General Concepts

Aspects of Viral Epidemiology

Viruses must enter cells to multiply. Transmission may be horizontal (between different individuals), or vertical (between mother and offspring either before, during, or immediately after birth).

Portals of Entry and Exit

Portals of entry and exit in horizontal transmission include all body surfaces, or the blood stream, by arthropod bite. Vertical transmission may occur in the ovum, via the placenta, during birth, or in the colostrum or milk. The mode of exit is not necessarily the same as the portal of entry.

Viral Zoonoses

Some human viral infections are acquired from an animal source, which may be via an arthropod in which the virus may multiply.

Epidemiologic Features of Viral Infections

Each kind of viral infection is characterized by a particular mode(s) of transmission, a reasonably well-defined incubation period, a typical period of communicability, and a proportion of subclinical cases. Many infections have a seasonal incidence.

Evolution of Viruses

Viruses, especially those with RNA genomes, have a very high rate of mutation (see chapter 42 on virus genetics). Many viruses undergo recombination, and those with segmented genomes may undergo reassortment. Evolutionary changes are due to the interplay of genetic variability and natural selection, often during the transmission phase.

INTRODUCTION

Within the field of medical virology, pathogenesis (see Ch. 45) concerns the processes by which viruses infect individuals and cause disease, whereas epidemiology examines the transfer and persistence of viruses in human populations. Epidemiology and evolution are linked because epidemiologic mechanisms of transfer largely determine the natural selection component of viral evolution. Since viruses multiply only within cells, the epidemiology of viral diseases does not involve multiplication in food, water, or soil. However, some viruses that infect man may multiply and persist in other animals, such as arthropods, rodents and bats.
Portals of Entry and Exit

The human body presents three large epithelial surfaces to the environment—the skin, the respiratory mucosa, and the alimentary tract, and two lesser surfaces—the genital tract and the conjunctiva (Fig. 48-1). To gain entry to the body, viruses must either (1) infect cells in one of these surfaces, (2) otherwise breach the surface (by trauma, the bite of an arthropod or animal, or injection, transfusion or transplantation), or (3) be transmitted congenitally. Viruses escape from the body via the same surfaces, often but not necessarily by the route used as a portal of entry.

FIGURE 48-1 Body surfaces as sites of viral infection and shedding.

Infection via the Skin

Intact skin has a tough outer layer of cornified cells. This barrier protects the body from infection, but is frequently breached by trauma or by inoculation (e.g., by a needle or an insect bite (Table 48-1). Virus inoculation by injection or transfusion is now common as a result both of medical procedures and of social practices such as sharing needles by intravenous drug users. In Western society, hepatitis B and hepatitis C viruses are usually transmitted in this way; less often, cytomegalovirus, Epstein-Barr virus (EBV), and the human immunodeficiency viruses (HIV) may be transferred in this manner. Hepatitis B and hepatitis C viruses may also be transferred by minor "surgical" procedures like tattooing, dentistry, ear piercing, and even (in the past) arm-to-arm vaccination.
Infection by arthropod bite is important for the large number of viruses that multiply in both arthropods and vertebrates (the arboviruses, which include most togaviruses and flaviviruses, the Orbivirus genus of the reoviruses, and all bunyaviruses except the hantaviruses). In such infections the virus is usually injected directly into small blood vessels. In contrast to the many viruses that enter the body through the skin, only a few are shed from it in an infectious form. Herpes zoster lesions usually shed few virus particles, but they are epidemiologically important in that adults shedding virus may transmit chickenpox to susceptible children. Some viruses that infect humans by the respiratory tract may be shed from superficial lesions of the oral mucosa, (e.g., measles, and in the past, smallpox viruses) or from infected salivary glands, (e.g., mumps virus).

