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The term “epidemiology” was originally used for the science of major, humanity-threatening diseases. Today, it refers to the science of all transmissible and non-transmissible diseases in a population, irrespective of whether they occur frequently in time or space. In the field of microbiology, epidemiology deals with diseases which are caused by transmissible agents such as bacteria, viruses or prions, and in particular with the spread and consequences of infections. Therefore, epidemiological studies are very important for the health of the world population, and are the basis for general and veterinary measures such as quarantine or vaccinations to prevent and control pandemics and epidemics. Furthermore, they allow the development of guidelines and regulations for vaccinations and other measures that prevent infections.

Exo-epidemiology is confined to the investigation of the dissemination of the pathogen after its release from the organism. It includes their survival in the environment, their whereabouts in certain reservoirs and their retransmission to humans or animals. In contrast, endo-epidemiology deals with the way and manner in which pathogens spread within the organism and where they may persist and mutate. Epidemiology records not only the incidence of infections, diseases and deaths, but also attempts to obtain data on the disease pattern in which the aetiological relationship to a specific pathogen is not known (disease in search of virus), and this leads to the identification of diseases caused by a known virus (virus in search of disease). It extends the knowledge of the cause of infectious diseases by monitoring epidemics or pandemics and assessing the course of infectious diseases and their consequences for a population. If clusters of specific symptoms result,

this can be an indication of the appearance of new viruses or particularly virulent strains. The survey of epidemiological data also includes the influence of living standards, social structure and human behaviour patterns, such as sexual promiscuity or drug abuse, but also veterinary relevant parameters such as stock densities, animal transport, animal markets, animal shows, seasonality, climate, vector density and mating season on the transmission frequency and infection time. The migrations of populations because of eviction or rural exodus and the associated negative social consequences, such as poor hygiene, and the declining effectiveness of public health authorities can facilitate the dissemination of infectious diseases. In antiquity, diseases such as plague, smallpox, influenza and measles spread along the caravan routes and trade routes. The worldwide growth of tourism resulted in increased contacts with previously unknown pathogens that were imported by infected people in a naive (for the pertinent pathogen) population of a country. Whereas these processes were long-lasting even a few decades ago, viruses are now spread worldwide within a few days or weeks. This was clearly demonstrated by the rapid spread of the infection with SARS coronavirus in 2003 from Southeast Asia to Europe and North America (► Sect. 14.8). The change of production processes in industry and agriculture and trade in consumer goods and waste as well as human interferences with the natural environment cause new distribution patterns of infections. Until a few years ago, animal pathogenic viruses, such as avian influenza virus, spread worldwide by bird and animal migrations (► Sect. 16.3). In addition, pathogens are today a worldwide problem through the international trade in farm animals, which often extends beyond continental borders.

Some brief explanations of the basic concepts commonly used in epidemiology for specific parameters or infectious forms follow. An epidemic is a temporally and spatially limited occurrence of an infectious disease in a population. Examples are rubella, measles and chickenpox. By contrast, a pandemic is defined as a global, time-limited or unlimited accumulation of infections, as is found in influenza or acquired immunodeficiency syndrome (AIDS). Endemic diseases are sporadic, spatially and temporally limited or unlimited appearing infectious diseases which can occur between epidemic phases. Morbidity describes the number of ill individuals in relation to the population size, and mortality is defined as the number of deaths that occur from a particular infection within a population; both are usually referred to 10^4 or 10^5 people or animals. By contrast, lethality is defined as the number of deaths in relation to the total number of people affected by a particular infectious disease. Excess mortality is the temporary accumulation of deaths as a result of an infection, such as flu or AIDS, which surpasses the long-term average mortality. Herd immunity is defined as the immunological protection that exists against a virus (measles, rubella and influenza viruses) in the population at a given time, regardless of whether it is caused by infection with the pertinent pathogen or by vaccination. The herd immunity of a population varies with the different viruses. It depends on transmission mechanisms, environmental conditions such as temperature and humidity and the population density, including vaccination discipline. To attain effective herd immunity, a vaccination rate of over 90 % of the population is usually considered necessary (e.g. measles, mumps and rubella).

