68 Epidemiology and control of community infections

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KEY POINTS

- The surveillance of infection provides the basis for appropriate investigation and preventive action.
- The infectious process involves three main factors: the micro-organism, the host and the environment.
- Herd immunity indicates the degree to which a community is susceptible to infection.
- Infection is spread in five ways: from person to person, from healthy carriers, from animal sources, from environmental sources and as a result of an organism situated in an area of the body where it is harmless gaining access to a more dangerous site.
- Infection may manifest itself as: a sporadic case, an outbreak, an epidemic or a pandemic.
- Outbreaks have three main patterns of spread: from a single source, from one person to another, or from a single source with subsequent person-to-person spread.
- The epidemiological investigation of an outbreak involves an analysis concerning: the persons involved, the place it occurred and the time those infected became ill.
- Vigilance and high-quality surveillance are necessary in order to have an early warning of emerging infections.

When you can measure what you are speaking about and express it in numbers, you know something about it; when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind.

William Thomson, Lord Kelvin
(Popular Lectures and Addresses, 1891)

Good surveillance does not necessarily mean the making of right decisions but it reduces the chances of wrong ones.

Alexander Langmuir, 1963

Once is happenstance, twice is coincidence, the third time it's enemy action.

Ian Fleming
(Goldfinger, Jonathan Cape, 1959)

Attempts to observe and record diseases in order to devise means of determining their cause and control have a long history. Hippocrates (460–361 BC), 'the father of medical science', and Herodotus (484–425 BC), 'the father of history', both related environmental factors to health. Hippocrates, when writing of the occurrence of diseases, distinguished between the 'steady state', the 'endemic state' and the abrupt change in incidence, the 'epidemic'.

Probably the first public health measures based on case reports of infectious diseases, taken by a European government, occurred in 1348 when the Republic of Venice excluded ships with affected people on board in order to control outbreaks of pneumonic plague (the *black death*). Fifty years later, again in Venice, the concept of *quarantine* was introduced when ships from plague-stricken areas had to stay outside the harbours for 40 days (*quaranta giorni*).

In addition, because of the fear of a plague epidemic, the first of the *Bills of Mortality*, in which causes of death were recorded, was published in London in 1592. In 1662 John Graunt (1620–1674), in his book *Natural and Political Observations Made Upon the Bills of Mortality*, was the first to count the number of persons dying in London from specific illnesses and to advocate the value of obtaining numerical data on a population in order to study the causes of disease (Table 68.1). In 1837 the office of the Registrar General was established to develop the work started by John Graunt; the English physician William Farr (1807–1883) added reports to those of

Table 68.1 Selection of causes of death in London taken from the Bills of Mortality, 1632

Causes of death	No. of deaths
Chrisomes[a] and infancy	2268
Consumption[b]	1797
Fever	1108
Aged	628
Smallpox	531
Teeth	470
Abortive and stillborn	445
Bloody flux[c], scouring[d] and flux	348
Dropsy[e] and swelling	267
Convulsions	241
Childbed	171
Measles	80
Ague[f]	43
King's evil[g]	38

[a]A child who died during the first month of life or a child who died unbaptized.
[b]Usually pulmonary tuberculosis.
[c]Dysentery
[d]Diarrhoea.
[e]Oedema.
[f]Malaria.
[g]Tuberculosis of the skin.

the Registrar General that dealt with infectious diseases, occupational diseases, accidents or hazardous work conditions.

The importance of keen observation of disease in order to deduce the likely cause has been demonstrated on many occasions. In 1849, 34 years before the identification of *Vibrio cholerae* by Robert Koch (1843–1910), John Snow (1813–1858), a London physician, proved by epidemiological observation that cholera was mainly spread by drinking infected water and not through the air in the form of miasmas, as was commonly thought at the time. Similarly, William Budd (1811–1880), a general practitioner from Devon, showed in 1873 how typhoid was spread, even though it was not until 1885 that the typhoid bacillus was first isolated in the laboratory. More recently, William Pickles (1885–1969), a general practitioner in Wensleydale, Yorkshire, was able to elucidate many of the epidemiological characteristics of hepatitis and other infections well before microbiological advances were to confirm his observations.

