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Phil. Trans. R. Soc. Lond. B 1985 **310**, 259-274
doi: 10.1098/rstb.1985.0115

Phil. Trans. R. Soc. Lond. B **310**, 259–274 (1985)
Printed in Great Britain

Infectious animal disease and its control

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The control of infectious diseases in the main food-producing animals is considered and the main factors involved in the epizootiology of disease are presented. The properties of infectious agents and their natural history together with factors that influence the spread and development of disease are summarized. The factors in intensive animal husbandry that affect the occurrence of infectious disease and its control are considered. These include population density, population movement, management, hygiene and genetic constitution of the host. They encourage the appearance of new diseases, changes in the character of established diseases and the development of pathogenicity in infectious agents that were previously of no importance. Intensive animal husbandry has also increased the importance of multifactorial disease, which includes diseases that require more than one infectious agent or one or more infectious agents plus other factors for their cause.

The methods of control of infectious disease currently available are described and the success and difficulties of their control on a global, national and local (farm or enterprise) basis are considered. Examples of diseases of global importance where national and world programmes of control and eradication have been of varying success are described. Examples of diseases that are enzootic throughout the world and the procedures used for their control are also described. The technological opportunities for the improvement of the control of infectious disease in the future are discussed. It is considered that developments in molecular biology and immunology will provide improvements in diagnostic tools and will revolutionize the development of animal resistance to disease and the production and use of vaccines.

1. Introduction

Infectious disease has been chosen for consideration because globally these diseases have in the past, are at present and are likely to remain in the future of major concern. The most important diseases of agricultural species have an infectious agent forming at least part of their cause. The increasing intensivism of modern animal husbandry, particularly in the western world, has encouraged infectious disease and resulted in the emerging importance of so-called multifactorial disease. Improvements in disease control and animal management systems has reduced the incidence of, or eradicated in some cases, many of the well recognized epizootic and enzootic diseases which caused severe morbidity and mortality in the past. The greater competition and lowered profit margins in the agricultural animal industries has led to an ever-increasing adoption of sophisticated management systems. This has resulted in an increasing significance of infections that reduce productivity with little or no overt clinical signs or mortality. This paper will be concerned with the control of infectious disease in the main food-producing animals: cattle, sheep, pigs and poultry.

2. Epizootiology of infectious disease

Although some of the major plagues have been controlled empirically, for most diseases a sound knowledge of their epizootiology (the factors concerned with their cause and distribution) is necessary as a foundation for the design and application of control measures.

There is a number of properties of causative agents important in the epizootiology of infectious disease. In general, each causative agent causes a characteristic disease but virulence may vary between strains of an agent. Another important property of infectious agents that varies between them but also can vary from strain to strain of a single agent is the ability to spread from animal to animal. A combination of high virulence and ease of spread has serious consequences.

Some causative agents exist in more than one serotype. This is particularly important where recovery from the consequences of infection with one serotype does not provide protective immunity against another. Infection may or may not result in immunity; more commonly it does but the duration can vary. Both these factors are important to the development of herd or flock immunity and resistance to subsequent exposure to the agent. Finally, resistance to survival outside the body and in animal products is closely connected with spread of infection.

The natural history of an infection includes the routes of infection, the distribution of the infectious agent within the body, its persistence in the body, and the routes, frequency and persistence of shedding of the agent. These are all important factors in the spread and persistence of infection in a population. Persistent infections of individuals, even when shedding occurs only sporadically, form important reservoirs of infection. Horizontal transmission can be by direct contact or by indirect contact through the medium of inanimate fomites, mechanical vectors, biological vectors or other species acting as a reservoir. Infections can also be transmitted vertically, that is from dam or sire to offspring either congenitally or, for some retroviruses, genetically.

A large number of other factors can influence the development, incidence and spread of disease. The principal factors which influence or control a host's susceptibility to infection, or if it is infected, the development of disease, are genetic constitution, immune status and age at infection. Factors outside the host may cause stress to animals. Stress can result in the exacerbation of disease in an infected animal or may increase susceptibility to infection.

In addition to those factors associated with the causative agent, the host, and methods of spread of infectious agents there is a number of other factors affecting spread of disease which should be considered. These include climate, topography and trade. Temperature and humidity effect the survival of micro-organisms outside the body and the activity of biological vectors. Interrelated with temperature and humidity is wind, which can disperse infectious agents either directly or through the dispersal of biological vectors such as arthropods.

Topographical features also influence the spread of airborne disease by affecting wind and air movements and the movement of infected animals. Deserts, mountains and forests restrict the movement of domesticated and feral animals. Water is even more restrictive, allowing islands a privileged position with respect to disease control.

