Chapter 5
Principles of Infectious Disease Epidemiology

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In this chapter, principles and concepts of modern infectious disease epidemiology are presented. We delineate the role of epidemiology for public health and discuss the characteristics of infectious disease epidemiology. This chapter also includes definitions of important terms used in infectious disease epidemiology.

5.1 Definition and Aims of Epidemiology

Giving a universally valid definition of epidemiology is difficult. Epidemiology is not a science with a clearly defined field of application in contrast to anatomy or gastroenterology, which target specific parts or aspects of the human body. Rather it is a scientific method which can be applied to a broad range of health and medical problems, from infectious diseases to health care. Epidemiology is a constantly changing field of science, because new questions arise in population health and new statistical techniques are developed and adapted from other sciences. In times of modern information technologies and high-speed computers, new opportunities arise for data collection and storage on a large scale and for application of advanced bio-informatic and modelling techniques. In the era of globalization, many health problems are relevant on a global scale and intervention strategies have to be developed on an international level. In particular, for infectious disease epidemiology, global spread is increasingly important as demonstrated by the spread of the human immunodeficiency virus (HIV) and the pandemic spread of influenza A.

Definition: Epidemiology

The word "Epidemiology" is derived from Greek words meaning *study upon populations* (epi-upon, demos-people, logos-study).

A broader definition of epidemiology from *A Dictionary of Epidemiology* has been widely accepted. According to this definition, epidemiology is *the study*

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A. Krämer et al. (eds.), *Modern Infectious Disease Epidemiology*,
Statistics for Biology and Health, DOI 10.1007/978-0-387-93835-6_5,

of the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems (Last 2001).

The crucial point is that epidemiology concerns itself with populations or groups of population in contrast to clinical medicine, which deals with individuals (patients). Therefore, epidemiology describes health and disease in terms of frequencies and distributions of determinants and conditions in a population or in a specific group of a population. Epidemiology also includes the study of associations between specific diseases and factors to which populations are exposed. In this way, risk factors or protective factors which are associated with a health status of an individual or with some conditions can be identified. These associations can be identified because risk factors and diseases are not randomly distributed in populations but rather there are population groups where some diseases and associated factors occur more often than in other population groups. Commonly, risk factors are distributed by age and often also differ for men and women.

Based on the distribution of risk factors among different population groups, the concept of "vulnerable" population can be derived. This group is at higher risk for certain conditions because of the existence of a risk constellation favouring these conditions.

Epidemiological methods can be used to show statistical associations, but causal relationships have to be established by clinical and biological research. Epidemiological studies often aim at generating statistical evidence that identify factors, which play an important role in acquisition of infection and the development of a disease. Causality between these factors and the outcome might be more or less plausible or strong. Some criteria which demonstrate a possible causal relationship between identified factors and disease have been developed (causal criteria by Hill; Rothman and Greenland 2008). Based on epidemiological studies, specific hypotheses that tell us which potential factors may play a causal role in the development of certain diseases can be generated. Providing a final proof for the causality of these associations is a task of other sciences like clinical medicine or microbiology.

5.2 Epidemiology and Public Health

Epidemiology is the fundamental science of public health and provides the evidence on which public health professionals should base their decisions and strategies (Detels et al. 2002). In this way, epidemiology provides the tools for the control of diseases and health promotion. More specifically, some important tasks of epidemiology for public health are

- To elucidate the aetiology of a disease
- To describe the spectrum of a disease (what kind of symptoms occur and how frequently do they occur)

- To describe the natural history of a disease (what disease stages does a patient typically go through)
- To identify risk factors and protective factors (which factors enhance or prevent occurrence of a disease)
- To estimate disease burdens and health-care needs of a population
- To predict disease trends (to extrapolate from observations about time trends in risk factors and the future occurrence of the disease)
- To evaluate the effectiveness of interventions and public health programs

Spatial and temporal relations between the distribution of risk factors and the occurrence of disease can be established using surveillance methods and epidemiological studies. The information obtained in this way permits the identification of risk and protective factors and the analysis of time trends and spatial clustering of diseases. Knowledge of the spatial distribution and temporal trends of diseases is an important prerequisite for the effective application of preventive and interventive measures in order to reduce corresponding disease burdens. We want to illustrate the contributions of epidemiology to public health with the example of HIV/AIDS.

