no specific antiviral chemotherapy, although pooled human gamma globulin can be used to abort virus infections

Epidemiology

Type A is fecal:oral transmission, Type B is via inoculation and close contact although both viruses can be transmitted by either route. Hepatitis B appears to be associated with drug addicts and homosexuals as well as through parenteral injections

Vaccine

Formalin-treated HBsAg (Dane particles) from capsid carriers has proven effective; subunit proteins synthesized by recombinant DNA technology are being developed

The presence of HBs Ag in serum means

Significance of Hepatitis B Antigens and Antibodies in Serum

Component Present in Serum

<u>HBsAg</u>	<u>Anti-HBs</u>	<u>Anti-HBc</u>	<u>Interpretation</u>
+	-	-	Prodromal period or early acute disease. Person is considered infectious.
+	-	+	Acute disease or chronic carrier. Person is considered infectious.
-	+	+	Convalescing from the disease or immune.
-	+	-	Immune via disease or vaccination.
-	-	+	Recovered from disease and lost reactivity. Antibody of IgG class; low level. or Recent disease; serum taken after HBsAg disappeared, before anti-HBs. Anti-HBc should be high. Such people are infectious.

SLOW VIRUSES

Diseases caused by viruses and virus-like agents belonging to different taxonomic groups, and linked together by the fact that they are all characterized by spongiform encephalopathy, and a long incubation period. Some of these agents may be PRIONS, small proteinaceous infectious particles

Subacute sclerosing panencephalitis (SSPE)

Infectious measles virus has been isolated from brain tissue and lymph nodes of affected individuals with a history of measles

Kuru

The disease seems to have resulted from cannibalism. Kuru has been found only in a single tribe in New Guinea

Progressive Multifocal leukoencephalopathy

A rare disease of the CNS. Papovavirus JC has been isolated from affected tissues

Creutzfeld-Jakob disease

A rare disease of the CNS which has been transmitted to chimpanzees by inoculation of material from the brains of patients

Multiple sclerosis

A CNS disease suspected to be of viral etiology. There is serological evidence suggesting that measles virus may be involved

Match the virus with the disease

A. measles

B. JC papovavirus

1. multiple sclerosis
2. subacute sclerosing panencephalitis
3. progressive multifocal leukoencephalopathy

(answers at bottom of page)

1=A
2=A
3=B

ONCOGENIC VIRUSES

Properties of oncogenic viruses

1. Both RNA and DNA viruses from several taxonomic groups have been shown to be oncogenic
2. Oncogenic viruses spread 2 ways:
 - a) Pre-natal (vertical) transmission from one generation to the next
 - b) Post-natal (horizontal) transmission
3. It appears that some or all of the genes of some oncogenic viruses may be integrated into host DNA; the RNA viruses being integrated by a RNA-dependent DNA polymerase (reverse transcriptase)

Transformation in vitro

The properties of transformed cells include:

1. Loss of contact inhibition
2. Altered cell morphology
3. The presence of new antigens, both in the membrane (tumor specific transplantation antigens) and intracellularly
4. The ability to proliferate rapidly with concomitant high energy demand
5. Altered chromosomal morphology and/or number
6. Ability to grow in soft agar and produce tumors when injected into an appropriate host

In Burkitts lymphoma, the c-myc gene translocates from one chromosome to another in proximity to one of the immunoglobulin gene loci. This does not occur in other EB virus infections such as _____.

POXVIRUSES

Viruses in this group include those responsible for the lesions of molluscum contagiosum in man

HERPESVIRUSES

1. This group causes Marek's disease, a form of lymphomatosis, in chickens, as well as leukemia and reticulosarcoma in non-human primates, renal carcinoma in frogs, and lymphoma in rabbits
2. Epidemiological evidence suggests Herpes simplex type 2 may be associated with cervical carcinoma, although papilloma virus #16 seems a better candidate
3. EB virus is associated with Burkitt's lymphoma (a B cell malignancy) and nasopharyngeal carcinoma

Herpes viruses are associated with the following cancers

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

PAPOVAVIRUSES

1. Papillomaviruses

These cause benign papillomas (warts) in man and other mammalian species. In man, condyloma acuminatum causes a genital wart which is usually benign, but may become malignant (e.g. cervical and laryngeal carcinoma)

2. Polyomavirus

It induces the formation of sarcomas and carcinomas in diverse animal species

3. SV 40 virus and Adenoviruses

In experimental conditions, they induce malignant neoplasms in mice, and causes transformation in vitro of cells of many species.

