Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
EVs, they encode other types of defense molecules. Among these are the inhibitor of apoptosis (iap) genes. The iap of AMEV has been well characterized and functionally inhibits apoptosis. A related AMEV gene that functions to inhibit apoptosis is a homolog of the baculovirus pan-caspase inhibitor, p35.

Another novel protein expressed by AMEV is a Cu–Zn superoxide dismutase (SOD). Although a number of the orthopoxviruses encode genes with homology to this class of SODs, neither the VV or myxoma virus proteins are functional in that capacity, although they are present within the virion. The SOD expressed by AMEV is functional as an SOD but is not essential for virus growth in culture. The deletion of the sod gene from AMEV appears to have no effect on the growth of the virus in gypsy moth larvae.

Summary

It is clear that this large subfamily of the family Poxviridae provides a wealth of possible information about the basic mechanisms of the poxvirus lifecycle. There appear to be a number of interesting variations on the molecular details which define this overall family of viruses. There are clear similarities to the vertebrate poxviruses in virion morphology, double-stranded DNA genome, cytoplasmic life cycle, and RNA expression. Yet the differences between the CVs and EVs are significant and represent an area of research that has not been fully explored. The data that have been obtained from genomic sequencing has been essential to identifying some of the different proteins that are present in the EVs, as well as identifying potentially missing homologs of VV proteins. It is important to note that there are large differences at the DNA level between the two sequenced EVs, indicating that there is probably a wide variety of unique features within the EVs as a group. As more sequence information becomes available, the diversity of this family of viruses may become more evident.

See also: Apoptosis and Virus Infection; Baculoviruses: Molecular Biology of Nucleopolyhedroviruses; Poxviruses; Vaccinia Virus.

Further Reading

Afonso CL, Tulman ER, Lu Z, et al. (1999) The genome of Melanoplus sanguinipes entomopoxvirus. Journal of Virology 73: 533–552.
Becker MN and Kurstak E (1991) The entomopoxviruses. In: Kurstak E (ed.) Viruses of Invertebrates pp. 179–195. New York: Marcel Dekker.
Bawden AL, Glassberg KJ, Diggans J, et al. (2000) Complete genomic sequence of the Amsacta moorei entomopoxvirus: Analysis and comparison with other poxviruses. Virology 274: 120–139.
Becker MN, Greenleaf WB, Ostrov DA, and Moyer RW (2004) Amsacta moorei entomopoxvirus expresses an active superoxide dismutase. Journal of Virology 78: 10265–10275.
Becker MN and Moyer RW (2007) Subfamily Entomopoxvirinae. In: Mercer A, Schmidt A, and Weber O (eds.) Poxviruses, pp. 251–269. Basel: Birkhäuser.
Gubser C, Hue S, Kellam P, and Smith GL (2004) Poxvirus genomes: A phylogenetic analysis. Journal of General Virology 85: 105–117.
Li GJ, Liston P, and Moyer RW (2005) Functional analysis of the inhibitor of apoptosis (iap) gene carried by the entomopoxvirus of Amsacta moorei. Journal of Virology 79: 2335–2345.
Li GJ, Liston P, Schokman N, Ho JM, and Moyer RW (2005) Amsacta moorei entomopoxvirus inhibitor of apoptosis suppresses cell death by binding grim and hid. Journal of Virology 79: 3684–3691.
Miller LK and Ball LA (1998) The Insect Viruses. New York: Plenum.
Moss B (2001) Poxviridae: The viruses and their replication. In: Knipe DM and Howley PM (eds.) Fields Virology, 4th edn., pp. 2849–2883. Philadelphia: Lippincott Williams & Wilkins.
Upton C, Slack S, Hunter AL, Ehlers A, and Roper RL (2003) Poxvirus orthologous clusters: Toward defining the minimal essential poxvirus genome. Journal of Virology 77: 7690–7700.
Winter J, Hall RL, and Moyer RW (1995) The effect of inhibitors on the growth of the entomopoxvirus from Amsacta moorei in Lymantria dispar (gypsy moth) cells. Virology 211: 462–473.
Direct contact transmission Involves actual physical contact between an infected subject and a susceptible subject (e.g., kissing, biting, coitus).