From these beginnings the surveillance of infection has assumed national and international proportions. National surveillance is carried out in different countries, for example at the Centers for Disease Control and Prevention (CDC) in Atlanta, USA. In the UK, information on infectious diseases and environmental hazards is collated for each devolved country by different public health agencies. General Practitioners and other clinicians also undertake regular recording of disease voluntarily. The European Centre for Disease Prevention and Control in Stockholm collects such data for each European country and, on a worldwide basis, the World Health Organization (WHO) provides important liaison and support. This international co-operation is vital as 'germs do not recognize boundaries'.

Probably the most outstanding achievement of international surveillance was the development of a programme for smallpox eradication. The multidisciplinary approach adopted by the WHO, in which programmes were community based with measurable goals and constant monitoring, resulted in the last endemic case being recorded in October 1977; smallpox was officially declared eradicated in December 1979.

EPIDEMIOLOGY: DEFINITIONS AND PRINCIPLES

Epidemiology is usually defined as *the study of the nature, distribution, causation, mode of transfer, prevention and control of disease*. It has also been regarded as 'the natural history of disease' or as 'the human face of ecology'. Closely linked with the study of epidemiology is the concept of surveillance, which is probably the most effective infection control technique available. Surveillance is defined as: *the epidemiological study of a disease as a dynamic process involving the ecology of the infectious agent, the host, the reservoirs, the vectors as well as the complex mechanisms concerned in the spread of infection and the extent to which this spread will occur*. There are three main elements of surveillance of infection:

1. the systematic collection of pertinent data
2. the orderly consolidation and evaluation of the data
3. the prompt dissemination of the findings, especially to those who can take appropriate action.

Surveillance provides for the recognition of acute problems requiring immediate local, national or international action, and for further assessment by revealing trends or facilitating forecasts. It also provides a rational basis for planning and implementing efficient control measures and for their evaluation and continuing assessment. Although particularly appropriate to the study of infectious diseases, epidemiological principles are also used to elucidate the causes of non-communicable diseases.

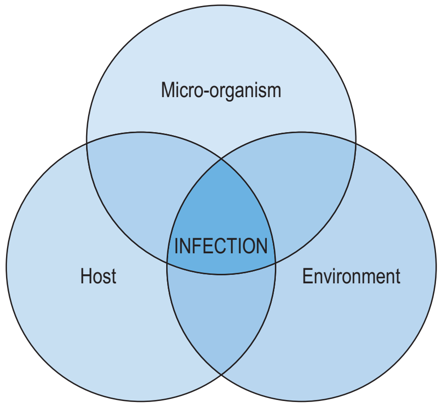

Fig. 68.1 The three main factors involved in the infectious process.

The infectious process is a dynamic state involving three main factors: the micro-organism, the host and the environment (Fig. 68.1).

The micro-organism

Since few micro-organisms are harmful to man, the concept of *virulence* (the degree of pathogenicity of an infectious agent indicated by fatality rates and/or its ability to invade and damage the tissues of the host) must be recognized. The degree of virulence depends on *invasiveness* (the capacity of the organism to spread widely through the body) and *toxigenicity* (the toxin-producing property of the organism) (see Ch. 13). A further variable is the *dose* of the organism, as well as virulence. A small number of organisms of high virulence is usually sufficient to cause disease in a susceptible person, whereas if the organism is of low virulence it often fails to cause disease. Another variable is the *portal of entry*. Many organisms have a predilection for a particular tissue or organ. For example, the causal organism of typhoid fever, *Salmonella typhi,* usually causes disease only when it enters the human body through the mouth in food or water (see Ch. 24).

The host

The reaction of the host to a micro-organism will depend on the ability to resist infection. The individual may not possess sufficient resistance against a particular pathogenic agent to prevent contraction of infection when exposed to the organism. Alternatively, the individual may possess specific protective antibodies or cellular immunity as a result of previous infection or immunization. However, immunity is relative and may be overwhelmed by an excessive dose of the infectious agent or if the person is infected via an unusual portal of entry; it may also be impaired by immunosuppressive drug therapy, concurrent disease or the ageing process. These properties were particularly evident in the influenza H1N1 pandemic of 2009 when infection was mainly seen in younger persons as those over the age of 60 had acquired immunity from previous exposure.