**Infection via the Respiratory Tract**

In modern Western society the respiratory tract is by far the most common route of viral infection. The average human adult breathes in about 600 L of air every hour; small suspended particles (<2 µm diameter) pass down the pharynx and a few reach the alveoli. Viruses in such droplets may initiate infection if they attach to cells of the respiratory tract. Many respiratory viruses are also transferred by contact with contaminated fingers or fomites (inanimate carriers). The viruses commonly referred to as the respiratory viruses multiply only in the respiratory tract and cause colds, pharyngitis, bronchiolitis, and pneumonia; other viruses that initiate infection via the respiratory tract can produce generalized infections (Table 48-2).

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**TABLE 48-1 Viruses That Initiate Infection by Penetration of Skin or That Cause Direct Infection of Genital or Conjunctival Mucosa**

<table>
<thead>
<tr>
<th>Route</th>
<th>Family or Genus</th>
<th>Specific Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penetration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor trauma</td>
<td>Hepadnaviridae</td>
<td>Hepatitis B virus</td>
</tr>
<tr>
<td></td>
<td>Papillomavirus</td>
<td>All types</td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>HSV-1, HSV-2</td>
</tr>
<tr>
<td></td>
<td>Poxviridae</td>
<td>Molluscum contagiosum virus, milker's nodes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>parapoxivirus, vaccinia virus, cowpox virus,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>orthopoxivirus</td>
</tr>
<tr>
<td>Arthropod bite</td>
<td>Retroviridae</td>
<td>HIV-1, HIV-2</td>
</tr>
<tr>
<td>Mechanical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological</td>
<td>Poxviridae</td>
<td>Tanganyikavirus</td>
</tr>
<tr>
<td></td>
<td>Alphavirus</td>
<td>All species</td>
</tr>
<tr>
<td></td>
<td>Flavivirus</td>
<td>All species</td>
</tr>
<tr>
<td></td>
<td>Reoviridae</td>
<td>Colorado tick fever virus</td>
</tr>
<tr>
<td></td>
<td>Bunyaviridae</td>
<td>LaCrosse virus, sandfly fever virus, Rift Valley fever virus</td>
</tr>
<tr>
<td>Bite of vertebrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection</td>
<td>Rhabdoviridae</td>
<td>Rabies virus</td>
</tr>
<tr>
<td>Genital tract</td>
<td>Herpesviridae</td>
<td>B herpesvirus</td>
</tr>
<tr>
<td></td>
<td>Hepadnaviridae</td>
<td>Hepatitis B virus</td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>Cytomegalovirus, EBV</td>
</tr>
<tr>
<td></td>
<td>Filoviridae</td>
<td>Ebola virus, Marburg virus</td>
</tr>
<tr>
<td></td>
<td>Rotoviridae</td>
<td>HIV-1, HIV-2, HTLV-1</td>
</tr>
<tr>
<td></td>
<td>Flaviridae</td>
<td>Hepatitis C virus</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adenoviridae</td>
<td>Some types</td>
</tr>
<tr>
<td></td>
<td>Picornaviridae</td>
<td>Enterovirus 70, coxsackievirus 24</td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>HSV-1</td>
</tr>
</tbody>
</table>
The respiratory tract sheds many different viruses and is the main route of excretion for all viruses that initiate infection by respiratory means.

**Infection via the Alimentary Tract**

Although the surface of the alimentary tract is potentially exposed to a great number and variety of viruses, the harsh conditions in the stomach and duodenum protect it from many viruses. For instance, viruses that have a lipid-containing envelope are usually inactivated by the acid, bile salts and enzymes that occur in the stomach and duodenum. Infection via the gut, therefore, is due to viruses that resist these chemicals. These viruses multiply in the cells of the small intestine and are excreted in the feces (Table 48-3). Such viruses usually resist environmental conditions and may cause water- and food-borne epidemics.