11.1 How Are Viral Infections Transmitted?

Horizontal transmission refers to all types of infection of an organism by another organism, i.e. the transmission of a pathogen between hosts of a generation. This includes the homologous transmission of a virus from person to person, as well as the heterologous transmission from animals to humans (zoonosis) and vice versa. Pathogens spread by horizontal transmission in a population during epidemics, pandemics or endemics. This can be directly, for example, by virus-containing aerosols or droplets that are released when sneezing or coughing during infectious diseases of the upper respiratory tract (such as infections with influenza viruses, coxsackieviruses, adenoviruses and paramyxoviruses; ► Sects. 14.1, ► 15.3, ► 16.3 and ► 19.4), or indirectly. Indirect transmission is known, among others, for rhinoviruses (► Sect. 14.1), which are transmitted by droplet infection, and also via contaminated hands, doorknobs or similar household items commonly used by infected and uninfected people such as towels. Dirt and smear infections contribute especially to the dissemination of virus-induced gastrointestinal or renal diseases. Here, the pathogen is excreted in the faeces or urine, and is transmitted by contamination with this material because of inadequate hygiene. Canine parvovirus has been spread very efficiently worldwide by the soles of shoes which were contaminated with viruses from dog excrements. In regions with a low hygienic standard, sewage is discharged untreated into rivers and seas. This practice and also fertilization of plants with human faeces, which is widespread in some countries, can lead to contamination of food with polioviruses, enteroviruses, hepatitis A viruses (► Sect. 14.1) and caliciviruses (► Sect. 14.2) – an important cause of epidemics. Mussels thrive particularly well in such polluted waters and simultaneously enrich hepatitis A viruses. Hantaviruses and arenaviruses (► Sects. 16.1 and ► 16.2) are excreted in the faeces of infected rodents, and thus are disseminated into the ground. In the case of contact with such contaminated earth, there is a risk of infection with the relevant pathogens. Similarly, organ transplants can lead to transmission of such viruses and also herpesviruses (Epstein–Barr virus or cytomegalovirus; ► Sect. 19.5). In the worst case, all viruses which have a more or less pronounced viraemic phase or are situated in the organ at the time of graft removal can be transmitted by transplants. In fact, lymphocytic choriomeningitis and rabies have been transmitted in this way (► Sects. 15.1 and ► 16.1). Many viruses are present in the saliva and can be transmitted to babies by kissing or mouth-to-mouth feeding. In other cases, the virus is present in the semen or the cervical secretions and can be transmitted by sexual intercourse. This is particularly true for human immunodeficiency virus (HIV), papillomaviruses and some herpesviruses (► Sects. 18.1, ► 19.3 and ► 19.5). Viruses that are present in the blood during the disease (hepatitis B and hepatitis C viruses, HIV, parvovirus, cytomegalovirus), are transmitted by smeared blood, for example, perinatally during the birth process from the infected mother to the neonate, but also through contaminated blood products or stored blood (► Sects. 14.5, ► 18.1, ► 19.1 and ► 20.1).

Some viral species are transmitted by arthropods (ticks, mosquitoes). The animals are infected with the pathogen when it is taken up with the blood when

stinging or biting. After reproduction in ticks or insects, the virus can be transmitted to other organisms through biting or stinging. This form of heterologous transmission is found, for instance, in yellow fever virus, dengue virus, tick-borne encephalitis virus, togaviruses and orbiviruses, and in some bunyaviruses (► Sects. 14.5, ► 14.6, ► 16.2 and ► 17.2). On the other hand, rabies virus enters the wound and thus the organism through the bite of infected vertebrates (► Sect. 15.1). The geographic distributions of viruses that are transmitted by arthropods are mostly identical to those of the mosquitoes and ticks that they use as vectors. Shifts and changes in climate conditions, as are to be expected because of global warming, can lead to the occupation of new regions and niches by insects and the viruses that are associated with them.

Dissemination of viruses among people who live in close contact with each other is known as nosocomial infection. Such infections are commonly observed in nursing homes, kindergartens and hospitals. In these communities, many pathogens spread swiftly. The concept of iatrogenic infection refers particularly to the spread of pathogens by medical procedures such as organ transplants and blood transfusions, and by improperly performed medical interventions, such as the use of contaminated equipment, syringes or needles. Iatrogenic transmissions have frequently been observed in bovine leukaemia virus infections in which the virus was transmitted through the use of insufficiently disinfected needles from animal to animal and from flock to flock.