RETROVIRUSES

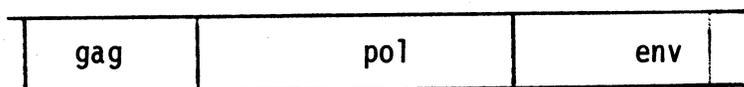
1. These enveloped viruses contain single-stranded RNA; the virion also contains the enzyme reverse transcriptase which, together with certain other enzymes, produces double-stranded DNA homologous to the virion RNA

2. Oncornaviruses can induce leukemia and other blood malignancies, sarcomas, and mammary cancer in experimental animals; AIDS in man (HIV)

3. The oncogene hypothesis proposes that the viral genome consists of at least 2 sets of genes, one of which controls the process of oncogenesis, and the other the production of infectious virus; either, neither or both sets may be evoked by endogenous or exogenous factors

4. Retroviruses pick up host cell genes (e.g., the c-onc gene)

SAMPLE RETROVIRUS GENOME



The gag gene encodes capsid proteins, which are synthesized as a polyprotein precursor and then split by a protease. The pol gene encodes reverse transcriptase. The env gene encodes glycoprotein spikes in the envelope. In addition HIV and HTLV-1 have a tat gene whose action is unknown but is thought to be involved in regulation of viral replication.

VIRUSES AND HUMAN CANCER

Burkitt's lymphoma

Specific antigen and nucleic acid of Epstein-Barr (EBNA) herpesvirus is present in cells cultured from cases of Burkitt's B cell lymphoma. This virus also appears to be responsible for infectious mononucleosis. Patients with Burkitt's lymphoma have a high incidence and high titers of antibody against EB virus

Nasopharyngeal carcinoma

EB herpesvirus has been detected in cells obtained from cases of nasopharyngeal carcinoma, and patients show high titers of anti-EB herpesvirus antibody

Carcinoma of the uterine cervix

Papilloma virus, serotype 16, seems to be etiologically associated with cervical cancer

Hepatocellular Carcinoma

Hepatitis B virus has been associated with primary carcinoma of the liver

Kaposi's Sarcoma

1. Human Immunodeficiency Virus 1 (HIV), a Retrovirus, is etiologically associated with Kaposi's sarcoma and AIDS. It is antigenically different from all other retroviruses.
2. Individuals with AIDS suffer from infections by opportunists such as Pneumocystis, Candida, Cryptococcus and Cryptosporidium. CMV infections are often activated.
3. There will be inverted CD4:CD8 lymphocyte ratios (due to the CD4 "target" of this virus) and normal to elevated levels of IgG, etc. The disease is particularly common in homosexuals, hemophiliacs, and intravenous drug users. Neonates are involved via transplacental passage of the virus. High incidence of the virus is reported in various African countries

Epstein-Barr virus causes 3 human diseases. They are

1. _____
2. _____
3. _____

HIV has a tropism for CD4/CD8 lymphocytes.

HUMAN T-CELL LYMPHOTROPIC VIRUSES

A human Retrovirus has been isolated from numerous cases of adult T-cell leukemia and lymphoma. The HTLV agents have a marked affinity for mature T cells. Clusters of HTLV disease have been reported from the Caribbean basin and the southern United States.

Review Statements

The protein coat (capsid) of true viruses functions to maintain infectivity of nucleic acid in the extracellular state, serves as an antigen in vaccines, and aids in the penetration of virions into susceptible cells.

One of the first events which occurs after a virulent virus infects a cell is cessation of host cell macromolecular biosynthesis.

Interferon is a viral inhibitor produced in virus infected cells.

On recovering from infection with herpesvirus hominis, type I, the patient develops neutralizing antibodies.