Trade is also responsible for movement of animals and their products. There has been movement of animals and their products for centuries and one could list many diseases which have been introduced to the United Kingdom by the importation of infected animals or their products. A well documented example is rinderpest (cattle plague), which was introduced into

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the United Kingdom in 1865 through the importation of infected cattle (Hall 1962). Other examples in the nineteenth century are contagious bovine pleuropneumonia in about 1840 and foot-and-mouth disease in 1892 (Anon. 1965). Each of these importations produced epidemics of the respective disease. These and other incidents resulted in legislation during this and the last century to control the importation of animals and in this century the importation of meat, animal products and materials. These controls have been extremely successful with several epidemic diseases and severely restricted the appearance in Great Britain of others. However, less dramatic diseases, but nevertheless economically important to the animal industry, continue to be imported with infected animals. It is relatively easy to legislate for known disease, especially where there is a thorough knowledge of its epizootiology, but impossible to do so for unknown disease or those where knowledge of their epizootiology is lacking. Examples are the introduction to Great Britain of the acute form of Marek's disease in domestic fowl in 1965 (Biggs *et al.* 1965) and enzootic bovine leukosis in 1972–73 (Loxam *et al.* 1978), both virus-induced neoplastic diseases. Enzootic bovine leukosis has a long incubation and the infection was present in Great Britain for about 5–6 years before it was recognized. Infection with Maedi–Visna virus was first noted in 1979 but lesions of the disease were not noted until two years later (Dawson *et al.* 1979; Grimshaw *et al.* 1981). The Maedi–Visna virus is a slow virus and the disease has an incubation period of several years.

Most of these importations were the results of a desire to improve the genetic stock available in the country. The need to have the best genetic stock available in the world so as to remain competitive and to satisfy the particular needs of the consumer has resulted in increasing pressure for access to the world gene pool by importation of stock. Inadvertantly, infectious agents of disease previously unrecognized in this country or of disease previously unrecorded have been imported.

3. Factors in intensive animal husbandry affecting infectious disease and its control

(*a*) *Population density*

Population density is probably the most important factor in intensive animal husbandry affecting infectious disease. Population density, whether considered as number of animals per unit area of house or feed lot, the size of house or feed lot, the number of houses or feed lots comprising a holding or the concentration of holdings within a geographical area affect the spread and replication of infectious agents. The high population densities used in intensive animal husbandry allow the rapid spread and replication of infectious agents. This, together with the evolutionary pressures provided by the widespread use of vaccines and other control measures, encourages mutations in infectious agents of importance to disease. These include changes in antigens, virulence and ability to spread in a susceptible population.

(*b*) *Population movement*

Population movement assists the spread of infection. The adoption of intensive husbandry systems and increasing size of the organizations controlling the farm animal industry has resulted in greater movement of animals not only within a nation but also internationally. Not only does such movement nationally assist in the spread of infection but international

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movement, either to improve the gene pool of a species in a country or as part of international breeding companies activities, has introduced a wide range of diseases to Great Britain some of which have already been mentioned in §2.

(*c*) *Management*

The large holdings and integrated enterprises associated with the adoption of intensive animal husbandry systems are conducive to the spread of infectious disease if not properly managed. Good management is particularly important in relation to the movement of animals and contact, whether direct or indirect, between animals on different premises and of different ages and generations. However, large enterprises provide the opportunity for the design and implementation of programmes and procedures to control and prevent disease.

(*d*) Hygiene

The large concentrations of animals present where intensive animal husbandry is practised leads to potentially serious accumulations of infectious agents. The efficiency with which the cleaning and disinfection of premises is performed is therefore clearly important and any defect in hygiene places large numbers of animals at risk.

(*e*) *Genetic constitution*

The trend to fewer breeders associated with increasing intensiveness in animal production reduces the gene pool available for selection. It also increases the impact of inadvertent selection for susceptibility to a disease and increases the distribution of inadvertent infection with vertically transmitted agents.