The transmission of an infection between generations (from mother to fetus) is referred to as vertical transmission. This happens when pregnant women are acutely infected with certain viruses (rubella virus, cytomegalovirus, parvovirus B19; ► Sects. 14.6, ► 19.5 and ► 20.1), and the pathogen is transplacentally transmitted to the fetus. Similarly, this also applies when the viral genome is inherited by the next generation as an integrated part of the genetic information of the cell (e.g. of the egg or sperm cell). This vertical transmission from parents to offspring is known primarily for endogenous retroviruses (► Sect. 18.1) or for bovine and porcine pestiviruses (► Sect. 14.2).

11.2 Where Do Human Pathogenic Viruses Reside?

Where viruses reside in the time between their epidemic occurrences is often unclear. Sporadic cases of apparent infections occur repeatedly; in such cases, the virus is probably transmitted by healthy people with asymptomatic (inapparent) infections. Some viral species are able to survive in the environment for considerable time before they infect their hosts again; these include parvoviruses and rotaviruses (► Sects. 17.2 and ► 20.1), picornaviruses (► Sect. 14.1) and also poxviruses (► Sect. 19.6). Even now, poliovirus is occasionally reintroduced from countries that are not free of poliovirus infections (e.g. India and several African countries), and it proliferates in sero-negative people until a developing herd immunity or specific outbreak-control vaccinations eliminate the virus from the corresponding population. In contrast, other pathogens such as rubella virus and

most paramyxoviruses (► Sects. 14.6 and ► 15.3) are instable in the environment, and do not infect animals. They are completely eliminated from the organism by the immune system during the course of infection. Only little is known concerning their whereabouts during the periods between sporadically occurring infections or epidemics. The first appearance of such a viral species must have been linked to human urbanization because such a virus would disappear from small, isolated human populations; therefore, it must be a phylogenetically relatively new virus, which could maintain its infection chains only in populations with a relatively high density. The term “emerging virus diseases” includes infectious diseases in which the viruses have been transmitted to a new host (such as SARS coronavirus; ► Sect. 14.8) or appear again as re-emerging viruses after long periods of time, as is the case for some hantaviruses (► Sect. 16.2).

In contrast, herpesviruses show a completely different behaviour. They remain latent in the body after infection, and the lifelong latency with recurrent excretion phases facilitates the dissemination of the virus even after long intervals (► Sects. 18.1 and ► 19.5). HIV infections also appear clinically unnoticed for a long time, although in this case infectious viruses are always present in the blood. The same applies to viruses that produce persistent infections and are present over long periods in the blood and are excreted or released from the skin, such as hepatitis B virus, adenoviruses and papillomaviruses (► Sects. 19.1, ► 19.3 and ► 19.4). Therefore, they are considered as one of the phylogenetically old viruses, which are well adapted to humans and can survive even in small populations. However, the new highly sensitive methods for detection of viral nucleic acids show that, besides these forms of chronically persisting or latent infections with relapsing recurrence or reactivation, there is also latency of viral genomes in which neither reactivation of the viral genetic information nor the associated synthesis of virus products is observed. This DNA latency in the cells of different tissues has particularly been described for parvovirus B19 (► Sect. 20.1).

Sometimes, viruses infect certain animal species, and these are used as reservoirs for these pathogens, whence they can be transmitted to humans on certain occasions, or accidentally. Influenza viruses infect various bird species, which excrete them in the faeces. They can be transmitted to swine, just as the human virus types. In the case of double infections in swine, genome segments of both virus types can be recombined. In this manner, new reassortants of influenza viruses arise, which are occasionally pathogenic for humans and can spread pandemically in the population (► Sect. 16.3). Other viruses can bridge larger periods by having long incubation times. These include rabies viruses, which use foxes, badgers and bats as reservoirs. In this case, human infections represent the end of the infection chain, and a further dissemination is generally not possible (► Sect. 15.1). Even other viruses are able to leave their natural reservoir, and can be transmitted to humans: different animal poxviruses, hantaviruses, Ebola virus, the pathogen of Lassa fever and flaviviruses, including tick-borne encephalitis virus (► Sects. 14.5, ► 15.4, ► 16.1, ► 16.2 and ► 19.6). They reach the human organism by contact with animals as well as by tick or mosquito bites, thus leaving their natural hosts, rodents or monkeys.