5.2.1 Example: Epidemiology and the HIV/AIDS Epidemic

A good example of the important role of epidemiology in collaboration with other relevant public health and medical disciplines is the research upon the AIDS epidemic. At the beginning of the 1980s, the syndrome of acquired immunodeficiency (AIDS) was for the first time described in the United States. It was observed in a group of homosexual men in California and New York who had opportunistic infections and specific tumours.

5.2.1.1 Elucidating the Aetiology

At that time, various theories explaining the aetiology of this syndrome were postulated. Through targeted epidemiological studies it was found that an infectious agent was responsible for this syndrome. Sexual contact was identified as an important transmission route, because homosexual men who had many sexual partners contracted the disease more frequently than those with only few partners. Later the human immunodeficiency virus (HIV) was characterised in the laboratory as the cause of the disease and an antibody test was developed. Epidemiological studies had to a certain extent a filter function for gaining insight into this new infectious disease by sorting a wide set of potential aetiological factors and elucidating the infectious nature of the disease. This hypothesis was then checked in the laboratory and proven through the identification of the infectious agent. Thereafter, epidemiology had not lost its important role in the investigation of the HIV epidemic. On the contrary, epidemiological studies continue to play a significant role for surveillance and prevention of this globally devastating infectious disease.

5.2.1.2 Describing the Spectrum of Disease for HIV/AIDS

The human immunodeficiency virus (HIV) can lead to the acquired immunodeficiency syndrome (AIDS), which is characterized by a potpourri of different symptoms and diseases, ranging from certain opportunistic infections and tumours to neurological illnesses. A common pathogenetic feature underlying these clinical conditions is the deficiency of the immune system caused by HIV, which primarily infects and destructs specific cells of the immune system ($CD4^+$ T lymphocytes). Aim of epidemiology is to study the distribution of these clinical manifestations depending on the population and its risk factors.

5.2.1.3 Describing the Natural History of HIV Infection

Epidemiological studies can be used to gain information on the natural history of a disease. The natural history of a disease refers to the course of the disease without treatment, which is usually not observed in clinical medicine. Using the antibody test, it became possible to study certain risk groups for HIV infection in the population by way of screening and to follow up persons with and without HIV infection over time in cohort studies in order to understand the risk factors and the natural history of the infection and to identify factors predicting AIDS development. The natural history of HIV infection in its initial stages is characterized by acute retroviral syndrome, which is accompanied by fever, substantial viral pathology and viremia, followed by a long-lasting latent period, where a relative equilibrium between HIV and the immune system of the infected individual exists despite active viral replication. Following an early clinical stage, full-blown AIDS may develop, which is marked by a collapse of the immune system. In the context of clinical epidemiology, the question arises at which phase and when treatment of HIV-infected patients should be applied.

5.2.1.4 Risk Factors and Protective Factors for HIV Infection

The aim of epidemiology is to identify risk and protective factors, which are associated with a disease, and to define frequencies and distributions of these factors in the population. The prevalence of relevant risk factors can then be reduced by the application of specific public health interventions. For the example of HIV, the identification of risk factors includes studies about sexual behaviour and behaviour related to intravenous injections, while the study of protective factors includes, for example, the effect of circumcision on HIV incidence.

5.2.1.5 Predicting Disease Trends

Backcalculation techniques and time series analysis can be used for the prediction of epidemiological trends. For the HIV epidemic, backcalculation approaches were much used up to the era of widespread use of antiretroviral therapy (Rosenberg et al.

1991; Seydel et al. 1994; Verdecchia and Mariotto 1995). Recently, incidence-based measures have gained in importance, since testing rates have increased and methods to detect early HIV infection have become available.

5.2.1.6 To Estimate Disease Burdens and Health-Care Needs of a Population

Due to their dynamic nature the burden of infectious diseases is hard to project. Nevertheless, it is estimated that in 2030, HIV/AIDS will be the third leading cause of death and the leading cause of disability-adjusted life years worldwide (Mathers and Loncar 2006). The authors estimate that 12.1% of all disability-adjusted life years will be due to HIV/AIDS in 2030. This has large implications for the need for health care, in particular the need for antiretroviral treatment (ART) worldwide and may jeopardize the aims of the WHO for providing ART for those living with HIV especially in low-income countries.