IUDR (5-iodo-2'-deoxyuridine) is incorporated into viral DNA to produce faulty nucleic acid.

The etiologic agent of human warts (verrucae) is a papovavirus.

Commercially available influenza vaccine contains inactivated influenza virus, types A and B.

In general, enteroviral diseases are subclinical in nature with less than ten percent of the cases being severe.

Coxsackie A and B viruses cause herpangina and myocarditis, respectively.

Coxsackie viruses of Group B, are responsible for a considerable proportion of cases of aseptic meningitis.

The hepatitis B surface antigen (HBsAG) when found in banked blood renders it undesirable for use in blood transfusions.

The incubation period of serum hepatitis usually ranges from 50-180 days.

Hepatitis B virus is more resistant to chemical and physical agents than is hepatitis A virus (HAV).

The finding of Negri bodies, cytoplasmic inclusions in neurons, is specific for the pathologic diagnosis of rabies.

Togaviruses may infect the liver to produce yellow fever or the brain to cause encephalitis.

Virus-induced cell transformation may result in the formation of new enzymes and antigens as well as altered cell morphology and tumor formation.

Cell susceptibility range of a virus is determined by surface protein units of the capsid or envelope.

The Epstein-Barr virus causes infectious mononucleosis.

Rhinoviruses are acid labile and hence can not survive the acidity of the stomach; they do not colonize the GI tract as do the other Picornaviruses.

The picornaviruses are single strands of (+) RNA. During replication replicative intermediates (RI = double stranded RNA: a + RNA and a -RNA) are formed by the enzyme replicase.

Myxoviruses and paramyxoviruses also have an RI; however, these viruses have a (-) RNA as the parental type. Myxoviruses have eight distinct (-) RNA strands; paramyxoviruses only have one.

REOVirus RNA is double stranded RNA which exists in 10 distinct segments.

All (-) RNA viruses have a virion-bound transcriptase which synthesizes (+) RNA used as mRNA for protein synthesis.

Naked polio virus, (+) RNA, is able to penetrate mammalian cell membranes and establish an infection under appropriate laboratory conditions. Myxoviral (-) RNA can not do this because the purified RNA would not contain the transcriptase needed to make messenger RNA.

The oncornaviruses replicate through a DNA replicative intermediate. Reverse transcriptase synthesizes single stranded DNA from the parental RNA template. DNA polymerase then synthesizes double stranded DNA which is integrated into the host cell genome.

Measles is prevented by administration of an attenuated monovalent vaccine. It may be included with rubella and mumps vaccines to produce a polyvalent product.

Subacute sclerosing panencephalitis is thought to be caused by measles.

Complications of measles include encephalitis and pneumonia.

Clinical signs and symptoms of measles include photophobia, cough, coryza, conjunctivitis and Koplik spots.

The pathogenesis of measles and mumps include a primary infection of the respiratory tract followed by a viremia.

Mumps is a disease of secretory cells and often involves the pancreas.

Following the initial attack of mumps, long lasting protective immunity is produced.

Mumps is spread from the infected patient by droplets (aerosol) or fresh fomites.

Antibodies to the hemagglutinin spikes of influenza viruses are protective.

Type A influenza viruses are known to cause pandemics while types B and C influenza viruses are less likely to do so.

Antigenic drift is brought about by minor changes in type A influenza viruses while antigenic shift involves major changes in one or more of the glycoprotein spikes.

Orthomyxoviruses contain eight pieces of single stranded-RNA, and an RNA-dependent RNA polymerase.

Integration of viral genome is essential for transformation of cells.

Translocation of the c-myc gene to one of the immunoglobulin gene loci is characteristic of Burkitts lymphoma, but is not seen in infectious mononucleosis.

Parainfluenza viruses cause bronchitis, bronchiolites and croup in children and a common cold-like disease in adults.

Influenza viruses are replicated in both the cytoplasm and nucleus, mature in the cytoplasm and are released by budding through the modified cell membrane.

Paramyxoviruses resemble orthomyxoviruses morphologically but are larger and the genome is contained in one continuous RNA strand.

Respiratory syncytial virus commonly produces severe disease (bronchitis, bronchiolitis and croup) in infants.