Epidemic Major increase in disease incidence affecting either a large number of humans or animals or spreading over a large area.

Epidemiology The study of the determinants, dynamics, and distribution of diseases in populations.

Fomite An inanimate object that may be contaminated with virus and become the vehicle for transmission.

Herd immunity The immune status of a population that affects viral transmission rates. Often used in describing the elimination of a virus from a population when there are too few susceptible hosts remaining to sustain a transmission chain.

Horizontal transmission The transfer of infectious virus from one human or animal to another by any means other than vertical transmission.

Iatrogenic transmission Transmission via health care procedures, materials, and workers (e.g., physicians, nurses, dentists, veterinarians).

Incidence rate (or attack rate) A measure of the occurrence of infection or disease in a population over time – it refers to the proportion of a population contracting a particular disease during a specified period.

Mathematical model (epidemiological) A means to convey quantitative information about a host-virus interaction, such as an epidemic or an emerging disease episode, by the construction of a set of predictive mathematical algorithms.

Nosocomial transmission Pertains to infections acquired while a patient, human or animal, is in hospital.

Prevalence rate The ratio, at a particular point in time, of the number of cases currently present in the population divided by the number of subjects in the population at risk; it is a snapshot of the occurrence of infection or disease at a given time.

Species jumping (or host range extension) Referring to a virus that derives from an ancient reservoir life cycle in animals, but has subsequently established a new life cycle in humans or a different animal species and no longer uses, the original animal reservoir.

Transmission The process by which a pathogen is shed from one host and infects the next.

Vector-borne transmission Involves the bites of arthropod vectors (e.g., mosquitoes, ticks, sandflies).

Vertical or transplacental transmission Occurs from mother to fetus prior to or during parturition, either across the placenta, when the fetus passes through the birth canal, or via colostrum and milk.

Vertical transmission Transmission of virus from parent to progeny through the genome, sperm, or ovum or extracellularly (e.g., through colostrum or across the placenta).

Zoonosis Disease which is naturally transmitted to humans from an ongoing reservoir life cycle in animals or arthropods, without the permanent establishment of a new life cycle in humans.

Introduction

Viral disease epidemiology is the study of the determinants, dynamics, and distribution of viral diseases in populations. The risk of infection or disease in a population is determined by characteristics of the virus, the host, and the host population, as well as behavioral, environmental, and ecological factors that affect virus transmission from one host to another. Epidemiology attempts to meld these factors into a unified whole. The depiction of the interaction of factors favoring the emergence of a viral disease (Figure 1), called ‘the convergence model’, is taken from the US Institute of Medicine study, Microbial Threats to Health, Emergence, Detection and Response (National Academy Press, 2003). At the center is a box representing the convergence of factors leading to ‘the black box’, reflecting the reality that many unknown interactions are important virologically and epidemiologically.

The foundations of epidemiology predate the microbiological and virological sciences, starting with Hippocrates, the Greek physician and father of medicine, who in the fourth century BC made important epidemiologic observations on infectious diseases. John Snow is called the father of modern epidemiology because he developed excellent quantitative methods while studying the source of a cholera outbreak at the Broad Street pump in London in 1849. Snow was followed by William Farr, who in the 1870s advanced the use of vital statistics and clarified many of the principles of risk assessment and retrospective and prospective studies. Their vision is reflected in the fast-changing science of epidemiology which is now supported by advanced computer technology, sophisticated statistical methods, and very sensitive and specific diagnostic systems.

Assessment of Disease Occurrence and Outcome

By introducing quantitative measurements of disease trends, epidemiology has come to have a major role in improving our understanding of the overall nature of
disease and in alerting and directing disease control activities. Epidemiology is also effective in (1) clarifying the role of particular viruses and viral variants as the cause of disease, (2) clarifying the interaction of viruses with environmental determinants of disease, (3) determining factors affecting host susceptibility, (4) unraveling modes of transmission, and (5) field testing of vaccines and antiviral drugs.