A combination of the factors discussed encourages the unpredictable appearance of new diseases and changes in the character of established diseases. These are features of intensive animal management. Examples of apparently new diseases are swine vesicular disease in pigs (Henderson 1981), inclusion body hepatitis (McFerran *et al.* 1976) and infectious stunting syndrome in chickens (Vertommen *et al.* 1980). The origins of new diseases of this kind can be multifarious. In some cases it is the origin that is unknown, for example Newcastle disease which first occurred in Indonesia in 1926 (Lancaster 1981) and swine vesicular disease in Italy in 1966 (Mann 1981). In other cases the new disease appears to be the result of changes in husbandry and management providing circumstances for agents to be important pathogens where previously they were only mildly so or even non-pathogenic. This is particularly true of respiratory and enteric disease. There is a further source of disease that is indirectly associated with intensive animal husbandry. The need for widespread use of vaccines has increased the risk of accidents. These have ranged from inadequate inactivation, which was a possible source of the virus causing the foot-and-mouth outbreaks in France and the Isle of Wight in 1981 (King *et al.* 1981), to contamination of vaccines with unknown viruses, for example contamination of Marek's disease vaccines with reticuloendotheliosis virus (Yoshida *et al.* 1980) and possibly egg-drop syndrome–1976 adenovirus (Anon. 1978). In the latter, a pathogen was established in the chicken population of the world that was not previously present in that species. Another feature of intensively husbanded animals is the importance of multifactorial disease.

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4. Multifactorial disease

Multifactorial disease may be caused by a single agent, a number of single agents or multiple agents. As already described, even with diseases caused by single agents, there are many other factors which effect the outcome of infection. From this standpoint all disease is multifactorial and the use of this term therefore has to be clearly defined. The term 'multifactorial disease' has been applied to (i) a disease process which can be reproduced by each of a number of infectious agents and, in some instances, a mixture of these agents is found in the disease, (ii) a disease in which more than one infectious agent is required to produce the disease and (iii) diseases in which one or a mixture of infectious agents together with other factors, usually associated with the environment, are required for their production.

An example of the first category is mastitis in cattle, which can be reproduced by a number of single agents that are rarely found as mixtures. Another example is enteritis in most species where a wide range of agents including bacteria, viruses and protozoa, have been implicated. Although several may be present in both diseased and normal animals it is presumed that there is not a requirement for more than one agent interacting with another, although they may do so. A group of diseases which could belong to this category, because a similar pathology is present in all, are the vesicular diseases – foot-and-mouth disease, vesicular stomatitis, swine vesicular disease and vesicular exanthema. However, traditionally they are not in this category because the aetiology of each is well established and their epizootiology differ. The causative viruses of these diseases belong to three families but they produce the same pathological lesion. The four diseases can only be differentiated with certainty by the identification of the causative virus. This group and the causative organisms of mastitis, a single disease process, illustrate that there is nothing unusual about this category. Because an infectious agent causes a disease similar to that produced by other agents does not make it different in understanding, diagnosis and control from the more classical diseases. The term 'multifactorial disease' should be restricted to the categories of disease which require the interaction of more than one infectious agent or one or more infectious agents with other factors to produce disease. An example of the former (category (ii) above) is the synergistic effect between swine influenza virus and *Haemophilus influenza suis* in pneumonia in pigs (Shope 1931), neither of which produce clinical signs on their own. Another is the interaction between the infectious bronchitis virus *Escherichia coli* and *Mycoplasma* spp. in the fowl; although infectious bronchitis virus and *Mycoplasma* spp. can produce disease on their own, they allow certain serotypes of *E. coli* to gain entry via the respiratory tract and produce serious disease (Gross 1984). Both respiratory and enteric disease not produced by the recognized pathogens may well come into the latter category (category (iii) above). Viruses, mycoplasma and bacteria, and viruses, bacteria and protozoa are present together in respiratory and enteric disease respectively. It is also probable that other factors are required in the causation of these complex diseases.

5. Methods of control

Infectious disease is important both economically and from the point of view of animal welfare and its control should be considered from an individual animal, farm or enterprise basis. It may also be of national or worldwide importance to the livestock industry. The options available for disease control are similar for a farm, an enterprise, a state or a geographical area.

However, the factors influencing choices may be different because execution of the chosen programme can be better controlled on farms and enterprises than on a national or international scale. For a detailed consideration of the control of infectious diseases in farm animals reference should be made to Webster (1983), Biggs (1983), Payne (1983) and Sellers (1983).

(a) *Treatment*

Although treatment is used, particularly with bacterial disease, it indicates failure of prevention. Even so it has a value particularly with respect to the individual animal and as an adjunct to preventative measures.

(b) *Prevention*

There are a number of approaches to prevention and they are not mutually exclusive.

(i) *Chemoprophylaxis*

Chemoprophylaxis is used particularly for parasitic disease; for example it is at present the only method of controlling avian coccidiosis (see §7*a* (iv)).