5.2.1.7 To Test the Effectiveness of Interventions

Extensive studies have been undertaken to evaluate the effectiveness of various prevention strategies to reduce HIV transmission. Prevention strategies that have been tested in large epidemiological studies were among others mass treatment for sexually transmitted infections (Korenromp et al. 2005) and the effect of circumcision on HIV transmission (Auvert et al. 2005; Gray et al. 2007). While mass treatment for sexually transmitted infections did not prove to be a strategy with lasting success, the results from the circumcision trials have been very promising (see also Chapter 18).

5.3 Characteristics of Infectious Disease Epidemiology

Infectious diseases are caused by pathogens that are transmitted either directly between persons or indirectly via a vector or the environment. They are therefore also called “communicable diseases”, because their transmission relies on some form of contact between individuals of a population. The fact that transmission occurs makes the epidemiology of infectious diseases different from the epidemiology of non-communicable diseases for the important reason that the risk of contracting the disease depends on its prevalence in the population.

The spread of an infectious disease through populations is determined by characteristics of the infectious agent, the host, and the environment. Infectious agents are characterized by their biological properties, their host spectrum and natural occurrence; host characteristics are, for example, susceptibility to specific diseases, immune status, socio-demographic and contact behaviour. The interaction between host and pathogen is modulated among others by immune response, virulence of the pathogen, behavioural responses to disease symptoms and pathogen

adaptation to treatment. Environmental factors determine the conditions under which the host–pathogen interaction takes place and influences pathogen survival and host behaviour. Environmental factors include physical factors (e.g. climate), biological factors (e.g. insects that transmit the infectious agent), as well as social factors such as sanitary conditions and quality of health-care services.

Definition: Infectious disease

An *infectious disease* is defined as a disease caused by an infectious agent or its toxic products. This agent can be transmitted by an infected person, an animal or a reservoir directly or indirectly through a vector (e.g. alternate host).

Just like other fields of epidemiology, infectious disease epidemiology is concerned with populations, instead of dealing with individual patients. At the centre of the focus of infectious disease epidemiology is the relationship between an infectious agent and its host, its routes of transmission and the environment in which transmission takes place. In contrast with non-communicable diseases, an infected individual (case) can be an initial source for further infections, thereby leading to chains of transmissions in a population. If these are clustered in time they will be recognized as an outbreak and will require localized intervention to break transmission chains. Inapparent and subclinical infections and carriers of infection may be sources for further infections without being identified as infectious cases. Some persons or population groups may be immune against an infection due to vaccinations or after prior exposure to the infection.

Important questions studied in infectious disease epidemiology concern the transmissibility and virulence of pathogens, the course of clinical or sub-clinical infections and the duration of protective immunity. Also, in contrast to the epidemiology of non-communicable diseases, in infectious disease epidemiology the study of human contact patterns play an important role. These can be contacts between humans, between humans and animals, between humans and vectors, or between humans and their environment. Epidemiological studies are conducted to determine why an infectious disease occurs endemically or epidemically and what causes differences in the occurrence of infections among populations and within populations.

In Page et al. (1995) the transmission of infectious disease is described by a chain of six elements that are needed in order for infection and disease to occur in an individual. This interaction is referred to as the “chain of infection” (Fig. 5.1). Each element must be present and lie in sequential order for an infection to occur. Intervention can target any of those six elements of the cycle.

The *portal of entry* is the way an infectious agent enters a susceptible host. The portal of entry is usually the same as the portal of exit from the host (Timmreck 1994). For example, measles virus exits the respiratory tract of the host and enters the respiratory tract of a new host. In the case of gastrointestinal infections an infectious agent is located in faeces and can be carried to the mouth of the new host by improperly washed hands. Other portals of entry are the skin (e.g. schistosomes), the mucous membrane (sexually transmitted diseases), the blood (HIV) and the transplacental mode of entry (toxoplasmosis).

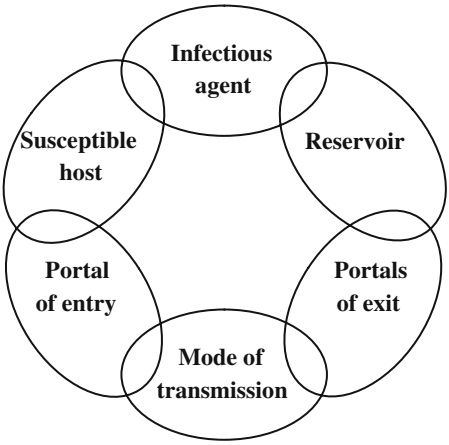

Fig. 5.1 The chain of infection

The *portal of exit* is the route by which the infectious agent leaves the host. The portal of exit is usually dependent on the localization of the infectious agent in the host. The most common portals of exit are respiratory tract (e.g. influenza, measles, mumps, and rubella), genitourinary tract (HIV, syphilis), gastrointestinal tract (hepatitis A, *Salmonella*), through skin (hepatitis B through needles), placenta (toxoplasmosis).