Herd immunity

Herd immunity is an important element in the balance between the host population and the micro-organism, and represents the degree to which the community is susceptible or not to an infectious disease as a result of members of the population having acquired active immunity from either previous infection or prophylactic immunization (see p. 731).

Herd immunity can be measured:

1. *Indirectly* from the age distribution and incidence pattern of the disease if it is clinically distinct and reasonably common. This is an insensitive and inadequate method for infections that manifest subclinically.
2. *Directly* from assessments of immunity in defined population groups by antibody surveys (sero-epidemiology) or skin tests; these may show 'immunity gaps' and provide an early warning of susceptibility in the population. Although it may be difficult to interpret the data in absolute terms of immunity and susceptibility, the observations can be standardized to reveal trends and differences between various defined population groups in place and time.

The decision whether to introduce herd immunity artificially by immunization against a particular disease will depend on several epidemiological principles.

- The disease must carry a substantial risk.
- The risk of contracting the disease must be considerable.
- The vaccine must be effective.
- The vaccine must be safe.

The effectiveness and safety of immunization programmes are monitored by observing the expected and actual effects of such programmes on disease transmission patterns in the community by appropriate epidemiological techniques.

The environment

The environment plays a major role in the causation, spread and control of infection. In the UK, the

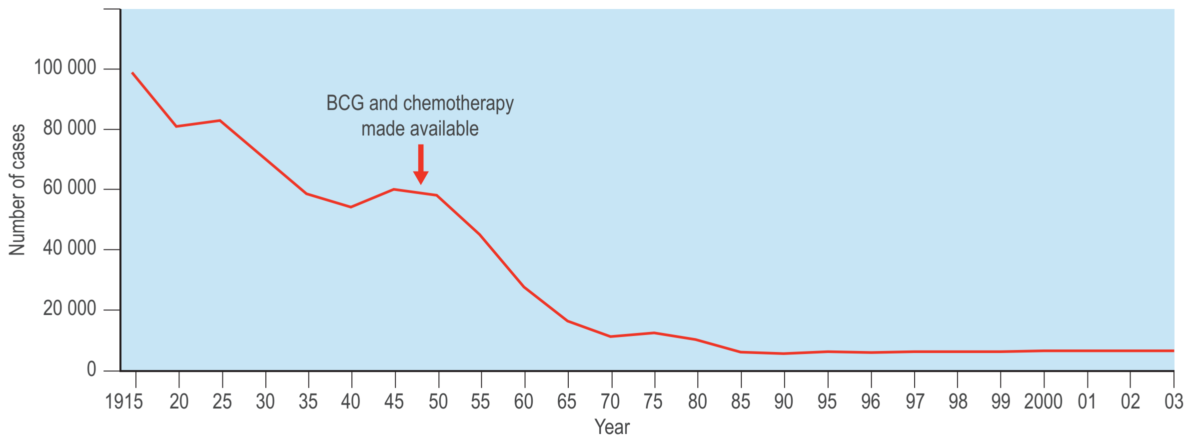

Fig. 68.2 Notifications of tuberculosis in U.K., 1915–2008.

disappearance of relapsing fever, plague and cholera, the rarity of indigenous typhoid fever and the relative infrequency of bacillary dysentery are all indications of the improvements that have taken place in environmental conditions.

The decrease in overcrowding and infestation, together with the demand for cleaner water supplies and better sanitation, have been of paramount importance in producing these dramatic advances. This is well illustrated in the case of tuberculosis, which was declining before the availability of chemotherapy and mass Bacillus Calmette–Guérin (BCG) vaccination in countries where socio-economic conditions were improving (Fig. 68.2). Paradoxically, better living conditions may unexpectedly create new problems; for example, poliovirus infection, previously experienced mainly in early childhood, is usually postponed in more favoured communities to older ages when paralysis is a more likely complication unless there is an adequate immunization programme.