**TABLE 48-3 Viruses That Initiate Infection via the Alimentary Tract**

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>Family</th>
<th>Specific Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth or oropharynx</td>
<td>Poxviridae</td>
<td>Monkeypox virus</td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>HSV, EBV, cytomegalovirus</td>
</tr>
<tr>
<td>Intestinal tract</td>
<td>Reoviridae</td>
<td>Rotaviruses</td>
</tr>
<tr>
<td>Producing enteritis</td>
<td>Caliciviridae</td>
<td>Norwalk agent and related viruses</td>
</tr>
<tr>
<td></td>
<td>Adenoviridae</td>
<td>Several types</td>
</tr>
<tr>
<td>Producing generalized disease, usually without local symptoms</td>
<td>Picornaviridae</td>
<td>Many enteroviruses including polioviruses and hepatitis A virus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatitis E virus</td>
</tr>
<tr>
<td>Usually symptomless</td>
<td>Caliciviridae</td>
<td>Some enteroviruses</td>
</tr>
<tr>
<td></td>
<td>Picornaviridae</td>
<td>Some adenoviruses</td>
</tr>
<tr>
<td></td>
<td>Adenoviridae</td>
<td>Reoviruses</td>
</tr>
<tr>
<td></td>
<td>Reoviridae</td>
<td>Coronavirus (rarely)</td>
</tr>
</tbody>
</table>

Recently, the significance of trauma to the mucosa of the lower rectum as a result of anal intercourse has been highlighted by the frequency of sexually transmitted viruses, notably HIV in homosexual men.

**Infection via the Genital Tract**

During the last decade the list of sexually transmitted viruses (Table 48-4) of the female genital tract has been enlarged by the demonstration of heterosexual transmission of HIV, the human T-cell lymphotropic virus type 1 (HTLV-1) and other viruses (Table 48-4).

**TABLE 48-2 Viruses That Initiate Infection via the Respiratory Tract**

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>Family</th>
<th>Specific Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local respiratory infection</td>
<td>Orthomyxoviridae</td>
<td>Influenza A and B viruses</td>
</tr>
<tr>
<td></td>
<td>Paramyxoviridae</td>
<td>Parainfluenza viruses, respiratory syncytial virus</td>
</tr>
<tr>
<td>Coronaviridae</td>
<td></td>
<td>Rhinoviruses, a few enteroviruses</td>
</tr>
<tr>
<td>Adenoviridae</td>
<td></td>
<td>Many serotypes</td>
</tr>
<tr>
<td>Generalized disease, usually without initial respiratory symptoms</td>
<td>Herpesviridae</td>
<td>Varicella virus, EBV, cytomegalovirus</td>
</tr>
<tr>
<td></td>
<td>Papovaviridae</td>
<td>BK virus, JC virus</td>
</tr>
<tr>
<td></td>
<td>Parvoviridae</td>
<td>Erythema infectiosum virus</td>
</tr>
<tr>
<td></td>
<td>Paramyxoviridae</td>
<td>Mumps virus, measles virus</td>
</tr>
<tr>
<td></td>
<td>Togaviridae</td>
<td>Rubella virus</td>
</tr>
<tr>
<td></td>
<td>Picornaviridae</td>
<td>Some enteroviruses</td>
</tr>
<tr>
<td></td>
<td>Bunyaviridae</td>
<td>Hantaviruses</td>
</tr>
<tr>
<td></td>
<td>Arenaviridae</td>
<td>Lymphocytic choriomeningitis virus, Lassa fever virus</td>
</tr>
<tr>
<td></td>
<td>Poxviridae</td>
<td>Smallpox virus (in the past)</td>
</tr>
</tbody>
</table>

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possibly hepatitis C virus. The importance of genital transmission of particular papillomaviruses in the causation of cervical carcinoma is receiving much attention (see Ch. 66). Genital ulcers due to herpes simplex type 2 (HSV-2), a sexually transmitted virus, are important in themselves and increase the likelihood of heterosexual transmission of HIV.