The comparison of disease experience between populations is expressed in the form of ‘rates’. The terms ‘incidence rate’ and ‘prevalence rate’ are used to describe quantitatively the frequency of occurrence of infection or disease in populations. ‘Incidence rate’ (also called attack rate) is defined as the ratio of new cases occurring in a population to the size of the population during a specified period of time. Prevalence rate is the ratio of the total number of cases occurring in a population to the size of the population during a specified period of time. ‘Sero-prevalence rate’ relates to the occurrence of antibody to a particular virus in a population. Because viral antibodies, especially neutralizing antibodies, often last a lifetime, seroprevalence rates usually represent cumulative experience with the virus. The term ‘case–fatality rate’ is used to indicate the percentage of subjects with a particular disease that die from the disease. All these rates may be affected by various attributes that distinguish one individual from another: age, sex, genetic constitution, immune status, pregnancy, nutritional status, and various behavioral and medical care and patient management parameters. The most widely applicable attribute is age, which may encompass immune status as well as various physiological variables.

A viral disease is characterized as ‘endemic’ when there are multiple or continuous chains of transmission resulting in continuous occurrence of disease in a population over a period of time. ‘Epidemics’ are peaks in disease incidence that exceed the endemic baseline or expected rate of disease. The size of the peak required to constitute an epidemic is arbitrary and is related to the background endemic rate and the anxiety that the disease arouses (e.g., a few cases of rabies is regarded as an epidemic, whereas a few cases of influenza is not). A ‘pandemic’ is a worldwide epidemic.

**Epidemiologic Studies**

A proper description of an outbreak of disease or an epidemic must include the parameters of ‘person (or subjects in the case of animals), place, and time’. Such descriptive information is a necessary first step in describing the occurrence, distribution, course, threat, and anticipated action response to the initial recognition of a cluster of cases of disease. Much of the initial
Case-Control Studies and Cohort Studies

There are two basic analytic techniques used to investigate relationships between cause and effect and to evaluate risk factors of disease. These are the ‘case-control study’ and the ‘cohort study’. In the case-control study, investigation starts after the disease has occurred – it is a retrospective study, going back in time to determine causative events. Although this kind of study does not require the creation of new data or records, it does require careful selection of the control group, matched to the test group so as to avoid bias. The retrospective case-control study lends itself to quick analysis and is relatively inexpensive to carry out. In the cohort study, the prospective study, investigation entails the gathering of new data to identify cause–effect relationships. This kind of study is expensive and does not lend itself to quick analysis as groups must be followed until disease is observed. However, when cohort studies are successful, proof of cause–effect relationship is often incontrovertible.

Molecular Epidemiologic Studies

The term ‘molecular epidemiology’ is used to denote the use of any of a large number of molecular biological methods in support of epidemiologic investigations. For example, with herpesviruses, restriction endonuclease mapping has provided a means of identification of unique viral genotypes – in an epidemiologic study recognized as the first based upon viral molecular characterization, the source of herpes simplex virus 1 causing disease in a hospital newborn nursery was traced to one persistently infected nurse rather than any of several other possible shedders. With rotaviruses and bluetongue viruses, polyacrylamide gel electrophoresis of the segmented viral RNA has been used epidemiologically, for example, to unravel outbreaks involving multiple viral variants. Panels of monoclonal antibodies have been used to distinguish virus variants for epidemiologic purposes; they have been particularly useful in elucidating host-range and geographic variants of rabies virus. Today, partial sequencing has become the most commonly used molecular acuity, and an insightful ‘index of suspicion’.

Etiologic Studies and the Proof of Causation

One of the landmarks in the history of infectious diseases was the development of the Henle-Koch postulates which established the evidence required to prove a causal relationship between a particular infectious agent and a particular disease. These simple postulates were originally drawn up for bacteria, but were revised in 1937 by Rivers and again in 1982 by Evans in attempts to accommodate special cases, such as viral diseases, especially animal diseases, in need of this kind of relationship between a particular infectious agent and a particular disease. These simple postulates were originally drawn up for bacteria, but were revised in 1937 by Rivers and again in 1982 by Evans in attempts to accommodate special cases, such as viral diseases, especially animal diseases, in need of this kind of relationship between a particular infectious agent and a particular disease. These simple postulates were originally drawn up for bacteria, but were revised in 1937 by Rivers and again in 1982 by Evans in attempts to accommodate special cases, such as viral diseases, especially animal diseases, in need of this kind of relationship between a particular infectious agent and a particular disease.