In the following we introduce some of the central concepts of infectious disease epidemiology.

5.3.1 Exposure

One of the central concepts of epidemiology is the *exposure* of an individual to a potential disease-causing agent or substance. In case of an infectious disease, their exposure to infectious agents – a pathogen – can lead to infection, but does not necessarily lead to disease. Infectious agents can be prions, viruses, bacteria, fungi or parasites. The disease can then be caused either by the pathogens themselves after replication in the infected host or by their toxic products. The exposure to an infectious agent depends on its transmission route. Different outcomes of an exposure to an infectious agent can be observed (Fig. 5.2). The outcome may or may not depend on the infectious dose or the inoculum size. For very infectious pathogens a small dose may result in infection of the host, while for less infectious pathogens higher doses of a pathogen are needed for infection. For example, exposure to hepatitis B virus via sexual contact has a much higher probability for resulting in infection than does exposure to HIV. For some infections the relationship between infectious dose and probability of infection can be quantified by dose–response relationships (Teunis et al. 1999).

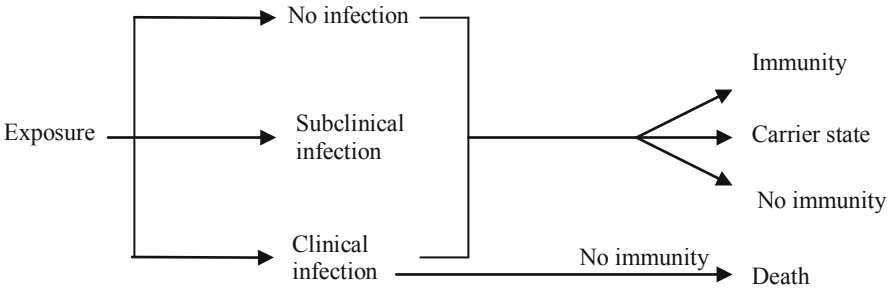

Fig. 5.2 The different outcomes of an exposure to an infectious agent (modified from Giesecke 1994)

5.3.2 Infection

What is actually meant by *infection*? For most pathogens, infection describes the event that the pathogen can establish itself in the host individual and reproduce itself or some stages of its life cycle. For some pathogens one has to distinguish between colonization (a settlement of the pathogen on the skin or other body tissues), where an individual has no clinical signs or symptoms of disease, and invasive infection, when the pathogen permeates through certain barriers of the host like the skin or the mucous membrane and causes symptomatic infection. In pathology, an inflammation caused by an infectious pathogen (or other damaging agents) is characterized by following four phenomena: redness and hyperthermia of, e.g. affected skin areas followed by swelling, pain and loss or impairment of function.

Infections with different pathogens, but also with the same pathogen in different individuals, can differ widely in their natural history. Some infections are acute and exist only for a few hours, days or weeks (e.g. measles, mumps, influenza, diarrhoea), while others after a short acute phase can become chronic and might remain detectable for decades (e.g. hepatitis B and C, HIV). These differences reflect how the human immune system can deal with different pathogens, which in turn depends on a pathogen's genetic variability and on where it is localized in the host.

The *clinical* manifestations of an infection can also differ widely between individuals. An infection may lead to a carrier stage where an infected individual displays no symptoms. Nevertheless, the presence of pathogens can be detected in carriers by means of microbiological tests (serological tests or direct methods to detect the presence of pathogens). Carriers are of large importance for the spread of infections and for intervention, because they are not easily recognized or detected. A carrier of an infection is usually not aware of his/her infection and the risk they pose towards their direct contacts. Therefore, susceptible contact persons do not take precautions against being infected. It is difficult to target public health measures to prevent risky contacts and to identify sources of infection (e.g. hepatitis B infection, HIV). Under these conditions, only systematic screening of entire population groups may ensure that effective interventions are implemented.