<table>
<thead>
<tr>
<th>Site</th>
<th>Family</th>
<th>Specific Viruses</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular</td>
<td>Adenoviridae</td>
<td>Human type 8 virus, and others</td>
<td>Conjonctivitis</td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>HSV-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poxviridae</td>
<td>Vaccinia virus (occidental)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Picornaviridae</td>
<td>Enterovirus 70, coxsackievirus A24</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paramyxoviridae</td>
<td>Newcastle disease virus</td>
<td></td>
</tr>
<tr>
<td>Genital</td>
<td>Papoviridae</td>
<td>Human papillomaviruses 16, 18, others</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herpesviridae</td>
<td>HSV-2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytomegalovirus</td>
<td>Conjonital disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Papoviridae</td>
<td>Human papillomaviruses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepadnaviridae</td>
<td>Hepatitis B virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retroviridae</td>
<td>HIV-1, HIV-2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flaviviridae</td>
<td>Hepatitis C virus</td>
<td></td>
</tr>
<tr>
<td>Excretion in urine</td>
<td>Herpesviridae</td>
<td>Cytomegalovirus</td>
<td>Generalized disease</td>
</tr>
<tr>
<td></td>
<td>Togaviridae</td>
<td>Rubella virus</td>
<td>Rubella</td>
</tr>
<tr>
<td></td>
<td>Paramyxoviridae</td>
<td>Measles virus, mumps virus</td>
<td>Measles, mumps</td>
</tr>
<tr>
<td></td>
<td>Arenaviridae</td>
<td>Hepatitis B virus</td>
<td>Hepatitis</td>
</tr>
<tr>
<td></td>
<td>Bunyaviridae</td>
<td>Hantavirus</td>
<td>In urine of rodents</td>
</tr>
</tbody>
</table>

A few viruses are shed in the urine of humans or, in the case of arenavirus and hantavirus infections, of rodents. The viruses from rodent urine may then cause human disease as a result of the inhalation of dust containing virus particles (hemorrhagic fever in the case of arenaviruses and hemorrhagic fever with renal syndrome or hantavirus pulmonary syndrome from hantavirus infections).

**Infection of the Conjunctiva**

Viruses of several families occasionally infect the conjunctiva directly (Table 48-4), but conjunctivitis in generalized diseases such as measles is caused by virus that reaches the conjunctiva through the bloodstream.

**Vertical Transmission**

Vertical transmission refers to the transfer of virus from parent to offspring, and may occur via the ovum, across the placenta, during birth, or via the mother's milk. Viruses that cross the placenta include rubella virus and cytomegaloviruses, which may cause congenital defects or severe neonatal disease, and HIV.

The classic examples of vertical transmission of viruses in animals are lymphocytic choriomeningitis virus in mice, transmitted via the cytoplasm of the egg or the placenta, and the retroviruses that cause avian leukosis and sarcoma and murine leukemia. The retroviruses are transferred either as an integrated DNA copy of the viral RNA genome, or more rarely, in birds, as infectious virions via the egg. HTLV-1, the retrovirus that causes adult T-cell leukemia/lymphoma (see Ch. 62), appears to be transmitted horizontally, although integrated provirus is found in the lymphocytes of affected individuals.

Vertical transmission of cytomegalovirus may occur through the mother's milk, and both cytomegalovirus and herpes simplex virus type 1 can be transmitted from parents to infants by salivary contamination. Then, because of its long latency and the periodic recurrence of lesions, the same virus may be transferred to the next generation. In small, isolated human populations, infections with zoster-chickenpox may be maintained by a similar cycle, zoster in the grandmother causing chickenpox in the grandchild by horizontal transmission. Perinatal transmission of hepatitis B virus is important in much of Africa and Asia because it is common and often produces a persistent infection that may lead to cirrhosis of the liver or primary hepatocellular carcinoma.
Viral Zoonoses

A wide range of viruses that can cause human diseases survive in nature as infections of other animals; humans are only occasionally infected, and infection of humans is usually unimportant for viral survival. These infections are called zoonoses (Table 48-5); many are caused by arboviruses (viruses that are transmitted by arthropod vectors) and some are due to direct infection. However, some arbovirus infections, notably dengue and yellow fever, can be maintained indefinitely by human-to-human mosquito transmission, although both have animal reservoir hosts also.