In recent years, areas of urban deprivation, particularly in western countries, have been blighted by the culture of illicit drug injection and its associated infections, such as human immunodeficiency virus (HIV) and hepatitis C, acquired through the sharing of injecting equipment. These may also be associated with spore forming bacteria, such as clostridia and anthrax bacilli contracted through soil contamination of drugs.

THE SPREAD OF INFECTION

Infection spreads in well-defined epidemiological patterns. Knowledge of these will lead to an understanding of the best methods of control, or even eradication, and enables an estimate to be made of the likelihood of this happening.

Infection spread directly from one person to another

Among this group can be included such highly infectious diseases as chickenpox. Infection is passed directly from a person with the disease to a susceptible contact. Diseases in this category are usually clinically apparent and healthy carriers are not a feature. When it is possible to diminish the number of susceptibles in the target population then eradication becomes feasible, as has happened with smallpox.

Infection in which healthy carriers are involved

Because apparently healthy individuals may harbour the bacilli responsible for such diseases as typhoid, paratyphoid and diphtheria, often for long periods after having acquired the infection, it is possible for such infections to be transmitted to others and the source remains undetected. For certain infections, such as hepatitis C virus infection, the healthy carrier state may last several decades.

Infection in which persons harbour the organism before the onset of clinical illness

Organisms such as *Streptococcus pneumoniae* may not cause the person any harm until an event such as a skull fracture allows for the transfer of the bacterium from the middle ear to the cerebrospinal space where it can cause a potentially fatal meningitis.

Infection derived from animal sources

Diseases derived from animals, such as leptospirosis, Q fever, anthrax, rabies and brucellosis, are known as *zoonoses*. These diseases are spread by direct contact with the animal concerned or indirectly by such means as the ingestion of infected milk and contact with infected bone products, etc.

Infections derived from environmental sources

The spread of legionellae from cooling towers and air conditioning units to cause legionnaires' disease is an example of illness derived from an infected environment. By dealing appropriately with the infected source by use of biocides in the water, the population can be protected.

OUTBREAKS OF INFECTION

The crowding together of human beings (or for that matter animals) provides the necessary conditions to allow micro-organisms to multiply and spread. When human beings led nomadic lives there was less opportunity for outbreaks to occur; the main opportunities came when large numbers gathered for a pilgrimage or had other reasons for a meeting. These clusterings facilitated the spread of infection, resulting in outbreaks; the subsequent dispersal of the group enabled the causative organism to be carried elsewhere.

The threat of outbreaks in overcrowded and difficult conditions is particularly well illustrated in military history; on many occasions the germ has been as important in determining the outcome of a campaign as the sword or gun. The typhoid bacillus caused severe effects during both the American Civil War (1861–1865) and the Boer War (1899–1902). The use of typhoid vaccine in the latter years of the First World War meant that the main impact of typhoid in this war subsided after 1916. The pandemic of influenza in 1918–1919, in which about 700 million people were infected with approximately 22 million deaths, was a scourge of military camps and affected many servicemen returning home from the First World War. Several outbreaks of meningococcal meningitis have occurred in pilgrims to Mecca.

Nomenclature of outbreaks

The term *outbreak* is often confused with other epidemiological terms used to enumerate infection:

1. *Sporadic case*: a person whose illness is not apparently connected with similar illnesses in another person.
2. *Outbreak*: the occurrence of cases of a disease associated in time or location among a group of persons. A *household outbreak* involves two or more persons resident in the same private household and not apparently connected with any other case or outbreak. A *general outbreak* involves two or more persons who are not confined to one private household.
3. *Epidemic*: the large-scale temporary increase in the occurrence of a disease in a community or region that is clearly in excess of normal expectancy.
4. *Pandemic*: the occurrence of a disease that is clearly in excess of normal expectancy and is spread over a whole geographical area, usually crossing national boundaries.