For example, early in the investigation of human acquired immunodeficiency syndrome (AIDS), before its etiology was established, many kinds of viruses were being isolated from patients and many candidate etiologic agents were being advanced. Prediction that the etiologic agent would turn out to be a member of the family Retroviridae was based upon years of veterinary research on animal retroviruses and animal retroviral diseases. This prediction was based upon recognition of common biologic and pathogenetic characteristics of AIDS and animal retroviral diseases. This prediction guided many of the early experiments to find the etiologic agent of AIDS; later, after human immunodeficiency virus (HIV1) was discovered, its morphological similarity to equine infectious anemia virus, a prototypic member of the genus Lentivirus, family Retroviridae, was the key to unraveling confusion over the fact that the human virus killed host lymphocytes rather than transforming them as typical oncogenic retroviruses would do. Ever since, this essence of comparative medicine has been guiding HIV/AIDS research in many areas, including drug design,
diagnostics, and vaccine development. HIV/AIDS epidemiologic research has often been intertwined with research on the several simian immunodeficiency viruses (SIVs).

Seroepidemiologic Studies
Seroepidemiology is useful in public health and animal health investigations and in research to determine the prevalence or incidence of particular infections, to evaluate control and immunization programs, and to assess past history when a 'new' virus is discovered. When paired serum specimens are obtained from individuals several weeks apart, the initial appearance of antibody in the second specimen or a rise in antibody titer indicates recent infection. Similarly, the presence of specific immunoglobulin M (IgM) antibody in single serum samples, indicating recent infection, may be used in seroepidemiologic studies. Correlation of serologic tests with clinical observations makes it possible to determine the ratio of clinical to subclinical infections.

Sentinel Studies
Because of advanced diagnostic/serologic methods, sentinel studies can yield many valuable data in timely fashion about impending disease risks. For example, sentinel chicken flocks are set out for the early detection of the presence of arboviruses such as West Nile virus in the United States. These flocks are bled and tested weekly for the presence of virus or antiviral antibody; they provide an early warning of the levels of virus amplification that occur before epidemics.

Vaccine Trials
The immunogenicity, potency, safety, and efficacy of vaccines are first studied in laboratory animals, followed by small-scale closed trials, and finally in large-scale open trials. Such studies employ epidemiologic methods, rather like those of the cohort (prospective) study. In most cases, there is no alternative way to evaluate new vaccines, and the design of trials has now been developed so that they yield maximum information with minimum risk and acceptable cost.

Virus Transmission among Individuals
Viruses survive in nature only if they are able to be transmitted from one host to another, whether of the same or another species. Transmission cycles require virus entry into the body, replication, and shedding with subsequent spread to another host.

Virus Entry
Portals of virus entry into the body include the skin, respiratory tract, intestinal tract, oropharynx, urogenital tract, and conjunctiva. In some cases, viruses use a particular portal of entry because of particular environmental or host-behavior factors and in other cases because of specific viral ligands and host-cell receptors. In many cases, disruption of normal host-defense mechanisms leads to entry that might otherwise be thwarted; for example, papillomavirus may enter the deep layers of the skin via abrasions, acid-labile coronaviruses may enter the intestine protected by the buffering capacity of milk, and influenza viruses may enter the lower respiratory tract because a drug has dampened ciliary action of the respiratory epithelium.

Virus Shedding
The exit of virus from an infected host is just as important as entry in maintaining its transmission cycle. All portals used by viruses to gain entry are used for exit. The
important elements in virus shedding are virus yield (from the standpoint of the virus, the more shedding the better) and timeliness of yield (again, the earlier the shedding the better). Viruses that cause persistent infections often employ remarkable means to avoid host inflammatory and immune responses so as to continue shedding. For example, the epidemiologically important shedding of herpes simplex viruses 1 and 2 that perpetuates the viruses in populations requires recrudescence of persistent ganglionic infection, centrifugal viral genomic transit to peripheral nerve endings, and productive infection of mucosal epithelium, all in the face of established host immunity.