### TABLE 48-5 Viruses Responsible for Viral Zoonoses

<table>
<thead>
<tr>
<th>Family</th>
<th>Species</th>
<th>Reservoir Host</th>
<th>Mode of Transmission</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poxviridae</td>
<td>Cowpox virus</td>
<td>Cattle, cats, rodents</td>
<td>Contact, skin abrasions</td>
<td>Skin pustule</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cattle</td>
<td>Contact, skin abrasions</td>
<td>Skin nodule</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sheep, goats</td>
<td>Contact, skin abrasions</td>
<td>Skin ulcer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Humans, squirrels,</td>
<td>Contact, including oral</td>
<td>Generalized with rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>? Rodents, monkeys</td>
<td>Inject bite (mechanical)</td>
<td>Skin nodule</td>
</tr>
<tr>
<td>Bunyaviridae</td>
<td>Hantavirus</td>
<td>Rodents</td>
<td>Contact</td>
<td>Hemorrhagic fever</td>
</tr>
<tr>
<td>Flaviviridae</td>
<td>Rabies virus</td>
<td>Carnivores, bats</td>
<td>Animal bite, respiratory</td>
<td>Central nervous system disease</td>
</tr>
<tr>
<td>Arenaviridae</td>
<td>Ebola, Marburg virus</td>
<td>? Monkey</td>
<td>Contact, injection</td>
<td>Hemorrhagic fever</td>
</tr>
<tr>
<td>Orthomyxovirida</td>
<td>Influenza A virus</td>
<td>Birds, pigs, horses</td>
<td>Respiratory</td>
<td>Fever and cough</td>
</tr>
<tr>
<td>Arenaviridae</td>
<td>Lympohocytic chorio-meningitis</td>
<td>Rodents</td>
<td>Respiratory, contact</td>
<td>Hemorrhagic fever</td>
</tr>
<tr>
<td></td>
<td>virus, Lassa virus, Junin Virus,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Machupu virus</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 48-5 (continued)

<table>
<thead>
<tr>
<th>Family</th>
<th>Species</th>
<th>Reservoir Host</th>
<th>Mode of Transmission</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunyaviridae</td>
<td>California encephalitis virus</td>
<td>Mammals, monkeys</td>
<td>Mosquitoes</td>
<td>Fever, encephalitis</td>
</tr>
<tr>
<td></td>
<td>La Crosse virus</td>
<td>Mammals, birds</td>
<td>Mosquitoes</td>
<td>Fever, encephalitis</td>
</tr>
<tr>
<td></td>
<td>Tashyna virus</td>
<td>Mammals</td>
<td>Mosquitoes</td>
<td>Fever, encephalitis</td>
</tr>
<tr>
<td>Phlebovirus</td>
<td>Sandfly fever virus</td>
<td>Humans, monkeys</td>
<td>Mosquitoes</td>
<td>Fever, myalgia</td>
</tr>
<tr>
<td></td>
<td>Ricketts fever virus</td>
<td>Mammals, monkeys</td>
<td>Mosquitoes</td>
<td>Fever, myalgia</td>
</tr>
<tr>
<td>Nairovirus</td>
<td>Crimean-Congo hemorrhagic fever</td>
<td>Mammals, birds</td>
<td>Ticks</td>
<td>Fever, (encephalitis)</td>
</tr>
<tr>
<td>Reoviridae</td>
<td>Colorado tick fever virus</td>
<td>Mammals, ticks</td>
<td>Ticks</td>
<td>Hemorrhagic fever</td>
</tr>
</tbody>
</table>

*a* Reassortment involved

Epidemiologic Features of Viral Infections

Some epidemiologically important features of viral diseases of man are set out in Table 48-6. The control of these infections requires knowledge not only the mode of transmission but also of the incubation period, period of...