Types of outbreak

There are three main patterns of outbreak that may be revealed by the construction of graphs of occurrence of cases over time:

1. *The explosive outbreak*. This is characterized by the occurrence of a large proportion of cases in a relatively short period of time (Fig. 68.3); there is a sharp rise and fall in the number of infected persons, because the usual cause of such an event is a common source that infects the people concerned. This type of outbreak is also frequently termed a *common source outbreak* or *a point source outbreak*. This pattern of infection is often discovered when water or food becomes contaminated, although other vehicles of infection can also be responsible for this type of outbreak.
2. *Person-to-person spread*. Outbreaks caused by infections that are spread from person to person

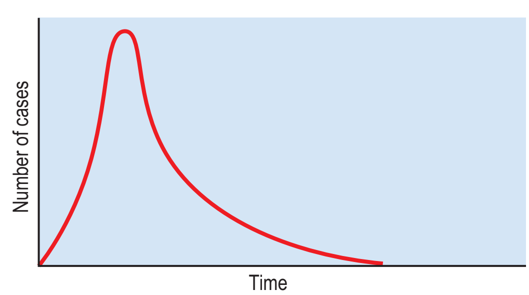

Fig. 68.3 Epidemic curve apparent when there is an explosive (common or point source) outbreak.

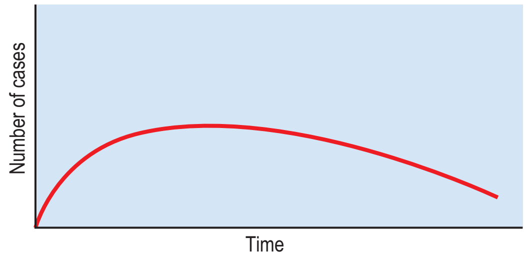

Fig. 68.4 Epidemic curve apparent when there is person-to-person spread of infection.

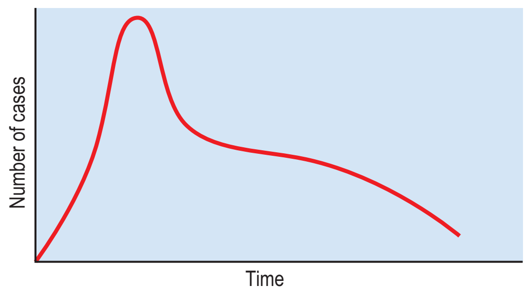

Fig. 68.5 Epidemic curve apparent when there is person-to-person spread subsequent to a common source outbreak.

usually have a more protracted course, taking longer than explosive outbreaks to build up and to subside. An infective agent may be passed from person to person by a variety of routes. Diseases such as dysentery, hepatitis type A and gastroenteritis, which are usually spread by the faecal–oral route, often follow this pattern of spread (Fig. 68.4).

3. *Explosive outbreaks with subsequent person-to-person spread*. This pattern is often apparent when there is contamination of a common water or food source and the initial cases subsequently infect their contacts. Thus, the pattern of the outbreak is a combination of that seen with an explosive outbreak, but followed by a slower decline (Fig. 68.5).

Analysis of outbreaks

The investigation of an outbreak should be approached in a logical and methodical way. The cause may be elucidated by determining details of the *persons* involved, the *place* where they had been and the *time* when they became ill.

The fundamental pieces of information that should be sought whenever an outbreak occurs are as follows:

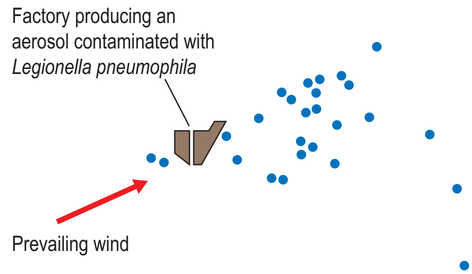

Fig. 68.6 Occurrence of legionnaires' disease in persons living downwind from a factory with an evaporative condenser contaminated with *Legionella pneumophila.*

1. *WHO gets infected*? What is their age? For example, if a possible food-borne outbreak affects mainly children, could the source be milk or ice-cream?
2. *WHERE were those who became infected*? Where have they recently been? For example, in a hospital outbreak were they all in the same surgical ward? Could a member of the operating staff be a carrier of a pathogen? In a community outbreak of legionnaires' disease were those affected living downwind from a source of infection (Fig. 68.6)?
3. *WHEN did the infection occur*? By knowing the incubation period of the infection and the date of onset of symptoms, it may be possible to trace back to an event that was attended by all those affected.
4. *WHAT was the common factor*? For example, in a food poisoning episode, the ingestion of an article of food by most of those affected but not by those unaffected may be a vital piece of evidence.
5. *HOW did those involved become infected*? For example, abscess formation among recently immunized persons might be due to contaminated vaccine.
6. *WHY did the infection occur*? For example, the reheating of meat may be the cause of a *Clostridium perfringens* food-poisoning outbreak.