**Modes of Virus Transmission**

Virus transmission may be ‘horizontal’ or ‘vertical’. The vast majority of transmission is horizontal, that is, between individuals within the population at risk. Modes of horizontal transmission of viruses can be characterized as direct contact, indirect contact, common vehicle, airborne, vector-borne, iatrogenic, and nosocomial. Vertical or transplacental transmission occurs between the mother and her fetus or newborn. Some viruses are transmitted in nature via several modes, others exclusively via one mode (see Table 2).

‘Direct contact transmission’ involves actual physical contact between an infected subject and a susceptible subject (e.g., kissing, Epstein–Barr virus, the cause of mononucleosis, biting (e.g., rabies); coitus (sexually transmitted viral diseases)). Indirect contact transmission occurs via ‘fomites’, such as shared eating utensils, improperly sterilized surgical equipment, or improperly sterilized non-disposable syringes and needles.

‘Common vehicle transmission’ pertains to fecal contamination of food and water supplies (e.g., norovirus diarrhea). Common vehicle transmission commonly results in epidemic disease.

‘Airborne transmission’ typically results in respiratory infections (and less typically in intestinal infections), but these infections may also be transmitted by direct and

| **Table 2** Examples of human and animal virus transmission patterns |
| **Infectious agent/disease** | **Mode of transmission** | **Portal of entry** |
|----------------------------|--------------------------|------------------|
| Influenza virus/influenza | Contact/direct/indirect via droplets and droplet nuclei | Respiratory tract |
| Rhinoviruses/common cold | Contact/direct/indirect via droplets and droplet nuclei and fomites | Respiratory tract |
| Rubella virus/congenital rubella | Contact/direct/indirect via droplets and droplet nuclei | Respiratory tract |
| Rotaviruses/diarrhea | Vertical/congenital | Transplacental |
| Poliovirus/polioymyelitis | Contact/direct/indirect via fomites | Intestinal tract (oral) |
| Norovirus/diarrhea | Common vehicle/fecal contamination of water | Intestinal tract (oral) |
| Hepatitis A virus/hepatitis | Common vehicle/fecal contamination of food | Intestinal tract (oral) |
| Variant Creutzfeldt–Jakob disease prion/prion disease (spongiform encephalopathy) | Common vehicle/bovine spongiform encephalopathy prion contamination of beef or beef products | Intestinal tract (oral) |
| Herpes simplex virus/genital herpes | Contact/direct (sexual) | Genital tract |
| Human immunodeficiency virus 1/acquired immunodeficiency syndrome (AIDS) | Contact/direct (sexual), contact/direct (blood) | Genital tract, bloodstream, transplacental, at birth and via breast feeding |
| Rabies virus/rabies | Vertical/congenital | Skin (bite wound) |
| Russian spring summer encephalitis virus/encephalitis | Zoonotic/contact/direct (saliva) | Skin (tick bite) |
| Dengue viruses/dengue | Zoonotic/arthropod-borne | Skin (mosquito bite) |
| Sin Nombre and related viruses | Zoonotic/contact/direct (rodent urine, saliva and feces) | Respiratory tract |
| Lassa virus | Zoonotic/contact/direct (rodent urine, saliva and feces) | Respiratory tract and intestinal tract (oral) |
| Ebola and Marburg viruses | Zoonotic/reservoir host unknown; secondary cases contact/direct/ nosocomial and iatrogenic | Index cases unknown, likely respiratory tract or skin and mucous membranes; secondary cases, contact and iatrogenic (injection) |
| Leukemia viruses/leukemias (proven only in animals) | Vertical/germ-line | Transmitted as genetic trait |
indirect contact. Airborne transmission occurs via large droplets and via very small droplet nuclei (aerosols) emitted from infected persons during coughing or sneezing (e.g., influenza) or from environmental sources. Large droplets (>10 μm in diameter) settle quickly, but droplet nuclei evaporate forming dry particles (<5 μm in diameter) which remain suspended in the air for extended periods. Droplets may travel only a meter or so while droplet nuclei may travel over much longer distances.

‘Vector-borne transmission’ involves the bites of arthropod vectors (e.g., mosquitoes, ticks, and sandflies).