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communicability, and seasonal incidence. Not all infections cause disease; inapparent infection (which may nevertheless be responsible for new cases) is the rule with many viruses, especially enteroviruses and some of the herpesviruses. Only in a few diseases, such as measles, does virtually every infection of a susceptible individual cause obvious clinical disease.

### TABLE 48-6 Epidemiologic Features of Some Common Human Viral Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mode of Transmission</th>
<th>Incubation Period* (days)</th>
<th>Period of Communicability*</th>
<th>Incidence of Subclinical Infections*</th>
<th>Season of Maximum Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Respiratory</td>
<td>1-2</td>
<td>Short</td>
<td>Moderate</td>
<td>Winter</td>
</tr>
<tr>
<td>Common cold</td>
<td>Respiratory</td>
<td>1-3</td>
<td>Short</td>
<td>Moderate</td>
<td>Spring, autumn</td>
</tr>
<tr>
<td>Bronchiolitis, group</td>
<td>Respiratory</td>
<td>2-5</td>
<td>Short</td>
<td>Moderate</td>
<td>Winter</td>
</tr>
<tr>
<td>ARD (adenovirus)*</td>
<td>Respiratory</td>
<td>5-7</td>
<td>Short</td>
<td>Moderate</td>
<td>Winter</td>
</tr>
<tr>
<td>Dengue</td>
<td>Mosquito bite</td>
<td>5-8</td>
<td>Short</td>
<td>Moderate</td>
<td>Summer</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>Salivary</td>
<td>5-8</td>
<td>Long</td>
<td>High</td>
<td>Summer</td>
</tr>
<tr>
<td>Enterovirus diarrhea</td>
<td>Alimentary</td>
<td>6-12</td>
<td>Long</td>
<td>Moderate</td>
<td>Winter</td>
</tr>
<tr>
<td>Rotavirus diarrhea</td>
<td>Alimentary</td>
<td>2-4</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Winter</td>
</tr>
<tr>
<td>Norwalk diarrhea</td>
<td>Alimentary</td>
<td>2-4</td>
<td>Moderate</td>
<td>High</td>
<td>Summer</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Enteric</td>
<td>5-20</td>
<td>Long</td>
<td>Low</td>
<td>Summer</td>
</tr>
<tr>
<td>Measles</td>
<td>Respiratory</td>
<td>9-12</td>
<td>Moderate</td>
<td>Low</td>
<td>Spring</td>
</tr>
<tr>
<td>Chickenpox</td>
<td>Respiratory</td>
<td>13-17</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Spring</td>
</tr>
<tr>
<td>Mumps</td>
<td>Respiratory</td>
<td>16-20</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Spring</td>
</tr>
<tr>
<td>Rubella</td>
<td>Respiratory, congenital</td>
<td>17-20</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Spring</td>
</tr>
<tr>
<td>Mononucleosis</td>
<td>Contact</td>
<td>30-50</td>
<td>Long</td>
<td>High</td>
<td>Nil</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Alimentary</td>
<td>15-40</td>
<td>Long</td>
<td>High</td>
<td>Summer</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Inoculation</td>
<td>50-150</td>
<td>Very long</td>
<td>High</td>
<td>Nil</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Inoculation</td>
<td>40-60</td>
<td>Very long</td>
<td>Moderate</td>
<td>Nil</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>Alimentary</td>
<td>30-40</td>
<td>Short</td>
<td>High</td>
<td>Nil</td>
</tr>
<tr>
<td>Rabies</td>
<td>Animal bite</td>
<td>30-100</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Warts</td>
<td>Contact</td>
<td>50-150</td>
<td>Long</td>
<td>Low</td>
<td>Nil</td>
</tr>
<tr>
<td>AIDS</td>
<td>Sexual contact, inoculation, congenital</td>
<td>1-10 years</td>
<td>Very long</td>
<td>Low</td>
<td>Nil</td>
</tr>
</tbody>
</table>

* Unless first appearance of symptoms. Diagnostic signs, e.g., rash or paralysis, may not appear until a few days later.
* Many viral diseases are transmissible a few days before symptoms occur. Long = >10 days; short = <4 days.
* High = >=90%; low = <10%.
* ARD, Acute respiratory disease.