Investigation of outbreaks

In the investigation of outbreaks it is important to have a standardized approach to the various steps involved. Such an approach might have the following as a basis:

1. *Verify the diagnosis*. It is always prudent to confirm that the clinical history is compatible

with the diagnosis. Occasional 'pseudo-epidemics' can occur, sometimes resulting from contamination of specimens.

2. *Establish the existence of an outbreak*. The increased interest of an investigator or a change in the mechanism of reporting can sometimes result in an increase in the number of reports of illness. It is important to check the previous level of investigation of a clinical entity or alteration in laboratory methods.
3. *Establish the extent of an outbreak*. Often the number of cases notified is only a proportion of the total number of those affected. It is necessary to seek out the additional cases or vital information may be lost.
4. *Identify common characteristics or experiences of the affected persons*. An individual history from each confirmed or suspected case is required to detect any common factor among those affected (e.g. eating the same item of food).
5. *Investigate the source and vehicle of infection*. In addition to ascertaining the general characteristics of the material suspected as being the source or vehicle of infection, appropriate laboratory investigation will often have to be done. Good co-operation with laboratory staff is vitally important. Increasingly, putative links between individuals who present with the same infection or infectious disease are confirmed or dispelled through the typing or sequencing of the genes of the organism involved.
6. *Analyse the findings*. The data should be analysed by various epidemiological criteria, especially persons, time and place. Denominators should be obtained to calculate attack rates.
7. *Construct and test a hypothesis*. On the basis of the evidence a hypothesis should be constructed concerning the origin of the outbreak. This may be confirmed by laboratory findings but action to control the outbreak may be needed in advance. The hypothesis may be tested by comparing information from cases with matched controls (case/control study).

Control of outbreaks

The investigation of an outbreak should be carried out as swiftly as possible so that adequate control measures can be started without delay. Knowledge of the *source of infection*, the *route of transmission* and the *persons at risk* should allow appropriate action to be taken to achieve success.

Sources of infection

These may be:

- human cases or carriers
- animal cases or carriers
- the environment.

If the initial cases have readily identifiable clinical features (e.g. chickenpox) then control is often easier as it is much more likely that the index case will be located.

On the other hand, it is more difficult to control diseases in which apparently healthy carriers are responsible, as it is necessary to search for an infected person who may be asymptomatic.

It may be important to isolate the case or carrier, and possibly to institute appropriate treatment, until the patient is no longer infectious. The degree of isolation will depend on the type of disease, as not all infections require strict isolation. For example, a patient with a highly infectious disease may require very strict isolation whereas the salmonella excreter will usually need only to cease food-handling activities and observe a high standard of personal hygiene until free from infection. In contrast to 'isolation', the term 'quarantine' applies to restrictions on the healthy contacts of an infectious disease.

If an animal reservoir is responsible, action has to be directed at ensuring that the source of infection is eradicated, withdrawn from consumption or rendered harmless, for example by the pasteurization of milk or the adequate cooking of meat.

When the environment is the source of an outbreak the control measures required will depend on the nature of infection and the mode of spread. In recent years, waterborne spread of legionnaires' disease (e.g. from shower-heads, air-conditioning systems or droplet spread from cooling towers) has become increasingly recognized (Fig. 68.7). Environmental measures, such as the use of biocides, can destroy the causative legionellae at their source and so prevent further cases.

The hospital setting is particularly dangerous as the presence of compromised patients can result in tragic consequences. Moreover, the increasing use of invasive techniques and the appearance of antibiotic-resistant strains of micro-organisms further compound the problem. The early detection of infection by effective surveillance, the emphasis on the cleanest possible environment and awareness among the staff of potential problems are among the measures that need to be stressed to control infection among hospital patients (see Ch. 69).