Infections with symptomatic or clinical manifestations may display a large variability in symptoms. These symptoms can be very specific for some infectious

diseases (e.g. typical rash and pox in smallpox) or they can be rather aspecific such as respiratory tract infections (fever and cough) or gastrointestinal infections (diarrhoea) such that a number of differential diagnoses are available. In the latter case a final diagnosis can be based only on laboratory testing of specimen.

Immunity after infection may or may not be protective against infection and may last for variable periods of time. Some infectious diseases confer lifelong immunity (e.g. measles), others confer some amount of immunity against severe symptomatic infection, but much less against sub-clinical infection (e.g. pertussis), and some confer no or negligible levels of immunity (e.g. Chlamydia infection). Finally, some pathogens invade the immune system itself and thereby not only limit the host's immune response against themselves but also enable other pathogens to invade the infected host (e.g. HIV and opportunistic infections). Immunity can be acquired either after natural infection or indirectly. Maternal antibodies protect the newborn child against many infections in the first few months of its life. After that, immunization for some infectious diseases is possible by vaccination. Also vaccine-induced immunity can be lifelong or temporary. In the latter case, repeated booster vaccinations are necessary to ensure protection against the infection.

5.3.3 Stages of Infection and Disease

During the course of an infection, different stages or time periods can be distinguished regarding the infectivity and manifestations of symptoms in the infected individual. The *latent period* is the time interval from infection to the start of the infectious period; the *incubation period* is the time interval from infection to the onset of clinical symptoms (Fig. 5.3). The *infectious period* is the time interval

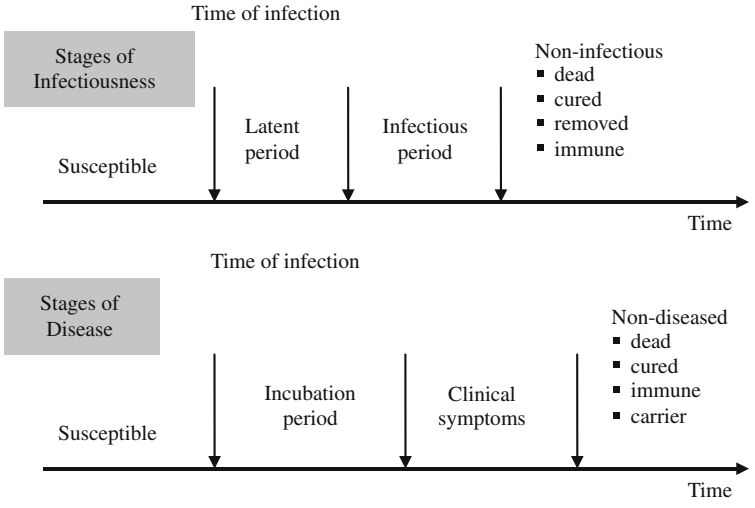

Fig. 5.3 Stages of infection and disease (modified according to Halloran 1998)

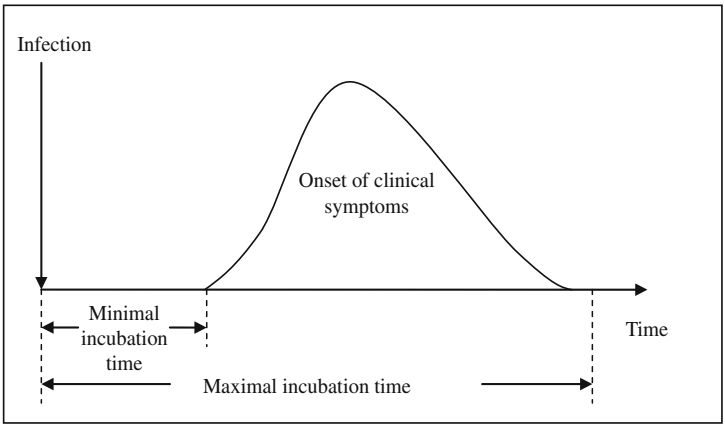

Fig. 5.4 Incubation time distribution

during which an infected person can transmit an infection to other susceptible persons.