(ii) *Husbandry, hygiene and management*

The contribution of husbandry, hygiene and management to the control of infectious disease is to minimize the challenge from the pathogen and maximize the capacity of the host to resist the challenge. The need to pay attention to husbandry, hygiene and management has become more acute with the development and adoption of intensive management systems. Increased stocking density requires greater attention to be given to the environment in the house and to its disinfection so as to maintain the load of pathogens at acceptable levels. Particular attention should be given to the movement of animals of different ages, populations or generations within farms and enterprises and between them. Attention must be paid to the general principles of spread of infectious agents and also to knowledge of the epizootiology of specific diseases for which the species and premises are at risk.

Although husbandry, hygiene and management can greatly contribute to the control of infectious disease, especially for the multifactorial diseases for which environmental factors are important, they seldom alone provide the desired control.

(iii) *Vaccines*

Vaccines are widely used to prevent and control infectious disease in fish, birds and mammals. They are in current use to control infections and disease produced by bacteria and their toxins, parasites including protozoa and helminths and by viruses. They are most commonly used for viral disease and particularly for those that were, and in some cases still are, epizootic and panzootic. However, with the development of intensive systems of husbandry and management they have become an indispensable component of disease prevention. They are particularly widely used in the modern poultry industry where it is usual for vaccines to be used for five to seven diseases. This is so even in the broiler industry in which the birds may only have a life of seven weeks. They are particularly important in the control of rapidly spreading infections and where animals are husbanded in large populations either on a farm or geographic basis. Vaccines can be used to prevent disease caused by single or multiple agents, to prevent disease spreading by ring vaccination or to assist eradication of disease.

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Vaccines should be efficacious, safe to use and of good quality. Those available today vary greatly in each of these characteristics. Even so, the requirements placed on vaccines today are greater than in the past. Originally vaccines were only required to prevent overt disease. Nowadays they may be required to prevent subclinical disease, reduction in growth and production and the spread of infection, and also not spread themselves.

(iv) *Genetics*

Intraspecies variability in susceptibility to disease is widespread in farm species. Evidence for genetically controlled resistance has been reported for numerous infectious diseases in cattle, sheep, pigs and poultry. These include diseases caused by viruses, bacteria, protozoa and helminths.

Genetic resistance may be to a single disease or be more general and can be controlled by simple Mendelian or by polygenic inheritance. Although selection for resistance to a single disease has and is being practised, for example leukosis virus infection and Marek's disease in the fowl, selection for resistance to a group of diseases through a common mechanism such as the immune response is a more attractive possibility. Selection for resistance to a single infectious agent could result in the selection of a mutant which bypasses the resistance mechanism. Selection for resistance of a more general kind is less likely to encourage the appearance of mutant infectious agents. Single-gene effects are more attractive to the breeder than polygenic control because selection for resistance is easier.

There are many constraints on the use of genetic resistance in the control of diseases. These include first, the lack of knowledge of the mode of inheritance of susceptibility to most diseases, second, selection for disease resistance may be closely linked with unwanted productivity traits, third, that selection may encourage the appearance of mutants, fourth, selection may not be cost effective, especially in species with long generation times and fifth, there may be difficulty finding or creating adequate selection criteria.

The selection for genetically controlled resistance to disease is likely to be practised in species with a high reproductive rate and short generation time and where breeding is controlled by a relatively small number of breeding companies, as for poultry and possibly pigs.

(v) *Control of biological vectors*

Control of biological vectors is particularly important where they form an obligatory part of the natural history of an infection because such control removes the source of infection to the primary host. The elimination of vectors is costly and usually only feasible on a local scale. For this reason, control of biological vectors should be undertaken in conjunction with procedures that isolate the animal from the vector.

(vi) *Eradication*

Eradication of an infectious disease requires the elimination of the infectious agent from a population and not only the overt signs of the disease. Eradication can be achieved for a farm, for a breed, for a vertically integrated enterprise that includes breeding, rearing and production, for a geographical area, or for a nation. For all of these situations reliable methods of recognition of the disease and infected animals and a knowledge of the epizootiology of the disease is required. Infected and in-contact animals, where they constitute a source of infection to other animals, have to be destroyed and activities which may reintroduce the infection must be controlled.

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6. Choice of method of control

None of the methods of control discussed are mutally exclusive; most diseases are controlled by a combination of methods. Choice of method will depend on a number of factors, which include the characteristics of the infectious agent, knowledge of the epizootiology of the disease, diagnostic tools available, the ability to control sources of infection, the species affected by the disease and infected with the causative agent, the availability and efficacy of vaccines, the genetic variation in susceptibility to the disease and the simplicity of identifying phenotypes and genotypes. The overriding factor is cost.

7. Success of control measures

The control of infectious disease can be considered on a global, state and local basis.