‘Iatrogenic transmission’ involves health care procedures, materials, and workers (e.g., physicians, nurses, dentists, and veterinarians).

‘Nosocomial transmission’ pertains to infections acquired while a patient, human or animal, is in hospital.

‘Vertical or transplacental transmission’ occurs from mother to fetus prior to or during parturition. Certain retroviruses are vertically transmitted in animals via the integration of viral DNA directly into the DNA of the germline of the fertilized egg. Other viruses are transmitted to the fetus across the placenta; yet others are transmitted when the fetus passes through the birth canal. Another vertical transmission route is via colostrum and milk. Vertical transmission of a virus may or may not be associated with ‘congenital disease’ (i.e., disease that is present at birth) which may be lethal (and the cause of abortion or stillbirth) or the cause of congenital abnormalities. The herpesviruses, especially cytomegaloviruses, and rubella virus cause important congenital diseases in humans, and pestiviruses, such as bovine viral diarrhea virus, in animals.

Common Patterns of Virus Transmission

Enteric infections are most often transmitted by direct contact and by fomites in a ‘fecal–oral cycle’ that may include fecal contamination of food and water supplies; diarrheic feces may also splash to give rise to aerosols (droplets and droplet nuclei). Respiratory infections are most often transmitted by the airborne route or by indirect contact via fomites in a ‘respiratory cycle’, that is, virus is shed in respiratory secretions and enters its next host through the nares during inhalation. The respiratory cycle is responsible for the most explosive patterns of epidemic disease in humans and all domestic animal species.

Influence of Virulence of the Virus

The virulence of the infecting virus may directly affect the probability of its transmission. The classic example of this is rabbit myxomatosis. In Australia, mosquito-borne transmission of myxoma virus was found to be most effective when infected rabbits maintained highly infectious skin lesions for several days before death. Highly virulent strains of the virus were found to kill rabbits so quickly that transmission did not occur, and naturally attenuated strains were found to produce minimal lesions that healed quickly and did not permit transmission. Virus strains at either extreme of this virulence spectrum were found not to survive in nature, but virus strains of intermediate virulence have circulated for many years.

Influence of the Clinical Status of the Host

Infection without recognizable disease is called ‘subclinical’ or ‘clinically inapparent’. Overall, subclinical infections are much more common than those that result in disease. Their relative frequency accounts for the difficulty of tracing chains of transmission, even with the help of laboratory diagnostics. Although clinical cases may be somewhat more productive sources of virus than subclinical infections, because the latter do not restrict the movement of the infected host, they can be most important as sources of viral dissemination. In most acute infections, whether clinically apparent or not, virus is shed in highest titers during the late stages of the incubation period, before the influence of the host-immune response takes effect. Persistent infections, whether or not they are associated with episodes of clinical disease, also play an important role in the perpetuation of many viruses in nature. For example, prolonged virus shedding can reintroduce virus into a population of susceptibles all of which have been born since the last clinically apparent episode of infection. This is important in the survival of rubella virus in some isolated populations. Sometimes the persistence of infection, the production of disease, and the transmission of virus are dissociated; for example, togavirus and arenavirus infections may have little adverse effect on their reservoir hosts (arthropods, birds, and rodents), but transmission may be very efficient. On the other hand, the persistence of infection in the central nervous system, as with measles virus in subacute sclerosing panencephalitis (SSPE), is of no epidemiological significance, since no infectious virus is shed from this site.

Influence of Host Population Immunity

With most viruses, endemic or epidemic transmission leads to a level of immunity in the host population that affects or even interrupts further transmission. The ‘herd immunity’ effect is countered in some cases by viral
infections that are transmissible from animals to man. The term ‘zoonosis’ is used to describe multiple-host examples, such as rabies and eastern equine encephalitis viruses. Between several different species of vertebrate host, for viruses that may have multiple hosts and spread naturally to another, as by birth or immigration, to maintain measles virus persistence of measles virus in a population depends upon a continuous supply of susceptible children. Analyses of the incidence of measles in large cities and in island communities have shown that a population of about half a million persons is needed to ensure a large enough annual input of new susceptible hosts, by birth or immigration, to maintain measles virus in the population. Because infection depends on respiratory transmission, the duration of epidemics of measles is correlated inversely with population density. If a population is dispersed over a large area, the rate of spread is reduced and the epidemic may last longer, so that the number of susceptible persons needed to maintain transmission chains is reduced. On the other hand, in such a situation a break in the transmission chain is much more likely. When a large proportion of the population is initially susceptible, the intensity of the epidemic builds up very quickly and attack rates are almost 100% (‘virgin-soil epidemic’). On the other hand, when measles vaccination programs are implemented properly the virus disappears completely from the regional population.