For a specific infectious disease the incubation period may vary widely between individuals. Therefore, incubation periods are often better described as incubation time distributions with a minimal, a mean or median and a maximal incubation time (Fig. 5.4). In outbreaks one frequently observes several generations of an infection, i.e. clusters of cases with typical time intervals between their days of symptom onset (Fig. 5.5). The first case, or index case, in an outbreak is of great importance because he or she brings the infectious disease into the community. Secondary cases are those infected by the index case, tertiary cases those infected by a secondary case, etc. The typical time interval between the onset of symptoms in a case and the onset of symptoms in the cases infected by him/her is called the *generation interval* or *serial interval*. The distribution of this interval is determined by the durations of

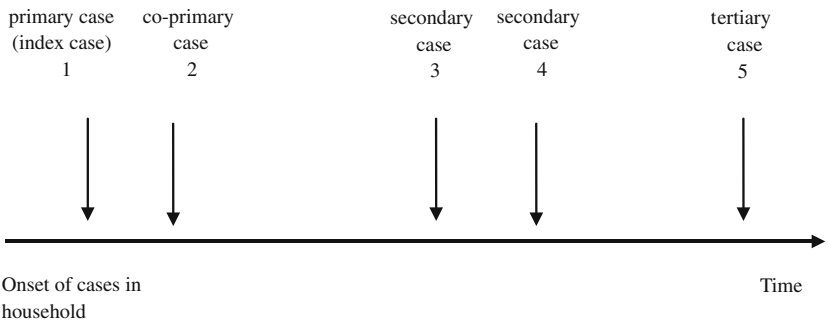

Fig. 5.5 Generations of an infection (modified according to Halloran 1998)

latent period and infectious period, and by the contact rates of infectious individuals (Fine 2003).

The reproduction number or *reproductive rate* of an infection is its potential to spread after invasion into a population. It depends on the proportion of immune persons in the population, the duration of the infectious period, the contact rates and the probability of transmission upon contact between an infected and a susceptible individual.

5.3.4 Virulence, Pathogenicity and Immunogenicity

There are different definitions of virulence in the literature, mostly based on the ability of a pathogen to cause host mortality. However, in many infectious diseases a virulence definition based on the death of a host is not useful, because we are more interested in the severity of symptoms rather than in death. In an absolute sense the capacity of a pathogen to cause symptoms is described as *pathogenicity*. By *virulence,* one usually refers to the pathogenicity of one (strain of a) pathogen in comparison with another. We therefore follow Casadevall and Pirofski (1999) in defining virulence as the relative capacity of a pathogen to cause damage in the host.

Pathogenicity and virulence are determined by the interaction between host and pathogen. Characteristics of infectious agents that affect virulence include their ability to proliferate, invade organisms and damage the host. These effects may be dependent on the infective dose, which is the number of organisms needed to cause an infection. A virulent pathogen can invade into the host organism with a small infectious dose. Characteristics of the host also play an important role in the ability of a pathogen to cause disease, that is, pathogenicity and virulence depend not only on the characteristics of the host such as resistance and immune system function but also on genetic factors, age, gender and other physiological conditions, e.g. pregnancy.

Immunogenicity is defined as the ability of a pathogen or a vaccine to evoke an immune response after an infection or a vaccination, which may lead to protection against re-infection with the same or similar pathogen. For some infections, immunity after natural infection is lifelong (measles or polio virus), while for others, immunity is temporary (pertussis) or strain specific (influenza). For some infections, immunity is acquired only after repeated re-infections and wanes if booster infections do not occur (malaria). For some infections, immunity is induced against symptomatic infection, but subclinical infection may still occur.

5.3.5 Routes of Transmission

An infectious agent may be transmitted to a susceptible host in many ways. These routes of transmission are classified as direct and indirect transmission (Giesecke 1994). Direct transmission includes direct skin-to-skin contact and close contact that permits transmission via droplets and aerosols. Droplet spread occurs by sneezing,

coughing or talking at a short distance. Droplet spread is defined as direct transmission because it is transmitted by a direct spray over a few metres before droplets fall to the ground. Indirect transmission takes place through vectors or via the environment. A *vector* is an invertebrate animal that becomes infected from infected animals or persons and transmits the infection to other persons, e.g. the *Anopheles* mosquitoes that transmit malaria parasites from person to person. Vectors are typically insects or arthropods. Also, medical devices like injection syringes can act as vectors for disease transmission. Furthermore, environmental transmission occurs through water, food, soil, air, and solid surfaces depending on where a pathogen can best survive outside the host.

The *source of infection* is the initial point from which the infection passes to a person. In directly transmitted infections the source is an infected person. In indirectly transmitted infections, sources of infection can be different materials in the environment (e.g. objects, ground and water), contaminated or infected foods or infected animal vectors. A *reservoir* of infection is a living organism or a material in or on which an infectious agent lives and/or usually multiplies.