(a) *Global*

Most of the major plagues have been viral in origin because these are the most highly contagious infections. Many of them have been reduced in their importance from a global standpoint and eradicated from some nations and geographical areas. Three examples for which the epizootiology differs have been chosen for consideration.

(i) *Rinderpest* (*Scott* 1981)

Rinderpest is primarily a disease affecting domestic buffaloes and cattle, although it is probable that all cloven-hoofed animals are susceptible to infection. The causative agent is a morbillivirus and strains are immunologically homogenous, although they vary in their virulence and the ease with which they spread. The virus infects animals via the respiratory tract and is shed from the respiratory and intestinal tracts. Surviving animals are immune to the overt effects of infection and this immunity is assumed to be lifelong. The virus is perpetuated by repeating a short cycle of transmission by direct contagion from a sick to healthy animal. Indirect spread via fomites is possible but rare.

Rinderpest has been recognized since at least the 9th century. It is assumed that the disease was endemic in Asia because it spread widely into Europe in the wake of military operations involving the two continents. It was also introduced into Africa in the 1890s by military operations. The development of trade in livestock which followed the exploitation of steam power in transport spread the disease widely, although, with the exception of single introductions into Brazil and Australia, it has been restricted to the Eastern Hemisphere. The epizootics which periodically swept across Europe were so serious during the 18th and 19th centuries that governments in Europe were forced to establish veterinary inspectorates, departments and veterinary schools.

Ultimately the epizootics were controlled by slaughter of infected and in-contact animals and by control of importation of live animals from infected areas. In enzootic areas the disease has been eradicated or reduced by the use of vaccines, the properties of which have been improved over the years.

Low-risk areas (countries not linked geographically or commercially with enzootic areas) have been successfully kept free of rinderpest by prohibiting imports of live susceptible animals from enzootic and high-risk areas (countries linked geographically or commercially with enzootic areas). Epizootics in low-risk areas have been successfully controlled and the infection eradicated by slaughter of infected and in-contact animals.

High-risk countries reduce risks of introduction of the disease by vaccination and quarantine of animals from enzootic areas. Epizootics are localized by controls on the movement of animals and ring vaccination.

In countries in which the disease is enzootic, the losses are limited by vaccination, but the task is formidable. Even so, the geographical distribution of rinderpest has been greatly reduced over the years of this century. In 1900 it was endemic in most of Asia, parts of the Middle East, and Eastern Horn of Africa and the southern parts of Africa. In 1975 endemic infection was only present in northern equatorial Africa and in India and its near neighbours. The disease largely persists in Africa because of nomadism and as a sequel to strife. In India it persists because of religious prejudice and difficulties of control through the many state governments.

Rinderpest is an example of a disease that is relatively easy to control because of the stability of the causative virus in respect of its antigenic properties, the lifelong immunity and the need for close contact between infected and uninfected animals for infection to spread. It is also an example of a disease where religious and behavioural practices and disparate government activities militate against successful world eradication.

Despite the reasonable control in enzootic and high-risk areas the risks of epizootics and panzootics continue. In 1969 a panzootic swept across the Middle East, originating in Afghanistan and reaching countries on the eastern border of the Mediterranean. The disease was eradicated from all countries except Lebanon, which has acted as a focus for recent spread to Israel and Syria (Anon. 1983), a classic result of military operations. A resurgence in Africa (Scott 1984) has also occurred, which is believed to be the result of the worldwide recession which has prevented expensive vaccination cover to be properly maintained.

(ii) *Newcastle disease* (*Lancaster* 1981)

Newcastle disease virus is an avian paramyxovirus belonging to serotype 1. It is antigenically homogenous but strains vary greatly in their virulence and the ease with which they spread.

The disease was first recognized in 1926 in Indonesia and in Newcastle-upon-Tyne, England, from which it gets its name. Between 1926 and 1946 it was recognized in all continents but Antarctica. It is a disease with a worldwide distribution with the highest occurrence in developing countries. In most developed countries with modern intensively managed poultry, the infection and disease is rare and sporadic. However, serious world panzootics of highly virulent virus have occurred and are a constant threat to the poultry industries of developed countries. The source of such panzootics is uncertain, but it has been suggested that they may originate from members of the family Psittacidae resident in the tropical rain forests of South East Asia and South and Central America (Lancaster 1981). Whatever the sources, panzootics can be traced from these areas spreading throughout the rest of the world. The virus can survive for appreciable periods outside the body and can spread by fomites (Boyd & Hanson 1958). Airborne transmission of the disease has been recorded (Hugh-Jones *et al.* 1973), although the significance of this method of spread varies between strains of virus and geographic density of poultry populations.