Influence of Population Size

It is self-evident that the long-term survival of a virus requires that it be continuously transmitted from one host to another. In general, for rapidly and efficiently transmitted viruses such as many respiratory viruses, local survival of the virus requires that the susceptible host population be very large. A virus may disappear from a population because it exhausts its potential supply of susceptible hosts as they acquire immunity to reinfection with the same virus. Depending on duration of immunity and the pattern of virus shedding, the ‘critical population size’ varies considerably with different viruses and with different host species. The most precise data on the importance of population size in acute nonpersistent infections come from studies of measles. Persistence of measles virus in a population depends upon a continuous supply of susceptible children. Analyses of the incidence of measles in large cities and in island communities have shown that a population of about half a million persons is needed to ensure a large enough annual input of new susceptible hosts, by birth or immigration, to maintain measles virus in the population. Because infection depends on respiratory transmission, the duration of epidemics of measles is correlated inversely with population density. If a population is dispersed over a large area, the rate of spread is reduced and the epidemic may last longer, so that the number of susceptible persons needed to maintain transmission chains is reduced. On the other hand, in such a situation a break in the transmission chain is much more likely. When a large proportion of the population is initially susceptible, the intensity of the epidemic builds up very quickly and attack rates are almost 100% (‘virgin-soil epidemic’). On the other hand, when measles vaccination programs are implemented properly the virus disappears completely from the regional population.

Influence of Zoonotic Transmission Cycles

Because most viruses are host-restricted, most viral infections are maintained in nature within populations of the same or related species. However, there are a number of viruses that may have multiple hosts and spread naturally between several different species of vertebrate host, for example, rabies and eastern equine encephalitis viruses. The term ‘zoonosis’ is used to describe multiple-host infections that are transmissible from animals to man. The zoonoses, whether involving domestic or wild animals or arthropods, usually represent important problems only under conditions where humans are engaged in activities involving close contact with animals or exposure to arthropods.

Influence of Arthropod Transmission Cycles

Many viral zoonoses are caused by arboviruses. Arboviruses have two classes of hosts, vertebrate and invertebrate. Over 500 arboviruses are known, of which about 100 cause disease in humans and 40 in domestic animals; some of these are transmitted by ticks, some by mosquitoes, and yet others by phlebotomine flies (sandflies) or Culicoides spp. (midge). Arthropod transmission may be ‘mechanical’, where the arthropod acts as a ‘flying pin’, or more commonly, ‘biological’, involving replication of the virus in the arthropod vector. The arthropod vector acquires virus by feeding on the blood of a viremic person or animal. Replication of the ingested virus, initially in the arthropod’s gut, and its spread to the salivary glands takes several days; the interval varies with different viruses and is influenced by ambient temperature. Virions in the salivary secretions of the vector are injected into human or animal hosts during subsequent blood meals. Most arboviruses have localized natural habitats in which specific receptive arthropod and vertebrate hosts are involved in the viral life cycle. Vertebrate reservoir hosts are usually wild mammals or birds; humans are rarely involved in primary transmission cycles, although the exceptions to this generalization are important (e.g., Venezuelan equine encephalitis, yellow fever, and dengue viruses). Humans are in most cases infected incidentally, for example, by the geographic extension of a reservoir vertebrate host and/or a vector arthropod. Ecological changes produced by human activities disturb natural arbovirus life cycles and have been incriminated in the geographic spread or increased prevalence of arbovirus diseases.