11.3 To what Extent Are Most Viruses Optimally Adapted to their Hosts?

The currently predominant viral infections are the result of evolutionary processes between hosts and parasites which have taken place over very long time periods. Frequently, viral species related to human pathogens are found in various animal species. It is thought that these have adapted to humans during their evolution to become human pathogens, which remain permanently in the population after a certain period of time. If they are highly pathogenic for humans, then they will eliminate themselves from the population by destroying their hosts immediately. Therefore, the ideal situation is a balance between survival of the host and a more or less optimal viral replication with minimal damage. Examples for the optimal adaptation to a host are some arenaviruses (► [Sect. 16.1](#)), among them lymphocytic choriomeningitis virus and the causative agent of Lassa fever. Both viruses are highly adapted to their hosts, namely wild mice. These viruses are transmitted vertically during pregnancy to offspring, in which they induce an immune tolerance. These animals are healthy virus carriers, and excrete large amounts of viruses for life. However, if they infect humans, this frequently leads to severe diseases. Occasionally, new viral infections emerge in humans. This is particularly the case when contact occurs with rare and reclusive species which transmit the adapted pathogens to humans. An example in this context is the SARS epidemic of 2003. It is assumed that bats are the animal species that serves as the natural host of this very dangerous virus for humans (► [Sect. 14.8](#)). Other examples are human Nipah and Hendra infections, which are also transmitted by bats. Poliomyelitis was also a relatively well adapted human virus infection under living conditions with low hygiene standards. Here, the pathogen was usually transmitted during the first 6 months of life. Protective maternal IgG antibodies are still available in the infants at this time. Sequelae from the disease and occasionally paralysis are found only in infections occurring at an older age (► [Sect. 14.1](#)).

11.4 What Methods Does Epidemiology Use for Studying Viral Diseases?

The epidemiological methods which are especially used for viral diseases include survey and collection of data on the occurrence of specific disease clusters. This anamnesis constitutes the basis of all studies. Detection of specific antibodies, viral genomes or viral proteins in blood or tissue samples makes possible the diagnosis of acute or previous viral diseases (► [Chap. 13](#)).

Frequently, the aetiological role of a virus can no longer be evidenced by the fulfilment of the Henle–Koch postulates. These require the pathogen always be detectable in the patients, isolable from them, cultivable in pure culture and able to generate the disease after inoculation in a susceptible host (► [Chap. 1](#)). According to these criteria, many viruses cannot be characterized as pathogens of the infectious diseases caused by them, not least because many viruses cannot be propagated

Table 11.1 The Evans postulates

The prevalence of the disease should be significantly higher in populations exposed to the putative disease-causing agent than in control populations that have not been so exposed
Exposure to the pathogen is more frequent in the population with the disease than in the population without the disease
In prospective studies, the incidence of the disease should be significantly higher in populations exposed to the putative disease-causing agent than in those not exposed to it
In a region with exposure to the pathogen, the incubation periods should follow a normal distribution
All exposed individuals should react with an immune response, which can exhibit a biological variance
A measurable immune response should regularly appear after exposure to the putative pathogen either as a new response in those lacking this before exposure or as an increased response in terms of the corresponding parameters
Experimental reproduction of the disease should occur with higher incidence in animals appropriately exposed to the putative pathogen than in those not exposed to it
Elimination of the putative pathogen should result in a significant reduction of the incidence of the disease
Vaccination should lead to a decrease of the incidence of the disease in a population
The overall picture of the postulates should be plausible in a biological and epidemiological sense

in cell culture. Therefore, it is reasonable to extend these definitions. Helpful in this context are the so-called Evans postulates. They assess the association of a pathogen with a disease, even using indirect criteria. Essential aspects of the Evans postulates are summarized in [Table 11.1](#).

Nucleic acid sequencing and determination of restriction enzyme patterns of DNA sequences render it possible to compare the virus strains or variants that emerge during an epidemic or pandemic. They make possible molecular epidemiology, which allows one to identify certain people, animals or livestock as a source of infection. In this way, molecular pedigrees can be established, which allow conclusions to be drawn on the origin of the pathogen.

Another field of modern epidemiology is so-called modelling, which is the theoretical construction of the development of a viral infection in the population. By modelling, one can estimate the worst-case scenario by variation of individual parameters. For many questions this is an important factor.

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