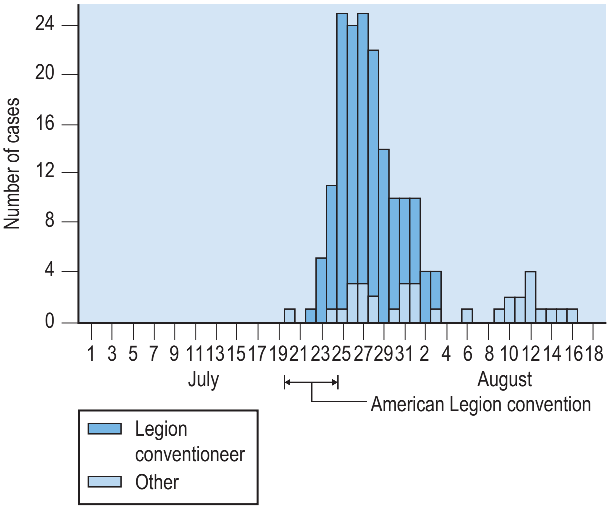

Fig. 68.7 Legionnaires' disease among those associated with a convention in a hotel in Philadelphia (July–August 1976); an example of an explosive outbreak.

Route of transmission

Infection may be spread by:

- direct or indirect contact
- air-borne transmission
- food and water-borne transmission
- insect-borne transmission
- percutaneous transmission
- sexual transmission
- transplacental transmission.

There are various ways in which the routes of transmission occurring during an outbreak may be blocked by measures appropriate to the route involved: effective hand washing; disinfection or disposal, if necessary, of the patient's belongings. Strict adherence to high standards of personal hygiene by the contacts of a case are also important measures.

When the disease is air-borne, overcrowding should be avoided and, where appropriate, dormitory or ward beds should be well spaced. In certain instances major isolation measures, such as those adopted to control the outbreak of severe acute respiratory syndrome (SARS) in 2003, need to be implemented. Indeed, the spread of the coronavirus, the air-borne infection responsible for SARS, throughout regions of the Far East (China, Vietnam and Singapore) and North America (Toronto), before it was brought under control, demonstrates how effectively international travel and overcrowding in major cities can facilitate the transmission of serious air-borne infections.

Food and *water* should be as free as possible from infection; otherwise their consumption can cause major outbreaks. To prevent *insect-borne transmission*, insect eradication policies and repellents should be considered. HIV is an infection that, commonly, is transmitted through the percutaneous, sexual and transplacental routes; the elimination of infected blood donations by blood donor testing, the provision of sterile needles and syringes for infected drug users, the use of condoms and the treatment of HIV-infected pregnant women with anti-retroviral therapy are measures that prevent the spread of this infection through these routes.

Persons at risk

Where indicated and feasible, susceptible persons at risk should be protected as soon as possible. Among the measures available, the following may need to be considered:

- immunization
- chemoprophylaxis for close contacts.

Immunity against several infectious diseases can be obtained by either active or passive immunization (see Ch. 70). Examples of rapid effective protection of communities by active immunization are the 'ring vaccination' policy used to protect close contacts of poliomyelitis and so stop more widespread dissemination of poliovirus, and the early (within 72 h of exposure) administration of measles vaccine to close contacts in an institution. Passive immunization, usually by means of human specific immunoglobulin, gives rapid protection to contacts of certain infections, such as hepatitis B, although protection is short lived. Chemoprophylaxis is effective in the protection of close contacts of meningococcal infections and diphtheria.

MATHEMATICAL MODELS

Mathematical modelling techniques attempt to define, by use of relatively simple estimates and assumptions, the dynamic conditions governing transmission of communicable agents.

Details of the multiplication and growth rates of micro-organisms and the spread of infection under natural or experimental conditions need to be known to simulate spread in defined communities. Measurable factors include:

- the number of infective persons or sources of introduction of infection

- the proportion of susceptible persons in a community at risk
- the duration of immunity
- the introduction of new susceptibles
- the removal rate of infective persons (by isolation, immunity or death)
- the response to vaccines and chemotherapeutic agents.