Control is largely by vaccination, but with variable success. Vaccination can be effective but also can be overcome by heavy challenge with virulent virus. For this reason good hygiene and

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management are essential and where this is not possible the disease tends to be enzootic and to occur with a high incidence, for example, in developing countries.

Newcastle disease is an example of a disease which has been largely controlled in developed countries where movement of poultry and their products can be monitored and poultry isolated from their environment. However, it is enzootic and occurs at a high incidence in a large part of the world. In these areas vaccination is used but it does not always control the disease. The inadequate control in enzootic areas is the result of a combination of the properties of the causative virus, lack of knowledge of essential parts of the epizootiology of the disease and the methods of husbandry used in developing countries.

Even in developed countries with well managed and controlled poultry industries there is no reason for complacency. Serious epizootics occurred in Europe and the U.S.A. in the early 1970s, which, in Great Britain, for example, killed four million birds in a space of three months (Anon. 1970) and cost the country an estimated £20M in one year (Allan & Stuart 1974). In the U.S.A. the cost of eradication of an outbreak of Newcastle disease in Southern California during 1971–4 was U.S. $56M (Lancaster 1981). More recently Newcastle disease has been introduced into Great Britain by infected racing pigeons (Alexander *et al.* 1984).

(iii) *Foot-and-mouth disease* (*Pereira* 1981)

Foot-and-mouth disease is caused by one of seven serotypes of virus belonging to the genus *Apthovirus*. There is no cross protection between serotypes and within serotypes there is antigenic heterogeneity with quantitative differences in cross immunity. The infection is highly contagious and the virus remains infective for long periods outside the body. Infection readily spreads by either direct contact or through animal products, fomites or aerosol. These factors favour wide and rapid spread of the disease and maintenance of the infection unless strict control measures are used.

Foot-and-mouth disease has at one time or another occurred in most parts of the world. The disease is enzootic in certain parts of the world, principally the countries of the Near East, Central Asia, Africa and South America. It is a permanent threat to all other countries who practice preventive measures. Disease-free countries or those with only sporadic incidence of disease are those which are able to control the importation of animals and animal and farm products from countries in which the disease is present. A number of these countries do not practice vaccination and their stock is fully susceptible to infection. In this situation rapid action is required should infection be inadvertently introduced. These countries practice slaughter of infected and in-contact animals. However, it is recognized that because of the increasing intensivism of farming it may be necessary in future to use ring vaccination around primary foci of infection.

Vaccinated animals are only immune to the serotype contained in the vaccine and are fully susceptible to serotypes not included. Vaccination is costly and requires international surveillance of the disease and serotyping of the infections throughout the world.

In countries and areas where the disease is enzootic, control is largely by vaccination. However, vaccines need to contain the serotypes and preferably subtypes prevalent in the area. No less than 80% of cattle in the area need to be vaccinated and this at intervals frequent enough to maintain immunity. If well implemented, vaccination can reduce the incidence of disease so that eradication can be considered by combining vaccination with a slaughter policy together with the other preventive procedures already discussed.

Rinderpest, Newcastle disease and foot-and-mouth disease were chosen as examples of diseases which present different problems for their control. These diseases are still enzootic in many parts of the world and can cause serious epizootics and panzootics. However, they are also diseases for which eradication alone or together with other methods of prevention have been practised in countries with well developed animal husbandry systems. Although all three diseases have been well controlled or eradicated in these countries the threat and occurrence of serious epizootics initiated from areas of enzootic disease still exists.

These diseases are not the only kinds which are of global importance. There are also those for which the causative agents have properties that do not favour eradication. These tend to be infections that are widespread, or even ubiquitous, in susceptible species and have the ability to survive outside the body for long periods. These may also be well controlled but they are continuously present and for various reasons are a potential or real threat to the animal industry. Two examples are avian coccidiosis and Marek's disease of the fowl.

(iv) *Avian coccidiosis* (*Reid et al.* 1984)

Coccidiosis is an enteric disease caused by seven or more species of protozoa belonging to the genus *Eimeria*. There would be no modern broiler industry without the control of this ubiquitous infection, which is achieved at present by the continuous prophylactic administration of anticoccidial drugs. Despite this the disease is of importance throughout the world (Anon. 1984) because, for many reasons, there are failures in the efficacy of such drugs, the most important of which is the development of resistance to these drugs. The poultry industry has therefore been dependent on the pharmaceutical industry continually producing novel drugs at great cost. A management difficulty in the use of drugs is compliance with withdrawal periods laid down by licensing authorities for most drugs, so that residues are not present in the meat.