Examples of directly transmitted infections include sexually transmitted infections (transmission by mucous membrane contacts), toxoplasmosis (transmission through the placenta), HIV and hepatitis B (transmission by sexual contact and via blood), herpes virus type 1 infection (skin-to-skin contacts), and influenza [transmission by coughing and sneezing (droplet spread)]. Examples of indirectly transmitted infections are hepatitis A (faecal–oral transmission), *Salmonella* (food), malaria (mosquitoes) and schistosomiasis (water) (Table 5.1).

In addition to their main host (human or vertebrate animal), some pathogens have one or several intermediate hosts (e.g. arthropod), in which they multiply and develop. In case of malaria the human is an intermediate host and sexual proliferation of the pathogen takes place in the *Anopheles* mosquito.

A human can also become an accidental host by unusual contact with an infectious agent that has animals as the main host (e.g. hantavirus pulmonary syndrome). Any infection that is transmitted from an animal to a human is called *zoonosis*. It is believed that many newly emerging infections in humans evolve from zoonoses.

Table 5.1 Frequent media of transmission and transmission routes for some infectious agents

Transmission medium	Pathogen	Transmission route
Foods	*Salmonella*	Foodborne
	Campylobacter	Faecal–oral
	Hepatitis A	
Water	Cholera	Water-borne
Sputum droplets	Influenza	Close contact
Air/aerosols	Tuberculosis	Airborne
	Chickenpox, *Legionella* infection	
Organ transplants	Cytomegalovirus	Transplant-borne
Blood	HIV, hepatitis C	Blood-borne
Sperm, body fluids	Hepatitis B	Sexual contact

5.3.6 Endemic Infectious Diseases and Epidemic Outbreaks

An *outbreak* is defined as the occurrence of an infection in a population with an excess of cases in space and time above the expected level. An outbreak can be small – sometimes two linked cases constitute an outbreak – or it can affect large parts of the population. A larger outbreak that affects a considerable proportion of a population is also called *epidemic*. A global outbreak that affects many or all countries worldwide is called a *pandemic*.

If an infectious disease can establish itself permanently in a population, it is called *endemic*. For many endemic infections, the prevalence remains more or less constant over time as long as no changes occur in intervention or prevention strategies. By prevention or intervention one can aim at *elimination* of an endemic infection from a population. Elimination on a global scale is called *eradication*. Elimination occurs if there is no natural circulation of a pathogen any longer in a population; eradication is reached if a pathogen does not circulate at all any more in the human population. Smallpox is the only infectious disease for which eradication has been achieved at present.

Many endemic infectious diseases have seasonally fluctuating incidence rates (Fisman 2007). The seasonality is due to climate conditions, which influence pathogen survival in the environment, and human contact patterns, which fluctuate due to activity patterns (e.g. school holidays).

5.4 Challenges of Infectious Disease Epidemiology

Transnational migration, changes in human behaviour, rapid urbanization and newly emerging infectious diseases such as SARS and BSE (mad cow disease) are the challenges of modern infectious disease epidemiology (see Chapter 2). In times of globalization, transnational migration is of great importance for the spread of infectious diseases. The border cannot be seen as a barrier anymore as many infectious diseases have a long incubation period, which makes it difficult to control the spread of infectious diseases. On the other side, migrant populations are often marginalized in the society, which makes them vulnerable to certain diseases (Tselmin et al. 2007). Socio-economic inequalities also play an important role in the spread of infectious diseases. The poor population often lives in overcrowded households with inadequate sanitation conditions. These people usually have a worse nutritional status which makes them more vulnerable to infectious diseases. Individuals from low socio-economic classes also may have limited access to primary health care.

Population groups at risk for infectious diseases may benefit from educational interventions to improve knowledge, beliefs and attitudes concerning prevention. Such efforts are crucial to stop the spread of infections. Closer interaction between academic research and populations at risk can be achieved by using the *community-based participatory research* (CBPR) approach, which actively involves the community studied in the research (Israel et al. 1998). The benefits of this type

of research are the following: (a) community members are considered to be the study partners and not just objects of research; (b) the knowledge of the community is used to better understand health problems in the community; (c) interventions can be directly conducted in the community. Close collaboration between communities and researchers is essential to develop adequate public health strategies that address community concerns (Kone et al. 2000). This approach is especially appropriate when research is conducted on sensitive issues such as HIV/AIDS or sexually transmitted diseases and has been successfully applied in infectious disease epidemiology.