Humoral immunity affects the behavior of viral infections as much in human populations as in individuals. The frequency of immunity in a population is sometimes called the herd immunity. Most generalized virus diseases are associated with lifelong immunity; therefore, in the absence of an animal reservoir or of recurrent infectivity, these diseases survive only in large populations and die out in small isolated communities. For example, even in the absence of vaccination, measles and poliomyelitis do not occur as endemic infections in remote populations of Eskimos or the populations of small islands.

In superficial infections of the respiratory and alimentary tracts, humoral antibodies are less important than secretory antibodies (IgA). However, IgA is produced for a much shorter period, so that reinfections with viruses such as respiratory syncytial virus are relatively common. Further, the effect of antibody in preventing respiratory and enteric infections is often circumvented by the great number of non-cross-reacting antigenic types of most viruses that cause superficial infections of these surfaces.

In conclusion, the main variables that determine the transmissibility of viruses are excretion (manner, duration, quantity of virus, and infectivity); environment (stability of the virus and the chance of contact with a new host); and immunity (the level of herd immunity among possible hosts). Many viral diseases have been brought under control by manipulating certain of these variables, for example, by immunization and by improving sanitation so as to reduce the possibility of contact (see Ch. 51).

**Evolution of Viruses**

Viral genomes undergo genetic change by mutation and by recombination. Recombination may be either intramolecular or, among viruses with divided genomes, by reassortment. Mutation in RNA viruses may be extremely rapid because there is no proof-reading mechanism for RNA polymerases, as there is for DNA polymerases. This situation is
compounded in the retroviruses, for there is no proof-reading mechanism for the reverse transcriptase either. Most of these mutations result in non-viable phenotypes. Whether the genetic changes lead to emergence of an altered phenotype depends on natural selection, which may occur within the infected cell, during spread of virus in the body, or the transmission of the virus from one host to the next.

For the practicing physician, virus evolution may appear to be an academic matter, because evolutionary changes usually occur over a time scale that is long compared with human life. However, sometimes genetic changes in viruses may occur rapidly as a result of evolutionary pressure. For instance, the highly virulent myxoma virus introduced into Australia to control the wild rabbit population evolved in a few years to a much more attenuated strain, enabling infected rabbits to survive for weeks instead of days, thereby increasing chances for transmission. Among influenza viruses, antigenic variation evolves toward decreased affinity for preexisting neutralizing antibodies during the course of an outbreak. Periodically, pandemics of influenza occur (most recently in 1957 and 1968), due to the spread of reassortant viruses with a novel hemagglutinin antigen. Because survival of a virus depends largely on its ability to circulate among its natural hosts, natural selection tends to favor those viruses that are better transmitted (usually less virulent), have a lower susceptibility to antibody, and have a greater ability to persist. Also, the ability of the virus to produce reactions that promote excretion, such as coughing and sneezing in respiratory infections and diarrhea in many enteric infections, is likely to be retained.

Contemporary society seems to be experiencing an increased development of new serotypes of several kinds of respiratory and enteric viruses, because of the evolutionary potential afforded by the human population explosion and the great increase in human mobility world-wide. Evolution allows influenza to remain potentially the most important of all human viral diseases (see Ch. 58). Genetic reassortment and exchange of influenza viruses between humans and animals, producing antigenic shift, periodically introduce new viruses to the human population; mutation and selection, producing antigenic drift, accounts for year-to-year variations in influenza A subtypes.

REFERENCES


Kramer MS: Clinical Epidemiology and Biostatistics. Springer-Verlag, New York, 1988