(v) *Marek's disease of fowl* (*Calnek* 1984)

Marek's disease is a serious neoplastic disease of the fowl caused by a herpesvirus. Infection is ubiquitous in populations of fowl and is present throughout the world (Anon. 1984) and the disease is most serious in intensively managed poultry. It has presented particular problems for its control because of the ubiquitous nature of the infection, the long survival of the causative agent outside the body and the young age at which infection usually occurs. Even so, vaccination of one-day-old chicks has been effective for the last fifteen years. However, viruses have recently appeared in the U.S.A. for which the currently available vaccines are not fully effective (Witter *et al.* 1980).

(*b*) *State*

State control of disease is concerned with exotic diseases and with diseases that are either of economic importance to the animal industry or a danger to man. The first category includes diseases of the nature of rinderpest, Newcastle disease and foot-and-mouth disease, which have already been discussed. Diseases that are a danger to man (zoonoses) may also be of serious consequence in their agricultural animal host. The main example of a disease of this kind, which has been the concern of many government veterinary departments is tuberculosis. There are others such as anthrax, brucellosis and ornithosis. The control or eradication of these diseases has been successful, although sporadic cases of bovine tuberculosis occur in certain parts of Great Britain, believed to be the result of endemic infections in wildlife and particularly in badgers

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(Anon. 1980). Finally the State is concerned with the control and eradication of enzootic diseases threatening the livelihood of the animal industry.

(c) *Local*

All the diseases that are considered to be threats on a global or national basis are also threatening to an agricultural enterprise and single farm premises. However, there are many diseases of economic or threatened economic importance that are not of sufficient concern to world and state authorities to warrant implementation of regulatory programmes for their control. Most of these infections occur widely in populations of farm animals and range in their effects from producing high levels of mortality to lowered production with no other overt signs of disease.

Whereas the diseases of global or state importance are controlled by combinations of vaccination, slaughter and movement control, those of local importance may be controlled by one or more of the methods described in §5. Whatever method is used, good management and hygiene is always of importance. Vaccines are used to prevent disease with variable success. In species where it is feasible, such as poultry, breeding programmes have included selection for 'livability'. This selects for a general resistance to disease but was notably ineffective with respect to many serious specific diseases. In the domestic fowl, where the potential of breeding for resistance to disease is greater than in other species of farm animal, attention is being paid to selection for resistance to specific diseases. Eradication of specific disease and the development of minimal disease stock has also been an important approach to control of disease, particularly in the highly intensively managed and husbanded species such as poultry and pigs. Chemoprophylaxis is used to prevent spread of (mainly) bacterial infection from infected to uninfected individuals and as a preventive when a population is at risk of infection, for example coccidioses in poultry. Management and hygiene is used specifically to control infectious disease. Housing and ventilation systems have been developed to reduce the chance of the introduction into housed animals of infections and the spread of infectious agents within a house.

8. Future technological opportunities for control of infectious disease

(a) *Control by state regulation and management and husbandry*

Control of infectious disease by the state through regulations or by an enterprise or farm through their choice of management and husbandry procedure is dependent on the recognition of the disease and the prevention of its introduction to a geographical area, nation, enterprise or farm, and on a knowledge of its epizootiology. The opportunity for developing better diagnostic tools and for controlling movement of pathogens through the application of embryo transfer techniques and better housing for intensively farmed stock will improve the control of infectious disease in the future.

(i) *Diagnostic tools*

For potential epizootic and panzootic diseases, surveillance of the disease is essential to institute methods for its control in countries where it is enzootic and promulgate procedures to ensure its exclusion from countries free of the disease. The more rapid and definitive the tests used for this surveillance the more useful the information. The action taken, whether on a world, national or local basis is dependent on detailed epizootiological and knowledge of the disease. The tools used for disease surveillance and for elucidating their epizootiology are similar. Essentially they are diagnostic tools identifying the causative agent or the host response to the agent. Modern molecular biological and immunological technology and application of developments in microelectronics and information technology will undoubtedly lead to more precision, greater speed and an ability to undertake a larger volume of diagnostic tests, the results of which will be better recorded and documented. Such tests will be useful not only in disease surveillance but also for rapid monitoring of the efficacy of vaccination, the immune status of populations and the movement of pathogens globally, nationally and even on a farm basis.

(ii) *Embryo transfer*

Although better disease surveillance will reduce the risks of introducing exotic disease there will always be risks attached to the movement of animals. The risks derived from the need to have access to the world gene pool of a species will also be reduced by the use of developments in storage of fertilized ova and embryos and the technology of embryo transfer. This will allow movement of genetic material with less risk of concomitant conveyance of pathogens, providing such embryos are derived from stock free of vertically transmitted pathogens.