Mathematical Modeling

From the time of William Farr, who studied epidemic disease problems in the 1870s, mathematicians have been interested in ‘epidemic curves’ and secular trends in the incidence of infectious diseases. With the development of computer-based mathematical modeling techniques, there has been a resurgence of interest in the population dynamics of infectious diseases. There has also been a resurgence in controversies surrounding the use of models; critics say ‘for every model there is an equal and opposite model’. So, the proof of the value of models lies in their practical application, and in recent years there have been more and more successes. For example, when for counterterrorism reasons universal
smallpox vaccination was being considered, models that showed that vaccine could be used effectively after rapid detection of a terrorism incident led to a decision to stockpile, but not widely use vaccine. As another example, when a foot-and-mouth disease epidemic raged in the United Kingdom in 2001, a model showed that only the most vigorous stamping-out campaign could get ahead of the movement of the virus across the country. The model, seeming eminently logical now, importantly provided the kind of veracity and political will needed to accelerate the stamping-out campaign.

Models may be used to determine (1) patterns of disease transmission, (2) critical population sizes to support the continuous transmission of viruses with short and long incubation periods, (3) the dynamics of endemicity of viruses that become persistent in their hosts, and (4) the variables in age-dependent viral pathogenicity. Computer modeling also provides useful insights into the effectiveness of disease control programs. Much attention has been given to modeling the future of the AIDS epidemic in the United States and the rest of the world. Such models usually start with historical data on the introduction of the etiologic virus, HIV1, proceed to the present stage of the epidemic where the disease has become well established in many countries and in fewer countries subject to prevention and treatment strategies, and then proceed to project its course into the future. During the first 10 years of the AIDS epidemic in the United States, African countries, and then in Asian countries, most models underestimated developing trends; more recently models have become more accurately predictive – but in many places more and more sobering.

Implications for Disease Prevention

Knowledge of the epidemiology and modes of transmission of infectious diseases is critical to the development and implementation of prevention and control strategies. Data on incidence, prevalence, and mortality contribute directly to the establishment of priorities for prevention and control programs while knowledge of viral characteristics and modes of transmission are used in deciding prevention strategies focusing on vaccine development and delivery, environmental improvements, enhancement of nutritional status, improvement in personal hygiene, and behavioral changes.

See also: Disease Surveillance; Viral Pathogenesis; Zoonoses.

Further Reading

Evans AS and Kaslow RA (eds.) (1997) Viral Infections of Humans. Epidemiology and Control, 4th edn. New York: Plenum Medical Book Company.
Heymann DL (ed.) (2005) Control of Communicable Diseases Manual, 18th edn. Washington, DC: American Public Health Association Press.
Mandell GL, Bennett JE, and Dolin R (eds.) (2000) Mandell, Douglas, and Bennett’s Principles and Practice of Infectious Diseases, 5th edn. New York: Churchill Livingstone.
Monto A (2005) The epidemiology of viral infections. In: Mahy BWJ and ter Meulen V (eds.) Virology: Topley and Wilson’s Microbiology and Microbial Infections, vol. 1. London and Washington, DC: Hodder Arnold and ASM Press.
Murphy FA, Gibbs EPJ, Horznick MC, and Studdert MJ (1999) Veterinary Virology, 3rd edn. New York: Academic Press.
Nathanson N (2006) Epidemiology. In: Knipe DM, Howley PM, Griffin DE, Lamb RA, and Martin MA (eds.) Fields Virology, 5th edn. Philadelphia: Lippincott Williams and Wilkins.
Nathanson N and Murphy FA (1997) Evolution of viral diseases. In: Nathanson N, Ahmed R, Griffin DE, et al. (eds.) Viral Pathogenesis, Philadelphia: Lippincott-Raven Press.
Nowak MA and May R (2001) Virus Dynamics: Mathematical Principles of Immunology and Virology. Oxford, UK: Oxford University Press.
Smolinski MS, Hamburg MA, and Lederberg J (2002) Emerging Microbial Threats to Health in the 21st Century. Institute of Medicine/ National Academy of Sciences. Washington, DC: National Academy Press.
Smolinski MS, Hamburg MA, and Lederburgh J (eds.) (2003) Microbial Threats to Health, Emergence, Detection and Response, 367pp. Washington: National Academies press.
Thrusfield MV and Bertola G (2005) Veterinary Epidemiology, 3rd edn. London: Blackwell Publishing.