Togaviruses are spread by the bite of an infected arthropod.

Mammals and birds are reservoir hosts for arboviruses.

Poliovirus is spread throughout the human body via the lymphatics and blood.

The portal of entry of enteroviruses is the oral cavity and the viruses invade through the oropharyngeal and intestinal mucosa.

ECHO viruses are responsible for many cases of aseptic meningitis.

Rhinoviruses (the etiologic agents of the common cold) are Picornaviruses.

Polio vaccines must be polyvalent as there are 3 antigenically distinct viruses.

The Sabin polio vaccine contains attenuated virus which is taken orally while the Salk polio vaccine is formalin-inactivated and is administered by injection.

Rhabdoviruses are single stranded, RNA-containing, bullet-shaped viruses; Rabies virus is a rhabdovirus.

Rabies virus is usually spread by the bite or lick of a rabid animal.

The rabies vaccine of choice contains inactive human diploid cell produced virus.

Rabies is usually diagnosed by immunofluorescence applied to brain tissue.

The Dane particle of hepatitis virus is composed of core antigen surrounded by surface antigen and is the infectious particle.

Type A hepatitis is spread primarily by the fecal-oral route and type B hepatitis is spread primarily by injection but both viruses can be spread by either route.

Non A, non B type hepatitis is spread primarily by injection.

All Retroviral genomes contain gag, pol and env genes; HIV and HTLV-1 also have a tat gene which is thought to be involved in regulation of viral replication.

Rotaviruses are REOviruses which are the causal agents of infantile diarrhea.

Pharyngeal-conjunctival fever is the most common syndrome associated with adenoviruses.

An eosinophilic, intracytoplasmic inclusion called the Guarnieri body is formed frequently in variola-infected cells.

The poxvirus virion contains several enzymes including a DNA-dependent RNA polymerase.

The pathogenesis of smallpox includes two viremia stages during which the virus is spread throughout the body.

Polyoma viruses produce tumors in many organs of many animals, especially mice.

A slow virus requires a prolonged incubation period (months to years) before appearance of disease.

Kuru (a disease seen in New Guinea) and Creutzfeldt-Jacob diseases are transmissible spongiform encephalopathies of humans.

Subacute sclerosing panencephalitis (SSPE) is a chronic, fatal disease of humans associated with a previous case of measles.

Rubella virus belongs to the Togavirus family.

Lasting protective immunity is usually produced upon convalescence from rubella.

Rubella virus is known to cross the human placenta and to infect the developing fetus.

Congenital rubella is the result of fetal infection during the first trimester of pregnancy. Following birth, virus may be excreted and cause a rubella outbreak in a newborn nursery.

An attenuated viral vaccine is effective in the prevention of rubella but should not be given to pregnant humans.

The "patient's immune response" to viral disease is the most commonly used diagnostic test. A four-fold rise in antibody titer between acute and convalescent serum specimens is considered diagnostic.

Cells transformed by viruses may be characterized by having the ability to induce tumors in animal hosts and possessing virus-specific tumor antigens.

Oncogenic viruses may be transmitted naturally in a vertical fashion, from one generation to another, or horizontally transmitted from one animal to another.

The provirus of an oncornavirus is a double-stranded DNA copy of the viral genome synthesized by a virion enzyme.

The capsid proteins in the progeny of a hybrid virus (e.g. polio RNA in a coxsackie capsid) will be directed by the genetic information of the nucleic acid donor.

RNA tumor viruses contain a reverse transcriptase and a single strand of RNA.

The Epstein-Barr virus (EBV) has been recovered from Burkitt's lymphoma tissue, from human patients with nasopharyngeal carcinomas, and from human patients with infectious mononucleosis.

Herpes simplex virus, type 1, may have produced latent infection in the majority of the human population.

Inclusion bodies in host cells infected with a herpes simplex virus are found in the nucleus.

Reactivation of a latent infection in the form of shingles (herpes zoster) occurs with the etiologic agent of varicella (chicken pox).

Herpes simplex virus may cause aseptic meningitis.