(iii) *Housing*

An understanding of the movement of pathogens into and within animal houses, together with developments and application of technologies of housing, ventilation and air filtration provide promise of reducing infectious disease in intensively housed animals.

(*b*) *Genetic resistance to disease*

For prevention of most infectious diseases, vaccination will remain the method of choice. Selection for resistance to disease, either for specific disease or for general disease resistance through genes controlling immune competence, is also an approach of promise for the future. However, knowledge of genetically controlled resistance to disease, particularly in the large farm animals, is limited. The long generation time in farm animals has been a major constraint in the past on the accumulation of a base of knowledge and on the practical application of such knowledge where available. Even in species with a relatively short generation time, such as poultry, selection for resistance to disease has been low in the priority of characteristics selected for by breeders. Even where single genes have been recognized as important, the process of introducing alleles by back-crossing is lengthy. The development of modern molecular biological techniques has opened horizons and they may well revolutionize selection for disease resistance. These techniques will help to identify genes of importance and to isolate them by cloning in suitable vectors together with providing methods for their introduction to germ lines of farm animals. Promise for such an approach has been provided by Palmiter *et al.* (1982) who achieved integration and expression of the growth hormone gene of the rat into the genome of the mouse, resulting in marked increase of the rate of growth in the mice. A candidate for such manipulation in the disease field is the *env* gene of avian leukosis viruses, the product of which should block receptors for virus infection in the fowl as the product of the *env* gene of E subgroup endogenous avian leukosis virus does in nature (Robinson *et al.* 1981). Another candidate is the B^{21} allele of the major histocompatibility locus of the fowl, which has been associated with resistance to Marek's disease (Briles *et al.* 1977).

(*c*) *Vaccines*

Vaccines will continue to be an important component of the armoury used to control disease. The prospects for improvement in respect of safety, purity, efficacy and ease of administration is promising. These developments will arise from the application of molecular biological and immunological techniques to identify immunogens and their important epitopes and the genes coding for them, and to manipulate such genes either for the *in vitro* production of the immunogens or for their presentation to the animal in a safe form which will stimulate protective immunity.

The use of purified immunogenic components of viruses has been considered as a means of increasing safety and efficacy of vaccines for animals (subunit vaccines) but they are likely to be too expensive for farm animals. However, recombinant DNA and other molecular biological techniques will allow the cloning of the appropriate genes and their introduction and expression in prokaryotic or eukaryotic cells and subsequent manufacture of the immunogens. Although these procedures could provide safer, purer and possibly more efficacious vaccines, such vaccines would require individual vaccination and appropriate adjuvants. An alternative using the same technology would be to engineer infectious organisms which are not pathogenic but stimulate effective protective immunity and these could be administered by aerosol, in the drinking water or in food. Conceptually, it is attractive to consider the excision from the genome of a pathogen the gene(s) ('pathogene') responsible for its pathogenicity; however, it is probable that the pathogenicity of most infectious agents is a polygenic trait and includes genes necessary for their replication. Immunogens and their coding genes are more readily identified. The recent reports of vaccinia virus recombinants with immunogen genes of influenza virus (Panicali *et al.* 1983; Smith *et al.* 1983*a*) hepatitis B virus (Smith *et al.* 1983*b*; Moss *et al.* 1984; Paoletti *et al.* 1984) *Plasmodium knowlesi* (Smith *et al.* 1984) and their immunogenicity in laboratory animals promises well for recombinants between other members of the poxviridae, or other viruses with large genomes and genes coding for protective immunogens of causative agents of diseases of agriculturally important species. The advantage of such viral vectors systems over vaccines available at present is that theoretically a number of genes coding for the immunogens of several infectious agents or a number of serotypes of one agent could be packaged into a single viral vector.

9. Conclusions

There are many factors other than the infectious agents contributing to the production of disease. Although the most devastating effects of some diseases have been controlled in the past with little knowledge of these factors, those diseases of importance today, and especially those that have emerged under intensive animal husbandry, require this knowledge for their effective control. Many of the potentially panzootic diseases causing high mortality or morbidity have been wholly or partly controlled. However, the better control of these diseases has increased the importance of those with less serious overt signs but serious consequences on productivity. These are important to the highly competitive agricultural animal industry of today. Intensive animal husbandry systems have encouraged such disease, much of which is multifactorial in aetiology. Although the prospect for the future control, or better control, of many infectious diseases by using the new technologies is promising, the various aetiological components of the multifactorial diseases will require dissection before appropriate control measures can be devised and implemented.

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