Other challenges of infectious disease epidemiology lie in the rapid development of genetic typing methods, which allow a more detailed picture of how strains of pathogens are genetically related and along which routes they might have spread through a population. At present a wealth of genotyping data are already available, but epidemiological studies to understand the relationship between transmission risks and the distribution of genotypes are still scarce.

Another pressing area of research for infectious disease epidemiology comes from the ability of pathogens to escape intervention pressure by evolutionary adaptation. For example, the development of resistance of pathogens against treatments (antibiotic resistance, resistance against antiviral medication) is causing increasing problems not only in hospitals, where multiresistant strains of pathogens have become endemic, but also in the treatment of tuberculosis and chronic hepatitis B.

References

Auvert BD, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, and Puren A (2005) Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 Trial. PLoS Med. 2:e298

Casadevall A and Pirofski LA (1999) Host-pathogen interactions: redefining the basic concepts of virulence and pathogenicity. Infect Immun. 67:3703–3713

Detels R, Holland W, and McEwen J (2002) Oxford Textbook of Public Health. Oxford: Oxford University Press

Fine PE (2003) The interval between successive cases of an infectious disease. Am J Epidemiol. 158:1039–1047

Fisman DN (2007) Seasonality of infectious diseases. Annu Rev Public Health. 28:127–143

Giesecke J (1994) Modern Infectious Disease Epidemiology. London Sydney Auckland: Arnold

Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, Kiwanuka N, Moulton LH, Chaudhary MA, Chen MZ, Sewankambo NK, Wabwire-Mangen F, Bacon MC, Williams CF, Opendi P, Reynolds SJ, Laeyendecker O, Quinn TC, and Wawer MJ (2007) Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 369:657–666

Halloran ME (1998) Concepts of infectious disease epidemiology. In KJRothman, S Greenland. Modern Epidemiology. Philadelphia: Lippincott-Raven,pp. 529–554

Israel BA, Schulz AJ, Parker EA, and Becker AB (1998) Review of community-based research: assessing partnership approaches to improve public health. Annu Rev Public Health. 19: 173–202

Kone A, Sullivan M, Senturia KD, Chrisman NJ, Ciske SJ, and Krieger JW (2000) Improving collaboration between researchers and communities. Public Health Rep. 115:243–248

Korenromp EL, White RG, Orroth KK, Bakker R, Kamali A, Serwadda D, Gray RH, Grosskurth H, Habbema JD, and Hayes RJ (2005) Determinants of the impact of sexually transmitted

infection treatment on prevention of HIV infection: a synthesis of evidence from the Mwanza, Rakai, and Masaka intervention trials. J Infect Dis. 191 Suppl 1:S168–S178
Last JM (2001) A Dictionary of Epidemiology.Oxford: Oxford University Press
Mathers CD and Loncar D (2006) Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 3:e442
Page RM, Cole GE, and Timmreck TC (1995) Basic Epidemiological Methods and Biostatistics. A Practical Guidebook. Boston London Singapore: Jones and Bartlett Publishers
Rosenberg PS, Biggar RJ, Goedert JJ, and Gail MH (1991) Backcalculation of the number with human immunodeficiency virus infection in the United States. Am J Epidemiol. 133:276–285
Rothman KJ, Greenland S and Lash TL, eds. (2008) Modern Epidemiology. 3rd. ed. Philadelphia: Lippincott Williams and Wilkins
Seydel J, Kramer A, Rosenberg PS, Wittkowski KM, and Gail MH. (1994) Backcalculation of the number infected with human immunodeficiency virus in Germany. J Acquir Immune Defic Syndr. 7:74–78
Teunis PF, Nagelkerke NJ, and Haas CN (1999) Dose response models for infectious gastroenteritis. Risk Anal. 19:1251–1260
Timmreck TC (1994) An Introduction to Epidemiology. Boston London Singapore: Jones and Bartlett Publishers
Tselmin S, Korenblum W, Reimann M, Bornstein SR, and Schwarz PE (2007) The Health Status of Russian-speaking Immigrants in Germany. Horm Metab Res. 39:858–861
Verdecchia A and Mariotto AB (1995) A back-calculation method to estimate the age and period HIV infection intensity, considering the susceptible population. Stat Med. 14:1513–1530