Herpes simplex virus, type 2, is associated with genital herpes (lesions of genital tract) and neonatal herpes; it has also been implicated in cervical carcinoma.

Adenosine arabinoside (Ara-A) has been used quite effectively in treating herpesvirus infections, including serious systemic infections.

Zoster (shingles) is a recurrent disease; the lesions appear unilaterally on the body, in a dermatome distribution.

Diagnosis of infectious mononucleosis can be done using a serological test for detecting heterophile antibody.

Non-A Non-B Hepatitis virus is the most common cause of transfusion associated hepatitis in the USA.

Peripheral ganglia are believed to be the sites of latency of herpes viruses.

Aspirin therapy in children with influenza or chickenpox is contraindicated due to the possible association of these conditions with Reye syndrome.

The predominant cell in the spinal fluid in viral meningitis is the lymphocyte. This is the same cell that would predominate in the perivascular cuffing also noted in these diseases.

The polio virus genome is +mRNA. This is also true of the togaviruses and rubella.

The REOvirus RNA is double-stranded.

The poliovirus genome is polycistronic, thus the synthesized polyprotein must be cleaved after synthesis.

Male homosexuals with AIDS may have HBsAg antibody in their serum in addition to antibody to the HIV virus.

Hepadnaviral DNA is circular (as is that of the parvoviruses); all other viruses have linear nucleic acids.

Virology Proficiency Test

This set of 40 questions was used in an examination given to sophomore Medical students. Their mean score was 80 percent. A score below 60 percent would probably suggest that the examinee is in need of more review of the Virology section of the text.

1. The genome of papovaviruses is
 - A. circular single stranded DNA.
 - B. circular double stranded RNA.
 - C. linear single stranded DNA.
 - D. circular double stranded DNA.

2. Rotavirus infections
 - A. follow the typical natural history of other enteroviruses.
 - B. are treated with ribovirin and fluids.
 - C. occur because of neglect in vaccination.
 - D. are important causes of diarrhea in young children.

3. Inhibits viral penetration and uncoating.
 - A. Acyclovir
 - B. Amantadine
 - C. Methisazone
 - D. Ara A
 - E. FUDR

4. RNA-dependent-RNA-polymerase may be found in the following viruses except
 - A. Parainfluenza.
 - B. Reovirus.
 - C. Influenza.
 - D. Western equine encephalitis.

5. Which of the following is the preferred post-exposure therapy for rabies?
 - A. Human anti-rabies immunoglobulin
 - B. Duck embryo virus vaccine
 - C. Human diploid cell culture virus vaccine
 - D. All of the above
 - E. A and C only

6. Which of the following statements about virions is not true?
 - A. They may contain lipids.
 - B. They are obligate intracellular parasites.
 - C. The symmetry of the nucleocapsid is dependent on the host cell in which it is propagated.
 - D. Antibodies to surface protein can neutralize infectivity.
 - E. Viruses with envelopes are usually sensitive to lipid solvents.

7. Which of the following statements is true for the rabies virus.
- A. A live attenuated virus vaccine is available for use in man.
 - B. Virus can be isolated from blood of the infected person in the last two weeks of disease.
 - C. Bats are the source for most cases of rabies in the USA.
 - D. The virus contains its own RNA dependent RNA polymerase.
8. An infectious RNA genome is characteristic of which of the following viruses?
- A. Rhabdovirus
 - B. Measles virus
 - C. Parainfluenza virus
 - D. Rhinovirus
9. Interferon
- A. once produced, persists for months.
 - B. requires T-lymphocytes for expression.
 - C. acts indirectly by blocking specific viral receptors.
 - D. synthesis can be induced in living cells exposed to viral or nonviral inducers.
10. The diagnosis of rubella infection in a newborn is accomplished by
- A. measuring IgM antibody in the mother.
 - B. measuring IgA antibody in the newborn.
 - C. isolation of virus from the placenta.
 - D. measuring IgM antibody in the newborn.
11. In comparing the differences between the orthomyxoviruses and the paramyxoviruses, one could say that:
- A. Orthomyxovirus replication is confined to the cytoplasm.
 - B. Paramyxoviruses have a primer requirement for transcription.
 - C. The rate of genetic recombination is higher for paramyxoviruses.
 - D. The genome of orthomyxoviruses is segmented.
12. Pandemics of influenza are due to
- A. antigenic drifting.
 - B. a mutant paramyxovirus.
 - C. extensive population migration.
 - D. antigenic shifting.
13. The influenza A virion
- A. contains 10 segments of RNA.
 - B. contains 8 segments of DNA.
 - C. induces host cell polymerase activity.
 - D. contains glycoproteins in the envelope.