Mathematical models can be used to predict institutional outbreaks and epidemics.

This approach has been used to attempt to forecast the number of cases of acquired immune deficiency syndrome, variant Creutzfeldt–Jakob disease and bovine spongiform encephalopathy that are likely to occur and the effect of control measures.

ASSOCIATION AND CAUSATION OF INFECTION

A problem commonly encountered by microbiologists and epidemiologists is the attribution of an infectious disease to a particular micro-organism. How do we determine whether the relationship is one of causation or merely a chance association?

Koch addressed this when he formulated his 'postulates' in 1891. These state that:

1. The organism must always be found in the given disease.
2. The organism must be isolated in pure culture.
3. The organism must reproduce the given disease after inoculation of a pure culture into a susceptible animal.
4. The organism must be recoverable from the animal so inoculated.

For many organisms pathogenic to man it is not possible to fulfil all of Koch's postulates; moreover, they are not applicable to the study of the transmission of infection within a population. For this purpose it is more appropriate to consider the following factors, suggested by the medical statistician Bradford Hill, to establish whether a disease is caused by a particular infectious agent:

1. *Strength*. What is the strength of the association? During the cholera epidemic in London in 1854, John Snow compared the death rates among persons drinking the sewage-polluted drinking water of the Southwark and Vauxhall Company with those receiving the purer water of the Lambeth Company; he discovered that the rate in the former was 14 times greater (Table 68.2). This strength of association allowed Snow to consider that polluted water was a cause of cholera, although at that time the causative organism itself had not been identified.
2. *Consistency*. Similar observations, made by different people at different times in different places, add confidence to a conclusion that causation is likely.
3. *Specificity*. If the association is limited to a specific group of persons, with a specific type of illness, who have all been subjected to the same specific infection, then a cause-and-effect relationship can be more strongly suspected.
4. *Temporality*. This can be of especial importance when persons in particular occupations become infected (e.g. leptospirosis in sewerworkers). The history of working in a particular environment *before* infection rather than vice versa is particularly relevant.
5. *Biological gradient*. If a dose–response curve is apparent then the evidence for causation is much stronger.
6. *Plausibility*. Is the possibility biologically plausible? The likelihood of veterinary surgeons becoming ill with a zoonotic infection from affected cattle which they have recently been treating seems biologically plausible.
7. *Coherence*. If all the evidence is coherent (e.g. if the same micro-organism is isolated from the index case, the vehicle of transmission and from the victims), this is strong support for causation.
8. *Experiment*. Is the frequency of infection reduced if certain preventive measures are taken? The beneficial effects of the pasteurization of milk to diminish the number of cases of milk-borne salmonellosis is presumptive evidence of a zoonotic relationship.
9. *Analogy*. Has there been similar evidence in the past? The known capacity of the rubella virus to cause congenital abnormalities in the infants of infected mothers makes it easier to accept the possibility of other viruses causing similar problems if maternal infection occurs.

Table 68.2 Deaths in London during the cholera epidemic of 1854 according to source of water supply

Water source	No. of houses supplied	Deaths
Southwark and Vauxhall Company (polluted)	10 000	71
Lambeth Company (non-polluted)	10 000	5

CONCLUSION

Because of the multifactorial causation of infection it is usually necessary to study the epidemiology of infection in a *multidisciplinary* manner. The microbiologist, the clinician, the epidemiologist, the infection control nurse, the veterinarian, the environmental health officer, and other appropriate personnel, must all be involved; the extent of the involvement will depend on the nature of the infection. Success will depend on the expertise and co-operation of these members of the team.

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Cymru NHS Wales: http://www.wales.nhs.uk

European Centre for Disease Prevention and Control: http://www.ecdc.europa.eu/

Health Protection Agency: http://www.hpa.org.uk/

Health Protection Scotland: http://www.hps.scot.nhs.uk/

Public Health Agency Northern Ireland: http://www.publichealth.hscni.net

World Health Organization: http://www.who.int/en/