- A = 1, 2, 3, correct
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14. Important factors involved in viral disease production include the
1. nutritional state of the host.
 2. immunologic status of host.
 3. virus dosage.
 4. age of the host.
15. Which of the following is/are true of the yellow fever virus?
1. An effective vaccine is available.
 2. Yellow fever virus is a bunyavirus.
 3. Both man and other animals may act as reservoirs.
 4. The insect vector for the virus is the sandfly.
16. Which of the following statement(s) is/are true for defective virus particles?
1. Formed in the course of a normal infection in the animal.
 2. Interfere with the replication of wild-type virus in the mixed infection.
 3. Contain less genetic information than wild-type virus.
 4. Increase in number with high multiplicities of infection.
17. Which pairs of viruses listed below are taxonomically related?
1. Dengue virus and yellow fever virus
 2. Rubella virus and mumps virus
 3. Poliovirus and rhinovirus
 4. Respiratory syncytial virus and influenza virus
18. Encephalitis caused by togavirus such as Eastern equine, Western equine and St. Louis encephalitis viruses
1. occurs most frequently in the summer and early autumn in the United States.
 2. could be eliminated by vaccinating or destroying all horses.
 3. is best prevented by mosquito control program.
 4. spread directly from human to human in severe epidemics.
19. Varicella-Zoster virus
1. causes chickenpox.
 2. has a tropism for nerve cells.
 3. is spread by respiratory secretions.
 4. can be activated to give manifestations in a dermatome distribution.

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20. Characteristic feature(s) of the herpes virus group include(s)
1. latent infections.
 2. presence of an envelope containing peplomers.
 3. budding from the nuclear membrane of a cell.
 4. induction of cytoplasmic inclusion bodies.
21. Which of the following statements is (are) true of Herpes simplex virus type 1?
1. It is antigenically related to herpes simplex type 2.
 2. It can cause venereal disease.
 3. The nucleocapsid contains a double strand of DNA.
 4. The most common primary infection seen is gingivostomatitis.
22. Which of the following is/are characteristic of hepatitis A virus?
1. Small non-enveloped icosahedral capsid with single-stranded nucleic acid genome.
 2. Previously known as "serum hepatitis".
 3. May be transmitted in a manner similar to poliovirus.
 4. Attenuated vaccine available.
23. Which of the following statements about viral hepatitis is/are true?
1. Hepatitis B is a DNA virus.
 2. NonA-NonB hepatitis is the most frequent cause of transfusion associated hepatitis in the USA.
 3. Pooled human gamma globulin can be used to passively immunize against hepatitis A.
 4. Routine screening of blood bank blood for hepatitis A virus is now being done.
24. With type B hepatitis
1. the finding of anti-HBcAg in the blood denotes a noninfectious state of the disease.
 2. several subtypes containing a common core antigen exist.
 3. HBcAg is the major component of the available vaccine.
 4. the presence of Hbs Ag antigen in the blood reflects infectivity of the blood.

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25. What feature(s) would you expect to be altered in a herpes simplex virus mutant resistant to acyclovir?
- 1. RNA polymerase.
 - 2. Thymidine kinase.
 - 3. Neuraminidase.
 - 4. DNA polymerase.
26. The disease called shingles is
- 1. caused by the same virus as the disease chickenpox.
 - 2. caused by a virus of the family Herpesviridae.
 - 3. due to reactivation of virus in dorsal root ganglia.
 - 4. increased in incidence by immunosuppression.
27. Example(s) of virus(es) capable of inducing persistent viral infections include(s):
- 1. Measles virus.
 - 2. Herpes simplex virus type 1.
 - 3. Hepatitis B virus.
 - 4. St. Louis encephalitis virus.
28. Inapparent (subclinical) viral infections
- 1. are important in developing life-long immunity.
 - 2. occur more often than apparent infections.
 - 3. can lead to latency of the virus.
 - 4. are seldom seen in children between 2 and 8 years of age.
29. A virus can cause disease in the host by
- 1. producing metabolites that result in cellular injury.
 - 2. inducing an antibody response.
 - 3. replicating in the cerebral spinal fluid resulting in increase in pressure.
 - 4. rendering vital target cells nonfunctional.
30. Replication of pox virus is unique in comparison to other DNA viruses in that
- 1. the virion does not possess viral enzymes.
 - 2. replication occurs only in the cytoplasm.
 - 3. the virion does not contain lipid.
 - 4. the viral DNA contains more than 100 genes.

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31. The major complication(s) of measles infection is/are:
- 1. encephalomyelitis.
 - 2. croup.
 - 3. pneumonia.
 - 4. loss of hair.
32. Transmission of respiratory syncytial virus (RSV) is mediated by
- 1. aerosols.
 - 2. fecal contamination of food stuffs.
 - 3. intimate contact with the infected patient.
 - 4. dirty diapers.
33. Parainfluenza infections
- 1. may be clinically similar to RSV infections.
 - 2. do not respond to acyclovir treatment.
 - 3. may be transmitted by large droplets.
 - 4. do not become epidemic.
34. The hemagglutinin of influenza A is
- 1. the target of neutralizing antibody.
 - 2. responsible for detaching the virion from the host cell.
 - 3. responsible for attaching the virion to the host cell.
 - 4. the target of ribavirin activity.
35. The neuraminidase of influenza A
- 1. is the target of amantadine activity.
 - 2. is a tetramer.
 - 3. is responsible for attachment of the virion to the host cell.
 - 4. may show antigenic drifting or shifting.
36. Early transcription of DNA virus genomes may be associated with
- 1. induction of viral DNA synthesis.
 - 2. non-structural viral proteins.
 - 3. protein(s) that binds to DNA.
 - 4. cell transformation.
37. Currently used inactivated vaccines include:
- 1. Polio.
 - 2. Influenza A.
 - 3. Hepatitis B.
 - 4. Rabies.

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38. Serious complication(s) of enterovirus infections include

1. stillbirth.
2. diarrhea resulting in dehydration.
3. hepatocellular carcinoma.
4. aseptic meningitis.

39. Antiviral agents include

1. 2-deoxy-D-glucose (Gluconil).
2. Amantadine.
3. Ribavirin.
4. Acyclovir.

40. Acyclovir works by

1. acting as a substrate for host thymidine kinase.
2. inhibiting viral DNA polymerase.
3. preventing uncoating of herpes virions.
4. being incorporated as a DNA chain terminator.

ANSWER SHEET

- | | |
|--------------|--------------|
| 1. <u>D</u> | 21. <u>E</u> |
| 2. <u>D</u> | 22. <u>B</u> |
| 3. <u>B</u> | 23. <u>A</u> |
| 4. <u>D</u> | 24. <u>C</u> |
| 5. <u>E</u> | 25. <u>C</u> |
| 6. <u>C</u> | 26. <u>E</u> |
| 7. <u>D</u> | 27. <u>A</u> |
| 8. <u>D</u> | 28. <u>A</u> |
| 9. <u>D</u> | 29. <u>C</u> |
| 10. <u>D</u> | 30. <u>C</u> |
| 11. <u>D</u> | 31. <u>B</u> |
| 12. <u>D</u> | 32. <u>B</u> |
| 13. <u>D</u> | 33. <u>A</u> |
| 14. <u>E</u> | 34. <u>B</u> |
| 15. <u>B</u> | 35. <u>C</u> |
| 16. <u>E</u> | 36. <u>E</u> |
| 17. <u>B</u> | 37. <u>E</u> |
| 18. <u>B</u> | 38. <u>C</u> |
| 19. <u>E</u> | 39. <u>E</u> |
| 20. <u>A</u> | 40. <u>C</u> |